

Impact of DHEA on GABA-agonist challenge in healthy young and older adults

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The primary goal of this dissertation research was to investigate the effect of dehydroepiandrosterone (DHEA) administration on recovery from a GABA-agonist challenge in healthy young and older adults. DHEA and its sulfate metabolite DHEA-S are natural steroid hormones that are produced primarily in the adrenal glands and act as precursors to other hormones (e.g., testosterone and estrogen) in the body. Animal studies have demonstrated antagonistic effects of DHEA and DHEA-S at the GABA receptor complex. When compared to young adults, the elderly have lower concentrations of DHEA and DHEA-S and recover more slowly from the CNS effects of benzodiazepines, the most commonly prescribed class of GABA-agonists. To investigate the role of DHEA and/or DHEA-S as excitatory steroids in the human brain, a GABA-agonist challenge study was proposed. Secondary goals included evaluations of SEM variability over repeated same-day testing and assessing the influence of age and endogenous concentrations of DHEA and DHEA-S on SEMs.

Both young (20 to 30 years) and older (60 to 79 years) men and women participated in this four-way crossover of placebo, DHEA, alprazolam plus placebo and alprazolam plus DHEA. For the 12.5 hours after the drug or placebo was administered, responses mediated via the GABA-A receptor complex (saccadic eye movements (SEMs), sedation, memory, and psychomotor performance) were assessed and blood samples were collected for the purpose of determining DHEA, DHEA-S, and alprazolam concentrations.

These data demonstrate that DHEA administration lessened alprazolam-induced impairment in young women, enhanced impairment in older men and women and did not alter impairment in young men. DHEA administration did not accelerate recovery from GABA-agonist challenge in the older subjects. In fact, the opposite effect was seen with the older men and women who demonstrated saccades with slower velocities and longer durations during the recovery phase of the DHEA/Alp treatment. A surprising outcome of this report is the number of older subjects who experienced impairment at a level where they were unable to complete the SEM

tasks in both treatments. The number of older subjects unable to perform the SEM tasks during the DHEA/Alp treatment was significantly greater than during the PL/Alp treatment.

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CHAPTER ONE

INTRODUCTION

Abbreviations:

AUC	area under the concentration-time curve
C _{max}	Maximum observed concentration
CNS	central nervous system
DHEA	dehydroepiandrosterone
DHEA-S	dehydroepiandrosterone-sulfate
GABA	gamma-aminobutyric acid
SEM	saccadic eye movements
t _{1/2}	apparent elimination half-life

Introduction

Dehydroepiandrosterone (DHEA) and its sulfate metabolite DHEA-S, (the most abundant steroid in the human body), are natural steroid hormones produced from cholesterol primarily in the adrenal glands. Often called the "mother hormone," DHEA acts as a precursor to other hormones in the body such as testosterone and estrogen. Synthetic versions of DHEA are marketed for their 'anti-aging' performance and are widely available as over-the-counter nutritional supplements.

DHEA was first isolated from human urine in the early 1930's by Dr. Adolf Butenandt (Butenandt & Dannenbaum, 1934) and in human blood in 1954 by Migeon and Plager (Migeon & Plager, 1954). The marked decrease in DHEA concentrations associated with aging was demonstrated as early as 1956 by the French biochemist, Max Fernand Jayle. Other than being a step in the metabolic pathway to androgens and estrogens, the function of DHEA in humans was not understood. Interestingly, the potential neuroactivity of DHEA was first explored in 1961 when Heuser and Eidelberg reported dose-dependent convulsions in mice after administration of DHEA (Heuser & Eidelberg, 1961). Although often studied in laboratory animals in the ensuing years, it was not until 1986 when the New England Journal of Medicine published a longitudinal study by Barrett-Connor et al. associating high concentrations of DHEA with less cardiovascular disease in older men (Barrett-Connor, Khaw, & Yen, 1986), that DHEA function and its relation to aging in humans came to be a popular subject for investigation. In fact, in 1990, Regelson et al. stated "DHEA modulates diabetes, obesity, carcinogenesis, tumor growth, neurite outgrowth, virus and bacterial infection, stress, pregnancy, hypertension, collagen and skin integrity, fatigue, depression, memory and immune responses." (Regelson, Kalimi, & Loria, 1990) This surge in human research culminated in June, 1995, when the New York Academy of Sciences held a major conference entitled "DHEA and Aging" and presented data from many of the world's renowned DHEA scientists. Results presented at this meeting proposed that, in addition to their role as sex hormone precursors, DHEA and DHEA-S had various other functions. Among these were protection of the circulatory system, enhancement of immune function, and increased insulin sensitivity. Additionally, both DHEA and DHEA-S were reported to have neuroactive properties and to enhance cognition, brain development, and memory, effects characterized as 'anti-aging.' The wide media coverage given to this conference served to heighten not only scientific but also public interest in DHEA as a possible panacea to the consequences of aging.

Presently, reported physiologic roles of DHEA and DHEA-S continue to vary and are, at times, contradictory. Several means of action of DHEA and DHEA-S, other than their role as sex hormone precursors, have been proposed. Studies have suggested that DHEA and/or DHEA-S may modulate immunity (Ledochowski, Murr, Jager, et al. 2001; Khorram, Vu, & Yen, 1997), reduce the risk of heart disease in men (Barrett-Connor, Khaw, & Yen, 1986; Porsová-Dutoit, Sulcová, & Stárka, 2000), treat depressive symptoms (Wolkowitz, Reus, Keebler, et al. 1999), aid in erectile dysfunction (Reiter, Pycha, Schatzl, et al. 1999) and improve affect (Morales, Nolan, Nelson, et al. 1994; Hunt, Gurnell, Huppert, et al. 2000). Furthermore, sex differences in response to oral administration of DHEA have been reported (Frye, Kroboth, Kroboth, et al. 2000; Morales, Haubrich, Hwand, et al. 1998).

Of particular interest are the reports of DHEA and DHEA-S activity within the central nervous system (CNS), especially since it is now known that the brain, in addition to the adrenals, is a steroidogenic tissue producing its own neuroactive neurosteroids. Baulieu and colleagues completed an elegant series of animal studies in the 1980's demonstrating that DHEA (and other steroids) were present in the CNS at concentrations higher than those of the periphery (Baulieu, Robel, Vatier, et al. 1987). More importantly, he advanced the concept of the brain as steroidogenic when he proved these CNS concentrations remained long after gonadectomy and adrenalectomy. Shortly thereafter, in agreement with the animal studies, DHEA was found throughout the human brain at concentrations 6.5 times that of plasma in deceased men and women aged 76 to 93. (Lacroix, Fiet, Benais, et al. 1987)

Subsequent studies furthered the theory that neuroactive neurosteroids alter neuronal behavior via actions at various neurotransmitter receptors (Wilson, 1992; Pollock, Perel, & Reynolds, 1990). Specifically, electrophysiological and in vitro animal studies have demonstrated that both DHEA and DHEA-S are active at the gamma-aminobutyric acid receptor complex (GABA-RC). The role of DHEA is more controversial with some researchers finding that DHEA does not bind to the GABA-RC (Sousa & Ticku, 1997) while others declare it an antagonist (Demirgören, Majewska, Spivak, et al. 1991; Majewska, 1992). Studies in rats demonstrate that DHEA also selectively enhances the response of excitatory amino acids on the N-methyl-D-aspartate receptor (Debonnel, Bergeron, & de Montigny, 1996). However, information from human studies regarding the neuroactive role of steroids is limited (McAuley, Reynolds, Kroboth, et al. 1995; Friess, Trachsel, Guldner, et al. 1995). Specifically, there are no known reports of in vivo human research demonstrating that DHEA and/or DHEA-S have direct GABA-antagonist activity.

Purpose

To investigate the role of DHEA and/or DHEA-S as neuroactive steroids with GABA-antagonist activity in the human brain, a GABA-agonist challenge study was proposed. It is known that the elderly, who have concentrations of DHEA and DHEA-S that are less than that in the young, recover more slowly from the CNS effects of benzodiazepines, the most commonly prescribed class of GABA-agonists. Previous research indicates that the concentration of DHEA may be related to the rate of recovery from such a challenge. The purpose of this research was to determine the effect of DHEA and DHEA-S concentrations on recovery from GABA-agonist (benzodiazepine) challenge in young and older men and women.

To test this, oral DHEA was administered to older adult volunteers between the ages of 65 and 79 to reproduce peak concentrations normally seen in the young between 20 and 30 years of age. A full description of the methods can be found in Chapter 2. Briefly, alprazolam, one of the top ten U.S. prescriptions dispensed in 2001 (RxIndex, The internet Drug Index, data furnished by NDC Health Retrieved February 26, 2003, from <http://www.rxlist.com/top200.htm>) was chosen as the GABA-agonist. Both young and older subjects participated in this four-way crossover of placebo, DHEA, alprazolam plus placebo and alprazolam plus DHEA. For the 12.5 hours after the drug or placebo was administered, responses known to be mediated via the GABA-A receptor complex (saccadic eye movements, sedation, memory, and psychomotor performance) were assessed and blood samples were collected for the purpose of determining DHEA, DHEA-S and alprazolam concentrations.

Background

Metabolism of DHEA. Figure 1.1 represents the synthesis and major metabolic pathways of DHEA and other steroids (Majewska, 1992; Sanger & Zivkovic, 1992; Robel & Baulieu, 1994; Orth & Kovacs, 1998; Wolf & Krischbaum, 1999).

Pregnenolone, the immediate precursor of DHEA, is derived from cholesterol after side-chain cleavage by CYP11A1 (cytochrome P450 scc). CYP17, a 17 α -hydroxylase with 17,20-desmolase activity, catalyzes the synthesis of DHEA from pregnenolone (Robel & Baulieu, 1994; Stoffel-Wagner, 2001). DHEA-S, quantitatively the most abundant steroid in humans (Nieschlag, Loriaux, Ruder, et al. 1973; Shealy, 1995) is metabolized from DHEA by hydroxysteroid sulfatransferase and can be converted back to DHEA by steroid sulfatase

(Kishimoto & Hoshi, 1972). DHEA can also be metabolized to androstenedione, and in turn testosterone and estrogens in tissues with sulfatase activity.

The adrenal cortex in humans and other primates secretes the greatest amounts of DHEA and DHEA-S. In men, the testes produce approximately 10-25% of DHEA and 5% of DHEA-S while in women the ovaries contribute only a minimal amount of both (Kroboth, Salek, Pittenger, et al. 1999). DHEA and DHEA-S are precursors to nearly 50% of androgens in men and 75% of estrogens in premenopausal women. After menopause, virtually all circulating estrogens are metabolized from DHEA (Baulieu, 1996). It is also known that DHEA and DHEA-S are produced de novo in the brain, hence their classification as neurosteroids (Baulieu, et al., 1987; Baulieu, 1998).

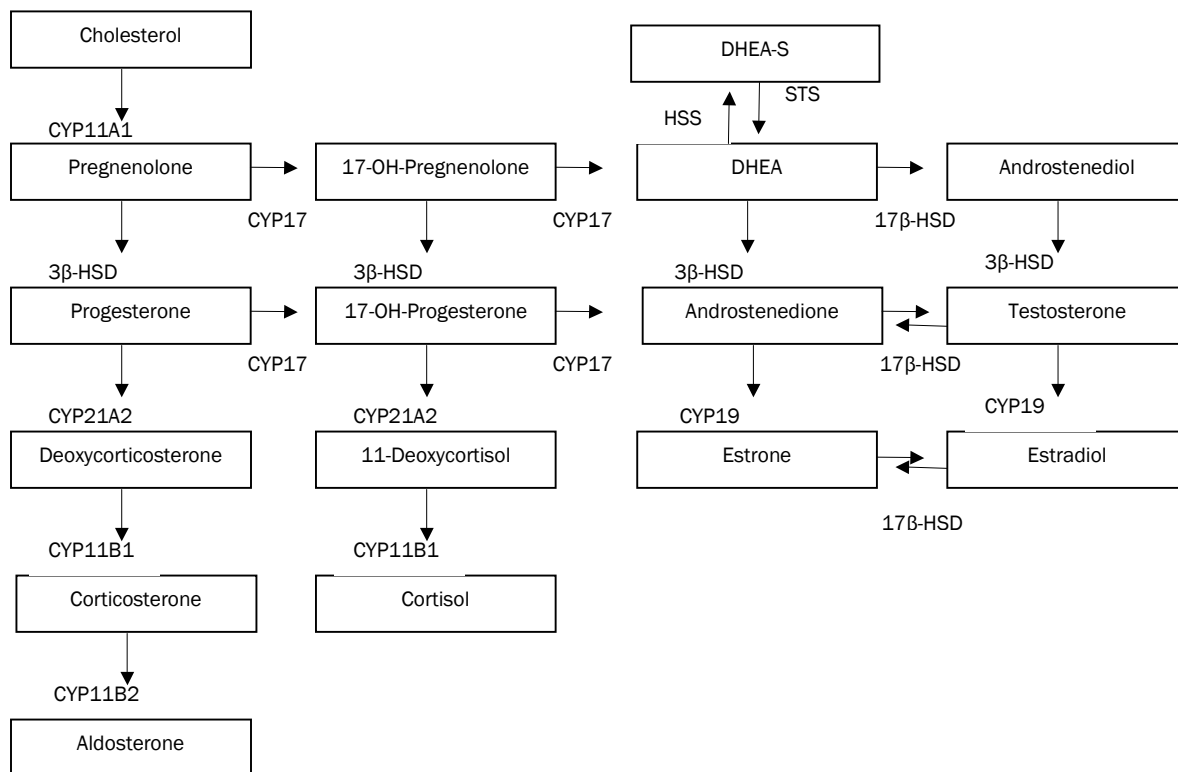


Figure 1.1. The steroidogenic pathway of DHEA. (CYP = Cytochrome P450; STS = Steroid sulfatase; HSS = Hydrosteroid sulfatase; HSD = Hydroxysteroid dehydrogenase.)

Similar to cortisol, DHEA secretion demonstrates a circadian rhythm. Unlike cortisol, this rhythm is age dependent as noted by a decrease in pulse amplitude, though not pulse frequency, with increasing age. Disease

status has also been associated with changes in the circadian rhythm of DHEA (Erb, Kadane, Tourney, et al. 1981; Goodyer, Herbert, Altham, et al. 1996; Heuser, Deuschle, Lippa, et al. 1998). The rhythmicity of DHEA-S is controversial with some researchers reporting systematic secretion (Montanini, Simoni, Chiossi, et al. 1988; Del Ponte, Di Monte, Graziani, et al. 1990; Liu, Laughlin, Fischer, et al. 1990) and others reporting none (Hall, Perry, & Spector, 1993; Moltz & Schwartz, 1986; Moltz & Schwartz, 1986; Kos-Kudla, Ostrowska, Marek, et al. 2001). The lack of systematic variation in DHEA-S concentrations may be attributed to its extended half-life of approximately 10 to 20 hours, a substantial increase over the 0.5 to 3 hour half-life of DHEA.

Age and Sex differences in DHEA. Concentrations of DHEA and DHEA-S are known to vary with age. High concentrations are present in the human fetus and decrease to minimal levels shortly after birth where they remain until the advent of adrenarche at approximately 6 to 8 years of age. At this point, adrenal production of DHEA and DHEA-S resumes and continues throughout life (Mesiano, Katz, Lee, et al. 1997). Circulating concentrations of DHEA peak during the mid-twenties then steadily decline from the third decade onward (Orentreich, Brind, Vogelmann, et al. 1992; Orentreich, Brind, Rizer, et al. 1984; Pavlov, Harman, Chrousos, et al. 1986; Baulieu, Thomas, Legrain, et al. 2000). DHEA levels tend to decrease at a rate of approximately 2% per year; concentrations in 70-year-old individuals are roughly 80% lower than those in young adults

It is widely accepted that women have lower DHEA-S concentrations when compared to men (Carlström, Brody, Lunell, et al. 1988; Morales, et al., 1998). It is unclear whether concentrations of DHEA in women differ from those in men; the literature reports both higher (Carlström, et al., 1988; Sulcová, Hill, Hampl, et al. 1997) and equivalent concentrations (Labrie, Bélanger, Cusan, et al. 1997; Frye, et al., 2000).

DHEA and DHEA-S kinetics. Reports of circulating concentrations of DHEA and DHEA-S after administration of DHEA are summarized in a review by Kroboth et al. (Kroboth, et al., 1999) The concentration-time course of orally administered DHEA has been reported in young healthy women (Schmid, Sala, Bonanno, et al. 1998), young healthy men (Bosy, Moore, & Poklis, 1998), older men (Arlt, Haas, Callies, et al. 1999), and post-menopausal women (Buster, Casson, Straughn, et al. 1992). However, all of these reports were after single dose administration of DHEA and most of them reported observations made at a single time point. A recent report characterizing the pharmacokinetics of DHEA and DHEA-S over a 24-hour period after single and repeated oral doses of DHEA in older men and women has established the presence of sex-based differences (Frye, et al., 2000).

Frye and colleagues have reported that after a single 200 milligram dose of DHEA, concentrations of DHEA were 5 to 6-fold greater than endogenous concentrations in both men and women. DHEA maximum concentration (C_{max}) and area under the curve (AUC) were higher, and the apparent elimination half-life ($t_{1/2}$) longer, in women compared to men. Achieved DHEA-S concentrations represented a 21-fold increase from endogenous levels in women yet only a 5-fold increase in men, essentially eliminating the difference normally seen between the sexes. DHEA-S C_{max} , AUC, and $t_{1/2}$ did not differ between men and women after a single dose.

Pharmacokinetic parameters were also estimated after 8 and 15 doses of DHEA 200 mg. daily. Concentrations of DHEA and DHEA-S after the 15th dose were comparable to those seen after a single dose. DHEA C_{max} and AUC were higher in women compared to men after both dose 8 and 15, and the $t_{1/2}$ longer after dose 8. There was no sex-based difference in $t_{1/2}$ after dose 15. The DHEA AUC for women tended to decrease across time but in men it remained constant. For DHEA-S, there was no difference between the women and men in either AUC or C_{max} after continued dosing. The difference in DHEA-S concentrations between men and women present before, but not after, oral administration of DHEA suggests a difference in the interconversion of DHEA and DHEA-S.

Saccadic eye movements as a GABA-RC-mediated response. Saccades are the brief, jerky movements the eye makes in order to refixate the fovea, i.e., to shift focus from one point to another in the visual field. Saccadic eye movement (SEM) motor neurons and their neurochemical modulation have been precisely identified and can be traced progressively from the brainstem through to the cerebral cortex (O'driscoll, Wolff, Benkelfat, et al. 2000; Fuchs, Kaneko, & Scudder, 1985; Sparks & Mays, 1990; Law, Svarer, Holm, et al. 1997; Robinson, 2000; Quaia, Lefevre, & Optican, 1999; Hikosaka & Wurtz, 1989). The central structures involved in the control of SEMs are the frontal cortex, basal ganglia, and cerebellum; the defined pathway consists of the frontal eye fields, caudate nucleus, substantia nigra, and superior colliculus.

Inhibitory synaptic connections involving GABA in the mediation of SEMs have been extensively documented through anatomical, electrophysiological, and pharmacological methods (1989). Specifically, GABAergic projections from the substantia nigra tonically inhibit the superior colliculus in order to prevent involuntary eye movements away from objects of interest, thereby aiding fixation (Hikosaka & Wurtz, 1983; Hikosaka & Wurtz, 1985a; Hikosaka & Wurtz, 1985b; Hikosaka & Wurtz, 1985b; Hikosaka & Wurtz, 1985a). Subsequently, when a saccade is required to foveate a new target, signals from the striatum restrain the

substantia nigra, again via a GABAergic pathway, thus liberating the superior colliculus to facilitate saccade generation.

Unlike psychomotor tests that require voluntary, conscious performance (Hindmarch, 1984; Hindmarch, 1980), the basic mechanics of SEMs, once initiated, are under involuntary control. This, coupled with the established role of GABA in the control of saccades (Sparks & Hartwich-Young, 1989), and the known benzodiazepine-induced drug effect on saccades (Bittencourt, Wade, Smith, et al. 1981; Kroboth, Folan, Bauer, et al. 1998; Tuk & Oberyé, 1997) make evaluation of SEMs an acceptable, and more sensitive (Williams & Bowie, 1999), indicator of drug response.

Summary. The full description of the design and methods of this research project can be found in Chapter 2. The goal of the research presented in Chapter 3 is to assess the stability of SEMs during repeated same-day testing in young and older men and women. Although SEM dynamics have shown little variability within a single testing session or when comparing single sessions between test days (Bollen, Bax, van Dijk, et al. 1993; Bollen, et al., 1993; van Steveninck, Verver, Schoemaker, et al. 1992), the influence of within-day repeated testing sessions over time in an older population has not been reported. The scoring program used to generate the SEM data required a certain amount of subjectivity on the part of the scorer. As such, Chapter 4 is dedicated to assessing the inter-rater reliability of the scoring program, which was created specifically for the purpose of measuring SEMs initiated while under the influence of a benzodiazepine. The majority of studies involving SEM dynamics generally report the velocity, accuracy and reaction time of the saccade. The purpose of the analysis presented in Chapter 5 is to evaluate the influence of age and endogenous concentrations of DHEA and DHEA-S on such saccade parameters. The purpose of the overall dissertation research project, i.e., to determine the effect of DHEA administration on recovery from GABA-agonist challenge is addressed in Chapters 6 and 7. Chapter 6 is limited to analysis of the concentration-time data while Chapter 7 addresses the pharmacodynamic response to alprazolam challenge, specifically during the recovery phase.

Collectively this work studying the effects of DHEA on recovery from alprazolam is of clinical significance in older men and women. It has been demonstrated that aging affects both the pharmacokinetics and pharmacodynamics of alprazolam. Previous studies have established that the aging are more sensitive to the effects of benzodiazepine and demonstrate decreased clearance (Greenblatt, Harmatz, & Shader, 1991; Greenblatt, Harmatz, Shapiro, et al. 1991; Bertz, Kroboth, Kroboth, et al. 1997; Smith, Divoll, Gillespie, et al. 1983; Thompson, Moran, & Nies, 1983; Bertz, Reynolds, Kroboth, et al. 1995). Compared to younger adults,

there is an increased use of benzodiazepines in the elderly (Miyamoto, Hirata, Miyamoto, et al. 2002; Tu, Mamdani, Hux, et al. 2001; Olfson & Pincus, 1994; Gleason, Schulz, Smith, et al. 1998). Despite the known beneficial effects, the increased prevalence of benzodiazepine use in the aging population is of concern. Benzodiazepine use in the older population has been associated with falls, hip fractures, and motor vehicle accidents (Ray, Griffin, Schaffner, et al. 1987; Ray, Thapa, & Gideon, 2000; Ray, Griffin, & Downey, 1989). The possibility that such events may be mediated by administration of a naturally produced GABA-antagonist is intriguing.

CHAPTER TWO

METHODS

Abbreviations:

Alp	Alprazolam
CS	card sorting task
DHEA	dehydroepiandrosterone
DHEA/Alp	DHEA + Alprazolam treatment
DHEA-S	dehydroepiandrosterone-sulfate
DSST	digit symbol substitution test
GCRC	General Clinical Research Center
HVLT	Hopkins Verbal Learning Test
NMDA	N-methyl-D-aspartate
NRSS	Nurse rated sedation scale
PL	Placebo
PL/Alp	Placebo + Alprazolam treatment
RMT	Randt memory test
SEM	saccadic eye movements

Introduction

The research project detailed in this chapter produced all data used in subsequent analysis as presented in Chapters 3, 4, 5, and 6. This chapter describes the overall study design, subject population, procedures, and process of data collection.

Methods

Study Design. This study was completed at the General Clinical Research Center (GCRC) of the University of Pittsburgh Medical Center. The protocol and consent forms were approved by the University of Pittsburgh Institutional Review Board. This randomized, double-blind, placebo-controlled, four-way crossover study was conducted in parallel in groups of young and older men and women. The study was designed to include 16 men and 16 women in both the young and older groups with each group of 16 comprised of 12 Caucasian and four minority volunteers. The study was divided into two phases and required four visits to the GCRC as indicated in Table 2A.

Table 2A. Treatment Assignment Scheme

	Phase I Treatment		Phase II Treatment	
	<u>Visit 1</u>	<u>Visit 2</u>	<u>Visit 4</u>	<u>Visit 5</u>
Block A	PL	DHEA	Alp	DHEA/Alp
Block B	PL	DHEA	DHEA/Alp	Alp
Block C	DHEA	PL	DHEA/Alp	Alp
Block D	DHEA	PL	Alp	DHEA/Alp

Note. PL = placebo, DHEA = Dehydroepiandrosterone, Alp = alprazolam.

Phase I was a placebo (PL) and DHEA crossover and Phase II was a PL plus alprazolam (PL/Alp) and a DHEA plus alprazolam (DHEA/Alp) crossover. The unblinded investigational drug pharmacist of the University of Pittsburgh Medical Center randomized subject numbers to one of the four blocks in order to balance by age, sex, and minority status. Visits within a phase were separated by a minimum of one and a maximum of five weeks; phases were separated by a minimum of one and a maximum of thirty-nine weeks. Alprazolam, DHEA and the placebo for DHEA were administered orally.

The times and dose amounts of DHEA in Phase I were adjusted as data were accrued in order to maximize the probability of obtaining concentrations between 10 and 20 ng/ml for each study group. As a result, the first five subjects recruited to the study received DHEA 150 mg at 0 hour and DHEA 50 mg at 6.5 hours during Phase I. Based on the concentration of DHEA noted in these subjects, the 0 hour DHEA dose for

Phase I was decreased to 50 mg for subsequent participants; the 6.5 hour dose remained the same. In order to achieve DHEA concentrations between 10 and 20 ng/ml in Phase II, the dose and time of administration of DHEA was individualized for each subject based on their DHEA concentration-time profile from Phase I. Tables 2B and 2C detail the dose amounts and time of administration of DHEA (or placebo) for each subject in Phases I and II, respectively. The majority of subjects received DHEA 50 mg at both 0 h and 6.5 h. Exceptions are noted in the Tables 2B and 2C. Identical doses of Alprazolam 2 mg were administered to all subjects at the same time (2.5 hour) for both visits in Phase II.

Table 2B. DHEA Dose Assignments for Phase I

Subject	0 hour	6.5 hour	Subject	0 hour	6.5 hour	Subject	0 hour	6.5 hour
1	50 mg	50 mg	28	50 mg	50 mg	54	50 mg	50 mg
3	50 mg	50 mg	29 ^a	150 mg	50 mg	55	50 mg	50 mg
4	50 mg	50 mg	30	50 mg	50 mg	56	50 mg	50 mg
5	50 mg	50 mg	31	50 mg	50 mg	57	50 mg	50 mg
7	50 mg	50 mg	33	50 mg	50 mg	58	50 mg	50 mg
8	50 mg	50 mg	34	50 mg	50 mg	59	50 mg	50 mg
9	50 mg	50 mg	35	50 mg	50 mg	60	50 mg	50 mg
10	50 mg	50 mg	36	50 mg	50 mg	61	50 mg	50 mg
11	50 mg	50 mg	37	50 mg	50 mg	66	50 mg	50 mg
12	50 mg	50 mg	38	50 mg	50 mg	102	50 mg	50 mg
14	50 mg	50 mg	39	50 mg	50 mg	106	50 mg	50 mg
15	50 mg	50 mg	40	50 mg	50 mg	111	50 mg	50 mg
16	50 mg	50 mg	41	50 mg	50 mg	112	50 mg	50 mg
17 ^a	150 mg	50 mg	42	50 mg	50 mg	113	50 mg	50 mg
18	50 mg	50 mg	43	50 mg	50 mg	114	50 mg	50 mg
19	50 mg	50 mg	44	50 mg	50 mg	120	50 mg	50 mg
20	50 mg	50 mg	45	50 mg	50 mg	140	50 mg	50 mg
21	50 mg	50 mg	46	50 mg	50 mg	145	50 mg	50 mg
22	50 mg	50 mg	47	50 mg	50 mg	146	50 mg	50 mg
23	50 mg	50 mg	48	50 mg	50 mg	149	50 mg	50 mg
24	50 mg	50 mg	50 ^a	150 mg	50 mg	160	50 mg	50 mg
25	50 mg	50 mg	51 ^a	150 mg	50 mg	206	50 mg	50 mg
26	50 mg	50 mg	52	50 mg	50 mg	213	50 mg	50 mg
27	50 mg	50 mg	53	50 mg	50 mg	245	50 mg	50 mg

Note. The dose amounts indicate the dose on the DHEA treatment day of Phase I.

^aThe first five subjects enrolled in the study received an initial DHEA dose of 150 mg. Subsequently, initial doses were decreased to 50 mg.

Table 2C. DHEA Dose Assignments for Phase II

Subject	0 hour	6.5 hour ^a	Subject	0 hour	6.5 hour ^a	Subject	0 hour	6.5 hour ^a
1	50 mg	50 mg	28	100 mg	50 mg	54	50 mg	100 mg
3	50 mg	50 mg	29	50 mg	100 mg	55	50 mg	50 mg
4	50 mg	50 mg	30	50 mg	50 mg	56	100 mg	50 mg
5	50 mg	50 mg	31	50 mg	50 mg	57	100 mg	50 mg
7	50 mg	50 mg	33	150 mg	100 mg	58	50 mg	50 mg
8	50 mg	50 mg	34	50 mg	50 mg	59	50 mg	50 mg
9	50 mg	50 mg	35	50 mg	50 mg	60	50 mg	50 mg
10	50 mg	50 mg	36	50 mg	50 mg	61	50 mg	50 mg
11	50 mg	50 mg	37	50 mg	50 mg	66	50 mg	50 mg
12	50 mg	50 mg	38	50 mg	50 mg	102	50 mg	50 mg
14	50 mg	50 mg	39	50 mg	50 mg	106	--	--
15	50 mg	50 mg	40	--	--	111	50 mg	50 mg
16	50 mg	50 mg	41	50 mg	50 mg	112	50 mg	100 mg
17	50 mg	100 mg	42	50 mg	50 mg	113	50 mg	50 mg
18	50 mg	50 mg	43	50 mg	50 mg	114	50 mg	50 mg
19	50 mg	50 mg	44	50 mg	50 mg	120	100 mg	50 mg
20	50 mg	50 mg	45	50 mg	50 mg	140	50 mg	50 mg
21	50 mg	50 mg	46	50 mg	50 mg	145	50 mg	50 mg
22	50 mg	50 mg	47	50 mg	50 mg	146	50 mg	50 mg
23	50 mg	50 mg	48	50 mg	50 mg	149	100 mg	50 mg
24	50 mg	50 mg	50	50 mg	100 mg	160	100 mg	50 mg
25	50 mg	50 mg	51	50 mg	100 mg	206	50 mg	50 mg
26	50 mg	50 mg	52	100 mg	50 mg	213	50 mg	50 mg
27	50 mg	50 mg	53	50 mg	100 mg	245	50 mg	50 mg

Note. The dose amounts indicate the dose on the DHEA treatment day of Phase II. A dash (-) indicates subjects who did not complete Phase II.

^aBased on data from Phase I, subjects 31 and 60 received the second dose of DHEA at 5 hours; subject 149 at 4 hours.

Subjects. Table 2D summarizes demographic information and dates of participation for all subjects enrolled in the study. A total of 42 women (26 young and 16 older) and 35 men (20 young and 15 older) completed informed consent and were enrolled in the study. Included in these 77 subjects were those who identified themselves as Black (n = 14), Hispanic (n = 2), Caucasian (n = 58), or Asian/Pacific Islander (n = 3). The young subjects were between the ages of 20 and 30 years; older subjects were between the ages of 66 and 78 years. Not all subjects completed all visits. Subjects who did not complete all four treatments were replaced with new subjects who were assigned the same subject number plus 100. Not all subjects were included in all analysis; subsequent chapter will identify those subjects used in each analysis.

All subjects were considered healthy by medical history and physical, and by laboratory screening. Screening took place within two weeks prior to participation in the study and included a routine and microscopic urinalysis, a complete blood count, a biochemical screening profile and a Structured Clinical Interview for Diagnosis of DSM IV Disorders, (SCID). Specifics of the screening can be found in Appendix A. Upon enrollment, a urine sample for drugs-of-abuse screening and a blood sample for blood alcohol determination was collected on each of the four visits. For young women, urine was also collected for a pregnancy test.

Excluded from the study were young women who had taken oral contraceptives and older women who had taken hormone replacement therapy (estrogen or progesterone) within the six months prior to study enrollment. Also excluded were volunteers known to have taken any enzyme-inducing (barbiturates, rifampin, etc.) or enzyme-inhibiting agents (e.g., erythromycin, ketoconazole) for a period of 30 days prior to the study day. Men and women selected for this study should not have taken any chronic and/or over-the-counter medications for the seven days prior to each study. Complete inclusion and exclusion criteria are included in Appendix A.

Procedure

Study Conditions. On the afternoon before each of the four treatment days, subjects were admitted to the GCRC. Subjects fasted from 10 p.m. on the evening of admission (water was permitted) until 7:30 a.m. the next day. At this time, subjects received a light breakfast and an intravenous catheter was placed in a forearm vein for the purpose of obtaining multiple blood samples throughout the treatment day.

To determine the concentrations of DHEA, DHEA-S, cortisol and alprazolam, blood samples were obtained at 0 h (prior to DHEA or placebo administration) and at 1, 2, 3, 3.5, 4.5, 5.5, 7, 8.5, 10, 11, 12.5, 16,

Table 2D. Subject demographic data and visit dates.

Subject	Sex	Race	Age (yr.)	Height (in.)	Weight (lb.)	Visit 1	Visit 2	Visit 3	Visit 4
1	Female	Caucasian	20	63	153	11/15/97	11/22/97	12/06/97	12/13/97
2	Female	Caucasian	20	68	135	1/10/1998	--	--	--
3	Female	Caucasian	30	68	169	05/20/98	05/27/98	06/03/98	06/10/98
4	Female	Caucasian	28	65	139	06/06/98	06/13/98	06/20/98	06/27/98
5	Female	Caucasian	24	61	121	07/11/98	07/18/98	07/25/98	08/01/98
6	Female	Caucasian	22	64	115	07/22/98	--	--	--
7	Female	Caucasian	23	68	140	09/12/98	09/19/98	09/26/98	10/03/98
8	Female	Caucasian	20	64	137	10/10/98	10/17/98	10/24/98	10/31/98
9	Female	Caucasian	22	68	143	11/14/98	11/21/98	12/05/98	12/12/98
10	Female	Caucasian	21	66	170	02/06/99	02/13/99	02/20/99	02/27/99
11	Female	Caucasian	22	67	136	04/17/99	04/24/99	05/01/99	05/08/99
12	Female	Caucasian	22	68	127	05/19/99	05/26/99	06/02/99	06/09/99
13	Female	Hispanic	30	64	130	08/18/97	--	--	--
14	Female	Black	23	63	110	01/24/98	01/31/98	10/31/98	11/07/98
15	Female	Black	27	66	125	02/14/98	02/21/98	02/28/98	03/07/98
16	Female	Black	22	70	144	10/17/98	10/24/98	01/23/99	01/30/99
17	Female	Caucasian	67	67	200	07/14/97	07/21/97	08/04/97	08/11/97
18	Female	Caucasian	68	59	192	11/18/97	11/25/97	12/02/97	12/09/97
19	Female	Caucasian	69	62	128	01/14/98	01/21/98	01/28/98	02/04/98
20	Female	Black	66	63	170	02/28/98	03/07/98	03/14/98	03/21/98
21	Female	Caucasian	67	63	170	04/22/98	04/29/98	05/06/98	05/13/98
22	Female	Caucasian	68	61	143	04/22/98	04/29/98	05/06/98	05/13/98
23	Female	Caucasian	72	63	126	06/17/98	06/24/98	07/01/98	07/08/98
24	Female	Caucasian	73	66	156	08/19/98	08/26/98	09/02/98	09/09/98
25	Female	Caucasian	75	62	142	01/24/00	01/31/00	02/07/00	02/14/00
26	Female	Caucasian	70	60	128	10/06/99	10/13/99	10/20/99	10/27/99
27	Female	Caucasian	68	63	154	09/06/00	09/13/00	09/20/00	09/27/00
28	Female	Caucasian	71	63	198	10/11/00	10/18/00	10/25/00	11/01/00
29	Female	Black	72	62	126	07/14/97	07/21/97	08/04/97	08/11/97
30	Female	Black	69	63	187	01/24/98	01/31/98	02/07/98	02/14/98
31	Female	Black	70	65	174	09/06/00	09/13/00	09/20/00	09/27/00
33	Male	Caucasian	22	69	133	09/27/97	10/04/97	10/18/97	10/25/97
34	Male	Caucasian	20	75	187	09/27/97	10/04/97	10/18/97	10/25/97
35	Male	Caucasian	21	69	187	09/27/97	10/04/97	10/18/97	10/25/97
36	Male	Caucasian	21	65	125	11/15/97	11/22/97	12/06/97	12/13/97
37	Male	Caucasian	25	74	186	07/29/98	08/05/98	08/12/98	08/19/98
38	Male	Caucasian	28	72	150	05/20/98	05/27/98	06/03/98	06/10/98
39	Male	Caucasian	29	68	154	08/05/98	08/12/98	08/19/98	08/26/98
40	Male	Caucasian	23	67	144	10/03/98	10/10/98	--	--

Table 2D. Subject demographic data and visit dates. (Cont'd)

Subject	Sex	Race	Age (yr.)	Height (in.)	Weight (lb.)	Visit 1	Visit 2	Visit 3	Visit 4
41	Male	Caucasian	28	71	170	11/14/98	11/21/98	12/05/98	12/12/98
42	Male	Caucasian	20	71	125	11/14/98	11/21/98	12/05/98	12/12/98
43	Male	Caucasian	21	68	179	01/09/99	01/16/99	01/23/99	01/30/99
44	Male	Caucasian	23	69	155	02/20/99	02/27/99	03/06/99	03/13/99
45	Male	Black	21	71	195	8/18/1997	8/25/1997	9/8/1997	9/15/1997
46	Male	Asian	29	70	149	09/27/97	10/04/97	10/18/97	10/25/97
47	Male	Hispanic	27	72	182	10/28/97	11/04/97	11/11/97	11/18/97
48	Male	Asian	21	67	146	06/06/98	06/13/98	06/20/98	06/27/98
49	Male	Caucasian	69	71	177	07/16/97	--	--	--
50	Male	Caucasian	69	73	186	07/14/97	07/21/97	08/04/97	08/11/97
51	Male	Caucasian	75	73	204	07/14/97	07/21/97	08/04/97	08/11/97
52	Male	Caucasian	73	66	188	02/25/98	03/04/98	03/11/98	03/18/98
53	Male	Caucasian	72	67	166	02/25/98	03/04/98	03/11/98	03/18/98
54	Male	Caucasian	68	70	170	04/22/98	04/29/98	05/06/98	05/13/98
55	Male	Caucasian	71	65	154	04/22/98	04/29/98	05/06/98	05/13/98
56	Male	Caucasian	72	68	190	04/25/98	05/02/98	05/09/98	05/16/98
57	Male	Caucasian	67	71	215	12/02/98	12/09/98	06/03/98	06/10/98
58	Male	Caucasian	68	70	189	06/17/98	06/24/98	07/01/98	07/08/98
59	Male	Caucasian	68	70	180	08/12/98	08/19/98	08/26/98	09/09/98
60	Male	Caucasian	74	70	193	04/07/99	04/14/99	04/21/99	04/28/99
61	Male	Black	68	64	164	09/23/98	09/30/98	10/07/98	10/14/98
66	Female	Caucasian	27	66	156	04/25/98	05/02/98	05/09/98	05/16/98
102	Female	Caucasian	20	64	119	07/07/99	07/14/99	07/21/99	07/28/99
106	Female	Caucasian	26	64	113	08/07/99	08/14/99	--	--
111	Female	Caucasian	29	63	157	02/19/00	02/26/00	03/10/00	03/18/00
112	Female	Caucasian	25	62	173	01/08/00	01/15/00	01/22/00	01/29/00
113	Female	Asian	20	65	117	11/14/98	11/21/98	01/09/99	01/16/99
114	Female	Black	21	67	156	04/08/00	04/29/00	05/06/00	05/20/00
120	Female	Caucasian	70	58	133	01/10/01	01/17/01	01/24/01	01/31/01
140	Male	Caucasian	24	75	173	02/27/99	03/06/99	03/20/99	03/27/99
145	Male	Black	26	67	259	01/20/01	01/27/01	02/03/01	02/10/01
146	Male	Black	26	70	177	06/19/99	06/26/99	07/10/99	07/17/99
149	Male	Caucasian	72	71	184	09/08/99	09/15/99	09/22/99	09/29/99
160	Male	Caucasian	78	65	163	06/21/00	06/28/00	07/12/00	07/19/00
206	Female	Caucasian	22	65	125	12/01/99	12/08/99	04/03/00	04/10/00
213	Female	Black	20	67	143	03/18/00	03/25/00	04/01/00	05/06/00
245	Male	Black	26	75	224	02/21/01	03/14/01	03/21/01	03/28/01

Note. Subject numbers 32, 62, 63, 64, and 65 were not recruited. A dash (--) indicates subject did not complete the visit.

20 and 23.5 h after dose administration. Since alprazolam was administered only in Phase II, the blood volume for samples in Phase II was 7.0 ml, while in Phase I it was 4.5 ml. Each blood sample was collected from the indwelling catheter in a forearm vein and placed in appropriately labeled vacuum tubes and centrifuged at 4°C for 15 minutes at 3000g. Serum was decanted and stored at -80°C.

Pharmacodynamic Assessment. During each of the four visits, response to the drug treatments was evaluated using a series of assessments that were conducted at multiple times throughout the treatment day as shown in Table 2E.

Table 2E. Schedule of Response Assessments

Assessment	Time of Assessment (h)														
	0	1	2	3	3.5	4.5	5.5	7	8.5	10	11.5	12.5	16	20	23.5
Blood	x	x	x	x	x	x	x	x	x	x	x	x	x	x	x
NRSS	x	x	x	x	x	x	x	x	x	x	x	x	x	x	x
DSST	x		x		x	x	x		x	x	x	x			
CS	x		x		x	x	x		x	x	x	x			
SEM	x		x		x	x	x		x	x	x	x			
RMT	x				x	x			x						
HVLT									x						

Note. Time 0 indicates baseline measurement. All other times are relevant to time after administration of DHEA or placebo. NRSS=Nurse Rated Sedation Score, DSST=digit symbol substitution, CS=card sorting, SEM=saccadic eye movements, RMT=Randt memory test, HVLT=Hopkins verbal learning test.

The full battery of pharmacodynamic assessments required approximately 10 minutes to complete and was assessed in the same order at each testing time: Nurse (observer) Rated Sedation scale (NRSS), Digit Symbol Substitution Test (DSST), card sorting (CS) task, memory test, (blood sample collection) and saccadic eye movement (SEM) task.

To control for learning effects, during the screening session subjects were required to practice the DSST and CS to a plateau, i.e., no improvement in score on two consecutive trials, and to become familiar with the SEM task. On the evening of admission to the GCRC for each of the four visits, subjects again practiced DSST, CS and SEMs. A final practice for DSST and CS was done prior to the baseline evaluation on the treatment day.

Sedation was assessed using the NRSS, a five point scale ranging from 0 (wide awake, alert) to 4 (sleeping soundly, not able to perform testing session). Psychomotor impairment was assessed using the DSST and CS task. DSST was originally developed as part of the Wechsler Adult Intelligence Scale (Wechsler, 1955). For this study, DSST consisted of a set of symbols associated with digits 0 through 9 in a key at the top of the paper. Below the key were 120 digits with a corresponding blank space. Subjects were instructed to use the key as a reference to draw the correct symbol in the blank space. The score was the number of symbols correctly

drawn within 90 seconds. CS required subjects to sort a deck of 52 playing cards by suits as quickly as possible with a maximum of 90 seconds allotted to complete the task; the score was the number of cards/sec.

Memory was assessed using the Hopkins Verbal Learning Test (HVL) and a modified Randt Memory Test (RMT). The HVL measured both recall and recognition of word lists over a number of trials. The HVL required subjects to learn a list of 16 words from four different semantic categories over five trials and was assessed once during each treatment day. RMT is a memory task in which a series of seven black and white line drawings of objects are presented at the rate of one per second. Immediately thereafter, a series of 15 drawings that includes copies of the original 7, plus 8 distracters, is presented to subjects to test their immediate recognition of pictures just presented. There were 16 forms of the test used in this study, one for each testing session. Consequently, no pictures were repeated throughout the four visits.

Saccadic eye movements (SEMs) were obtained using an infrared reflection technique (EyeTrac Model 210, Applied Science Laboratories), digitized at 500 Hz by a DATAQ 12-bit A/D converter (DATAQ Instruments, Akron OH) and recorded to removable media for off-line analysis with custom software. The resultant resolution was sufficient to detect saccades of 0.25° of visual angle. Visual presentations of targets for eye movements were presented on a computer screen using Micro Experimental Laboratory Software (Pittsburgh, PA: Psychology Software Tools).

The saccade targets were presented on a 17-inch computer screen as a white cross on a black background circumscribed by a white circle. Subjects were instructed to focus on the center of the cross and follow it as it changed positions. For each subject for each testing session, eye movements were calibrated during a process where the targets were presented in the horizontal plane in the following order: center, 16° left, 8° left, center, 8° right and 16° right. Subjects were instructed to fixate on each target as it appeared on the screen. During the SEM testing session, 48 trials (saccade targets) were presented in a pseudo-random order. In each trial, subjects began at center fixation and shifted their gaze to targets presented at one of the calibration target positions for 1.5 seconds, so that each target was presented 12 times. After a target was presented to the right or left, the target returned to center to begin the next trial. The timing and location of peripheral targets for saccades was unpredictable. Eye movements were recorded from both eyes. Data from only one eye were scored by choosing the eye with the most stable fixation data from the calibrated targets. The SEM data were scored using a computer algorithm to identify saccades. Saccades were identified when

eye acceleration exceeded $1200^{\circ}/\text{sec}^2$ and were defined as the time from that point until 25% of peak deceleration. Each saccade was visually inspected and measurements on the basis of this algorithm were verified. Saccades that occurred during blinks or that were not task-related were excluded. Scoring of each saccade provided quantification of latency, duration, peak velocity, and accuracy. Latency is the reaction time (msec) between target presentation and initiation of saccade, duration is the time (msec) required to complete the saccade, peak velocity ($^{\circ}/\text{sec}$) is the maximum velocity achieved during the saccade, and accuracy is the percent of target step amplitude gained by the saccade.

For each subject at each testing session, eye movements were separated according to the size of target amplitude (8° and 16°) and combined according to direction (left and right) allowing a maximum number of 24 scored trials per session per target amplitude. The subject-specific mean for saccades to each target amplitude was used in all subsequent analysis.

Drug treatment. Although readily available as an over-the-counter dietary supplement, DHEA is not currently marketed under FDA approval in the United States. However, the bioavailability of the DHEA formulation used in this study has been published (Buster, et al., 1992). DHEA doses were prepared as described by Buster et al. (Buster, et al., 1992) and supplied by Belmar Pharmacy of Lakewood, CO. Pharmacopoeia-grade DHEA (Diosynth Co., Chicago, IL) was micronized to $<10 \mu\text{m}$ particles and mixed with a wax vegetable oil matrix and compressed with a silica-based excipient into tablets containing DHEA 50 mg. Quality control assessment of the product is routinely done as described in our IND #48,123. Placebos for DHEA were also supplied by Belmar Pharmacy. Oral doses of alprazolam 2 mg were supplied by the Investigation Drug Pharmacy of the University of Pittsburgh Medical Center.

Assays

Alprazolam. For alprazolam and the internal standard, triazolam, a gas chromatographic-electron capture detection method (GC) was developed from previously published methods;(Greenblatt et.al., 1981 and Coassolo, et. al., 1983.) The assay was validated and used to determine serum alprazolam concentrations. After addition of the internal standard (triazolam 3 ng/0.5 ml), 0.5 ml aliquots of standards in blank serum, quality controls, and subject samples were extracted into 1.5% iso-amyl alcohol in toluene. The organic layer was dried under nitrogen and reconstituted samples were injected onto a 10 m x 0.32 mm x 0.25 μm capillary column (DB1701, J & W Scientific) in a Hewlett Packard 6890 gas chromatograph with helium as the carrier

gas and argon-methane (95:5) as the make-up gas. Alprazolam and triazolam were detected and quantified using a micro ^{63}Ni electron capture detector (μECD). Data were acquired and analyzed using an HP ChemStation. For each analysis group standard curves (0.25 to 20 ng/0.5 ml blank serum) were prepared by plotting peak-height ratios of alprazolam:triazolam versus the alprazolam concentrations. Subject and quality control sample concentrations were determined from the standard curves.

All standard concentrations were run in duplicate. Quality controls (0.3, 1.5, 3, 8 and 15 ng/0.5ml) were run in triplicate. Correlation coefficients were >0.99 . Coefficients of variation for precision and accuracy of all standards and quality control samples were $< 10\%$. For alprazolam the lower limit of quantitation was 0.25 ng/ml and the absolute recovery was 91%.

Steroids. The assays for steroid concentrations were done using ^{125}I -radioimmunoassay techniques (Diagnostic Systems Lab Inc.). Serum was assayed for DHEA, DHEA-S, and cortisol concentrations. The detection range and lower limit of detection, respectively, for each assay were: DHEA: 0.2 to 30 ng/ml and 0.009 ng/ml; DHEA-S: 50 to 8000 ng/ml and 17 ng/ml; cortisol: 0.5 to 60 $\mu\text{g}/\text{dl}$ and 0.11 $\mu\text{g}/\text{dl}$. The coefficient of variation for each was $<10\%$ throughout the range of the assay.

Summary

A total of 77 young and older men and women participated in this four-way crossover study of placebo, DHEA, PL/Alp and DHEA/Alp administration. During the 12.5 hours after dose administration, saccadic eye movements, psychomotor performance, memory, and sedation were assessed and blood samples were collected for determination of serum concentrations of DHEA, DHEA-S, cortisol and alprazolam. Steroid samples were assayed using RIA techniques and alprazolam concentrations were determined using GC methods.

CHAPTER THREE

REPRODUCIBILITY OF SACCADIC EYE MOVEMENTS, CARD SORTING, AND DIGIT SYMBOL SUBSTITUTION TASKS
IN YOUNG AND OLDER MEN AND WOMEN OVER 12.5 HOURS

Abbreviations:

CS	card sorting task
DSST	digit symbol substitution test
GCRC	General Clinical Research Center
SEMs	saccadic eye movements

Introduction

Saccadic eye movements (SEMs), the rapid and intermittent jumps the eye makes when moving between points of focus, have been used to study neurological and psychiatric disorders, and to assess response to the effects of various drugs and alcohol (Cowley, Roy-Byrne, Radant, et al. 1994; Baloh, Sharma, Moskowitz, et al. 1979; Clementz, Farber, Lam, et al. 1996; Blekher, Beard, O'Connor, et al. 2002). In particular, SEMs have been identified as a measurable response to GABA-ergic drugs (Ball, Glue, Wilson, et al. 1991; Glue, Wilson, Coupland, et al. 1995) and, as such, have been used to assess psychomotor impairment in response to benzodiazepine administration (Roy-Byrne, Fleishaker, Arnett, et al. 1993; Roy-Byrne, Wingerson, Radant, et al. 1996; Folan, Kroboth, Fabian, et al. 1999; Kroboth, et al., 1998). SEMs offer an advantage over other psychomotor tests (e.g., Digit Symbol Substitution Test, and Card Sorting) that are commonly used to determine dose-response relationships in pharmacodynamic studies. Psychomotor tests are influenced by the subject's degree of learning, alertness, fatigue, cooperation and motivation during each testing session (Hindmarch, 1984; Kroboth, Smith, & Erb, 1988). Unlike psychomotor tests, SEMs are dependent only to a limited extent on subject motivation and are, for the most part, an involuntary response. For example, in order to improve saccade accuracy, a subject may willingly delay reaction time between presentation of a target and initiation of an eye movement. However, once initiated, the velocity and duration of the eye movement cannot be voluntarily controlled. Furthermore, saccades of less than 20-degrees amplitude demonstrate a linear relationship between both velocity and amplitude, and duration and amplitude (Bahill, Clark, & Stark, 1975; 1999). Thus, any decrease in velocity is reflected in a decrease in amplitude. Although SEM dynamics have shown little variability within a single testing session, interindividual day-to-day differences, particularly in velocity, have been reported (Bollen, et al., 1993; Bollen, et al., 1993; van Steveninck, et al., 1992). What is unclear is whether or not changes are evident in velocity and other SEM parameters during repeated testing throughout a day. Repeated testing is necessary to fully characterize the concentration-effect and/or dose-response relationships of drugs. The objective of this study was to determine the reproducibility of specific SEM parameters (latency, velocity, duration and accuracy), Card Sorting (CS) scores, and Digit Symbol Substitution Test (DSST) scores during repeated same-day testing in healthy young and older men and women.

Methods

Study design and subjects. These data were collected from the placebo arm of the four-way crossover study that required subjects to complete four study visits at the General Clinical Research Center (GCRC) of the University of Pittsburgh Medical Center (see Chapter 2). Placebo was administered during either the first or second study visit. SEM tests were administered to all subjects as part of the screening process in order to ascertain each individual's ability to perform the test and to assist them in becoming familiar with the tasks that would be required on subsequent testing days. CS tasks and DSST were also administered to subjects during the screening process. To minimize learning effects, subjects were required to practice the CS and DSST to a plateau, i.e., no improvement in score on two consecutive trials, during screening. All subjects were admitted to the GCRC by 7:00 p.m. the evening prior to the study day at which time they again practiced SEMs, CS, and DSST. A final practice for CS and DSST was done in the morning prior to the baseline evaluation on each study day. Baseline evaluations of SEMs, CS and DSST were conducted in the morning prior to administration of the placebo treatment.

The 71 volunteers were medically and psychiatrically healthy women (22 young and 14 older) and men (18 young and 13 older). The age range for young subjects was 20 to 30 years and for older subjects 66 to 78 years. Table 3A contains mean ages for the four groups.

Table 3A. Mean age for the four groups of participants^a

GROUP	AGE (yr)
Young women (n=21)	23.2 (3.1) (20 - 30)
Young men (n=19)	23.9 (3.1) (20 - 29)
Older women (n=16)	69.7 (2.4) (66 - 75)
Older men (n=13)	70.9 (3.2) (67 - 78)

^aData are presented as mean, standard deviation, and range.

All subjects were non-smoking (by self-report) and before participating in the study were screened by medical and psychiatric history, physical examination, Structured Clinical Interview for Diagnosis of DSM IV Disorders (SCID) (First, Spitzer, Gibbon, et al. 1995), biochemical and hematological laboratory screen, urine drug screen, and blood alcohol concentration.

Evaluation of saccadic eye movements. The methods for SEM data collection, recording and scoring are detailed in Chapter 2. Briefly, the SEM recordings were obtained using an infrared reflection technique (EyeTrac Model 210, Applied Science Laboratories). The saccade targets were presented on a 17-inch computer screen as a white cross on a black background circumscribed by a white circle. During the SEM testing session, 48 trials (saccade targets) were presented. In each trial, subjects began at center fixation and shifted their gaze to one of four target positions. After a target was presented to the right or left, the target returned to center to begin the next trial. The timing and location of peripheral targets for saccades was unpredictable.

The SEM data were scored using a computer algorithm to identify saccades. Each saccade was visually inspected and measurements on the basis of this algorithm were verified. When multiple saccades were required to reach the target, only the initial, or primary saccade was scored. Scoring of each saccade provided quantification of latency, duration, velocity, and accuracy. For the purpose of this analysis latency is the reaction time (msec) between target presentation and initiation of saccade, duration is the time (msec) required to complete the saccade, velocity (degrees/sec) is the maximum or peak velocity achieved during the saccade, and accuracy is the percent of target step amplitude gained by the primary saccade.

SEM testing was conducted at ten times throughout the testing day: immediately prior to administration of placebo (0 hour) and at 2, 3.5, 4.5, 5.5, 7, 8.5, 10, 11.5 and 12.5 hours after administration of placebo. For each subject at each testing session eye movements were separated according to the target step amplitude (8-degrees and 16-degrees) and combined according to direction (left and right) allowing a maximum number of 24 scored trials per session per target amplitude. The subject-specific mean for saccades to each target amplitude was used in all subsequent analysis.

Evaluation of Card Sorting and Digit Symbol Substitution. CS required subjects to sort a deck of 52 playing cards by suits as quickly as possible with a maximum of 90 seconds allotted to complete the task; the score was the number of cards/sec. DSST, originally developed as part of the Wechsler Adult Intelligence Scale¹¹², required subjects to draw symbols corresponding to matching numbers. The score is the number of symbols drawn in 90 seconds. Both CS and DSST are described in more detail in Chapter 2. CS and DSST were collected at the same ten time points as the SEMs.

Statistical analysis. Significant differences between group means were tested using a repeated measures mixed-model analysis of variance (ANOVA). The four SEM parameters (latency, velocity, duration and

accuracy), CS score, and DSST score were used as the dependent variables. This study was a crossover design and subjects could have received placebo on either one of two study visits. Therefore, a term (order) was added to the model to determine if there was an effect due to order of placebo treatment, i.e., was there a difference in effect based on whether the placebo treatment was given the first study visit or the second study visit. Age group (young or old), sex, time (0, 2, 3.5, 4.5, 5.5, 7, 8.5, 10, 11.5, 12.5), order (1 or 2), and the sex-by-time interaction term were considered as fixed effects. Initial analysis demonstrated that the age groups differed from each other for each of the dependent variables tested. The sex-by-time interaction was statistically significant for one of the models. Subsequently, the subjects were divided into four age/sex groups: young women, young men, older women and older men, and were analyzed separately. Results were considered statistically significant if the observed p-value was less than or equal to a critical value of 0.05. All plotting was performed using GraphPad Prism version 3.02 for Windows, GraphPad Software; San Diego, California USA; www.graphpad.com (Motulsky, 1999). The ANOVA was performed using SAS Software (Cary, NC, version 8.02) (SAS Institute, 2000).

Results

Latency of saccades. Figure 3.1 represents the individual and mean data for latency to the 8-degree saccade targets in the young and older men and women. Data from the young groups and the older groups demonstrated no significant differences across time, ($p \geq 0.35$ and $p \geq 0.12$, respectively) for latency to the 8-degree saccades. For latency data from the 16-degree saccades, results (not shown) were similar in the young and older groups. There were no significant differences in the latency data between the sexes in either the young or older groups for both the 8 and 16-degree saccades ($p \geq 0.09$).

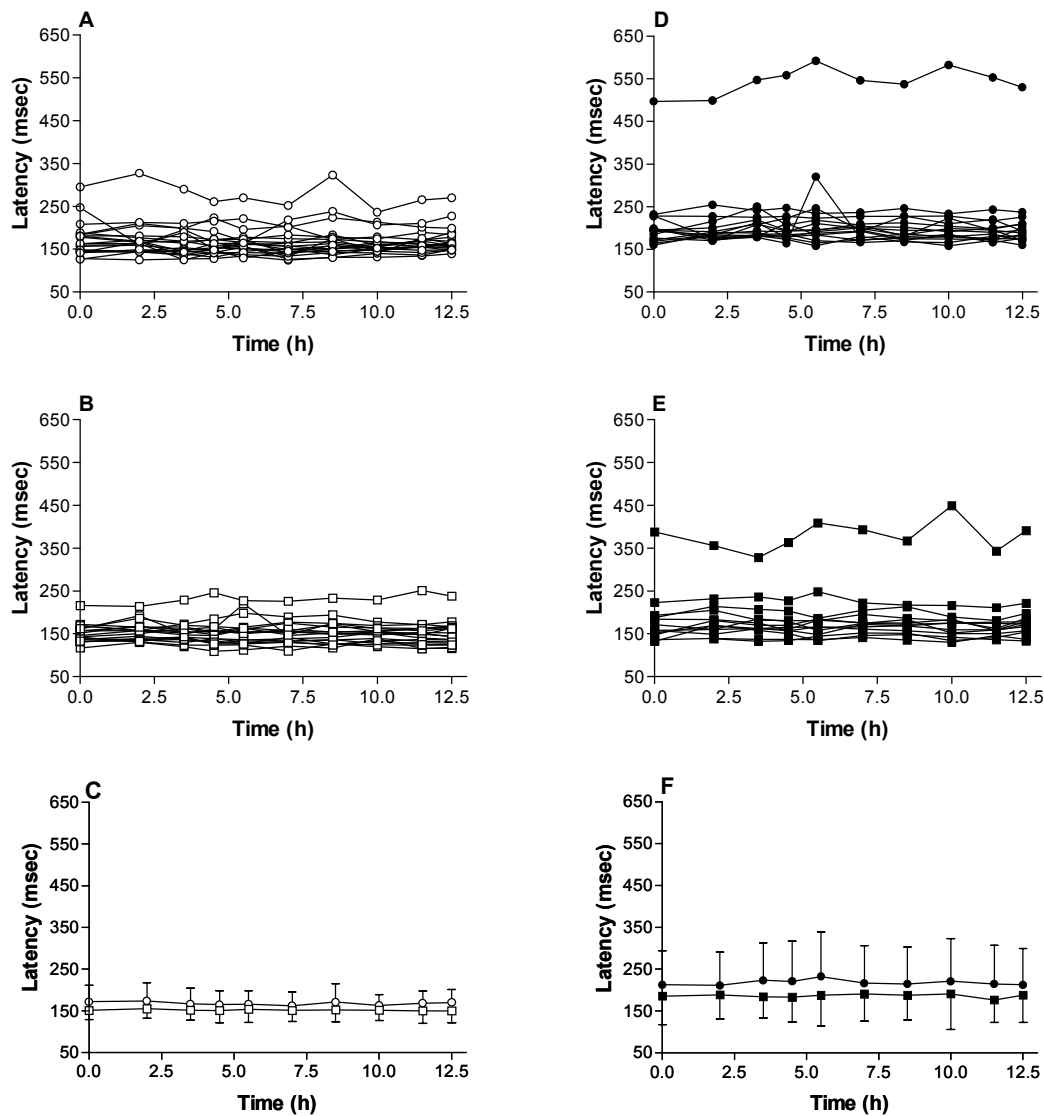


Figure 3.1. For 8-degree saccades: line plots of latency vs. time for individual data (A = young women (○), B = young men (□), D = older women (●), E = older men (■)) and mean data with standard deviations (C = young women and men; F = older women and men).

Peak Velocity of saccades. The individual and mean data for peak velocity of the 8-degree saccades in young and older men and women are shown in Figure 3.2. For mean peak velocity to the 8-degree saccades and the 16-degree saccades (not shown), there was no detectable time effect in the young women, the young men, and the older women, $p \geq 0.06$; for both targets there was a significant time-related difference in the older men's group, $p \leq 0.02$ with the greatest decrease from baseline (8.0%) occurring at the 5.5h time point. Similar to latency, there were no significant differences between data from the men and women in either the young or older groups ($p \geq 0.54$).

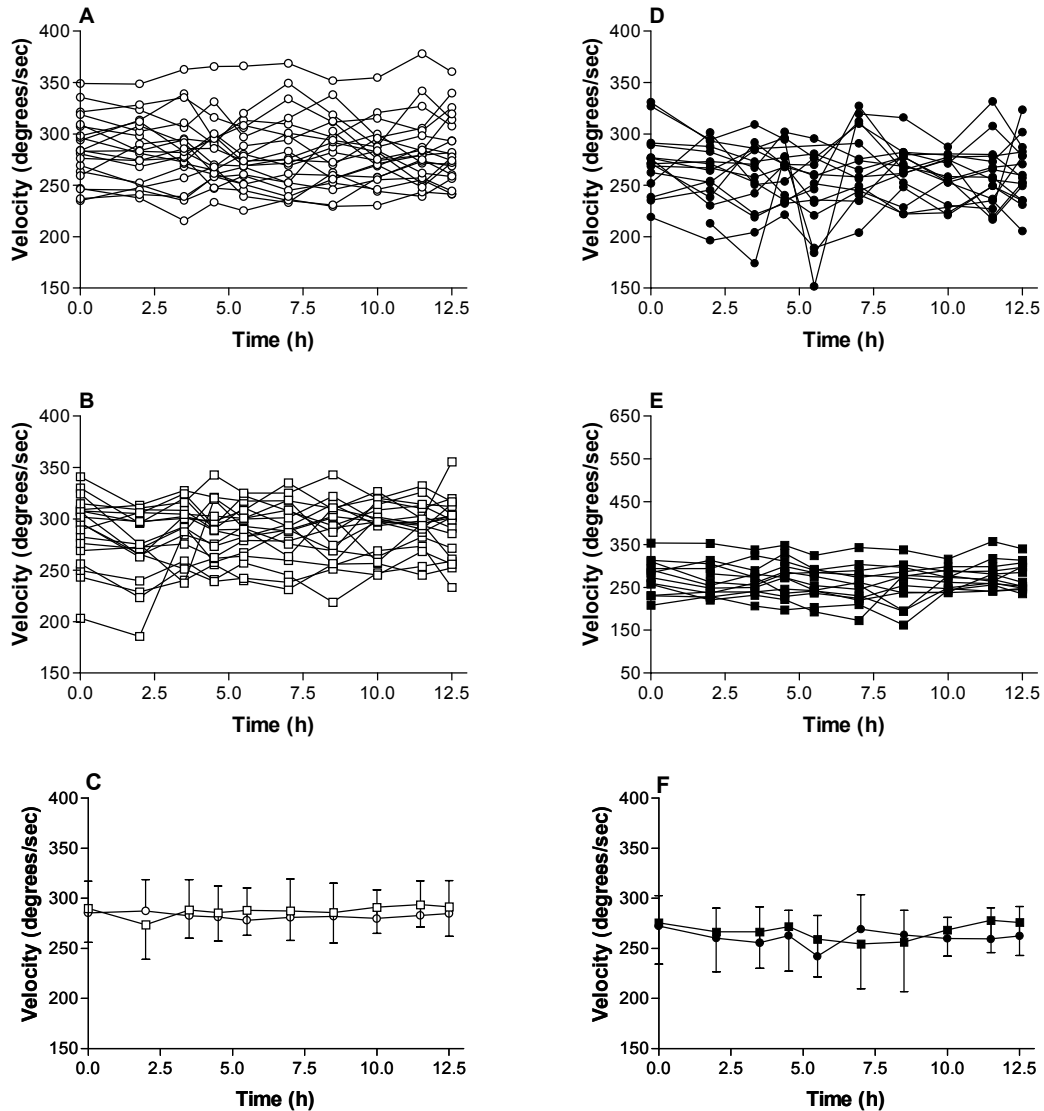


Figure 3.2. For 8-degree saccades: line plots of peak velocity vs. time for individual data (A = young women (○), B = young men (□), D = older women (●), E = older men (■)) and mean data with standard deviations (C = young women and men; F = older women and men).

Duration of saccades. Figure 3.3 illustrates the individual and mean duration data for both groups for the 8-degree saccades. Similar to the latency and velocity data, there were no significant time differences in the duration data from either the young women or young, or the older women, group for either the 8 or the 16-degree saccades ($p \geq 0.18$ for all). The older men displayed a significant time-related difference in the duration of both the 8 and 16-degree eye movements, ($p = 0.02$ and 0.006 , respectively). The longest

durations (i.e., a 16% increase from baseline measurements) were noted at the 7 h and 8.5 h testing times. There were no significant sex-related differences ($p \geq 0.79$) in duration for either the young or the older groups.

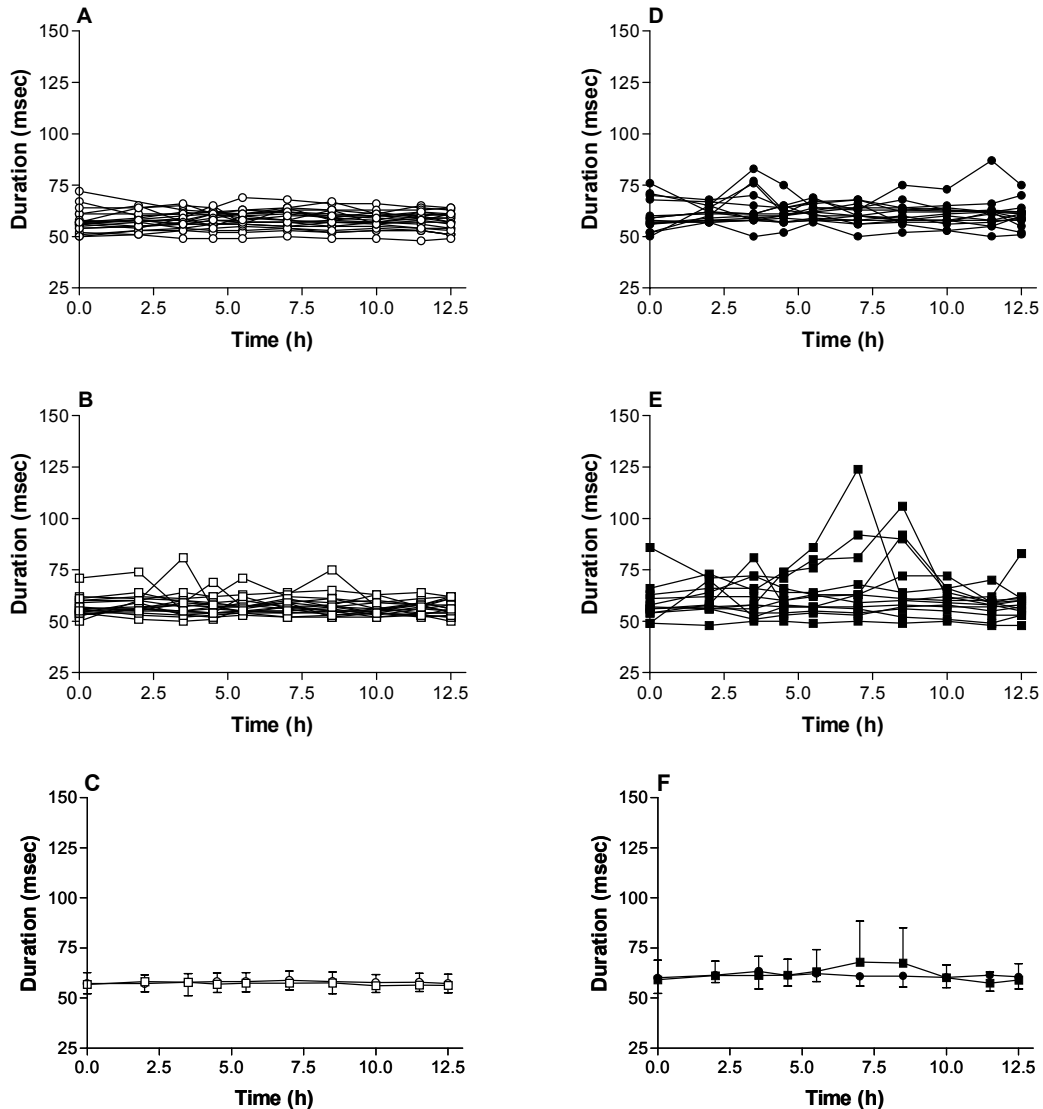


Figure 3.3. For 8-degree saccades: line plots of duration vs. time for individual data (A = young women (○), B = young men (□), D = older women (●), E = older men (■)) and mean data with standard deviations (C = young women and men; F = older women and men).

Accuracy of saccades. The accuracy data for the 8-degree saccades are represented in Figure 3.4 and include the individual and mean data for both young and older groups. There was a significant improvement over time in accuracy for the young women for the 16-degree saccades (greatest change from baseline = 4%; $p = 0.006$, not shown) but not for the 8-degree saccades ($p = 0.08$). This was in contrast to the

stability or lack of change in latency, velocity, and duration of saccades. Significant differences were also noted between the young men and women during the 16-degree saccade task, $p = 0.01$, but not the 8-degree task, with the women demonstrating greater accuracy than the men. For the older group there were no significant differences noted across time or between sexes for either the 8-degree or 16-degree saccade task ($p \geq 0.24$ for all).

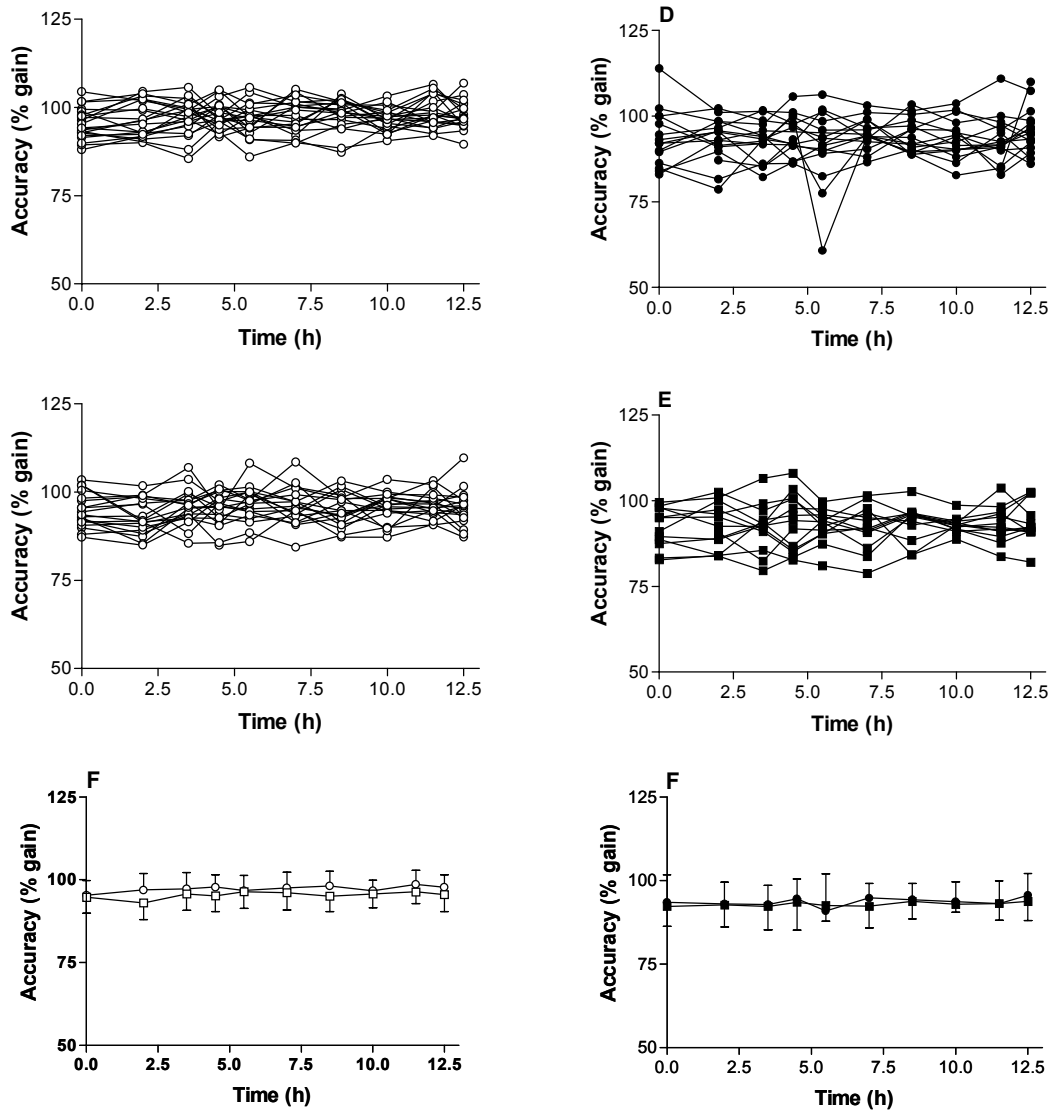


Figure 3.4. For 8-degree saccades: line plots of gain vs. time for individual data (A = young women (○), B = young men (□), D = older women (●), E = older men (■)) and mean data with standard deviations (C = young women and men; F = older women and men).

Card Sorting. The results of the CS task are represented in Figure 3.5. The young women demonstrated significant improvement (10% change from baseline) over time for CS, $p=0.04$. The young men showed no differences over time ($p = 0.11$) and were not different from the young women ($p = 0.66$). In the older groups, both men and women were stable over time and there was not a sex-based difference ($p \geq 0.31$ for all comparisons).

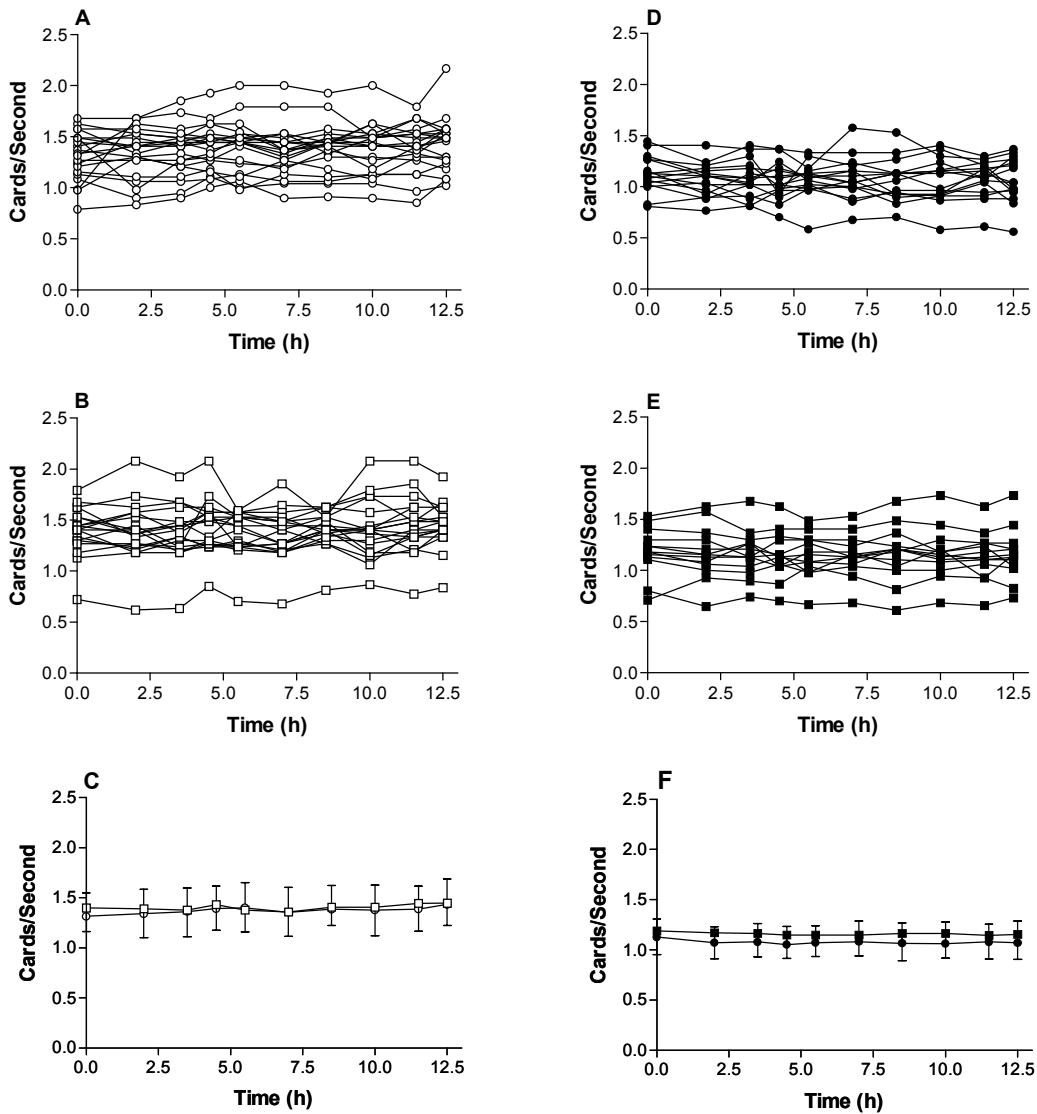


Figure 3.5. Card Sorting: line plots of number of cards/sec vs. time for individual data (A = young women (○), B = young men (□), D = older women (●), E = older men (■)) and mean data with standard deviations (C = young women and men; F = older women and men).

Digit Symbol Substitution. DSST results can be found in Figure 3.6. The young women had higher DSST scores than the young men ($p = 0.03$) and did not demonstrate a time-related effect ($p = 0.2$). The young men's DSST scores tended to improve with time ($p = 0.05$); the maximum change from baseline was 5%. DSST scores were stable throughout the testing day for both older groups ($p \geq 0.38$) and there were no differences between the older women and men, $p = 0.69$.

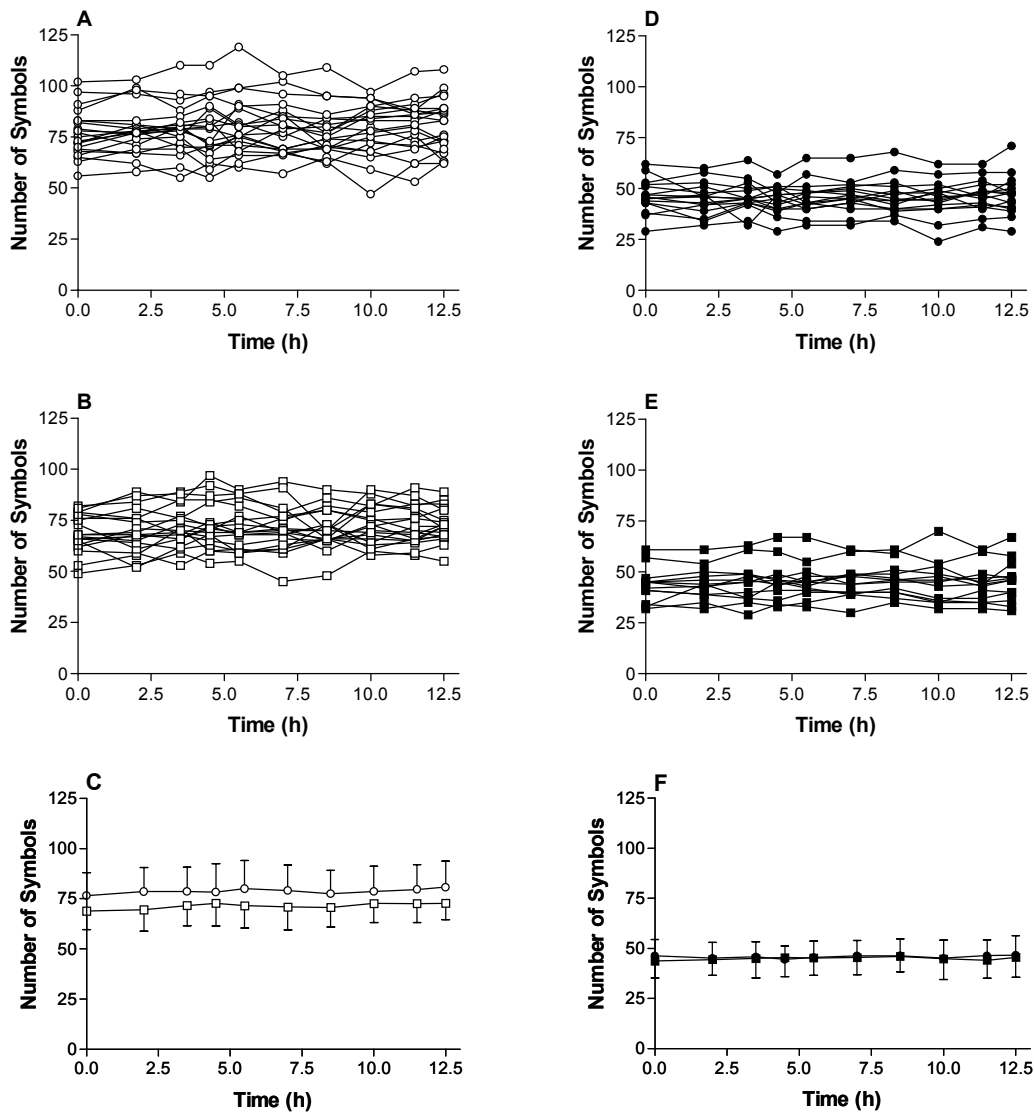


Figure 3.6. Digit Symbol Substitution: line plots of number of symbols vs. time for individual data (A = young women (O), B = young men (□), D = older women (●), E = older men (■)) and mean data with standard deviations (C = young women and men; F = older women and men).

For clarity, Table 3B summarizes the significance of the statistical models for the SEM, DSST, and CS data for each of the age/sex groups.

Table 3B. Statistical analysis of reproducibility of SEM and Psychomotor Test Data

	Age Sex groups			
	Young women	Young Men	Older Women	Older Men
<i>8-degree Saccades</i>				
Latency	--	--	--	--
Velocity	--	--	--	*
Duration	--	--	--	*
Accuracy	--	--	--	--
<i>16-degree Saccades</i>				
Latency	--	--	--	--
Velocity	--	--	--	*
Duration	--	--	--	*
Accuracy	*	--	--	--
<i>Psychomotor Tests</i>				
DSST	--	--	--	--
Card Sorting	*	--	--	--

Note: DSST is Digit Symbol Substitution Test. A dash (--) indicates no significant difference due to time within each age/sex group.

* Indicates statistically significant difference due to time within age/sex group, $p \leq 0.05$.

Discussion

Saccadic Eye Movements. These results demonstrate that SEM dynamics and results from CS and DSST tests are relatively stable over time for ten repeated testing sessions during 12.5 hours in young and older men and women. Although previous studies have examined repeated measurements of eye movements over time in young people under both drug and no-drug or placebo treatments (van Steveninck, et al., 1992; Glue, White, Wilson, et al. 1991; Ball, Glue, Wilson, & Nutt, 1991; Padoan, Korttila, Magnusson, et al. 1992), little information is available regarding repeated same-day testing of SEMs in an older population. A single report by Tuk et al., reported frequent testing (21 times over 8 hours) in a group of 21 patients whose ages ranged from 18 to 78 years (Tuk & Oberyé, 1997). However, there was no reference to breakdown of ages within this group and, more importantly, testing was done only after administration of an oral dose of either 10 or 20 mg of temazepam with no placebo control.

In the data reported here, latency, which is the reaction time (msec) between target presentation and initiation of eye movement, was the most stable of the SEM parameters across all four age/sex groups for both the 8-degree and 16-degree targets. This is consistent with earlier reports of latency evaluation in young (Green, King, & Trimble, 2000; Ball, Glue, Wilson, & Nutt, 1991; Glue, et al., 1991; van Steveninck, Schoemaker, Peiters, et al. 1991). However, in a study by van Steveninck et al., latency appeared to decrease with repeated testing (van Steveninck, et al., 1992) over an extended period of 33.5 h. It's important to note that van Steveninck's testing paradigm was quite dense during the first 16 h (40 testing sessions) and sparse during the remaining 17.5 h (3 testing sessions). Blekher and colleagues (Blekher, Ramchandani, Flury, et al. 2002) recently reported a decrease in latency when testing a group of adults three times within a 160 min. trial. It has been reported that shorter latencies, i.e., 'express saccades' may be achieved when subjects expect the saccade, attributed to frequent testing, such as in the van Steveninck study. The frequent testing results in a decreased tendency for target fixation (Fischer & Ramsperger, 1986) and thereby facilitates shorter reaction times. Additionally, learning or practice effects may occur when the target location is known, also resulting in decreased reaction times. Van Steveninck and group employed only 30-degree saccade targets in their study and while Blekher et al. employed four targets (7.5 and 15 degrees to either the left or right), it appears subjects did not practice the tasks prior to collection of study data. Hence, in these testing paradigms, learning may be occurring during the period of data collection. In contrast, the data reported here are from participants who were required to practice the SEM tasks at screening and again upon admission to the GCRC the evening prior to data collection, limiting the possibility of learning during the study day.

For peak saccade velocity, previous reports conflict concerning the stability over repeated testing times. Ball et al., report no change in saccade velocity when tested seven times over 30 minutes (Ball, Glue, Wilson, & Nutt, 1991). A recent study on the effect of sleep deprivation measured SEMs every 2 h for 40 h and found no variability in velocity for the first 22 h of testing (prior to sleep deprivation) (DeGennaro, Ferrara, Urbani, et al. 2000). Conversely, van Steveninck's group (van Steveninck, et al., 1992) reported a significant decrease in peak velocity within the first hour of testing (this included eight testing sessions). The change from baseline ranged among subjects from 6.2% to 12.1% and remained statistically significant throughout 15 h of testing, over 40 testing sessions. It is possible this decrease in velocity may be associated with fatigue attributed to the intensity of testing times and the large amplitude of the saccade target (30 degrees). Larger

saccades of greater than 17 degrees have been reported to be more fatiguing than shorter saccades of 10 and 15 degrees (Bahill & Stark, 1975).

In contrast, saccade duration seems to display little variation over time (Roy-Byrne, Cowley, Radant, et al. 1993), though reports are limited. In the data reported here, both mean peak velocity and duration of saccades remained stable throughout the testing day for both of the young groups and for the older women (for 8-degree and 16-degree targets). Only the older men demonstrated a significant effect of time: mean peak velocity decreased with an expected corresponding increase in duration of saccades, most notably between the 5.5 h and 8 h testing times for both target amplitudes. Interestingly, the study protocol provided for subjects to be served a smoothie (a 12 oz. frozen drink consisting of non-dairy milk substitute, frozen sorbet and fruit punch) at 4.5 h and 7 h, possibly inducing a post-prandial effect within certain subjects. For saccades to the 8-degree target, the overall impact of each observation within the group of older men was tested statistically using Cook's distance (Cook, 1977). Two subjects, (one at the 7 h testing session and one at time 8.5 h testing session) had the highest Cook's distance measurement. When data for these subjects from the identified time points were removed from the analysis, the model was no longer significant, thereby recognizing them as being influential to the model.

The accuracy of saccades was consistently reproducible for all groups to both the 8-degree and 16-degree targets with one exception. For the 16-degree target, the young women differed from the young men and they significantly improved throughout the 12.5 h course of testing. In a study of young men only, by DeGennaro et al., there were no changes in accuracy of saccades to targets stepped between 5 and 30 degrees of visual angle. However, it was noted that, other than instructing the subjects to avoid moving their heads, no measures were taken to assure head immobility. The combination of head and eye movements have a direct effect on accuracy of saccades (1999). Blekher and group studied the accuracy of 7.5-, 15-, and 30-degree saccades at four different times in both young men and young women as part of the placebo control in an investigation of alcohol effects and did not report any placebo effects (Blekher, et al., 2002). Although 38 of the 77 subjects in the alcohol arm of the study were young women, only a subset of the study population completed the placebo arm, precluding any sex-stratified analysis. Additionally, the study design was somewhat weak in that the placebo session was always conducted after the alcohol session.

Card Sorting and DSST. For CS, only one group demonstrated a time-dependent difference: the performance of the young women improved over time, in contrast to the stability of performance in the other three

groups. Previous data in young and older men from this lab report no changes in CS over an 8.5 h testing session though significance was approached ($p=0.057$). No significant placebo response within a day for CS when tested among 13 men and women aged 21 to 40 years on two occasions. However, there was a significant improvement of 7% between the first and second occasions, which were separated by 21 days (Bertz, et al., 1995).

For both groups of women and for the older men, the DSST scores from this study support previous reports that indicate that both young and older subjects demonstrate no change in DSST scores over time (Nikaido, Ellinwood, Jr., Heatherly, et al. 1990; Greenblatt, et al., 1991; Nikaido, Ellinwood, Jr., Heatherly, & Gupta, 1990). It's important to note that the studies referenced here, in addition to our own, provided for practice sessions in order to limit the amount of learning that might otherwise occur. Since the young men in this study demonstrated variability across the time points and tended to improve during the day, it may be that young men require more practice to reach a plateau. This is in contrast to a report by Nikaido and group who noted that young subjects (mean age approximately 26 years) required less practice than an older group (mean age approximately 67 years) before no substantial improvement was noted in task scores for a computerized digit substitution task. When data from a single young man (who had the least number of symbols drawn at times 7 h and 8.5 h) was removed from the analysis, the model was no longer significant. Although it appears he may be an outlier, subsequent analysis utilizing the Cook's distance measure (Cook, 1977) did not identify this individual as influential.

Overall, these data indicate that the SEM parameters are stable across testing in both young and older women and in young men. Although the velocity and resultant duration of saccades were more variable in older men this could be attributed to two possible outliers or to the somewhat smaller number of subjects in this group as compared to the other groups. Additionally, since the normal peak velocities to saccades of 8 and 16 degrees targets can range from 50 to 540 degrees/second and 50 to 725 degrees/second, respectively, it is improbable that the 8% magnitude of change in velocity noted in older men is of any clinical significance. These results also indicate that healthy men and women between the ages of 66 and 78 years of age are capable of completing the SEM tasks on multiple occasions within a 12.5 h period. To our knowledge, this is the first time that an older population has been tested on such a rigorous schedule similar to that required to characterize the time course of CNS-active drugs. These data also confirm the need for ample practice of both the DSST and CS tasks in order to limit learning effects, especially among a young population.

CHAPTER FOUR
RELIABILITY OF THE SCORING PROGRAM FOR SACCADIC EYE MOVEMENT DATA OBTAINED DURING GABA-
AGONIST IMPAIRMENT

Abbreviations:

ICC	intraclass correlation coefficient
SEMs	saccadic eye movements

Introduction

Pharmsac, (Pharmacodynamic Research Center and Neurobehavioral Studies Program, University of Pittsburgh, Pittsburgh PA) the program used to score the saccadic eye movements (SEMs) collected during this research study, is a modified version of a scoring program previously used in our laboratory. Pharmsac was specifically designed for us in order to facilitate the quantitative analysis of saccades in volunteers who have been exposed to pharmacologic challenges with sedative-like effects, e.g., alprazolam. The modifications made to the program allow the user (i.e., scorer) to manually mark and identify certain characteristics of the saccade that were previously controlled by a computerized algorithm. As such, a certain degree of subjective interpretation was introduced into the scoring procedures. To minimize this subjectivity and to standardize the scoring process, a Pharmsac scoring manual was created to guide users through proper scoring procedures and a process for training scorers was developed.

Inter-rater reliability is used to evaluate the extent of consensus between two or more individuals (e.g., raters, judges, scorers) on the implementation of a rating system. One form of inter-rater reliability is the intraclass correlation coefficient (ICC) which may be conceptualized as the ratio of between-groups variance to total variance. ICC will approach 1.0 when there is perfect inter-rater reliability. Intraclass correlations can be standardized as follows: 0.40 = poor, 0.40 to 0.59 = fair, 0.60 to 0.74 = good, and 0.75 to 1.00 = excellent (Viljoen, Roesch, & Zapf, 2002; Cicchetti, Showalter, & Tyrer, 1985). The purpose of this research is to determine the ICC of two scorers in order to assess the reliability of the Pharmsac saccadic eye movement scoring program. For each saccade parameter evaluated, a mean ICC greater than or equal to 0.60 (i.e., good or better), would be considered acceptable and, as such, validate the reliability of the Pharmsac software.

Methods

Study design and subjects. These data were collected during the alprazolam administration visits (the third and fourth visits) of the four-way crossover study that is described in Chapter 2. Subjects received alprazolam plus placebo on one visit and alprazolam plus DHEA on the alternate visit. Saccadic eye movements were tested at 10 time points over a 12.5 hour period during each of the two visits. Data from eight randomly chosen subjects (two from each of the age/sex groups: young women, young men, older women, older men) were evaluated by the same two scorers. Saccadic eye movement data from three time points during each of the two visits were scored. The time points were chosen to represent eye movement performance prior to alprazolam administration (0 h), near to peak drug effect (3.5 h after alprazolam

ingestion) and during recovery from drug effect (9.5 h after alprazolam ingestion). The scorers were blinded to treatment at the time of scoring. Scorers were instructed to have the Pharmsac manual available during each scoring session.

Rater Training. Prior to doing any individual scoring, the raters were trained (one-on-one) in the use of the software by an instructor using the scoring manual as a guide. The same instructor trained all raters. Additionally, group scoring sessions including several scorers and the instructor were held. During these sessions, the group would collectively view and score eye movements as a means of insuring joint understanding of the scoring process and compliance with the scoring manual. Finally, the rater scored data in the presence of the instructor before being judged ready to perform the task unsupervised.

Statistical Analysis. The specifics of the saccadic eye movement task and the scoring procedures are described in detail in Chapter 2. Briefly, for each subject at each testing session, eye movements were separated according to the target step amplitude (8-degrees and 16-degrees) and combined according to direction (left and right) allowing a maximum number of 24 scored trials per session per target amplitude. The subject-specific mean for saccades to each target amplitude was used in all subsequent analysis. Saccade measurements from the 8-degree targets were analyzed separately from the 16-degree target measurements. The four SEM parameters (latency, velocity, duration and accuracy) were used as the dependent variables. Scorer was the fixed effect. Based on the methods of Shrout and Fleiss (Shrout & Fleiss, 1979), scorers were conceived as a random selection of possible scorers, each of whom rated all eye movements from all randomly selected subjects such that each eye movement was evaluated by each scorer. Using a one-way mixed effect ANOVA, the ICC was calculated as the ratio of the covariance parameter estimates; that is, the variance component for each random effect (SEM parameter) was divided by the sum of the residual error variance plus the random effect variance. The ANOVA was performed using SAS Software (Cary, NC, version 8.02)(SAS Institute, 2000).

Results

Table 4A contains the ICCs for all SEM variables tested. For most SEM variables, ICC fell between .80 and 1.00.

Table 4A. Intraclass Correlation Coefficients

Visit	Session (h)	8-degree Targets				16-degree Targets			
		Duration	Gain	Latency	Velocity	Duration	Gain	Latency	Velocity
3	0	0.99	0.50	1.00	0.89	0.87	0.65	1.00	0.96
3	5.5	0.87	0.91	0.96	0.96	0.93	0.77	0.99	0.96
3	11.5	0.82	0.95	1.00	0.99	0.83	0.84	1.00	1.00
4	0	0.92	0.61	1.00	0.99	0.97	0.84	1.00	0.99
4	5.5	0.94	0.94	0.96	0.98	0.98	0.89	1.00	0.98
4	11.5	0.79	0.91	1.00	0.99	0.82	0.91	1.00	0.99
Mean ICC		0.89	0.80	0.99	0.97	0.90	0.82	1.00	0.98

Discussion

These data suggest that the average inter-rater reliability of the Pharmsac saccadic eye movement scoring program is excellent (i.e., $ICC \geq 0.75$) (Viljoen, Roesch, & Zapf, 2002; Cicchetti, Showalter, & Tyrer, 1985) for the duration, gain, latency, and velocity of saccades to both the 8-degree and 16-degree targets. Individually, the ICCs were excellent for all parameters at all time points except for gain to the 8-degree and 16-degree saccades which can be classified as fair and good, respectively.

The Pharmsac software allowed for subjective calibration of the individual saccades and for a combination of both subjective and programmed computation of the various saccade parameters. Although parameters were derived from only one eye, movements from both eyes were recorded and the scorers were required to review both recordings before choosing which eye was to be scored, based on clarity of tracing and absence of noise in the signal. Despite the opportunity for scorer bias, these data indicate that trained scorers with access to the Pharmsac scoring procedures manual produce reliable assessments of SEM data using Pharmsac software. The scorers who participated in this research were trained in the use of the Pharmsac program. Additionally, an instruction manual specific to Pharmsac was available during the scoring process.

CHAPTER FIVE

SACCADE PARAMETERS AND THEIR ASSOCIATION WITH AGE, SEX, DHEA, AND DHEA-S

Abbreviations:

CNS	central nervous system
DHEA	dehydroepiandrosterone
DHEA-S	dehydroepiandrosterone-sulfate
GABA	gamma-aminobutyric acid
GABA-RC	GABA-benzodiazepine-receptor-complex
NMDA	N-methyl-d-aspartate
SEM	saccadic eye movements

Introduction

Saccadic eye movements (SEMs) are rapid, brief, jerk-like movements made by the eye when the focus of vision is shifted from one point to another in the visual field. While the decision to initiate saccades is under volitional control, once initiated, the basic dynamics of these movements are not. For many reasons, saccades are ideal measures of central nervous system (CNS) activity for pharmacodynamic research. They are quantitative, reliable, and reproducible, and are measured non-invasively. In addition, the CNS pathways involved in the control of these eye movements and their neurochemical modulation have been studied in detail (O'driscoll, et al., 2000; Wurtz & Hikosaka, 1986; Fuchs, Kaneko, & Scudder, 1985; Sparks & Mays, 1990; Law, Svarer, Holm, & Paulson, 1997; Robinson, 2000; Quaia, Lefevre, & Optican, 1999).

Electrophysiological, pharmacological, and anatomical findings have documented inhibitory synaptic connections involving gamma-aminobutyric acid (GABA) in the control of eye movements. For example, the substantia nigra tonically inhibits (via GABAergic projections) the superior colliculus in order to prevent involuntary eye movements away from objects of interest (Hikosaka & Wurtz, 1983; Hikosaka & Wurtz, 1985b; Hikosaka & Wurtz, 1985a). When a saccade is required to fixate a new target, signals from the striatum inhibit the substantia nigra via a GABAergic pathway thus releasing the superior colliculus to facilitate saccade generation.

SEM dynamics have been studied extensively in young adults, and to a lesser extent in elderly individuals. In 1980, Spooner et al. compared the three visually controlled eye tracking systems (saccadic, smooth pursuit, and optokinetic) in subjects of various ages and demonstrated age-related declines in all three systems (Spooner, Sakal, & Baloh, 1980). While prolonged saccade latency has been associated with aging in the majority of studies, associations for saccade velocity and accuracy have not been as consistent. Some studies have indicated that velocity does not change with age (Abel, Troost, & Dell'Osso, 1983; Hotson & Steinke, 1988; Munoz, Broughton, Goldring, et al. 1998), while other studies have shown a significant decrease in velocity with age, particularly for saccades at amplitudes greater than 10° (Spooner, Sakal, & Baloh, 1980; Warabi, Manabu, & Kato, 1984; Sharpe & Zackon, 1987; Sweeney, Rosano, Berman, et al. 2001; Moschner & Baloh, 1994).

Dehydroepiandrosterone (DHEA) and its sulfate metabolite, DHEA-S, are endogenous hormones secreted by the adrenal cortex (Nieschlag, et al., 1973). Concentrations of both are age dependent, peaking in the third decade and decreasing thereafter (Sulcová, Hill, Hampl, & Stárka, 1997; Pavlov, et al., 1986; Carlström, et al., 1988). DHEA and DHEA-S are neurosteroids as they can be synthesized de novo in the brain (Majewska, Demirgören, Spivak, et al. 1990), where concentrations are considerably higher than in other organs (Corpechot, Robel, Axelson, et al. 1981). CNS concentrations appear to parallel those in the periphery (Robel & Baulieu, 1995; Lacroix, et al., 1987; Guazzo, Kirkpatrick, Goodyer, et al. 1996). On theoretical grounds, the overall effect of these neurosteroids in vivo should be excitatory based on in vitro activity at two receptors: 1) the GABA-benzodiazepine-receptor-complex (GABA-RC) (Olsen & Delorey, 1998), to which GABA, the major CNS inhibitory neurotransmitter, binds, and 2) the N-methyl-d-aspartate (NMDA) receptor, a major receptor for excitatory amino acids (Dingledine & McBain, 1998). In vitro, DHEA and DHEA-S act as noncompetitive negative modulators of the GABA-RC (Majewska, Demirgören, Spivak, & London, 1990; Demirgören, Majewska, Spivak, & London, 1991) while DHEA demonstrates agonist activity at the NMDA receptor (Debonnel, Bergeron, & de Montigny, 1996).

Despite the importance of endocrine modulations of the GABA-RC, and the role of GABA in the control of saccadic eye movements, little data are available regarding the possible relationship between SEM performance and concentrations of DHEA and DHEA-S. The objective of this study was to determine whether there are age- and/or sex-related patterns of SEM dynamics (peak velocity, latency, duration, and accuracy) and whether these are associated with endogenous concentrations of DHEA and DHEA-S.

Methods

Study design and subjects. The data used in this analysis were generated from a randomized, double-blind, placebo-controlled, four-way crossover study that required subjects to visit the GCRC on four separate occasions. Analyses presented in this chapter include only data collected during the baseline evaluation during the first of these four visits, i.e., prior to administration of any drug or placebo. Incorporated in the analysis are data from 68 medically and psychiatrically healthy volunteers. Fifty-six of these subjects were women (19 young and 11 older) and men (15 young and 11 older) who participated in the four-way crossover study described previously (see Chapter 2).

Twelve additional older subjects (six women and six men) participated in a separate study, but were screened and evaluated in the same way and are included in the analysis. The age range for young subjects was 20 to 30 years and for older subjects 66 to 78 years. Included in the 68 subjects are individuals who identified themselves as Black (n=10), Hispanic (n=1), Caucasian (n=55), or Asian/Pacific Islander (n=2).

Evaluation of saccadic eye movements. Saccadic eye movement data were collected and assessed as described in Chapter 2. For the purpose of this analysis, latency is the reaction time (msec) between target presentation and initiation of saccade, duration is the time (msec) required to complete the saccade, peak velocity ($^{\circ}$ /sec) is the maximum velocity achieved during the saccade, and accuracy is the percent of target step amplitude gained by the primary saccade.

For each subject at each testing session eye movements were separated according to the size of target amplitude (8° and 16°) and combined according to direction (left and right) allowing a maximum number of 24 scored trials per session per target amplitude. The subject-specific mean for saccades to each target amplitude was used in all subsequent analysis.

Analysis

Steroid concentration analysis. The assays for steroid concentrations were done using 125 I-radioimmunoassay techniques (Diagnostic Systems Lab Inc., Webster, TX). Serum was assayed for DHEA and DHEA-S concentrations. The detection range and lower limit of detection, respectively, for each assay were: DHEA: 0.2 to 30 ng/ml and 0.009 ng/ml; DHEA-S: 50 to 8000 ng/ml and 17 ng/ml. The coefficient of variation for each was <10% throughout the range of the assay. Blood samples for DHEA and DHEA-S were collected from an indwelling catheter in a forearm vein and placed in appropriately labeled vacuum tubes and centrifuged. Serum was decanted and stored at -80°C .

Data Analysis.

Analysis included descriptive statistics of age, DHEA and DHEA-S concentrations, and SEM dynamics for the four groups of subjects: young women, young men, older women, and older men. SEM data are shown graphically using box and whisker plots. The boxes extend from the 25th to the 75th percentile with a line at the median, while the whiskers extend to the highest and lowest

observed values. To determine whether hormone concentrations or saccade measures differed by age and/or sex, group means were compared using two-way analysis of variance (ANOVA). The dependent variable was the SEM parameter (or steroid concentration) while the fixed effects were sex, age, and the sex-by-age interaction term. The sex-by-age interaction term was not significant in preliminary analysis ($p > 0.07$ for all analysis) and was subsequently dropped from the model. Effects are reported as means and corresponding standard deviations (s.d.).

Stepwise multiple linear regression was used to assess the influence of age, steroid concentration, race, and sex on SEM dynamics. Results were considered statistically significant if the observed p-value was less than or equal to a critical value of 0.05. All plotting was performed using GraphPad Prism version 3.02 for Windows, GraphPad Software; San Diego, California USA; www.graphpad.com (Motulsky, 1999). All ANOVA and multiple linear regression analysis were performed using SAS Software (Cary, NC, version 6.09) (SAS Institute, 2000).

Results

The number of subjects and mean age data per group are presented in Table 5A, along with DHEA and DHEA-S concentrations.

Table 5A. Mean age and morning DHEA and DHEA-S concentrations for the four groups of participants^a

GROUP	AGE (yr)	DHEA (ng/ml)	DHEA-S (ng/ml)
Young women (n=19)	23.2 (3.2) (20 - 30)	14.1 (5.0) (2.6 - 21.4)	1723.6 (924.3) (134.86 - 4119.8)
Young men (n=15)	23.7 (3.2) (20 - 29)	14.3 (3.7) (8.39 - 20.3)	2451.4 (804.4) (1128.5 - 3996.2)
Older women (n=17)	69.4 (2.5) (66 - 75)	4.18 (2.9) (0.93 - 10.3)	172.3 (112.4) (37.9 - 375.1)
Older men (n=17)	70.5 (3.0) (67 - 78)	6.1 (4.9) (1.7 - 23.1)	843.6 (654.1) (91.7 - 2011.4)
Young vs. Older ^b	—	p=0.0001	p=0.0001
Men vs. Women ^b	—	p=0.30	p=0.0001

^aData are presented as mean, standard deviation, and range.

^bp-values were obtained by two-way ANOVA models.

Box plots of latency and duration of saccades to the 16° target for each group (i.e., young women, young men, older women, and older men) are presented in Figure 4.1 (latency) and Figure 4.2 (duration).

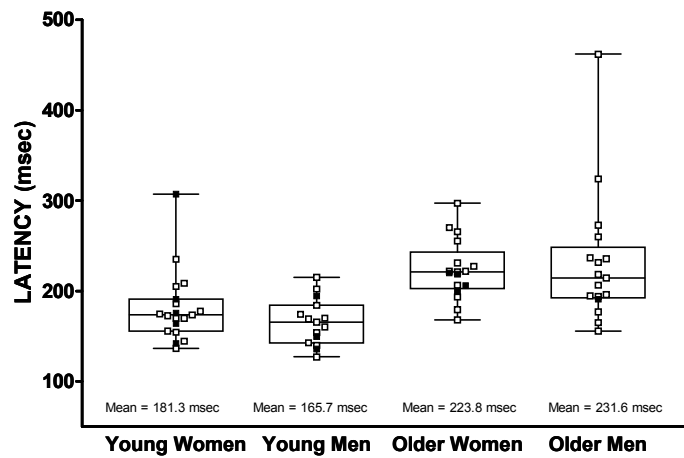


Figure 5.1 Boxplots of mean saccade latency to response time for 16° targets for each age/sex group. The box defines the interquartile range and the middle line represents the median. The whiskers extend to the highest and lowest values. The filled squares represent data from minority subjects and the empty squares represent data from Caucasian subjects. The latency in older subjects was significantly higher than in the young, $p < 0.0001$.

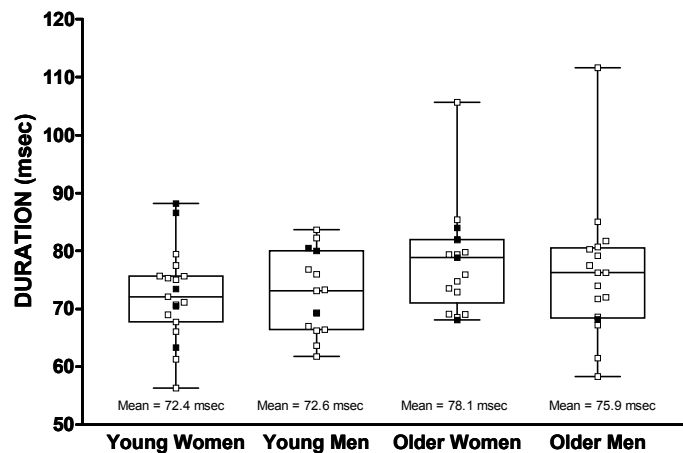


Figure 5.2. Boxplots of mean duration of saccades or 16° targets for each age/sex group. The box defines the interquartile range and the middle line represents the median. The whiskers extend to the highest and lowest values. The filled squares represent data from minority subjects and the empty squares represent data from Caucasian subjects. The saccade duration for older subjects was significantly different from that of the young, $p < 0.04$.

Data in Table 5A demonstrate that mean DHEA and DHEA-S values differed significantly between the age groups with the young having higher concentrations of both hormones than the older

subjects ($p = 0.0001$). The men had significantly higher DHEA-S concentrations than did the women ($p = 0.0001$). No differences were noted between sexes for DHEA ($p = 0.30$).

Latency (Fig. 5.1) differed by age ($p = 0.0001$) but not by sex, with the older subjects demonstrating longer latency to saccade initiation (mean = 227.7 msec; s.d. = 55.7) than the young (mean = 174.5; s.d. = 34.0). Findings were similar for latency to saccades to the 8° targets.

Similar to the results for latency, Figure 5.2 shows that the mean duration of the 16° saccades was longer ($p = 0.041$) in the older subjects (mean = 77.0 msec; s.d. = 10.4) than in the young subjects (mean = 72.5 msec; s.d. = 7.4), but was not significantly different between the sexes ($p = 0.65$). The duration of saccades to the 8° targets did not differ significantly by either age or sex ($p > 0.10$ for each).

In contrast to the results for latency and duration, the mean peak velocity for saccades to the 16° target for the older group (387.6°/sec; s.d. = 63.1) did not differ significantly from that of the young group (405.3°/sec; s.d. = 55.3). Peak velocity in men (397.6°/sec; s.d. = 61.5) did not differ from that in women (395.5°/sec; s.d. = 58.7); $p > 0.22$ for each comparison. Similarly, no differences were observed between age or sex groups for mean peak velocity to targets of 8° ($p > 0.16$). The average saccade gain (i.e., accuracy) to the 8° target did not differ by age ($p = 0.29$) but did differ significantly ($p = 0.023$) between men (0.92 s.d. = 0.07) and women (0.96; s.d. = 0.06). No differences were observed between age or sex groups for accuracy of saccades to the 16° targets ($p > 0.11$).

For saccade latency, results of stepwise multiple linear regression analyses indicate that age is a significant predictor for both the 8° ($r = 0.36$, $p = 0.002$) and 16° targets ($r = 0.51$, $p \leq 0.0001$). Addition of other variables (i.e., steroid concentration, race, or sex) did not improve the fit of the model.

Conversely, significant predictors for duration of saccades to 8° and 16° targets included DHEA ($r=0.27$, $p=0.023$; $r=0.30$, $p=0.014$) and DHEA-S ($r=0.26$, $p=0.033$; $r=0.30$, $p=0.012$), respectively; age and sex did not improve the fit of the model.

Discussion

Our results demonstrate significant age-related differences in saccade latency and duration, but not in the velocity or accuracy of saccades. Several studies have shown that increased saccade latency, or reaction time, is associated with aging (Abel, Troost, & Dell'Osso, 1983; Sharpe & Zackon, 1987; Abrams, Pratt, & Chasteen, 1998; Warabi, Manabu, & Kato, 1984; Whitaker, Shoptaugh, & Haywood, 1986; Sharpe & Zackon, 1987; Hotson & Steinke, 1988; Moschner & Baloh, 1994; Scialfa, Hamaluk, Skaloud, et al. 1999). Our data corroborate these results with a significantly longer latency in older adults for saccades to both the 8° and 16° targets. The increase in latency is consistent with age-related changes in motor function (Fozard, Vercruyssen, Reynolds, et al. 1994), possibly within the cortical eye fields or striatum or in their connections to brainstem saccade generators (Christakou, 2001). Although the 8° and 16° amplitudes of target steps used in our study are smaller than those used in some previous studies, they more closely emulate those seen in normal day-to-day eye movements (Bahill, Adler, & Stark, 1975). Consistent with a previous report by Munoz et al. (Munoz, Broughton, Goldring, & Armstrong, 1998) the mean duration of the 16° saccades observed in the present study for older subjects (mean=77.0msec; s.d.=10.4) was significantly longer than for the young (mean=72.5msec; s.d.=7.4).

In contrast, the mean duration to the smaller 8° targets did not differ significantly between the young and older subjects (59 msec and 57 msec, respectively). Likewise, no age-related differences in the peak saccade velocity to 8° and 16° targets were observed in this study, consistent with the results of some other studies (Abel, Troost, & Dell'Osso, 1983; Hotson & Steinke, 1988; Munoz, Broughton, Goldring, & Armstrong, 1998). Moschner et al. has found a significant slowing in peak velocity as age increases, but only when the amplitude of the saccade was greater than 20° (Moschner & Baloh, 1994). Others have drawn similar conclusions (Sweeney, Rosano, Berman, & Luna, 2001; Becker, 1989; Warabi, Manabu, & Kato, 1984), with Sharpe et al. noting a significant decrease in velocity when the amplitude of the saccade was 40°. In addition to the size of the saccade, recording methods also influence velocity (Becker, 1989) making it difficult to compare different studies.

DHEA concentrations in the multiple linear regression model explained a significant portion of variability in saccade duration. There is good rationale to expect a relationship between SEMs and DHEA. In vitro, DHEA is a non-competitive negative modulator of the GABA-RC and as such, should have an excitatory effect. We hypothesized that the well-documented age-related decrease in the circulating concentrations of DHEA over time would have an effect similar to that of an increase in GABA-agonist activity, which decreases SEM performance (Glue, et al., 1995; Roy-Byrne, Cowley, Greenblatt, et al. 1990; Kroboth, et al., 1998; Cowley, Roy-Byrne, Radant, et al. 1995; Ball, Glue, Wilson, & Nutt, 1991). Our results partially confirm this hypothesis. Systemic GABA agonists are well known to affect both the latency of saccades as well as saccade metrics such as duration. Our data indicate that DHEA and DHEA-S levels, which changed dramatically over the age span, were inversely related to saccade duration but not to well-established age-related changes in the latency of saccades. This suggests that DHEA and DHEA-S may differentially modulate GABA systems in different brain regions. The age-related changes in DHEA and DHEA-S observed in this study do not appear to alter activity in the cortical eye fields in a way that accounts for reductions in saccade latency shown by elderly individuals. However, DHEA and DHEA-S levels do appear to modulate activity within the brainstem or cerebellum, or in direct GABAergic projections to those regions, which are known to regulate the duration of saccades. One possibility is that this effect occurs by modulating GABA-mediated inhibition of the superior colliculus by the substantia nigra, a modulator of the initiation and termination of saccades (Hikosaka & Wurtz, 1983; Hikosaka & Wurtz, 1985a). DHEA and DHEA-S appear to modulate this pathway, or another GABAergic system intrinsic to the brainstem or cerebellum, to alter mechanisms that control the precise temporal synchronization of saccade onset and offset commands.

The relationship between eye movement activity and neuroendocrine levels seen in these data is correlational and, as such, the observed correlations of DHEA and /or DHEA-S with SEM dynamics must be viewed with caution. Multiple changes within the brain occur during normal aging that may conceivably affect the observed relationships. Studies in which steroid hormone concentrations are pharmacologically manipulated are needed to establish a direct linkage between changes in DHEA/DHEA-S and oculomotor function in the elderly.

Summary

Changes in saccadic eye movements (SEMs) have been associated with aging. With aging, there is also a decline in concentrations of the neurosteroids DHEA and DHEA-S, known to be noncompetitive negative modulators of the GABA-receptor complex. GABA tone plays an important role in the execution of saccadic eye movements. We evaluated the influence of age and endogenous concentrations of DHEA and DHEA-S on SEM dynamics in sixty-eight women and men (ages 20 to 78) who volunteered for the study. Older adults had significantly longer latency and duration than young adults ($p \leq 0.041$); age had no effect on peak velocity. Using stepwise multiple linear regression analysis, age was a significant predictor of latency ($p \leq 0.002$), which is consistent with age-related changes in corticofugal inputs from the cortical eye fields to the brainstem regulating saccade initiation. This analysis also showed that DHEA and DHEA-S concentrations were significant predictors of duration ($p \leq 0.023$); this is likely explained by the GABAergic modulation of the connections from the superior colliculus and cerebellum to brainstem saccade generators.

CHAPTER SIX

CONCENTRATION-TIME PROFILES FOR ALPRAZOLAM, DHEA, DHEA-S AND CORTISOL AFTER ORAL
ADMINISTRATION OF PLACEBO PLUS ALPRAZOLAM OR DHEA PLUS ALPRAZOLAM IN YOUNG AND
OLDER HEALTHY ADULTS

Abbreviations:

AUC	area under the concentration-time curve
C _{max}	maximum observed concentration
DHEA	dehydroepiandrosterone
DHEA/Alp	DHEA plus alprazolam treatment
DHEA-S	dehydroepiandrosterone-sulfate
GABA	gamma-aminobutyric acid
PL/Alp	placebo plus alprazolam treatment

Introduction

It is expected that when a drug is administered, a response, or pharmacological event will result. The potency and duration of this observed response is assumed to be related to the dose of drug administered. However, the pharmacological effects, both therapeutic and undesirable, are often more closely associated with the concentration of drug in the body (Holford & Sheiner, 1981). Pharmacokinetics is the association of a drug's concentration-time profile to dose, route of administration, absorption, distribution, elimination and metabolism. Pharmacodynamics is the study of the pharmacological response relative to drug concentration. It is known there is interpatient variability in response to drugs. Equivalent drug dosage does not always produce comparable concentrations, nor do comparable concentrations consistently result in equivalent effects among patients, or even within patients. The source of variability can generally be attributed to variability in pharmacokinetics, pharmacodynamics, or even genetics. This pharmacokinetic-pharmacodynamic variability may be intra- or interindividual, may be associated with different populations based on, though not limited to, age, sex, ethnicity or disease process, or may be caused by concurrent drug use or even environmental factors (Marzo, 1997; Linder & Valdes, Jr., 2001; Johnson, 2001).

The overall purpose of this dissertation research, as stated in Chapter 1, is to determine the effect of dehydroepiandrosterone (DHEA) concentration on recovery from gamma-aminobutyric acid (GABA)-agonist (benzodiazepine) challenge in young and older men and women. To address this, both drug concentrations and drug responses were assessed in a design that required administration of both DHEA and the benzodiazepine, alprazolam. The current chapter provides analysis of the concentration-time data of alprazolam, DHEA, dehydroepiandrosterone-sulfate (DHEA-S), and cortisol during two visits: the DHEA plus alprazolam visit (DHEA/Alp) and the placebo plus alprazolam visit (PL/Alp). The objective of this analysis is to describe the concentration-time profiles in four different age/sex groups (young women, young men, older women, and older men) and to determine whether age- and/or sex-based differences exist. This analysis is a prerequisite to the subsequent research presented in Chapter 7, which deals primarily with the pharmacological response to alprazolam in the presence and absence of DHEA.

Methods

Study design and subjects. The data used in this analysis were generated from a randomized, double-blind, placebo-controlled, four-way crossover study that required subjects to be admitted to the General Clinical Research Center on four separate occasions. Analyses in this chapter include only data collected during Phase II, i.e., the third and fourth visits. Subjects received placebo plus alprazolam on one visit (PL/Alp) and DHEA plus alprazolam on the alternate visit (DHEA/Alp). In the afternoon before each of the visits, subjects were admitted to the GCRC and fasted from 10 p.m. on the evening of admission (water was permitted) until 7:30 a.m. the next day. At this time, subjects received a light breakfast and an intravenous catheter was placed in a forearm vein for the purpose of obtaining multiple blood samples throughout the treatment day.

Based on the DHEA concentration-time profile from Phase I of the study, the times and dose amounts of DHEA administered during Phase II were individualized to achieve DHEA concentrations between 10 and 20 ng/ml. The majority of subjects received DHEA 50 mg at both 0 h and 6.5 h. Exceptions are noted in Chapter 2, Tables 2.2 and 2.3. Identical doses of Alp 2 mg were administered by mouth to all subjects at the same time (2.5 h) for both visits in Phase II. To determine the concentrations of alprazolam, DHEA, DHEA-S, and cortisol blood samples were obtained at 0 h (prior to DHEA or placebo administration) and at 1, 2, 3, 3.5, 4.5, 5.5, 7, 8.5, 10, 11, 12.5, 16, 20 and 23.5 h after dose administration. Blood samples for determination of steroid and alprazolam concentrations were collected from the indwelling catheter in a forearm vein and placed in appropriately labeled vacuum tubes and centrifuged. Serum was decanted and stored at -80°C.

Table 6A summarizes demographic information for the 36 women (20 young and 16 older) and 33 men (16 young and 14 older) whose data are included in this analysis.

Table 6A. Mean age and Body Mass Index (BMI) for the four groups of participants^a

GROUP (Age/sex)	AGE (yr)	BMI
Young women (n=20)	23.40(3.11) (20 - 30)	23.32 (3.21) (19.31 - 31.64)
Young men (n=16)	23.88 (3.04) (20 - 29)	23.30 (2.84) (17.43 - 28.00)
Older women (n=16)	69.69 (2.37) (66 - 75)	28.40 (4.42) (22.32 - 38.78)
Older men (n=14)	71.07 (3.13) (67 - 78)	27.02 (1.78) (24.39 - 30.34)

^aData are presented as mean, standard deviation, and range

Assays

Alprazolam. For alprazolam and the internal standard, triazolam, a gas chromatographic-electron capture detection method (GC) was validated and used to determine serum alprazolam concentrations. The assay is described in detail in Chapter 2. Briefly, samples were injected onto a 10 m x 0.32 mm x 0.25 μ m capillary column (DB1701, J & W Scientific) in a Hewlett Packard 6890 gas chromatograph with helium as the carrier gas and argon-methane (95:5) as the make-up gas. Alprazolam and triazolam were detected and quantified using a micro ⁶³Ni electron capture detector (μ ECD). Data were acquired and analyzed using an HP ChemStation.

Steroids. The assays for steroid concentrations were done using ¹²⁵I-radioimmunoassay techniques (Diagnostic Systems Lab Inc.). Serum was assayed for DHEA, DHEA-S, and cortisol concentrations. The detection range and lower limit of detection, respectively, for each assay were: DHEA: 0.2 to 30 ng/ml and 0.009 ng/ml; DHEA-S: 50 to 8000 ng/ml and 17 ng/ml; cortisol: 0.5 to 60 μ g/dl and 0.11 μ g/dl. The coefficient of variation for each was <10% throughout the range of the assay.

Statistical Analysis. The subjects were divided into four age/sex groups: young women, young men, older women and older men. Concentration-time data were plotted for each subject for alprazolam and all steroid concentrations. Significant differences between groups were tested using a repeated measures mixed-model analysis of variance (ANOVA). For the initial analysis, alprazolam, DHEA, DHEA-S and cortisol concentrations were used as the dependent variable. Age/sex, treatment, time, and the age/sex-by-treatment interaction were considered as fixed effects. The interaction term was dropped from the model when it was not significant. Subjects were treated as random effects and the variance/covariance matrix was modeled using compound symmetry.

For alprazolam, the maximum observed concentration (C_{max}) for each subject was identified. Area under the concentration-time curve was calculated for each subject from 0 to 12.5 hours (AUC_{0-12.5}) and from 0 to 24 hours (AUC₀₋₂₄) using the trapezoidal rule (Gibaldi & Perrier, 1982). Significant differences between treatments and among age/sex groups were tested using a one-way ANOVA with AUC_{0-12.5}, AUC₀₋₂₄, and C_{max} as the dependent variable and either treatment or age/sex as the main

effect. To determine pairwise differences in $AUC_{0-12.5}$, AUC_{0-24} , and C_{max} between groups, least squares means was used as the post hoc analysis.

For DHEA, DHEA-S, and cortisol, mean maximum observed and mean concentrations from 0 to 12.5 hours for each age/sex group were calculated for both the PL/Alp and DHEA/Alp treatments. Additionally, the change in steroid concentrations between the two treatments was determined for each subject, at each time point for the same time period. Significant differences between treatments and among age/sex groups for both the mean steroid and change in steroid concentration were tested using a one-way ANOVA with either treatment or age/sex as the main effect. To determine pairwise differences between groups, least squares means was used as the post hoc analysis.

Results were considered statistically significant if the observed p-value was less than or equal to a critical value of 0.05. All plotting was performed using GraphPad Prism version 3.02 for Windows, GraphPad Software; San Diego, California USA; www.graphpad.com (Motulsky, 1999). The ANOVA was performed using SAS Software (Cary, NC, version 8.02) (SAS Institute, 2000).

Results

Alprazolam Concentrations. Individual and mean concentration time profiles for the two treatments PL/Alp and DHEA/Alp are presented in Figures 6.1 (young subjects) and Figure 6.2 (older subjects). None of the four age/sex groups demonstrated a difference in alprazolam concentrations between the two treatments, ($p = 0.52$). The older women had significantly greater concentrations ($p \leq 0.004$) when compared to the other three groups, whose data did not differ from each other ($p \geq 0.14$).

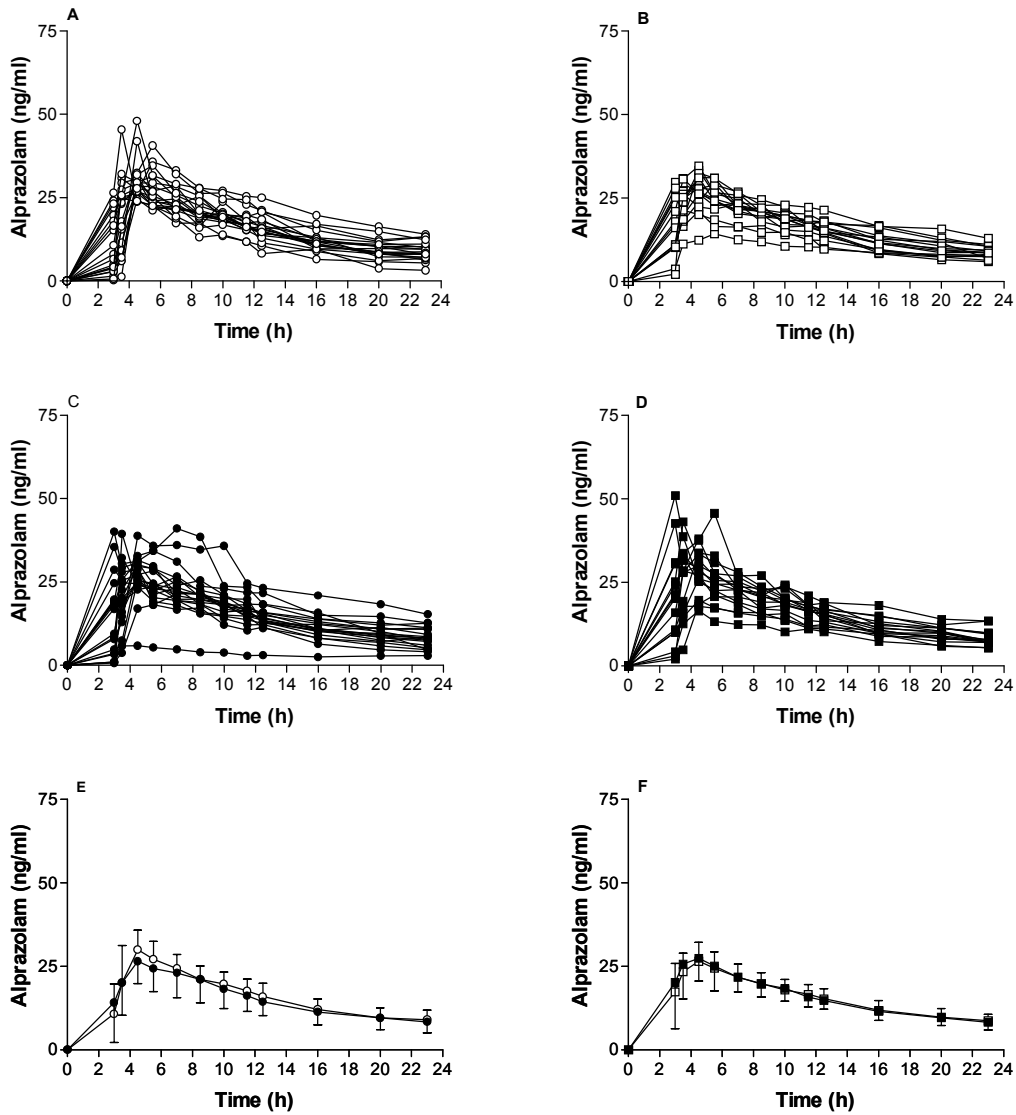


Figure 6.1. Line plots of alprazolam concentration vs. time from the young subjects. Individual alprazolam concentration data from the PL/Alp treatment are in panels A, young women (○), and B, young men (□). Individual alprazolam concentration data from the DHEA/Alp treatment are in panels C, young women (●), and D, young men (■). The mean data with standard deviations are in panels E (young women) and F (young men).

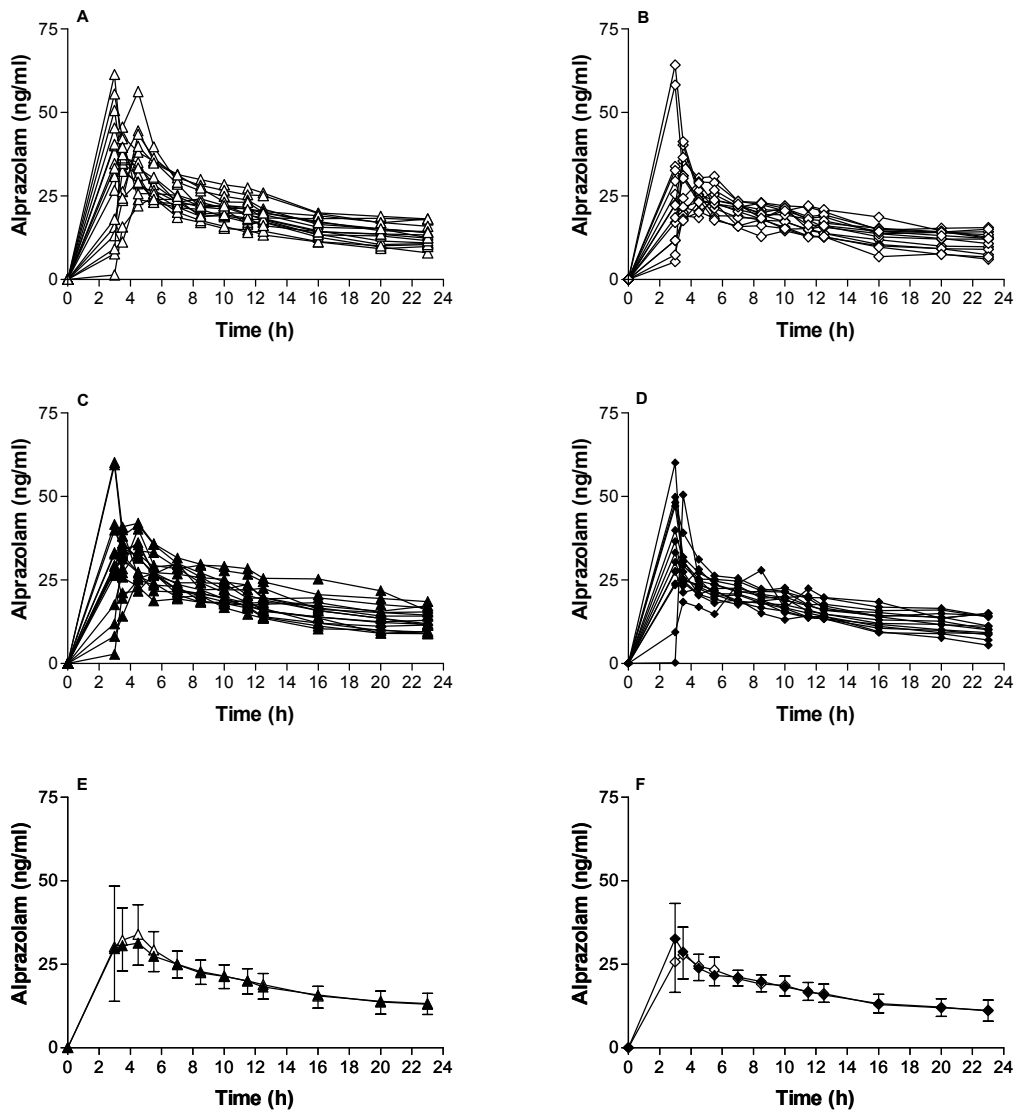


Figure 6.2. Line plots of alprazolam concentration vs. time from the older subjects. Individual alprazolam concentration data from the PL/Alp treatment are in panels A, older women (\triangle), and B, older men (\diamond). Individual alprazolam concentration data from the DHEA/Alp treatment are in panels C, older women (\blacktriangle), and D, older men (\blacklozenge). The mean data with standard deviations are in panels E (older women) and F (older men).

Table 6B contains the observed maximum alprazolam concentration values (Cmax) for both the PL/Alp and DHEA/Alp treatments. Peak alprazolam concentrations in the young women did not differ from those in either the young or older men. However, data from the older men revealed Cmax values significantly greater than those found in the young men and significantly less than those found in the older women. The older women demonstrated significantly higher Cmax values than any of the other age/sex groups.

Table 6B. Mean observed maximum alprazolam concentrations for the two treatments^a.

Group	PL/Alp Alprazolam Cmax	DHEA/Alp Alprazolam Cmax	Between treatment comparison
Young women (n = 20)	32.43 (6.52) ^{AC} (24.89 - 48.05)	29.64 (7.99) ^A (5.89 - 41.06)	p = 0.23
Young men (n = 16)	28.23 (4.99) ^A (14.25 - 34.61)	32.35 (10.26) ^{AB} (16.45 - 51.05)	p = 0.16
Elderly women (n = 16)	41.86 (10.36) ^B (24.70 - 61.43)	37.45 (9.94) ^B (27.02 - 60.24)	p = 0.23
Elderly men (n = 14)	34.42 (12.47) ^C (23.23 - 64.28)	38.30 (10.94) ^B (27.43 - 60.13)	p = 0.39
Among group comparison ^b	p = 0.0005	p = 0.03	

^aData are presented as mean, standard deviation and range. Superscripted uppercase letters indicate differences among the age/sex groups when the model was significant. Those with like letters were not different from each other.

^bp-values were obtained by one-way ANOVA models.

Table 6C includes the area under the alprazolam concentration-time curve (AUC) data for both treatments. Within each age/sex group there were no differences between the PL/Alp treatment and the DHEA/Alp treatment for either AUC_{0-12.5} or AUC₀₋₂₄, ($p \geq 0.13$ for all).

Table 6C. Area under the alprazolam concentration-time curve^a.

Group	Alprazolam ^b AUC _{0-12.5} PL/Alp	Alprazolam ^b AUC ₀₋₂₄ DHEA/Alp	Alprazolam ^b AUC _{0-12.5} DHEA/Alp	Alprazolam ^b AUC ₀₋₂₄ PL/Alp
Young women (n=20)	212.26 (27.12) ^A (158.82 - 275.09)	486.88 (131.63) ^A (105.60 - 755.77)	200.08 (53.49) ^A (42.61 - 299.87)	517.12 (72.92) ^A (375.49 - 680.17)
Young men (n=16)	201.16 (33.09) ^A (111.26 - 239.17)	498.87 (102.10) ^A (289.09 - 631.62)	205.29 (44.80) ^A (115.76 - 270.07)	493.08 (81.09) ^A (284.81 - 605.60)
Elderly women (n=16)	247.56 (40.17) ^B (170.70 - 328.17)	592.43 (98.79) ^B (458.23 - 778.99)	236.97 (40.32) ^B (177.00 - 310.01)	614.25 (96.76) ^B (429.14 - 814.24)
Elderly men (n=14)	199.91 (32.37) ^A (114.34 - 252.51)	514.70 (60.60) ^A (19.35 - 626.60)	206.54 (22.54) ^A (171.77 - 252.20)	500.76 (81.45) ^A (291.89 - 626.80)
Among group Comparison ^c	p = 0.0004	p = 0.02	p = 0.07	p = 0.0003

^aData are presented as mean, standard deviation and range. Superscripted uppercase letters indicate differences among the age/sex groups when the model was significant. Those with like letters were not different from each other.

^bThe area under the time curves were calculated for two different time periods: from 0h to 12.5 h (AUC_{0-12.5}) and from 0 h to 24 h (AUC₀₋₂₄).

^cp-values were obtained by one-way ANOVA models.

Steroid Concentration. The individual and mean concentration-time plots for the steroid concentration data can be found in Figures 6.3 through 6.8. Figures 6.3 and 6.4 contain the DHEA concentration data for the young and older subjects, respectively. As expected, there was a statistically significant increase in DHEA concentration over time after administration of DHEA during the DHEA/Alp treatment for each of the age/sex groups, $p < 0.001$ for all. For the PL/Alp treatment, overall concentrations did not differ between the sexes within each age group ($p \geq 0.32$), but were significantly higher in the young groups when compared to the older groups ($p > 0.0001$). During the DH/Alp treatment there were again no differences between sexes within age groups ($p \geq 0.14$); older men differed from both the young groups, the older women differed only from the young women ($p \leq 0.04$).

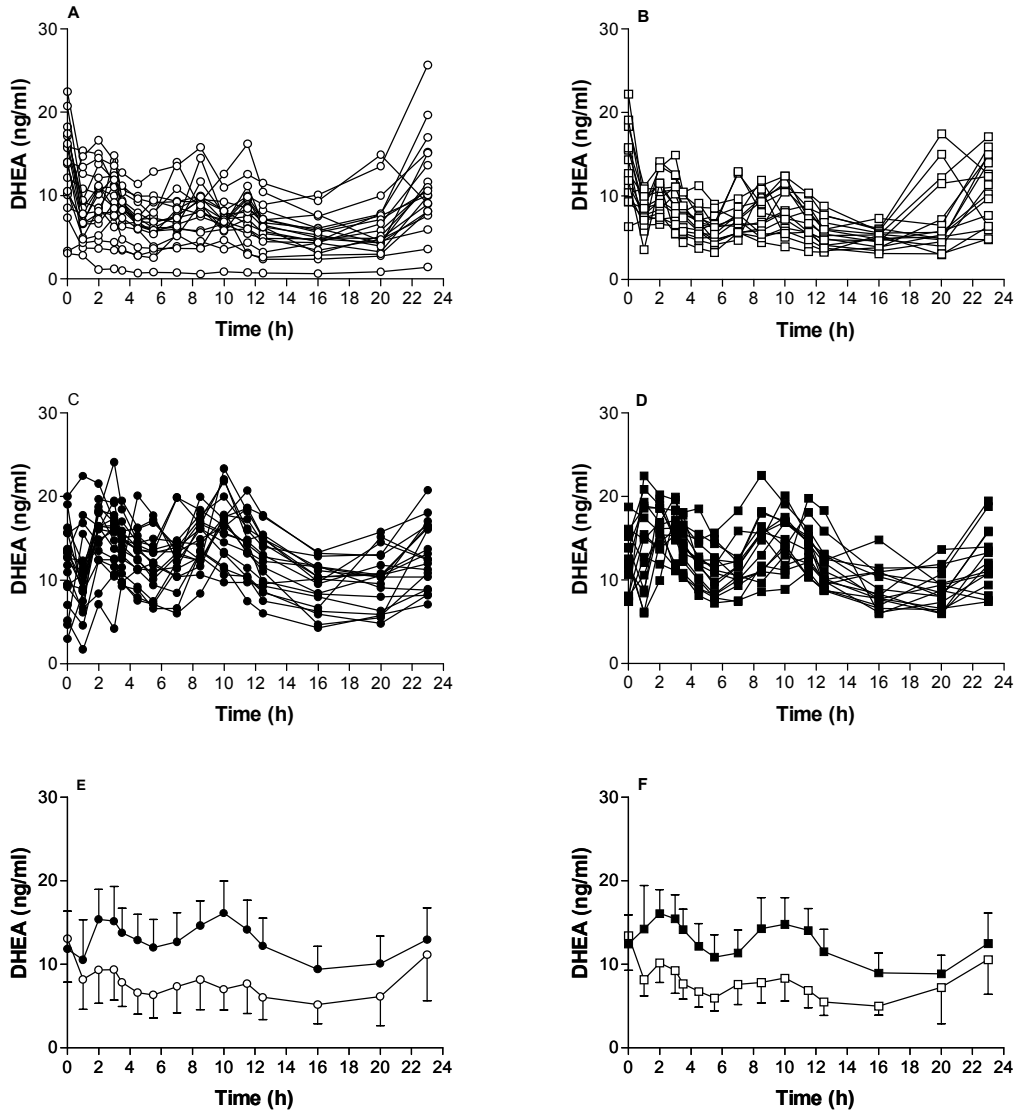


Figure 6.3. Line plots of DHEA concentration vs. time from the young subjects. Individual DHEA concentration data from the PL/Alp treatment are in panels A, young women (○), and B, young men (□). Individual DHEA concentration data from the DHEA/Alp treatment are in panels C, young women (●), and D, young men (■). The mean data with standard deviations are in panels E (young women) and F (young men).

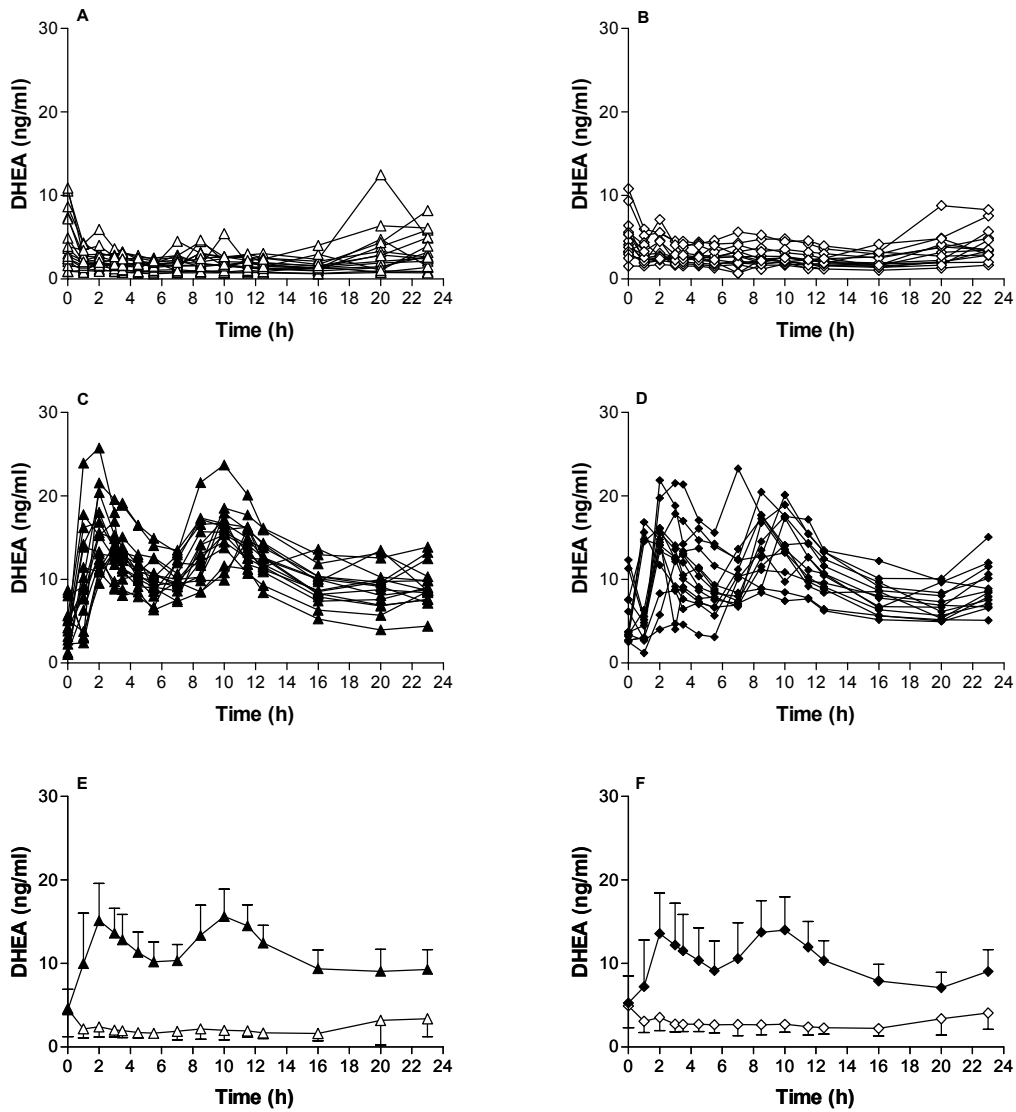


Figure 6.4. Line plots of DHEA concentration vs. time from the older subjects. Individual DHEA concentration data from the PL/Alp treatment are in panels A, older women (\triangle), and B, older men (\diamond). Individual DHEA concentration data from the DHEA/Alp treatment are in panels C, older women (\blacktriangle), and D, older men (\blacklozenge). The mean data with standard deviations are in panels E (older women) and F (older men).

The significant difference between treatments was also evident in the DHEA-S concentrations as presented in Figures 6.5 (young subjects) and 6.6 (older subjects). Similar to DHEA, DHEA-S concentrations were significantly higher during the DH/Alp treatment ($p < 0.0001$). All age/sex groups differed from each other during the PL/Alp treatment ($p < 0.0001$) with the young men having the highest concentrations and older women the lowest. The young women had higher concentrations than the older men. During the DH/Alp treatment, the young men had higher concentrations when

compared with the other three age/sex groups whose data did not differ from one another ($p = 0.002$).

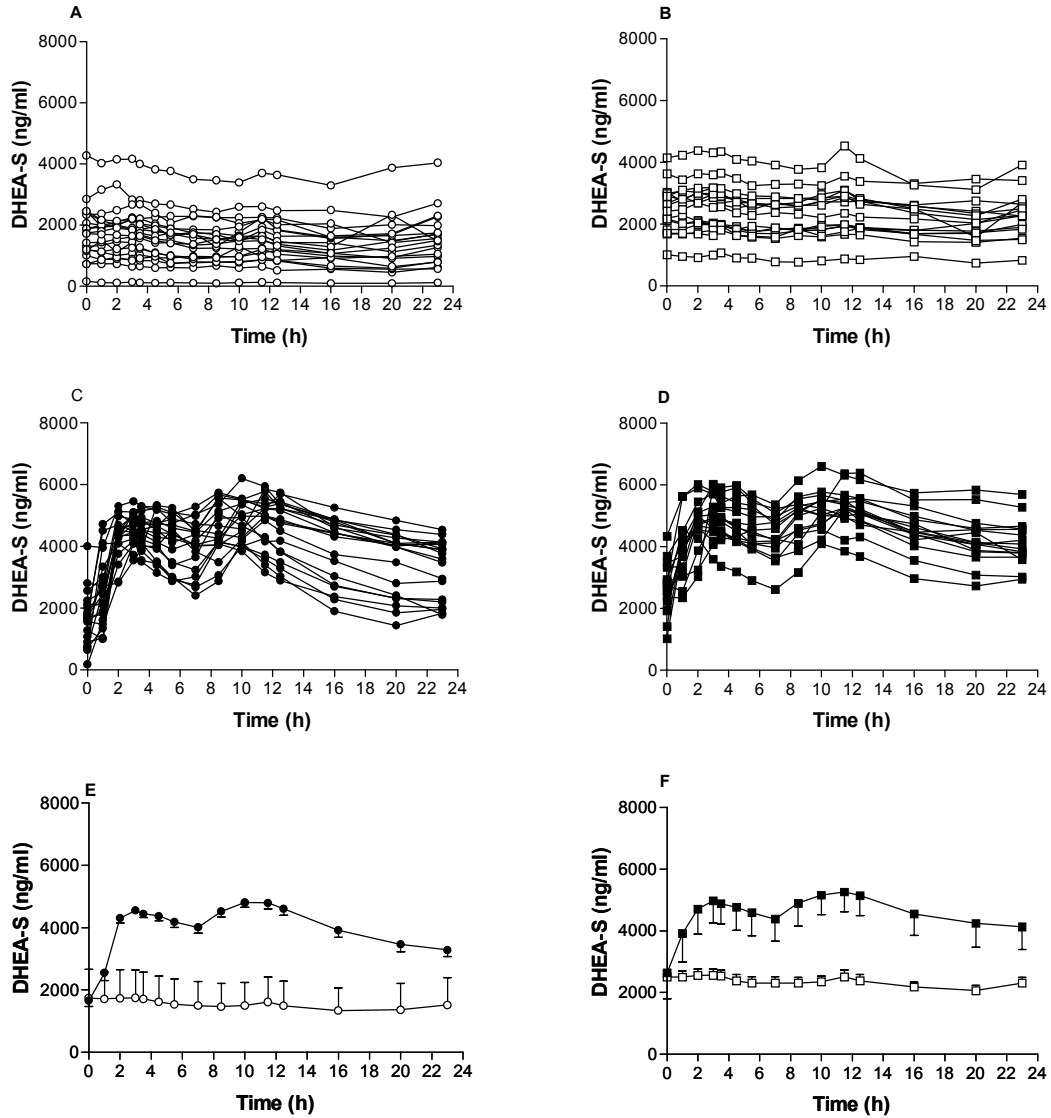


Figure 6.5. Line plots of DHEA-S concentration vs. time from the young subjects. Individual DHEA-S concentration data from the PL/Alp treatment are in panels A, young women (○), and B, young men (□). Individual DHEA-S concentration data from the DHEA/Alp treatment are in panels C, young women (●), and D, young men (■). The mean data with standard deviations are in panels E (young women) and F (young men).

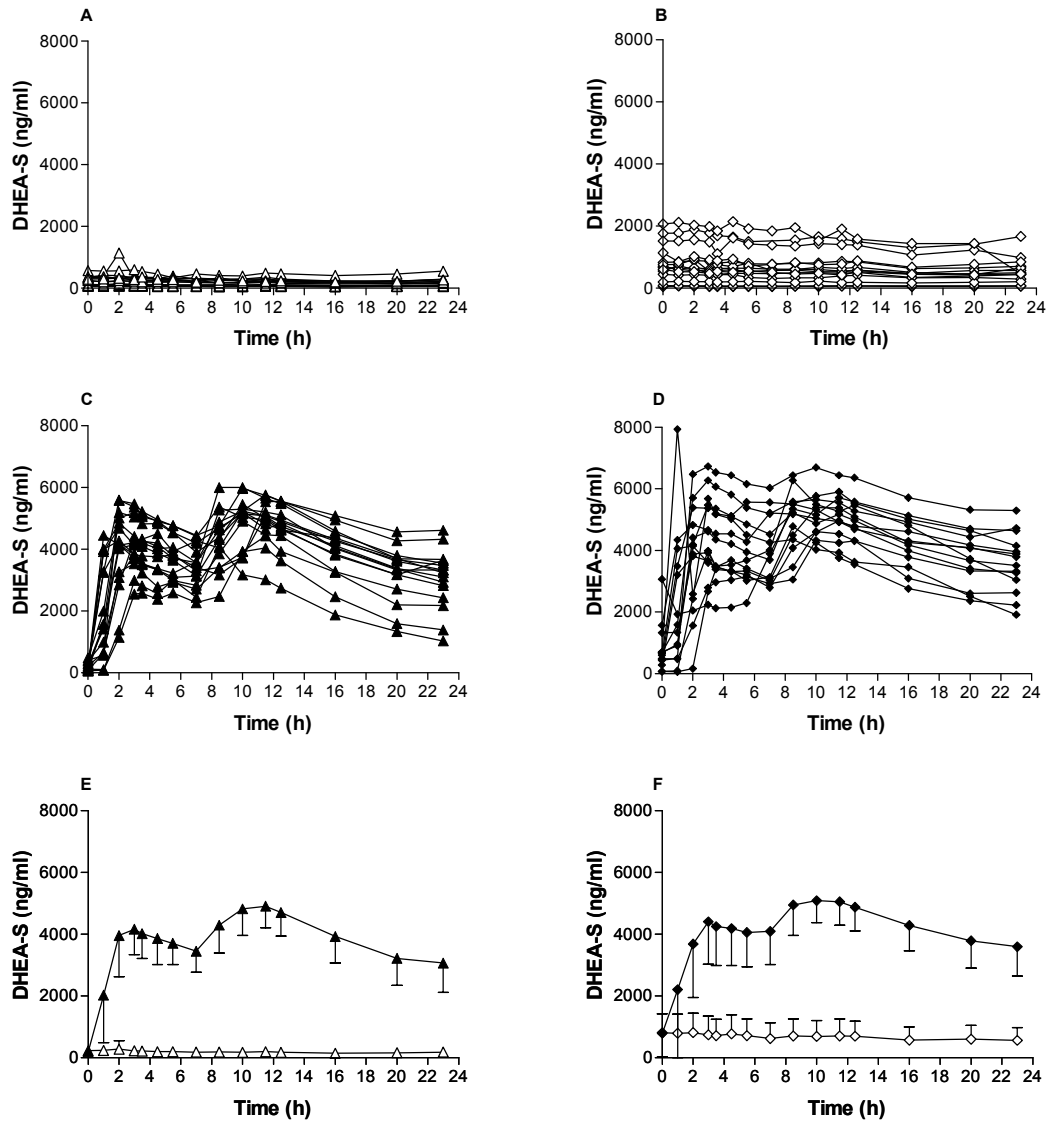


Figure 6.6. Line plots of DHEA-S concentration vs. time from the older subjects. Individual DHEA-S concentration data from the PL/Alp treatment are in panels A, older women (\triangle), and B, older men (\diamond). Individual DHEA concentration data from the DHEA/Alp treatment are in panels C, older women (\blacktriangle), and D, older men (\blacklozenge). The mean data with standard deviations are in panels E (older women) and F (older men).

The cortisol concentration-time data are illustrated in Figure 6.7 for the young subjects and Figure 6.8 for the older subjects. For each of the age/sex groups, the cortisol concentrations did not differ between the PL/Alp treatment and the DHEA/Alp treatment, nor were they different among the age/sex groups $p \geq 0.31$ for all.

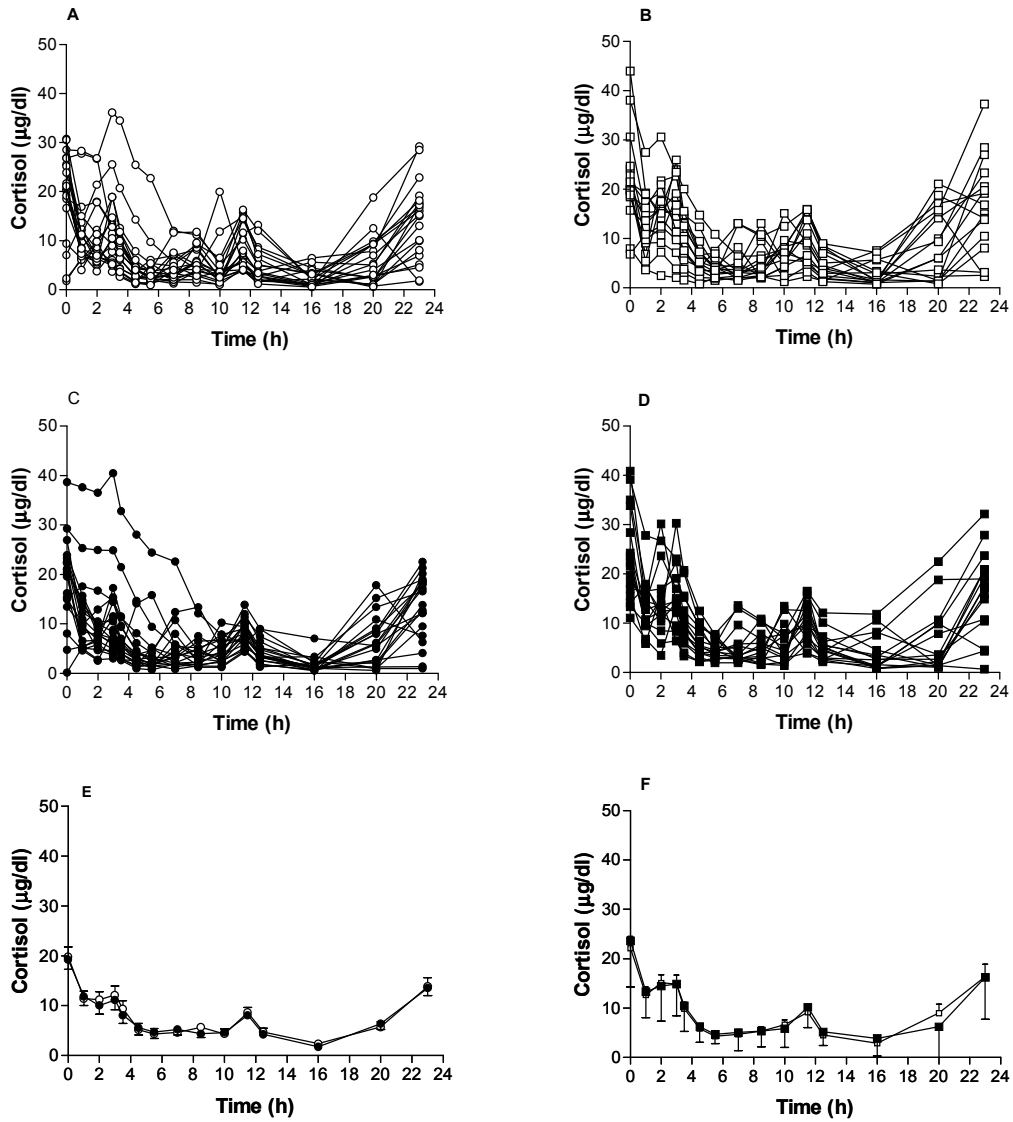


Figure 6.7. Line plots of cortisol concentration vs. time from the young subjects. Individual cortisol concentration data from the PL/Alp treatment are in panels A, young women (○), and B, young men (□). Individual cortisol concentration data from the DHEA/Alp treatment are in panels C, young women (●), and D, young men (■). The mean data with standard deviations are in panels E (young women) and F (young men).

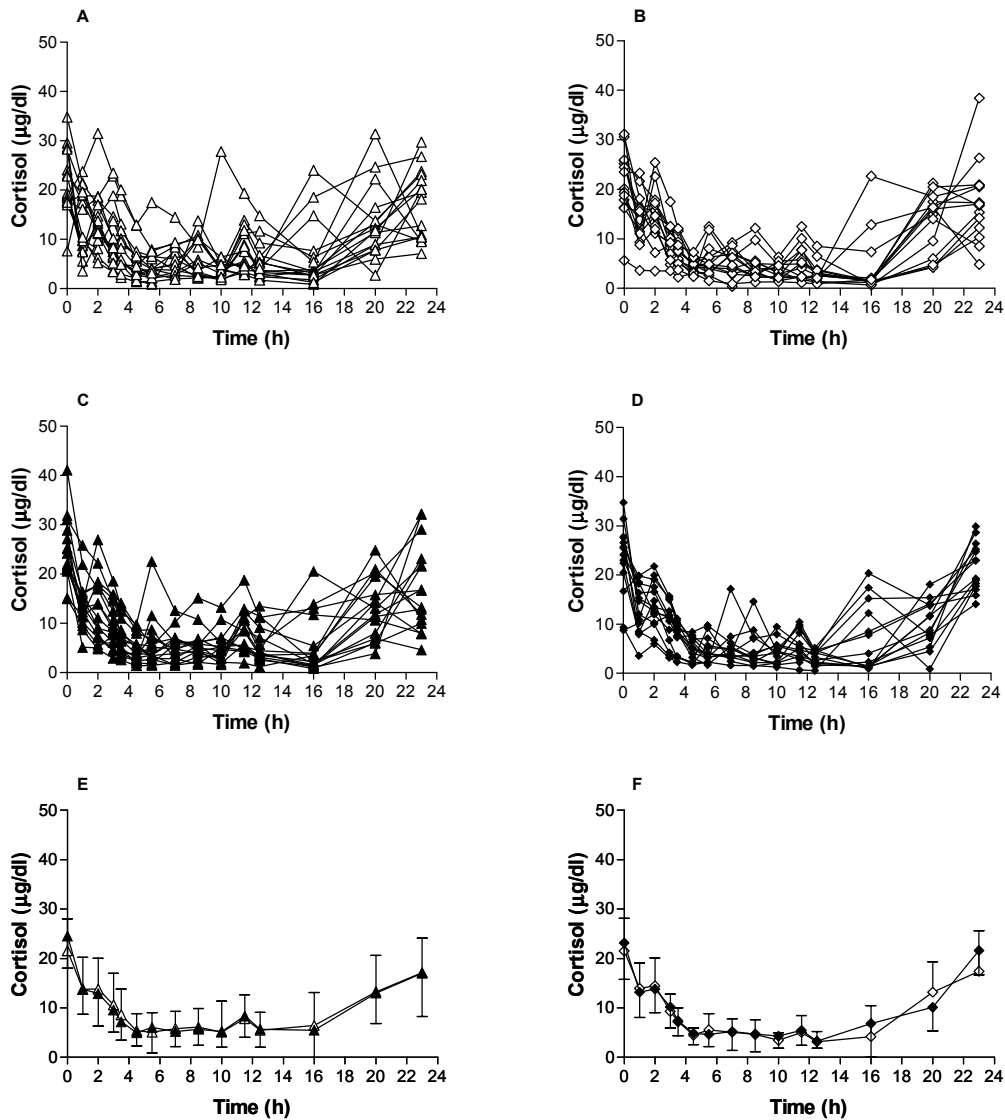


Figure 6.8. Line plots of cortisol concentration vs. time from the older subjects. Individual cortisol concentration data from the PL/Alp treatment are in panels A, older women (\triangle), and B, older men (\diamond). Individual cortisol concentration data from the DHEA/Alp treatment are in panels C, older women (\blacktriangle), and D, older men (\blacklozenge). The mean data with standard deviations are in panels E (older women) and F (older men).

The mean DHEA, DHEA-S, and cortisol concentration data from the two treatments are presented in Table 6D (PL/Alp) and in Table 6E (DHEA/Alp). During the PL/Alp treatment the mean DHEA and DHEA-S concentration data for both the young women and men were significantly higher than either the older women or older men. There were no differences between the sexes in either the young or older group for the DHEA mean data. For mean DHEA-S concentration data, all age/sex groups differed from each other with the young men having the highest concentration and the older women

having the lowest; concentration data from the young women were greater than the older men. There were no significant differences among the age/sex groups for mean cortisol concentrations.

Table 6D. Mean steroid concentration data from the first 12.5 h of the PL/Alp treatment day^a.

Group	DHEA (ng/ml) during PL/Alp	DHEA-S (ng/ml) during PL/Alp	cortisol (µg/dl) during PL/Alp
Young women (n=20)	8.08 (3.81) ^A (0.58 - 22.46)	1618.05 (819.25) ^A (99.42 - 4277.36)	8.47 (7.26) (0.92 - 36.16)
Young men (n=16)	8.12 (3.10) ^A (3.24 - 22.21)	2435.62 (781.69) ^B (769.12 - 4536.96)	9.62 (7.46) (0.80 - 43.97)
Elderly women (n=16)	2.17 (1.48) ^B (0.61 - 10.90)	209.20 (146.12) ^C (53.03 - 1146.66)	9.10 (6.99) (0.90 - 34.80)
Elderly men (n=14)	2.93 (1.43) ^B (0.68 - 10.81)	732.38 (553.23) ^D (50.73 - 2140.81)	8.14 (6.55) (0.39 - 31.15)
Among group comparison ^b	p < 0.0001	p < 0.0001	p = 0.59

^aData are presented as mean, standard deviation and range. Superscripted uppercase letters indicate differences among the age/sex groups when the model was significant. Those with like letters were not different from each other.

^bp-values were obtained by one-way ANOVA models.

Table 6E. Mean steroid concentration data from the first 12.5 h of the DHEA/Alp treatment day^a.

Group	DHEA (ng/ml) during DHEA/Alp	DHEA-S (ng/ml) during DHEA/Alp	cortisol (µg/dl) during DHEA/Alp
Young women (n=20)	13.45 (3.95) ^A (1.72 - 24.12)	4071.69 (1203.23) ^A (180.46 - 6206.49)	8.12 (7.42) (0.19 - 40.46)
Young men (n=16)	13.45 (3.50) ^A (6.02 - 22.54)	4610.93 (999.66) ^B (1022.55 - 6603.58)	9.96 (7.44) (1.39 - 40.88)
Elderly women (n=16)	11.98 (4.35) ^{AB} (1.00 - 25.77)	3679.41 (1551.51) ^A (61.34 - 6004.13)	9.09 (7.00) (1.14 - 41.05)
Elderly men (n=14)	10.83 (4.71) ^B (1.18 - 23.29)	3973.49 (1711.96) ^A (57.82 - 7939.09)	8.34 (6.80) (0.56 - 34.79)
Among group comparison	p < 0.005	p < 0.001	p = 0.41

^aData are presented as mean, standard deviation and range. Superscripted uppercase letters indicate differences among the age/sex groups when the model was significant. Those with like letters were not different from each other.

^bp-values were obtained by one-way ANOVA models.

For the DHEA/Alp data, DHEA concentrations were higher in the young women and young men when compared to that of older men, but not the older women. Within the older group, there was not a sex-associated difference for DHEA. For the mean DHEA-S concentrations, the young men had significantly higher concentrations than any of the other age/sex groups whose data did not differ from each other. There were no significant differences among the age/sex groups for the mean cortisol data.

Tables 6F, 6G and 6H present the mean observed maximum concentrations of DHEA, DHEA-S and cortisol (respectively) during the first 12.5 h for both the PL/Alp and DHEA/Alp treatments.

Table 6F. Mean observed maximum DHEA concentrations (0 – 12.5 h) for the two treatments^a.

Group	PL/Alp Maximum DHEA (ng/ml)	DHEA/Alp Maximum DHEA (ng/ml)	Between treatment comparison ^b
Young women (n=20)	14.06 (4.82) ^A (3.07 - 22.46)	18.23 (3.24) (12.04 - 24.12)	p = 0.003
Young men (n=16)	13.63 (3.95) ^A (7.84 - 22.21)	18.73 (2.34) (14.27 - 22.54)	p < 0.0001
Elderly women (n=16)	4.95 (3.09) ^B (1.15 - 10.90)	17.33 (3.26) (11.90 - 25.77)	p < 0.0001
Elderly men (n=14)	5.12 (2.57) ^B (1.74 - 10.81)	17.41 (2.89) (13.42 - 23.29)	p < 0.0001
Among group comparison ^b	p < 0.0001	p = 0.49	

^aData are presented as mean, standard deviation and range. Superscripted uppercase letters indicate differences among the age/sex groups when the model was significant. Those with like letters were not different from each other.

^bp-values were obtained by one-way ANOVA models.

Table 6G. Mean observed maximum DHEA-S concentrations (0 – 12.5 h) for the two treatments^a.

Group	PL/Alp Maximum DHEA-S (ng/ml)	DHEA/Alp Maximum DHEA-S (ng/ml)	Between treatment comparison ^b
Young women (n=20)	1896.93 (945.39) ^A (153.78 - 4277.36)	5205.10 (595.24) (4160.24 - 6206.49)	p < 0.0001
Young men (n=16)	2672.39 (827.27) ^B (1074.02 - 4536.96)	5487.58 (567.00) (4534.00 - 6603.58)	p < 0.0001
Elderly women (n=16)	305.98 (274.28) ^C (74.70 - 1146.66)	5190.49 (586.83) (4040.95 - 6004.13)	p < 0.0001
Elderly men (n=14)	861.96 (638.75) ^D (62.32 - 2140.81)	5615.82 (926.0) (4333.29 - 7939.09)	p < 0.0001
Among group comparison ^b	p < 0.0001	p = 0.21	

^aData are presented as mean, standard deviation and range. Superscripted uppercase letters indicate differences among the age/sex groups when the model was significant. Those with like letters were not different from each other.

^bp-values were obtained by one-way ANOVA models.

Table 6H. Mean observed maximum cortisol concentrations (0 – 12.5 h) for the two treatments^a.

Group	PL/Alp Maximum CORTISOL (ng/ml)	DHEA/Alp Maximum CORTISOL (ng/ml)	Between treatment comparison ^b
Young women (n=20)	22.34 (6.66) (7.18 - 36.16)	20.75 (6.69) (10.26 - 40.46)	p = 0.45
Young men (n=16)	24.03 (7.87) (12.54 - 43.97)	25.31 (8.48) (13.36 - 40.88)	p = 0.66
Elderly women (n=16)	23.91 (5.51) (16.97 - 34.80)	24.86 (6.29) (14.95 - 41.05)	p = 0.65
Elderly men (n=14)	22.16 (6.53) (5.65 - 31.15)	23.63 (6.80) (9.36 - 34.79)	p = 0.57
Among group comparison ^b	p = 0.78	p = 0.21	

^aData are presented as mean, standard deviation and range. Superscripted uppercase letters indicate differences among the age/sex groups when the model was significant. Those with like letters were not different from each other.

^bp-values were obtained by one-way ANOVA models.

During the PL/Alp treatment, DHEA Cmax for the young group was greater than that in the older groups (p < 0.0001), but did not differ between the sexes within each age group (p ≥ 0.87); DHEA-S Cmax also differed among the age/sex groups during the PL/ALP treatment with the highest in the young men and the lowest in the older women. Cortisol Cmax did not differ among the groups

during the PL/ALP treatments. There were no differences among the age/sex groups in mean observed maximum concentrations during the DH/Alp treatment for DHEA, DHEA-S or cortisol.

The mean change in steroid concentrations between the PL/Alp and the DHEA/Alp treatments can be seen in Table 6I.

Table 6I. Mean change in steroid concentrations between the PL/Alp and DHEA/Alp treatments during the first 12.5 h of data collection^a.

Group	Change in DHEA concentrations (ng/ml)	Change in DHEA-S concentrations (ng/ml)	Change in cortisol concentrations (µg/dl)
Young women (n=20)	5.37 (4.27) ^A (-9.12 - 16.35)	2453.65 (1303.05) ^A (-747.36 - 5386.09)	-0.35 (4.26) (-16.30 - 13.41)
Young men (n=16)	5.33 (3.77) ^A (-10.31 - 14.28)	2175.31 (1005.62) ^A (-294.55 - 4358.39)	0.34 (4.01) (-9.98 - 17.37)
Elderly women (n=16)	9.81 (4.75) ^B (-6.70 - 23.84)	3470.21 (1550.84) ^B (-197.32 - 5946.27)	0.00 (4.90) (-21.78 - 16.97)
Elderly men (n=14)	7.90 (4.93) ^C (-1.59 - 21.13)	3233.65 (1783.71) ^B (-451.30 - 7176.19)	0.20 (3.90) (-15.06 - 16.94)
Among group comparison	p < 0.0001	p < 0.0001	p = 0.68

^aData are presented as mean, standard deviation and range. Superscripted uppercase letters indicate differences among the age/sex groups when the model was significant. Those with like letters were not different from each other.

^bp-values were obtained by one-way ANOVA models.

The young women and men had smaller changes in DHEA concentration when compared to the older groups. Overall, the greatest change was noted in the older women who were significantly higher than the other three age/sex groups, including the older men. The change in DHEA-S did not demonstrate sex-based differences in either the young or older groups, but the older men and women had a significantly greater change than that seen in the young. The change in cortisol concentrations was not different among the age/sex groups.

Discussion

This study describes the concentration-time profiles of alprazolam, DHEA, DHEA-S and cortisol after administration of PL/Alp or DHEA/Alp to healthy young and older adults. These data demonstrate relatively little variability in alprazolam concentrations between the two treatment days

for each of the age/sex groups (the young women, young men, older women and older men). It is interesting to note the greater alprazolam concentrations demonstrated in the older women when compared to the other three groups. Previous studies, though not altogether consistent, suggest that differences in the pharmacokinetics of alprazolam between the young and elderly exist, but mostly in older men (Greenblatt, Divoll, Abernethy, et al. 1983; Kroboth, McAuley, & Smith, 1990; Dehlin, Kullingsjo, Liden, et al. 1991). This is in contrast to the current data that indicate consistently higher $AUC_{0-12.5}$, AUC_{0-24} , and C_{max} only in the older women. Obesity is known to prolong alprazolam half-life (Abernethy, Greenblatt, Divoll, et al. 1984) and although the older women in this study had significantly greater BMIs than both of the young groups, they did not differ from the older men. An age-related change in women but not men may indicate the influence of menopause on drug metabolism. When compared to young women, erythromycin and alfentanil, both substrates for CYP3A4, the enzyme responsible for metabolism of alprazolam, demonstrate decreased clearance in postmenopausal women (Harris, Benet, & Schwartz, 1999) without a corresponding decrease in older men. The calculation of clearance and half-life was not done in this study since estimates of such parameters require that sampling continue for a minimum of 3 to 5 half-lives. Alprazolam's expected half-life is 12 to 15 h and, for these data, the final sample was collected at 21 h after administration of alprazolam.

The age groups chosen for this study are representative of the ages when DHEA production is at its peak (20 to 30 years) or near its nadir (65 to 79 years) (Kroboth, et al., 1999). The age related decrease in both DHEA and DHEA-S concentrations is well known and has been extensively reviewed (Barrou, Charru, & Lidy, 1997; Baulieu, et al., 2000; Baulieu, 1995; Kroboth, et al., 1999). These data confirm that endogenous DHEA and DHEA-S concentrations are greater in the young groups when compared to the older men and women. For DHEA, there were no differences between the sexes within each age group. Although DHEA concentrations have been reported to be higher in women than in men (Sulcová, Hill, Hampl, & Stárka, 1997), not all studies are in agreement (Labrie, et al., 1997; Frye, Kroboth, Stone, et al. 1998). For DHEA-S, the men had greater concentrations than the women, supporting previous data (Orentreich, Brind, Rizer, & Vogelmann, 1984; Labrie, et al., 1997; Frye, et al., 1998). Similarly, the data presented here indicate that the older men's DHEA-S concentrations were higher than in older women, though the order of magnitude differed. We report

older women's DHEA-S concentrations to be 70% less than the older men, in contrast to Labrie, et al, who report a 50% difference between older men and women. In agreement with previous studies (Orentreich, Brind, Rizer, & Vogelman, 1984; Carlström, et al., 1988), the young women had DHEA-S concentrations approximately 35% less than the young men.

Reports of the cortisol response to DHEA administration are not conclusive. Cortisol concentrations have been reported to remain unchanged or to decrease after both single and repeated doses (Wolf, Köster, Kirschbaum, et al. 1997; Labrie, Bélanger, Cusan, et al. 1997). Previous data from our lab demonstrated significantly decreased cortisol concentrations after repeated administration of DHEA, and a trend toward a decrease after a single administration of DHEA (Kroboth, Amico, Stone, et al. 2003). The data presented here indicate no differences in cortisol concentrations between treatments, or among the four age/sex groups. This is in agreement with Labrie et al. who reported no change in cortisol concentrations after single and multiple percutaneous administration of DHEA to older men and women. Although the cortisol response to stress may be altered in the elderly (Giordano, DiVito, Lanfranco, et al. 2001; Bergendahl, Iranmanesh, Mulligan, et al. 2000), studies agree that basal cortisol concentrations are similar between healthy young and older adults (Kudielka, Schmidt-Reinwald, Hellhammer, et al. 2000; Lupien, Lecours, Schwartz, et al. 1995).

In order to test the hypothesis that DHEA concentration would impact recovery from GABA-agonist challenge in young and older men and women, it was important to reproduce, in the elderly, the DHEA concentrations observed in the young. Collectively, these data indicate that two oral doses (separated by 6 h) of DHEA 50 mg duplicate DHEA and DHEA-S concentrations as seen in the young, maintain the concentrations over a 24 h period after, and do not alter cortisol concentrations. Additionally, alprazolam (2 mg, oral) administered to young and older men and women on two separate occasions separated by one week results in reproducible concentration-time profiles.

CHAPTER SEVEN

THE EFFECT OF DHEA ADMINISTRATION ON RECOVERY FROM GABA-AGONIST CHALLENGE

Introduction

In vitro animal studies have demonstrated that both dehydroepiandrosterone (DHEA) and its sulfated metabolite, DHEA-S are active at the gamma-amino butyric acid receptor complex (GABA-RC) (Demirgören, Majewska, Spivak, & London, 1991; Majewska, 1992; Sousa & Ticku, 1997), though information from human studies regarding neuroactive steroids is limited (McAuley, et al., 1995; Friess, et al., 1995). The elderly have concentrations of DHEA and DHEA-S that are less than that in the young (Orentreich, et al., 1992; Orentreich, Brind, Rizer, & Vogelman, 1984; Pavlov, et al., 1986; Baulieu, et al., 2000). It is known that the elderly are more sensitive to the CNS effects of GABA agonists such as benzodiazepines and may recover more slowly from such effects (Greenblatt, et al., 1991; Bertz, et al., 1997; Thompson, Moran, & Nies, 1983). Previous research indicates that the concentration of DHEA may be related to the rate of recovery from the GABA-agonist effects of such drugs (Kroboth, Salek, Stone, et al. 1999).

Based on these data, we proposed the hypothesis that DHEA administered to older adults accelerates recovery from GABA-agonist challenge. We used a classical pharmacological agonist-antagonist paradigm that called for administration of the GABA-agonist in one treatment and the GABA-agonist plus DHEA, the antagonist, in the other. The benzodiazepine, alprazolam, was chosen as the probe GABA-agonist. Alprazolam, an anxiolytic with known GABA agonist activity, has been successfully used in our lab to produce concentration-dependent decreases in saccade velocity and DSST scores (Kroboth, et al., 1998). Because the concentrations of both DHEA and alprazolam can theoretically affect intensity of GABA response, concentrations of both were assessed. The concentration-time data for alprazolam, DHEA, DHEA-S and cortisol is presented in Chapter 6. Saccadic eye movement and psychomotor tasks were used as measures of intensity of response and recovery. The current chapter provides analysis of the response versus time data for the saccadic eye movement tasks, Digit Symbol Substitution Test (DSST), and card sorting (CS) task in order to describe the recovery from alprazolam challenge in the presence and absence of an oral dose of DHEA in four different age/sex groups (young women, young men, older women, and older men).

Methods

Study design and subjects. The data were generated from a randomized, double-blind, placebo-controlled, four-way crossover study that required subjects to visit the General Clinical Research Center on four separate occasions. Analyses in this chapter include only the response data collected during Phase II, i.e., the third and fourth visits. Subjects received placebo plus alprazolam (PL/Alp) on one visit and DHEA plus alprazolam (DHEA/Alp) on the alternate visit. During each of the visits, response to the drug treatments was evaluated using saccadic eye movement measurement (SEM), digit symbol substitution test (DSST) and card sorting (CS). A series of assessments that were conducted at multiple times throughout the treatment day: immediately prior to administration of placebo or DHEA (0 hour) and at 2, 3.5, 4.5, 5.5, 7, 8.5, 10, 11.5 and 12.5 hours thereafter. Samples for the purpose of determining drug and steroid serum concentrations were also collected at these times. The analysis of the concentration time data for alprazolam, DHEA, DHEA-S, and cortisol is reported in Chapter 6. Complete details of the study design and subject inclusion/exclusion criteria are described in Chapter 2.

During screening, SEM tests were administered to all subjects in order to ascertain each individual's ability to perform the test and to assist them in becoming familiar with the tasks that would be required on subsequent testing days. CS tasks and DSST were also administered to subjects during the screening process. To minimize learning effects, subjects were required to practice the CS and DSST to a plateau, i.e., no improvement in score on two consecutive trials, during screening. All subjects were admitted to the GCRC by 7:00 p.m. the evening prior to the study day at which time they again practiced SEMs, CS, and DSST. A final practice for CS and DSST was done in the morning prior to the baseline evaluation on each study day.

Table 7A summarizes demographic information for the 36 women (20 young and 16 older) and 33 men (16 young and 14 older) whose data are included in this analysis.

Table 7A. Mean age for the four groups of participants^a

<u>GROUP (Age/sex)</u>	<u>AGE (yr)</u>
Young women (n=20)	23.40(3.11) (20 - 30)
Young men (n=16)	23.88 (3.04) (20 - 29)

Older women (n=16)	69.69 (2.37) (66 - 75)
Older men (n=14)	71.07 (3.13) (67 - 78)

^aData are presented as mean, standard deviation, and range

Evaluation of saccadic eye movements. The methods for SEM data collection, recording and scoring are detailed in Chapter 2. Briefly, the SEM recordings were obtained using an infrared reflection technique (EyeTrac Model 210, Applied Science Laboratories). The saccade targets were presented on a 17-inch computer screen as a white cross on a black background circumscribed by a white circle. During the SEM testing session, 48 trials (saccade targets) were presented. In each trial, subjects began at center fixation and shifted their gaze to one of four target positions. After a target was presented to the right or left, the target returned to center to begin the next trial. The timing and location of peripheral targets for saccades was unpredictable.

The SEM data were scored using a computer algorithm to identify saccades. Each saccade was visually inspected and measurements on the basis of this algorithm were verified. When multiple saccades were required to reach the target, only the initial, or primary saccade was scored. Scoring of each saccade provided quantification of velocity (VEL), latency (LAT), duration (DUR), and accuracy (ACC). For the purpose of this analysis velocity (degrees/sec) is the maximum or peak velocity achieved during the saccade, latency is the reaction time (msec) between target presentation and initiation of saccade, duration is the time (msec) required to complete the saccade, and accuracy is the percent of target step amplitude gained by the primary saccade.

SEM testing was conducted at ten times throughout the testing day. For each subject at each testing session eye movements were separated according to the target step amplitude (8 degrees and 16 degrees) and combined according to direction (left and right) allowing a maximum number of 24 scored trials per session per target amplitude. The subject-specific mean for saccades to each target amplitude was used in all subsequent analysis. In this chapter, only saccades to the 8-degree target are presented.

Evaluation of DSST and CS. DSST, originally developed as part of the Wechsler Adult Intelligence Scale (Vogel, Barker, Gibbons, et al. 1976), required subjects to draw symbols

corresponding to matching numbers. The score is the number of symbols drawn in 90 seconds. CS required subjects to sort a deck of 52 playing cards by suits as quickly as possible with a maximum of 90 seconds allotted to complete the task; the score was the number of cards/sec. Both CS and DSST are described in more detail in Chapter 2. CS and DSST were collected at the same ten time points as the SEMs.

Statistical Analysis. The subjects were divided into four age/sex groups: young women, young men, older women and older men and these groups were used for all subsequent analysis.

The numbers of subjects unable to perform the SEM tasks were calculated at each time point for the two treatments. A Mantel-Haenszel chi-square was computed to determine whether the number of subjects unable to perform the SEM tasks differed between the two treatments within each age/sex group. The statistical model used in the analysis included all time points from 0 h to 12.5 h.

The percent change in effect from baseline was calculated for the 12.5 h time point for VEL, LAT, DUR, ACC, DSST and CS for each subject for both treatments. Data are presented graphically in a scatter plot with a horizontal line indicating the 10% threshold. Data less than or equal to 10% were considered to be equivalent to baseline evaluations.

Differences between treatments at each time point were determined for the four SEM parameters. Specifically, the value of the SEM parameter during the PL/Alp treatment was subtracted from that of the DHEA/Alp treatment. Age/sex groups means were calculated and plotted on an x-y graph with a horizontal line drawn at zero (the center of the y-axis) indicating no change in value between the two treatments. If the value of the SEM parameter increases as performance improves, as it would with velocity, data above the horizontal line specifies greater improvement in performance during the DHEA/Alp treatment and data below the line indicates impairment. Plots for SEM data that demonstrate a decrease in value with improved performance, e.g., latency, are represented in the opposite direction.

Effect versus time data were plotted for each subject for the four SEM parameters (VEL, LAT, DUR, and ACC), DSST, and CS. In keeping with the hypothesis that DHEA would accelerate the recovery from a GABA-agonist challenge, only data collected during the 7 h to 12.5 h time period was used. This time period begins 4.5 h after alprazolam administration and occurs subsequent to the maximum alprazolam concentrations in most subjects. Also, the greatest number of subjects unable

to complete the SEM tasks due to the effects of alprazolam occurred prior to the 7 h time point, limiting the amount of data available for analysis. Including data only from the 7 h to 12.5 h time period provided data from the greatest number of subjects.

Initial analysis of the recovery time period used a data set that excluded observations from those subjects who could not complete the SEM tasks during a visit. Significant differences between groups were tested using a repeated measures mixed-model analysis of variance (ANOVA). VEL, LAT, DUR, ACC, DSST, and CS were used as the dependent variable. Treatment, time, and the treatment-by-time interaction were considered as fixed effects. Subjects were treated as random effects and the variance/covariance matrix was modeled using compound symmetry. The interaction term was dropped from the model when it was not significant.

A subsequent analysis of recovery data was conducted for the SEM parameters using censored data. Specifically, data missing due to the effects of alprazolam were assigned a minimum (for VEL and ACC) or maximum (for LAT and DUR) value and a censored regression model was executed. Tobit analysis (Long, 1997) was performed using the PROC LIFEREG procedure in SAS (SAS Institute, 2000) with the SEM parameter as the dependent variable and treatment, time and the treatment-by-time interaction as the independent variable. The interaction term was not significant and was subsequently dropped from the model. For VEL and ACC, data were left-censored at the assigned minimum values. For LAT and DUR, data were right-censored at the assigned maximum values.

The mean maximum observed effects for VEL, LAT, DUR, ACC, DSST and CS for each subject for both treatments were identified. Significant differences between treatments and among age/sex groups were tested using a one-way ANOVA with the maximum observed effect as the dependent variable and either treatment or age/sex as the main effect. To determine pair-wise differences in maximum observed effect between groups, least squares means was used as the post hoc analysis.

Results were considered statistically significant if the observed p-value was less than or equal to a critical value of 0.05. All plotting was performed using GraphPad Prism version 3.02 for Windows, GraphPad Software; San Diego, California USA; www.graphpad.com (Motulsky, 1999). The ANOVA and Tobit analyses were performed using SAS Software (Cary, NC, version 8.02) (SAS Institute, 2000).

Results

Table 7B displays the number of subjects in each treatment who were unable to complete the SEM tasks due to the sedating effects of alprazolam. When all time points were included in the statistical model, the number of young subjects able to complete the SEM task did not differ between the two treatments. The number of older women and older men who were able to complete the SEM task during the PL/ALP treatment was greater than the number able to complete the tasks during the DHEA/ALP treatment, ($p \leq 0.0006$ for both).

Table7B. Subjects unable to complete SEM tasks during PL/Alp and DHEA/Alp treatments

Age/Sex Group		TIME (hours)								
		0	3.5	4.5	5.5	7	8.5	10	11.5	12.5
Young Women n = 20	PL/Alp	--	--	--	--	--	--	--	--	--
	DHEA/Alp	--	--	1	--	--	--	--	--	--
Young Men n = 16	PL/Alp	--	1	2	1	--	--	--	--	--
	DHEA/Alp	--	1	1	1	--	--	--	--	--
Older Women n = 16	PL/Alp	--	10	5	3	4	2	1	--	--
	DHEA/Alp	--	9	8	7	7	2	1	1	--
Older Men n = 14	PL/Alp	--	4	2	2	1	--	--	--	--
	DHEA/Alp	--	6	4	3	3	--	--	--	--

(--) indicates all subjects were able to complete the SEM task.

Figures 7.1 and 7.2 contain composite scatter plots of all SEM parameters and DSST and CS scores for the 12.5 h assessment represented as percent change from baseline values. The symbols below the horizontal line identify those values that are less than or equal to baseline values indicating no impairment. The majority of young subjects are no longer impaired at the 12.5 h assessment time whereas the majority of older subjects continue to have values greater than 10% of baseline.

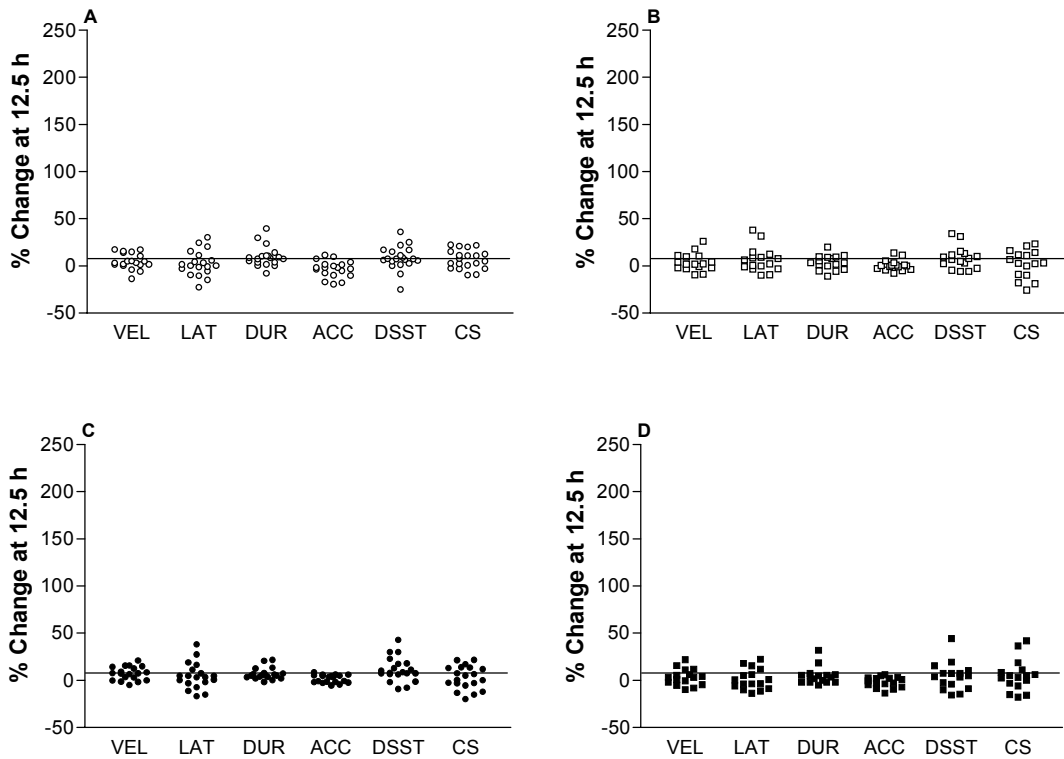


Figure 7.1. Scatter plots of percent change in performance from baseline at the 12.5 h time point for the young women (panels A and B), and young men (panels C and D). The SEM variables, VEL (velocity), LAT (latency), DUR (duration), and ACC (accuracy) are from saccades to the 8 degree target. DSST= digit symbol substitution test and CS = card sorting. The horizontal line indicates the 10% threshold. Values are considered to be equivalent to baseline if they are $\leq 10\%$ of baseline values. Hollow symbols indicate PL/ALP treatment, filled symbols indicate DHEA/ALP treatment.

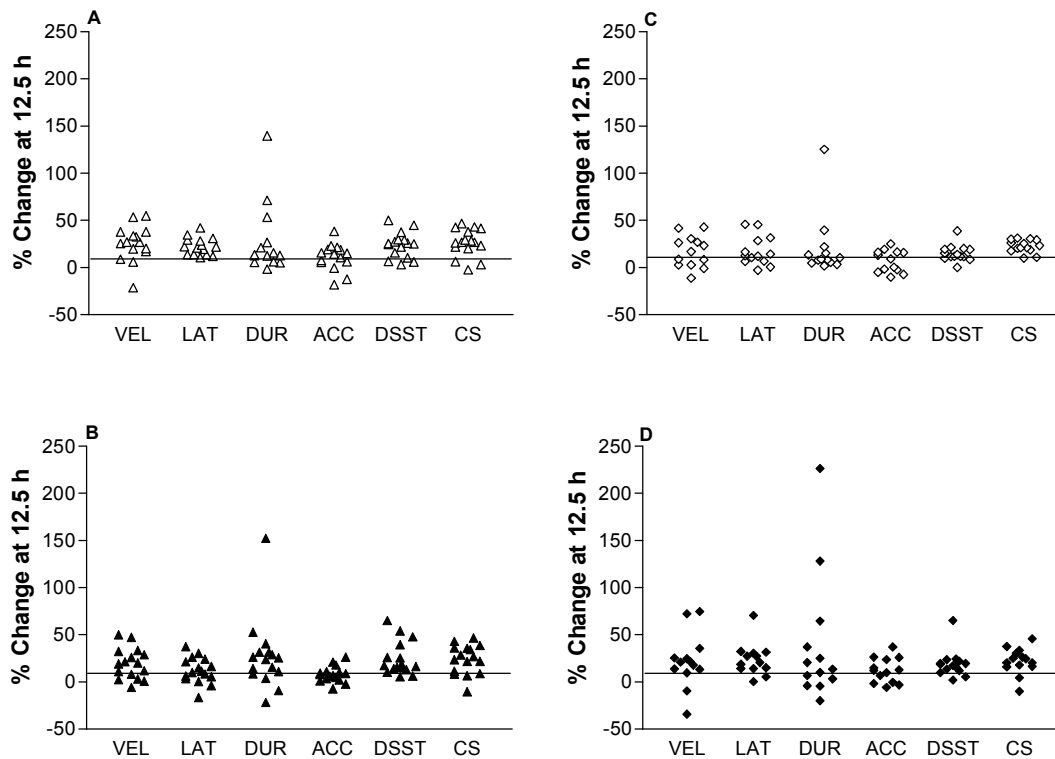


Figure 7.2. Scatter plots of percent change in performance from baseline at the 12.5 h time point for the young women (panels A and B), and young men (panels C and D). The SEM variables, VEL (velocity), LAT (latency), DUR (duration), and ACC (accuracy) are from saccades to the 8 degree target. DSST= digit symbol substitution test and CS = card sorting. The horizontal line indicates the 10% threshold. Values are considered to be equivalent to baseline if they are $\leq 10\%$ of baseline values. Hollow symbols indicate PL/ALP treatment, filled symbols indicate DHEA/ALP treatment.

SEM parameters. Individual and mean velocity (8 degree) versus time profiles for the two treatments PL/Alp and DHEA/Alp are found in Figures 7.3 (young subjects) and Figure 7.4 (older subjects). Results from the ANOVA analysis indicate that during the recovery phase, velocity to the 8 degree saccades in the young women was significantly higher in the DHEA/Alp treatment, ($p = .0002$), indicating that DHEA enhanced recovery. In contrast, velocity for the older men was significantly lower in the DHEA/Alp treatment during recovery, ($p = 0.02$). Data from the older women indicated a trend towards a decrease ($p = 0.06$) similar to the older men. There was no difference in velocity between treatments for the young men ($p = 0.86$). For the Tobit analysis, statistical results were similar.

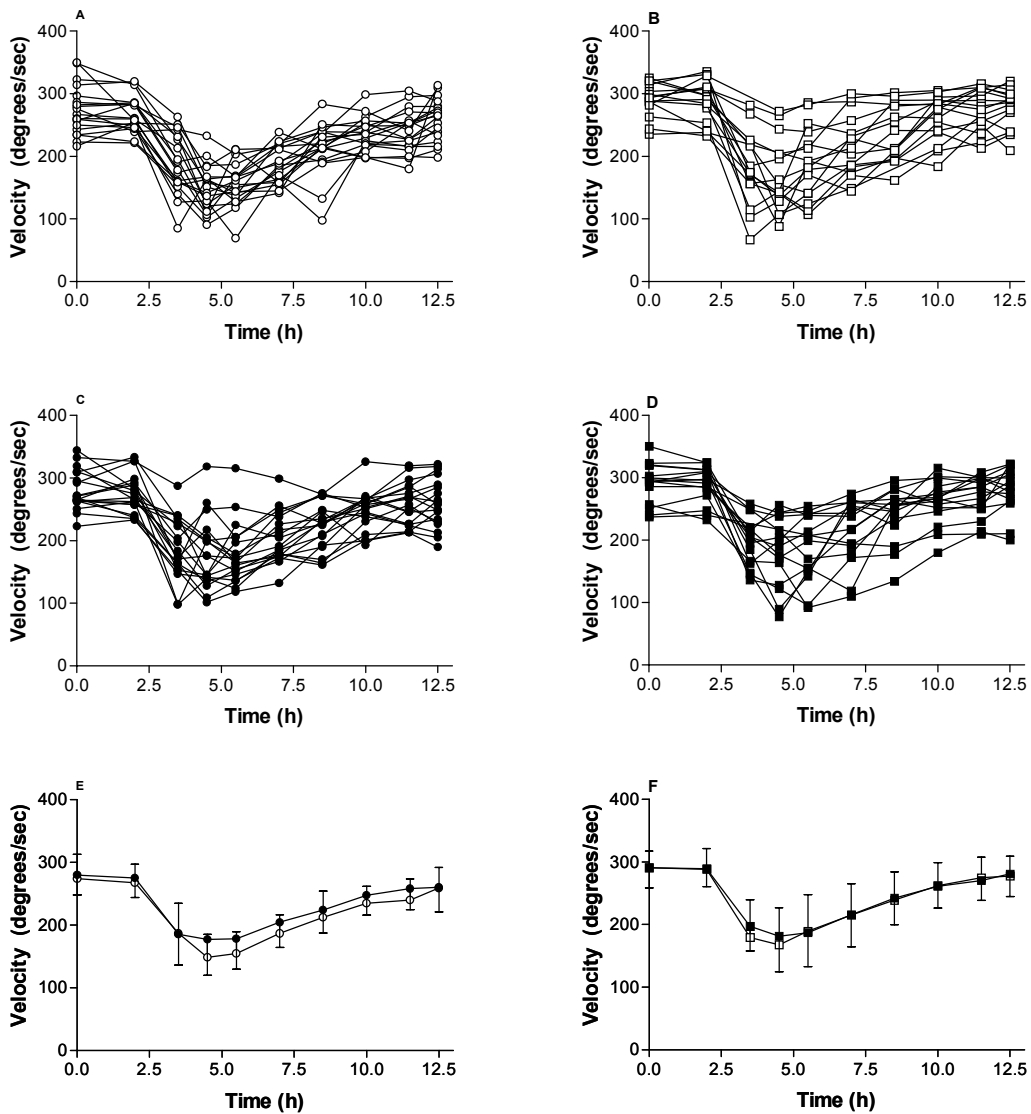


Figure 7.3. Line plots of velocity vs. time for the 8-degree saccades for the young subjects. Individual velocity data from the PL/ALP treatment are in panels A, young women (○), and B, young men (□). Individual velocity data from the DHEA/ALP treatment are in panels C, young women (●), and D, young men (■). The mean data with standard deviations are in panels E (young women) and F (young men).

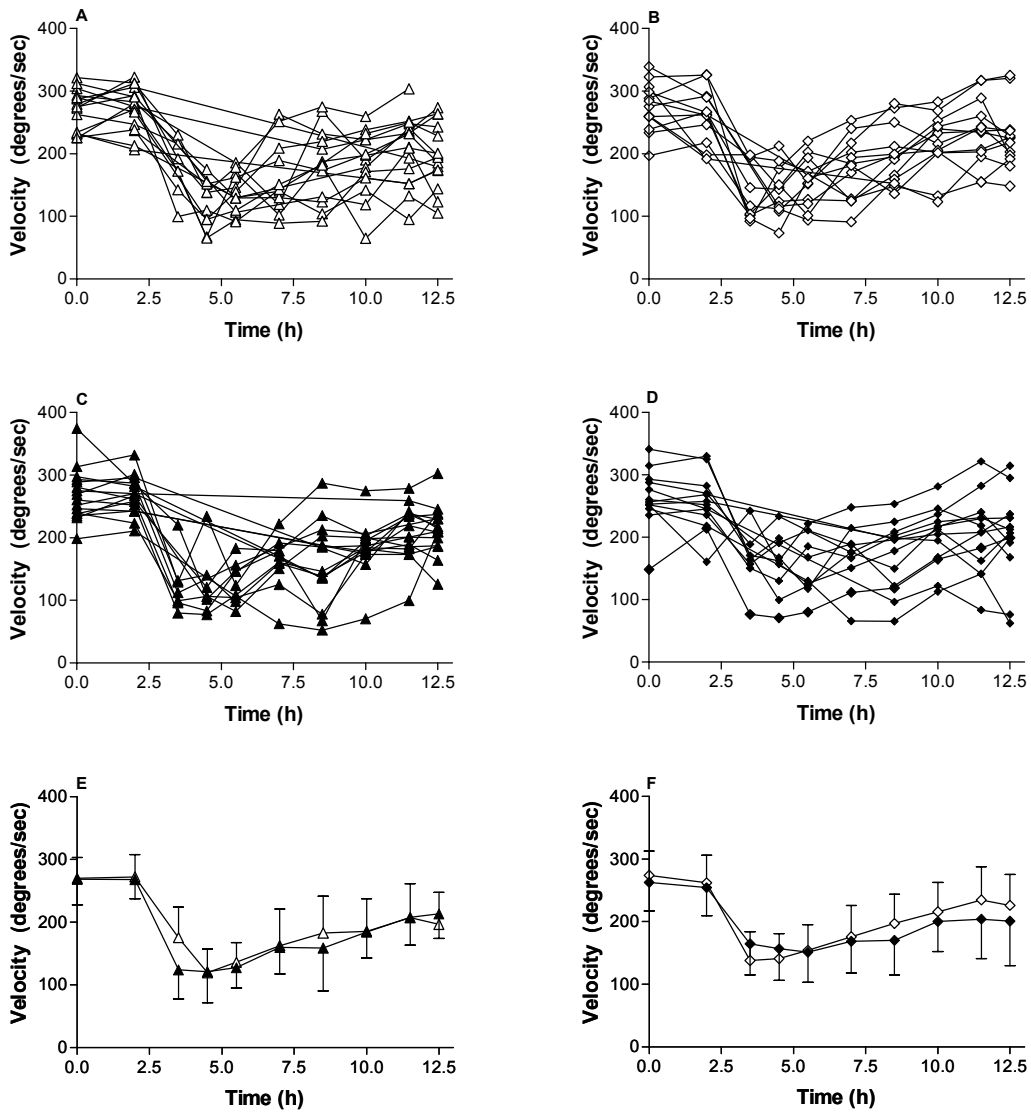


Figure 7.4. Line plots of velocity vs. time for the 8-degree saccades for the older subjects. Individual velocity data from the PL/Alp treatment are in panels A, older women (\triangle), and B, older men (\diamond). Individual velocity data from the DHEA/Alp treatment are in panels C, older women (\blacktriangle), and D, older men (\blacklozenge). The mean data with standard deviations are in panels E (older women) and F (older men).

Figure 7.5 illustrates the change in velocity between the PL/Alp and DHEA/Alp treatments. The velocity during the PL/Alp treatment was subtracted from that of the DHEA/Alp treatment. Since velocity decreases with impairment, points below the horizontal line indicate greater impairment during the DHEA/Alp treatment while points above indicate an improvement. The majority of data points for the young women are above the line representing improved performance in the DHEA/Alp

treatment. Data points for the young men are close to zero demonstrating little change in velocity between the two treatments. Data from the older men and women are below the line signifying poorer performance in the DHEA/Alp treatment.

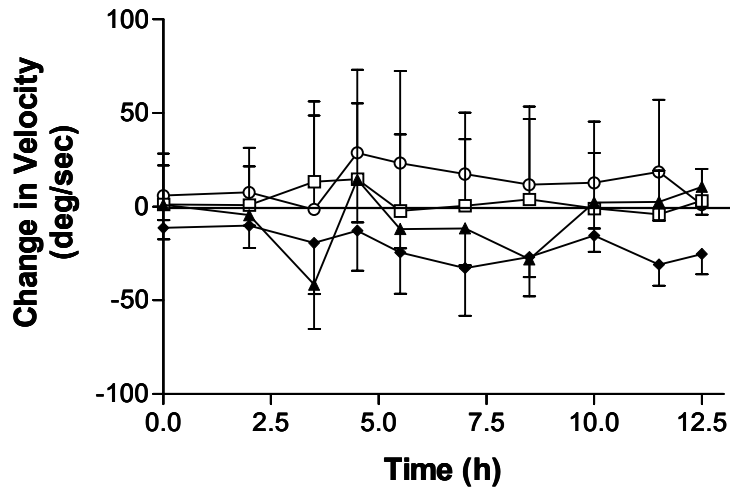


Figure 7.5. Line plots of change in velocity between the two treatments (DHEA/Alp – PL/Alp) for the young women (O), young men (□) older women (▲), older men. Points above the horizontal line represent improvement during the DHEA/Alp treatment. Points below the horizontal line indicate greater impairment during the DHEA/Alp treatment.

The individual and mean latency (8 degree) versus time plots for both treatments can be found in Appendix F. Figure 7.6 is the change in latency between the PL/Alp and DHEA/Alp treatments for the four age/sex groups. Latency increases with impairment, hence, points above the horizontal line indicate greater impairment during the DHEA/Alp treatment while points below indicate an improvement. Latency during the recovery phase did not differ between treatments in any of the age/sex groups, ($p \geq 0.24$). The Tobit analysis was in agreement with these results from the mixed effects ANOVA model.

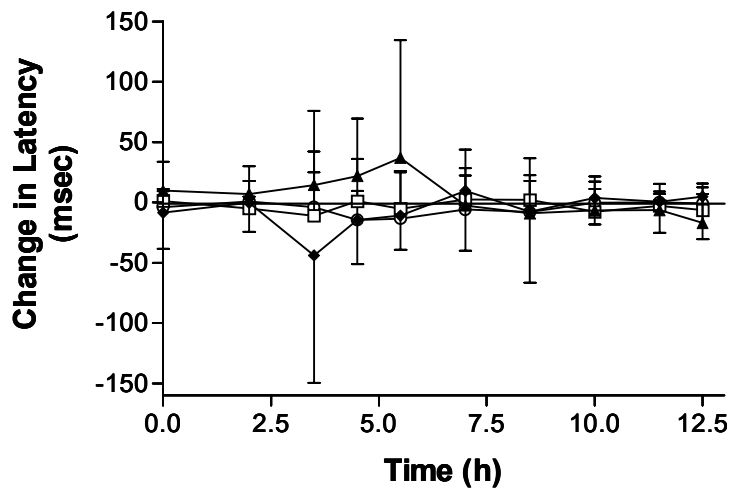


Figure 7.6. Line plots of change in latency between the two treatments (DHEA/Alp – PL/Alp) for young women (O), young men (□), older women (▲), older men. Points above the horizontal line indicate greater impairment during the DHEA/Alp treatment. Points below the horizontal line represent improvement during the DHEA/Alp treatment.

For duration, the individual and mean response versus time plots for both treatments can be found in Appendix F. Figure 7.7 is the change in duration between the PL/Alp and DHEA/Alp treatments. Duration increases with age so that points above the horizontal line indicate greater impairment during the DHEA/Alp treatment while points below indicate an improvement. As expected, results of duration are consistent with those of velocity. In the young women, the duration of saccades to the 8 degree targets during the recovery phase was significantly shorter ($p = 0.007$) for the PL/Alp treatment when compared to the DHEA/Alp treatment. An opposite effect was noted in older women ($p = 0.03$) with the DHEA/Alp treatment producing longer durations. There were no significant differences in duration during this time period for either the young or older men ($p \geq 0.23$). For the Tobit analysis, results were similar except for data from the older women, which no longer demonstrated a difference between the two treatments ($p = 0.38$).

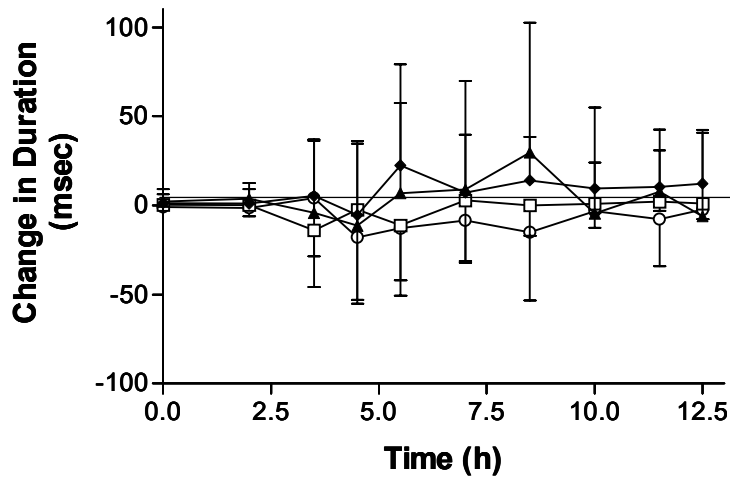


Figure 7.7. Line plots of change in duration between the two treatments (DHEA/Alp – PL/Alp) for young women (O), young men (□) older women (▲), older men. Points above the horizontal line indicate greater impairment during the DHEA/Alp treatment. Points below the horizontal line represent improvement during the DHEA/Alp treatment.

Individual and mean effect versus time data for accuracy of saccades to the 8 degree targets are in Appendix F. Figure 7.8 shows the change in accuracy between the PL/Alp and DHEA/Alp treatments. Since accuracy decreases with impairment, points below the horizontal line indicate greater impairment during the DHEA/Alp treatment while points above indicate an improvement. Results from the ANOVA model indicate that accuracy of saccades did not differ between treatments for any of the groups, though the older men indicated a trend ($p = 0.06$) towards a decrease in accuracy in the DHEA/Alp treatment compared to the PL/Alp treatment. For all other groups, $p \geq 0.16$. The results from the Tobit analysis confirm a treatment difference for the older men, ($p = 0.02$) but not for the other three age/sex groups, ($p \geq 0.36$).

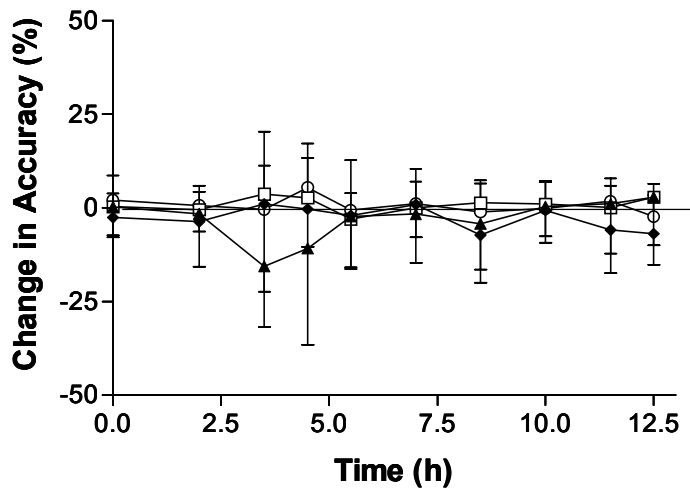


Figure 7.8. Line plots of change in accuracy between the two treatments (DHEA/Alp – PL/Alp) for the young women (O), young men (□) older women (▲), older men. Points above the horizontal line represent improvement during the DHEA/Alp treatment. Points below the horizontal line indicate greater impairment during the DHEA/Alp treatment.

Table 7C contains the observed minimum velocity (due to the effects of alprazolam) for the four age/sex groups during both treatments. The minimum velocity (i.e., the maximum drug effect) was not different between the PL/Alp and DHEA/Alp treatments for any of the groups. Within the PL/Alp treatment, there were no differences among the groups. Minimum velocity during the DHEA/PL treatment differed among the age/sex groups with the older women having the slowest velocity and the young men the highest velocity. Minimum velocity did not differ between the older men and young women.

Table 7C. Mean maximum effect for velocity (degrees/sec) from 0 h to 12.5 h to the 8 degree saccades for the two treatments^a.

Group	PL/ALP Minimum Velocity	DHEA/ALP Minimum Velocity	Between treatment p value ^b
Young women (n = 20)	133.79 (36.60) (69.15 - 203.00)	152.00 (41.54) ^{AB} (97.99 - 274.23)	0.16
Young men (n = 16)	154.59 (63.18) (66.99 - 272.25)	164.03 (54.83) ^B (77.18 - 243.88)	0.65
Elderly women (n = 16)	120.16 (40.75) (64.83 - 207.10)	118.04 (49.83) ^C (52.21 - 245.99)	0.89
Elderly men (n = 14)	117.70 (27.60) (73.12 - 171.83)	125.62 (40.46) ^{AC} (62.61 - 191.56)	0.56
Among group comparison ^b	0.09	0.02	

^aData are presented as mean, standard deviation and range. Superscripted uppercase letters indicate differences among the age/sex groups when the model was significant. Those with like letters were not different from each other.

^bp-values were obtained by one-way ANOVA models.

Table 7D contains the data for maximum latency values for the PL/Alp and DHEA/Alp treatments. The maximum latency (i.e., the maximum drug effect) was not different between the PL/Alp and DHEA/Alp treatments for any of the groups. Within the PL/Alp treatment, the older men and women demonstrated significantly longer latencies when compared to the young. For the DHEA/PL treatment, maximum latency in the older women differed significantly from both of the young groups, but not from the older men. The older men did not differ from either the young women or the young men.

Table 7D. Mean maximum effect for latency (msec) to the 8 degree saccades from 0 h to 12.5 h for the two treatments^a.

Group	PL/ALP Maximum Latency	DHEA/ALP Maximum Latency	Between treatment comparison ^b
Young women (n = 20)	230.68 (39.20) ^A (177 - 322)	220.20 (31.57) ^A (187 - 306)	p = 0.36
Young men (n = 16)	207.50 (53.61) ^A (140 - 350)	205.88 (44.90) ^A (144 - 289)	p = 0.92
Elderly women (n = 16)	286.53 (98.26) ^B (221 - 646)	298.38 (113.78) ^B (178 - 660)	p = 0.75
Elderly men (n = 14)	291.07 (122.81) ^B (168 - 553)	259.85 (86.45) ^{AB} (158 - 490)	p = 0.46
Among group comparison ^b	p = 0.008	p = 0.003	

^aData are presented as mean, standard deviation and range. Superscripted uppercase letters indicate differences among the age/sex groups when the model was significant. Those with like letters were not different from each other.

^bp-values were obtained by one-way ANOVA models.

The maximum duration data from both treatments for the four age/sex groups are in Table 7E. The maximum duration of saccades to the 8 degree targets did not differ between treatments for any of the age/sex groups. Within the PL/Alp treatment duration among the young and older men and women were similar. This was also true for the duration data during the DHEA/ALP treatment.

Table 7E. Mean maximum effect for duration (msec) of the 8 degree saccades from 0 h to 12.5 h for the two treatments^a.

Group	PL/ALP Maximum Duration	DHEA/ALP Maximum Duration	Between treatment comparison ^b
Young women (n = 20)	132.05 (39.92) (77 - 223)	112.65 (34.57) (56 - 191)	p =0.11
Young men (n = 16)	119.13 (47.40) (58 - 191)	117.06 (61.16) (58 - 233)	p =0.91
Elderly women (n = 16)	141.81 (51.89) (69 - 263)	140.56 (61.07) (79 - 284)	p =0.95
Elderly men (n = 14)	118.85 (43.33) (59 - 193)	118.38 (65.60) (62 - 284)	p =0.98
Among group comparison ^b	p = 0.44	p = 0.47	

^aData are presented as mean, standard deviation and range. Superscripted uppercase letters indicate differences among the age/sex groups when the model was significant. Those with like letters were not different from each other.

^bp-values were obtained by one-way ANOVA models.

Data describing the maximum impairment in accuracy from both treatments for the four age/sex groups are in Table 7F. The minimum accuracy of saccades did not differ between treatments for any of the age/sex groups. Within the PL/Alp treatment, the elderly men demonstrated significantly less accuracy when compared to the young men and women, but not the older women, who were not different from either of the young groups. During the DHEA/Alp treatment, saccades in the young were more accurate than those in the elderly. There were no sex-based differences demonstrated within the age groups.

Table 7F. Mean maximum effect for accuracy (%) to the 8 degree saccades from 0 h to 12.5 h for the two treatments^a.

Group	PL/ALP Minimum Accuracy	DHEA/ALP Minimum Accuracy	Between treatment comparison ^b
Young women (n = 20)	0.74 (0.11) ^A (0.52 - 0.93)	0.77 (0.12) ^A (0.58 - 0.94)	0.32
Young men (n = 16)	0.74 (0.15) ^A (0.43 - 0.98)	0.73 (0.09) ^A (0.47 - 0.86)	0.86
Elderly women (n = 16)	0.66 (0.14) ^{AB} (0.45 - 0.91)	0.63 (0.15) ^B (0.33 - 0.85)	0.56
Elderly men (n = 14)	0.62 (0.13) ^B (0.44 - 0.83)	0.60 (0.11) ^B (0.38 - 0.75)	0.76
Among group comparison ^b	0.03	0.0003	

^aData are presented as mean, standard deviation and range. Superscripted uppercase letters indicate differences among the age/sex groups when the model was significant. Those with like letters were not different from each other.

^bp-values were obtained by one-way ANOVA models.

DSST and CS. Individual response versus time data for the DSST and CS tests are contained in Appendix F. Mean data are presented in Figures 7.9 (DSST) and 7.10 (CS). When compared to the PL/Alp treatment during the recovery phase, DSST scores were significantly higher for the DHEA/Alp treatment in young women ($p = 0.05$). The difference in DSST scores between treatments was not significant in any of the other age/sex groups ($p \geq 0.13$). For CS, there were no differences between the PL/Alp and the DHEA/Alp treatments for any of the age/sex groups.

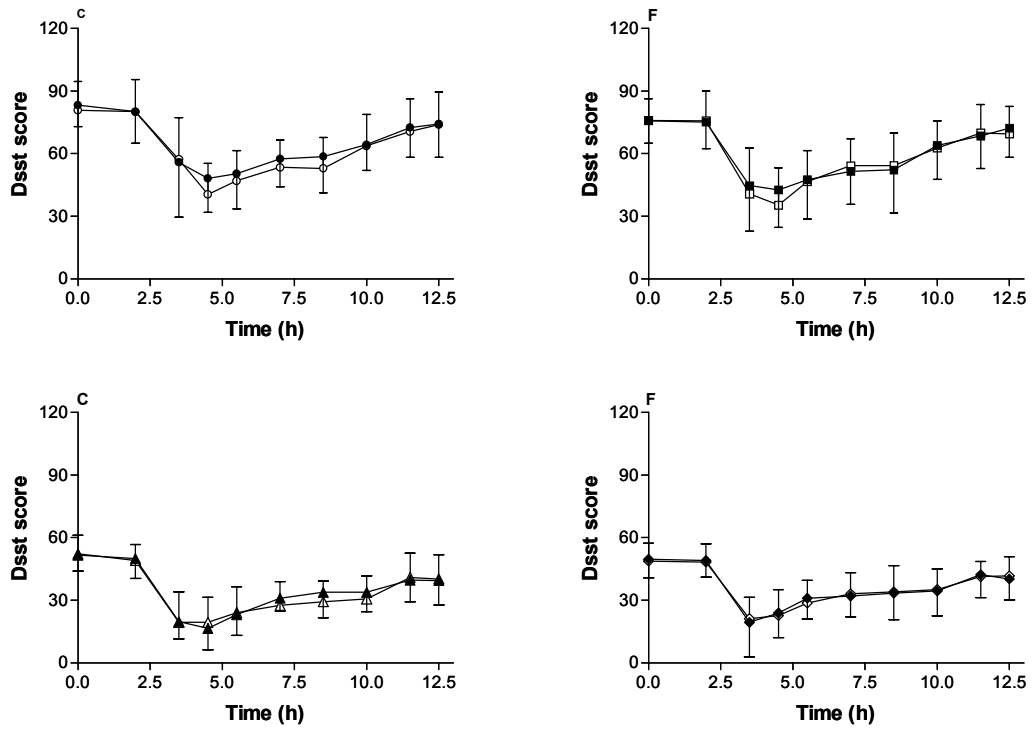


Figure 7.9. Line plots of mean DSST score vs. time for the young women (panel A), young men (panel B), older women (panel C) and older men (panel D). Empty symbols denote data from the PL/Alp treatment, filled symbols denote data from the DHEA/Alp treatment.

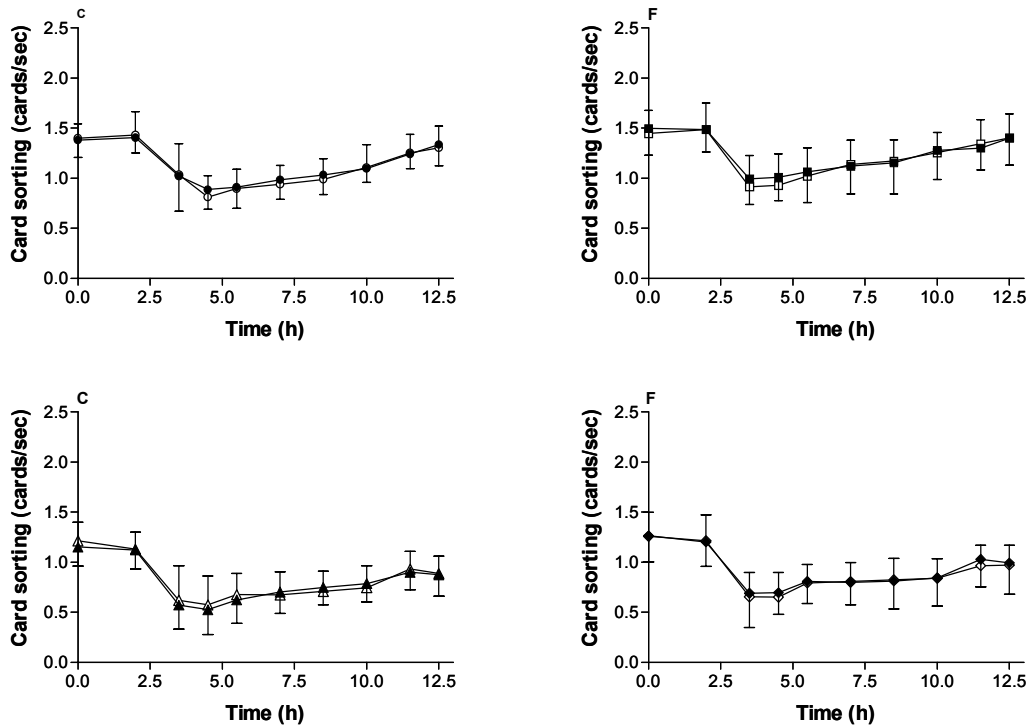


Figure 7.10. Line plots of mean CS score vs. time for the young women (panel A), young men (panel B), older women (panel C) and older men (panel D). Empty symbols denote data from the PL/Alp treatment, filled symbols denote data from the DHEA/Alp treatment.

Table 7G includes the mean minimum (maximum drug effect) DSST scores for the four age/sex groups for both treatments. Minimum DSST scores were different between the treatments in the young women, but not in any of the other groups. Analysis of data from both treatments showed differences among the age/sex groups with the older women having the lowest score and the young women the highest. Data from the older men were lower than that of the young men.

Table 7G. Mean maximum effect for DSST score from 0 h to 12.5 h for the two treatments^a.

Group	PL/ALP Minimum DSST	DHEA/ALP Minimum DSST	Between treatment comparison ^b
Young women (n = 20)	34.90 (11.08) ^A (11 - 59)	39.90 (15.84) ^A (7 - 70)	p = 0.0003
Young men (n = 16)	29.75 (17.60) ^B (5 - 67)	31.19 (17.72) ^B (3 - 61)	p = 0.47
Elderly women (n = 16)	12.44 (8.34) ^C (1 - 31)	13.38 (7.86) ^C (4 - 33)	p = 0.30
Elderly men (n = 14)	17.00 (8.96) ^D (3 - 36)	16.50 (11.38) ^C (2 - 42)	p = 0.68
Among group comparison ^b	p < 0.0001	p < 0.0001	

^aData are presented as mean, standard deviation and range. Superscripted uppercase letters indicate differences among the age/sex groups when the model was significant. Those with like letters were not different from each other.

^bp-values were obtained by one-way ANOVA models.

The data in Table 7H include the minimum number of cards per second for all groups during both treatments. The young men sorted significantly fewer cards per second during the PL/Alp treatment than in the DHEA/Alp treatment. There were no differences in CS between treatments for the other groups. During both treatments, the age/sex groups differed from one another. Overall, the older women had the lowest CS scores and the young men has the highest. The older men had lower CS scores than the young women.

Table 7H. Mean maximum effect for Card Sorting (cards/sec) from 0 h to 12.5 h for the two treatments^a.

Group	PL/ALP Minimum CS	DHEA/ALP Minimum CS	Between treatment comparison ^b
Young women (n = 20)	0.76 (0.21) ^A (0.33 - 1.13)	0.79 (0.21) ^A (0.41 - 1.18)	p = 0.14
Young men (n = 16)	0.83 (0.29) ^B (0.30 - 1.33)	0.91 (0.27) ^B (0.50 - 1.27)	p = 0.007
Elderly women (n = 16)	0.40 (0.23) ^C (0.08 - 0.87)	0.42 (0.15) ^C (0.20 - 0.76)	p = 0.41
Elderly men (n = 14)	0.52 (0.20) ^D (0.16 - 0.95)	0.52 (0.23) ^D (0.26 - 0.93)	p = 0.94
Among group comparison ^b	p < 0.0001	p < 0.0001	

^aData are presented as mean, standard deviation and range. Superscripted uppercase letters indicate differences among the age/sex groups when the model was significant. Those with like letters were not different from each other.

^bp-values were obtained by one-way ANOVA models.

Discussion

This study describes the pharmacological response to alprazolam in the presence and absence of orally administered DHEA as measured by SEMs, DSST and CS. To our knowledge, the data presented here are unique in that both men and women in two age groups with disparate endogenous DHEA and DHEA-S concentrations were assessed, allowing for age- and sex-specific analysis. These data demonstrate that DHEA administration enhanced alprazolam-induced impairment in older men and women. Conversely, in the DHEA/ALP treatment, the young women experienced less impairment. In the young men, there was no difference in impairment between the two treatments. Thus, contrary to our hypothesis, DHEA administration did not accelerate recovery from GABA-agonist challenge in the older subjects. In fact, the opposite effect was seen with the older men and women whose saccades showed slower velocities and longer durations during the recovery phase of the DHEA/Alp treatment. A surprising outcome of this report is the number of older subjects who experienced impairment at a level where they were unable to complete the SEM tasks in both treatments. Remarkably, and in direct

contrast to our hypothesis, the number of older subjects unable to perform the SEM tasks during the DHEA/Alp treatment was significantly greater than during the PL/Alp treatment.

There are three possible explanations for the results observed in the older subjects. First, the oral administration of DHEA may have disrupted the body's normal secretory rhythm. Second, DHEA administration resulted in very high concentrations of both DHEA and DHEA-S, allowing for increased concentrations of androstenedione, a precursor of the GABA-agonist, androsterone. And finally, the expected action of DHEA at the superior colliculus may have been confounded by its simultaneous action at the substantia nigra; both structures are crucial to initiation of SEMs. A discussion of these explanations ensues.

In the older men and women, the single oral doses of DHEA in this study achieved the targeted range of 10 to 20 ng/ml over an approximately 12 hour period of time, which differs from the normal physiological rhythm of DHEA secretion. Similar to cortisol, DHEA secretion demonstrates a circadian rhythm with the highest concentrations occurring in the morning hours. Unlike cortisol, this rhythm is age dependent as noted by a decrease in pulse amplitude, though not pulse frequency, with increasing age. The sustained high concentrations achieved after oral doses of DHEA may have altered the normal pulsatile frequency, possibly interrupting a neuroendocrine-based homeostasis.

An alternative explanation for the results found in the older subjects may be related to the concentrations of DHEA and/or DHEA-S in the brain. The design used in this study is based on assumptions that peripheral concentrations of DHEA and DHEA-S parallel those in the brain. This is based on evidence that changes in blood concentrations reflect those changes in CSF (Guazzo, et al., 1996; Lacroix, et al., 1987), and theoretically, the brain. Therefore, if the serum concentrations achieved in these older adults were indeed mirrored in the brain, it can be theorized that such supraphysiologic concentrations were high enough and sustained over a time period long enough to induce a desensitization of the DHEA excitatory response at the GABA-RC.

Previous data from our lab indicated that older men with lower concentrations of DHEA were more sensitive to the psychomotor impairing effects of alprazolam (Kroboth, et al., 1999), leading us to hypothesize that increasing the concentrations of DHEA would create a GABA-antagonist effect. The data presented here contrast with such a hypothesis and suggest the possibility of a u-shaped response curve. This can be explained by the potential metabolism of DHEA to androsterone, a hormone with

GABA-agonist activity (Kroboth, et al., 1999; Majewska, 1992), by way of androstenedione. Relative to endogenous concentrations, the amount of DHEA and DHEA-S available to the metabolic pathway for such a conversion was substantially greater in the older subjects than in the young. DHEA concentrations were increased by approximately 50% in the young subjects, while the older subjects demonstrated an increase of 500%. The changes in DHEA-S concentrations were even more prominent with the older women and men exhibiting increases of approximately 17- and 7-fold, respectively. In contrast, the young women and men demonstrated an approximate 2.5-fold increase in DHEA-S concentrations.

Finally, the greater SEM impairment noted in the older subjects during the DHEA/Alp treatment may be attributed to the complicated, yet well described, inhibitory synaptic connections involving GABA pathways during the mediation of SEMs. Specifically, the superior colliculus is tonically inhibited via a GABA-ergic pathway from the substantia nigra, which is itself inhibited by GABA. A GABA-agonist at the substantia nigra has the same effect as a GABA-antagonist at the superior colliculus; both result in irrepressible saccades and inability to fixate (Hikosaka and Wurtz, 1989). The anticipated GABA-antagonistic effect of DHEA was not specific to a particular brain region and, as such, may have been confounded by its simultaneous actions at multiple brain regions, particularly the substantia nigra and superior colliculus.

These explanations however, do not address those results noted in the young women and men. Specifically, data from the young women demonstrated a decrease in alprazolam-induced impairment during the DHEA/ALP treatment, while data from the young men indicate no difference in impairment between the two treatments. Potentially, the decrease in alprazolam-induced impairment noted in the younger women during the DHEA/Alp treatment, as compared to the PL/Alp treatment, may be attributed to the difference in alprazolam concentrations between the two treatments. Although not statistically significant, the alprazolam concentrations (presented graphically in Chapter Six) in the young women during the DHEA/Alp treatment were lower than during the PL/Alp treatment throughout the study day. These lower concentrations would correspond with less impairment. However, the alprazolam concentration-time profiles for the two treatments in the young men, who showed no change in impairment, were virtually superimposable. It would seem, therefore, that DHEA administration does not alter alprazolam-induced impairment in the young subjects.

Since the current data are not sufficient to determine actual brain concentrations, it must also be speculated that concentrations of DHEA achieved in the brain may have been too low to elicit the GABA-antagonist effect. Though unlikely, inadequate concentrations of DHEA in the brain would suggest that the effects of DHEA at the level of the GABA-RC might be bi-modal, following the same pattern of the neurosteroid, pregnenolone sulfate, which has recently been shown to be anxiolytic at low doses and anxiogenic at high doses (Majewska, 1992). (Le Mellédo & Baker, 2002)

In agreement with previous data (Kroboth, et al., 1998), the present data indicate that SEMs are a more sensitive measure of GABA-agonist effects than global measures such as DSST and CS. After administration of alprazolam, a number of subjects were unable to perform the SEM tasks, yet were still capable of doing the DSST and CS tests. This was true especially in the older men and women, 50% of who were unable to perform the SEM tasks at one hour after administration of alprazolam during both treatment days. Yet, at the same time point, all of the older men and women were capable of completing the CS tests while 85% of them completed the DSST tests. Therefore, whereas testing SEMs is labor-intensive and requires more time and greater expense, it is worth the effort involved.

Although reasons for the variability in response among the age/sex groups presented here are unclear and may be the result of interindividual differences it is interesting to speculate on whether a change in study design may have provided a different outcome. Attaining a DHEA target concentration for a short duration rather than a sustained plateau may have resulted in a different conclusion. Additionally, future explorations may want to target relative change in DHEA concentrations, rather than the achievement of absolute DHEA concentrations as presented here.

CHAPTER EIGHT
FUTURE DIRECTIONS

The primary goal of this dissertation research was to investigate the effect of DHEA administration on recovery from a GABA-agonist challenge in healthy young and older adults. Additionally, secondary goals included evaluations of SEM variability over repeated same-day testing, determining the inter-rater reliability of a software program modified to evaluate SEMs initiated while under the influence of a benzodiazepine, and assessing the influence of age and endogenous concentrations of DHEA and DHEA-S on SEMs.

Results indicate that after administration of an oral dose of DHEA, response to alprazolam was diminished in young women, enhanced in older men and women, and remained unchanged in young men. The study also determined that SEM measurements are stable within a testing day in both young and older men and women, use of the Pharmsac software by trained scorers produce reliable assessments of SEMs, that there are age-related differences in saccade latency and duration, and that DHEA and DHEA-S concentrations predict saccade duration.

Given these results and the design of this four-way crossover study, there are multiple opportunities for further investigation. Future considerations could be given to expanding the evaluation of the effects of DHEA administration on the time-specific SEM parameters. A comparison between the placebo alone and DHEA alone treatments would address the question of whether oral administration of DHEA affect SEMs and whether or not the relationship is altered by age, sex, and/or concentration. Evaluation of the association between endogenous DHEA and SEM parameters reported here were assessed at only one time point. The placebo treatment offers the opportunity to study the 24-hour DHEA diurnal profile in relation to SEMs with age and/or sex as covariates.

The data presented in this dissertation investigated the concentration-time data separately from the effect-time data. A direct comparison of the relationship between alprazolam concentration and effect for the PL/Alp and DHEA/Alp treatments for individual subjects would assess true differences in sensitivity, if any, due to DHEA administration. Drug impairment associated with alprazolam, corrected for DHEA concentration, may further explain the differences noted here. Also, the older subjects in this study experienced greater alprazolam-induced impairment than the young, especially during the eye movement tasks. As a result missing data was generated and proved difficult to handle in the analysis. Since the data was missing as a direct result of drug impairment, it

would be advantageous to develop a model that could take these data into account. Although not reported here, memory and sedation data were also collected during this study. Future analysis would include these parameters.

The sum total of this dissertation research was a statistical analysis of differences among age/sex groups in response to DHEA administration. The data presented here is from an extremely rich data set that has yet to be mined to its full capacity. In order to truly understand the influence of DHEA on GABA-agonist sensitivity, future directions should include studying the data from individuals and choosing optimal sampling times to include in the analysis. Methods to consider would be individual concentration-effect modeling and possibly a population pharmacokinetic/pharmacodynamic approach. Additionally, genetic variation that depends on factors besides age and sex, such as the environment and various inherent determinants, should not be overlooked. Pharmacokinetic studies have already identified allelic variants that influence drug response and drug-metabolizing enzymes. Studying genetic variants may be a reasonable approach to characterizing meaningful biological differences that would explain the variability presented here.

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APPENDIX A

Approval Letter
Protocol
Consent
Flowsheet

TITLE Dehydroepiandrosterone (DHEA) and GABA-Receptor Mediated Responses in Aged Adults

INTRODUCTION AND BACKGROUND

DHEA and DHEA-S. DHEA and DHEA-S have been widely publicized in both the lay press^{1,2} and in the scientific literature³⁻⁵ for their anti-aging effects. Electrophysiological studies have demonstrated that DHEA, a hormone secreted by the adrenal cortex in response to adrenocorticotrophin (ACTH),⁶ has GABA-antagonist effects.⁷ DHEA is metabolized to dehydroepiandrosterone-sulfate (DHEA-S), which also has GABA-antagonist effects.⁷ Despite the importance of the GABA receptor complex (GABA-RC) to the normal functioning of the central nervous system, information from human studies that describe the role of DHEA, DHEA-S, and other neurosteroid modulators of the GABA-RC is limited.^{8,9}

The GABA-RC and the Relevance of DHEA and DHEA-S. GABA, the major inhibitory neurotransmitter in the central nervous system, binds to the GABA-RC, a macromolecular, ligand-gated chloride ion channel complex that has distinct binding domains for GABA, benzodiazepines, barbiturates, and convulsants.¹⁰⁻¹² Naturally occurring agonists of the GABA-RC include tetrahydroxydeoxycorticosterone (THDOC), tetrahydroprogesterone (THP), and androsterone. These steroids enhance binding of GABA and benzodiazepines to their respective sites on the GABA-RC.¹²⁻¹⁶ These neurosteroids modulate synaptic events as well, leading Majewska to propose that neurosteroids may have a vital role in neuronal plasticity.¹² Naturally occurring noncompetitive antagonists of the GABA-RC include DHEA and DHEA-S.^{7,17} Critical to their role as modulators of the GABA-RC, both DHEA-S and pregnenolone sulfate can be desulfated and metabolized to antagonist steroids.

Influence of Age and Gender on DHEA and DHEA-S Concentrations. Unlike ACTH and cortisol in humans, plasma concentrations of DHEA and DHEA-S are age and gender dependent, with concentrations rising during puberty, peaking in the early 20's, and declining from the third decade onward.¹⁸⁻²⁰ Many have suggested that changes in adrenal secretion of DHEA with age may be explained by a decrease in 17,20-desmolase activity in the adrenal cortex.^{21,22}

Carlström et al. evaluated the influence of age and gender on DHEA and DHEA-S concentrations in a study of 590 women and 60 men and reported that women have a higher DHEA:DHEA-S ratio than men at ages 20 to 29, 30 to 39, 40 to 49 and 60 to 69.²³ While both DHEA and DHEA-S correlated negatively with age, the DHEA:DHEA-S ratio was unrelated to age. Women tended to have higher DHEA concentrations and lower DHEA-S concentrations. At age 20 to 29, mean DHEA concentrations for women and men, respectively, were 21.7 and 14.3 nM, while for ages 60 to 69, mean DHEA concentrations were 8.6 (women) and 7.4 (men) nM. DHEA-S concentrations for 20 to 29 year old women and men were 4191 and 6155 nM, respectively and for ages 60 to 69 were 1656 (women) to 2318 (men) nM.

To our knowledge, changes of this magnitude in concentrations of other neurosteroids have not been documented with aging. The decline in DHEA and DHEA-S concentrations with age are well documented; both have GABA-antagonist effects. Unless a proportionate decrease in GABA-agonist neurosteroids occurs, the loss of GABA-antagonist tone with age could cause an imbalance in the positive and negative modulation of the GABA-RC and reduce plasticity.

Human aging and the GABA-RC: Sensitivity to benzodiazepines. Benzodiazepines are the most commonly prescribed class of GABA-agonists, with women taking benzodiazepines more frequently than men.²⁴ In 1993, alprazolam (Xanax®) was the ninth most commonly prescribed drug in the United States.²⁵ There is clear evidence that the elderly respond differently than young adults to similar doses of benzodiazepines.²⁶ Diazepam,²⁷⁻²⁹ triazolam,³⁰ and alprazolam³¹ have been shown to produce more sedation and to impair memory and psychomotor performance to a greater extent in the elderly, who also have higher plasma concentrations than young adults. In addition, the duration of psychomotor impairment is longer in elderly than in the young.³¹

SPECIFIC AIMS

In this study, to evaluate the importance of DHEA as a modulator of GABA_A-receptor complex (GABA-RC) mediated responses, we have three specific aims:

1. To determine whether DHEA administered to elderly adults accelerates recovery from GABA-agonist challenge.
2. To test the effect of acute DHEA administration on neurobehavioral function in young and elderly adults.
3. To determine the effect of age and gender on alprazolam-induced increase in endogenous DHEA concentrations.

METHODS

Study Design. This is a randomized, double-blind, placebo-controlled, 4-way crossover study that will be conducted in parallel in groups of young and elderly men and women. The study is divided into two phases as indicated below: a placebo (PL) and DHEA crossover in Phase I and an alprazolam (AL) and DHEA+AL crossover in Phase II. The unblinded investigational drug pharmacist of the University of Pittsburgh Medical Center will randomize subject numbers to groups that will be balanced by age, gender, and minority status. Subjects who do not complete all four treatments will be replaced with new subjects who will be assigned the same numbers plus 100. Treatment days within a phase are separated by one week; phases will be separated by one or two weeks to allow for DHEA analysis between phases. The times and dose amounts of DHEA in Phase I will be adjusted as data is accrued to maximize the probability of obtaining concentrations between 10 and 20 ng/ml for each study group. Based on the DHEA concentration from Phase I, the dose of DHEA for Phase II will be individualized to achieve DHEA concentrations between 10 and 20 ng/ml. Details of drug administration, blood sampling and psychomotor testing are found in Appendix B.

	Phase I		Phase II	
	<u>Week 1</u>	<u>Week 2</u>	<u>Week 4</u>	<u>Week 5</u>
Group A	PL	DHEA	AL	DHEA+AL
Group B	PL	DHEA	DHEA+AL	AL
Group C	DHEA	PL	DHEA+AL	AL
Group D	DHEA	PL	AL	DHEA+AL

The design preserves blinding because the treatment arms paired in each phase are relatively equivalent in the expected level of sedation. The treatment pairing in the phases is legitimate since the major contrasts are between the two treatments within each phase, which are balanced for order (AL and DHEA+AL; placebo and DHEA).

The times and dose amounts of drug and/or placebo administration are approximate and dependent on concentrations achieved in Phase I. Times and doses are indicated below; treatments include a placebo for DHEA. Both alprazolam and DHEA will be administered by mouth. We have an approved IND (#48,123) for DHEA administration.

<u>Phase I Treatment</u>	<u>8:30 a.m.</u>	<u>11:00 a.m.</u>	<u>3:00 p.m.</u>
Placebo (PL)	Placebo for DHEA	---	Placebo for DHEA
DHEA	DHEA ≤150 mg	---	DHEA ≤150 mg
<u>Phase II Treatment</u>			
Alprazolam (AL)	Placebo for DHEA	Alprazolam 2 mg	Placebo for DHEA
DHEA+AL	DHEA 150 mg*	Alprazolam 2 mg	DHEA 50 mg*

* DHEA dose in Phase II will be determined based on the concentrations observed in Phase I. The maximum DHEA dose will not exceed 400 mg in either Phase.

Population Description. A sufficient number of subjects will be recruited for participation in this study so as to result in a total of 64 subjects who complete this four-way crossover study.

<u>Age Group</u>	<u>Age (years)</u>	<u>Men</u>	<u>Women</u>	<u>Age Group Total</u>
Young	20 to 30	16	16	32
Elderly	65 to 79	16	16	32
			TOTAL	64

Twelve subjects in each group will be Caucasian and four will be minority subjects. The number of minority subjects (25% per group) is greater than the representation in the local community and provides balance for order of treatment in groups A-D.

In the screening process, it is anticipated that some subjects will be identified who do not meet all of the inclusion criteria (e.g., abnormal SCID). For pilot study purposes, these volunteers may be studied in this protocol, but will not be included in the analysis of 64 subjects. Also for pilot purposes, subjects of ages 20 to 79 who do not meet inclusion criteria for healthy volunteers may be specifically recruited to participate in this study (e.g., stable patients with adrenal insufficiency, women taking hormone replacement therapy, patients with diabetes, obsessive compulsive disorder, etc.). For pilot study subjects, age- and gender-matched healthy volunteers will be recruited and evaluated. Up to 24 additional subjects will be evaluated in the pilot studies. The pilot study patients and their matched control volunteers will not be included in the analysis with the 64 healthy volunteers.

Inclusion/Exclusion Criteria A complete list of laboratory screenings and exclusion criteria is found in Appendix A. The subjects will sign an informed consent prior to laboratory screening, medical history, and physical examination. This will be performed free of charge to patients or third party payers. Vital signs and laboratory parameters listed in Appendix A will be evaluated. Subjects will be considered healthy if they have screening labs and vital signs within the normal reference range as defined by the clinical laboratory or judged clinically insignificant by the study investigators. The urine drug screen and blood alcohol concentration collected during screening must be negative. Age, height, weight, and alcohol consumption will be recorded in a demographic record.

Young or elderly women who have taken estrogen or progesterone as contraceptive or hormone replacement therapy during the three months prior to participation in the study will not be eligible to participate in the study of 64 healthy volunteers. Young women must not be pregnant. Subjects should not have received any known enzyme inducing (e.g., barbiturates, rifampin) or enzyme inhibiting agents (e.g., cimetidine, erythromycin) for 30 days prior to the study day. Men and women selected for this study will not have taken any chronic and/or over-the-counter medications for seven days prior to the first study day.

Study Conditions Informed consent procedures and screening for laboratory and psychiatric eligibility for the study occurs within 3 months prior to the first treatment day. Screening for medical eligibility occurs at the General Clinical Research Center (GCRC) of the University Pittsburgh Medical Center within 1 month prior to the first treatment day of Phase I. On the afternoon before each of the four treatment days, subjects will report to the GCRC. Young women will provide urine for pregnancy tests. Subjects will fast from 10 pm (water is allowed) until 7:30 am on the treatment day. At this time, subjects will receive a light breakfast and an intravenous catheter will be placed in a forearm vein for the purpose of obtaining multiple blood samples. In order to provide for subject safety in Phase II, subjects will remain in the study chair from time 2.5 to 8.5 h; after each test session from 8.5 to 12 h, subjects may ambulate with supervision for 15 min. The schedule of events can be found in Appendix B.

Pharmacokinetic Assessment For the purpose of determining the concentrations of alprazolam, and the steroids on each of the four treatment days, blood samples of either 4.5 ml (Phase I) or 7 ml (Phase II) each will be obtained at times indicated in Appendix B. Urine will be obtained in 12 hour intervals from 0 to 12 h and 12 to 23 h in each phase of the study. In addition, 3 ml samples will be obtained a total of 10 times during the entire study for testing lymphocyte function (Dr. Lotze's laboratory). The total volume of blood drawn for each subject including laboratory and alcohol screening will be approximately 395 ml. Each blood sample will be collected from an indwelling catheter in a forearm vein.

Pharmacodynamic Assessment Saccadic eye movements (SEMs), the very brief and rapid movements the eye makes when shifting from one point to another in the visual field, will be used as an assessment of response. Previous studies have demonstrated that changes in the velocity, latency, and accuracy of saccades are useful measures of the time course of effect of benzodiazepines.³²⁻³⁴ Other response assessments include digit symbol substitution (DSST), card sorting (CS), Randt Memory (RMT), Hopkins Verbal Learning (HVL) and Nurse (observer) Rated Sedation (NRSS). At the time of the screening session to determine eligibility for the study (within three months prior to the first treatment), subjects will practice digit symbol substitution and card sorting to a plateau, i.e., no improvement in score on two consecutive trials, in order to minimize learning during this study. At this time subjects will also be familiarized with the saccade tasks. One additional practice session of digit symbol substitution and card sorting will be done prior to the baseline evaluation on each of the four treatment days.

Analytical Technique Blood samples will be collected in appropriately labeled vacutainers and centrifuged. Plasma or serum will be decanted, transferred to appropriately labeled polypropylene tubes and stored at -80°C. Alprazolam concentrations will be analyzed using an established gas chromatography method at the Pharmacodynamic Research Center. Plasma for DHEA, DHEA-S, and cortisol concentrations and serum for progesterone concentrations will be assayed using ¹²⁵I-radioimmunoassay techniques (Diagnostic Systems Lab Inc.).

Data Analysis Most of the responses and corresponding drug concentrations are directly measured at each observation time. Summary measures will be used for Specific Aim #1. For Specific Aim #1 the primary response is the recovery from GABA-agonist challenge; this will be quantified by the slope of the SEM velocity vs. alprazolam concentration in the recovery phase, defined as all observations after the time of peak effect. Each subject and treatment-specific slope will be estimated using linear regression, if appropriate; otherwise non-linear curve fitting will be done, and the appropriate parameters compared. Other summary measures include DHEA area under the plasma concentration-time curve (DHEA-AUC) calculated by the linear trapezoidal rule. Appropriate graphical and numerical descriptives will be used to summarize the data for each subject (by treatment) and for each treatment group. Race-, gender- and age-specific plots include:

- concentration vs. time for DHEA, DHEA-S, and cortisol (four treatments), and alprazolam, (two treatments);
- response vs. time (four treatments) for digit symbol substitution, card sorting, memory, sedation and SEM variables: peak velocity, gain, duration:amplitude ratio and number of fractionated saccades.
- response vs. DHEA concentration (four treatments) and response vs. alprazolam concentration (two treatments) for digit symbol substitution, card sorting, memory, sedation and SEM variables: gain, peak velocity, duration:amplitude ratio and number of fractionated saccades.

Statistical Comparison of Treatments For each of the specific aims, the analysis assesses the influence of age, gender, and race on the corresponding outcome. A subgroup analysis of Caucasian subjects is planned as a check that the statistical adjustments for minority are adequate. For those response measures that follow a normal distribution, the analysis will be within the framework of a mixed-effects linear model.³⁵ When the normality assumption is suspect, a comparable analysis will be done within the Generalized Estimating Equation framework.³⁶ All plots and statistical comparisons will be performed on a Digital Equipment Corporation VAX cluster using SAS³⁷ software. A $p \leq 0.05$ will be considered the critical level of significance.

SIGNIFICANCE

DHEA and DHEA-S have considerable physiologic significance and clinical relevance as indicated in recent workshops sponsored by NIMH, FDA and NIA. Despite the abundance of information addressing DHEA effects on immunity and glucose metabolism, there is a lack of information about neurobehavioral effects. We will assess the role of DHEA as a modulator of GABA-RC responses. Although age and gender appear not to affect the GABA-RC directly, age and gender do influence response to GABA-RC agonists. For example, the elderly, who have greater impairment and slower rate of recovery than the young after benzodiazepine challenge are more prone to falls, a serious consequence of lingering benzodiazepine effects. This study will test the hypothesis whether the lower DHEA concentrations in the elderly explain the slower offset of psychomotor and sedative effects and whether acute administration of DHEA increases the rate of offset effect.

RISK/BENEFIT RATIO

The risks involved include the discomfort and inconvenience of having an I.V. catheter placed and blood samples collected with potential for pain, bruising, bleeding and infection. Potential side effects of alprazolam include drowsiness, headache, dizziness, dry mouth, and hiccoughs. Subjects will most likely experience drowsiness or sedation, expected effects, after alprazolam administration. Subjects will not be discharged from the GCRC until approximately 21 h after alprazolam administration and will be instructed not to drink alcohol or take sedatives the day they are discharged. Long term adverse reactions with DHEA are limited to rare reports. One time administration of DHEA has not produced any side effects. After oral administration of DHEA 1600 mg/day for 28 days, Welle et. al.³⁸ reported that one subject experienced increased lactate dehydrogenase and aspartate aminotransferase levels that returned to normal after discontinuing the DHEA. For the purpose of evaluating liver enzymes, a blood sample will be obtained at the end of each of the two Phases. A phone call will be made to each subject during the week after each treatment day for follow-up assessment. Other than payment for participation and their contribution to our knowledge of drug action and measurement of drug effect, there is no benefit to the subjects.

COSTS AND PAYMENTS

The procedures and medications involved in the study will not be charged to the subjects. The total payment for participating in the study will be \$600.00. There will be partial payment depending on the extent of the subject's involvement if the investigators require withdrawal from the study prior to completion or if the subject decides to withdraw from the study.

QUALIFICATION OF INVESTIGATORS

Patricia D. Kroboth, Ph.D. is Professor and Chairman of Pharmaceutical Sciences. Since 1980, when she joined the faculty at the University of Pittsburgh, she has conducted numerous clinical research studies; most have dealt with the question of how disease state, aging and hormones/other drugs modulate sensitivity to benzodiazepines.

Reginald Frye, Pharm.D., Ph.D. is Assistant Professor of Pharmacy and Therapeutics and has conducted many research studies. He has expertise in in vitro and in vivo assessment of drug metabolism as well as pharmacokinetics and has recently developed probes and analytical methodology for cytochrome P4503A4.

M. Margaret Folan, B.S.N., R.N. has been a research nurse in the Pharmacodynamic Research Center since 1988 and is currently a graduate student in the Clinical Scientist Ph.D. program in the School of Pharmacy. She has conducted pharmacodynamic studies, analyzed the resulting data and published the results.

John A. Sweeney, Ph.D. is Associate Professor of Psychiatry and Neurology and Director for the Neurobehavioral Studies Program at the Laboratories of Neuropsychopharmacology. He has been conducting studies of eye movements and their relationship to mental health since 1975.

Bruce G. Pollock, M.D., Ph.D. is Associate Professor of Psychiatry and Pharmacology, Director of the Geriatric Psychopharmacology Program and Principal Investigator of the Geriatric Psychopharmacology Core of the Mental Health Clinical Research Center for Late Life Mood Disorders(MH52247). He is well known for his contributions to psychopharmacology in general and drug metabolism in particular.

Gretchen Haas, Ph.D. is Associate Professor and Director of the Family and Psychosocial Studies Program in the Department of Psychiatry. Having been trained by the developers of the SCID diagnostic procedures for DSM-III-R/DSM-IV, she is highly familiar with the nuances of utilizing structured clinical diagnostic procedures in the assessment of both community control subjects and acutely ill psychiatric inpatients.

Frank J. Kroboth III, M.D. is Professor of Medicine at the University of Pittsburgh and Assistant Chief of Medicine, Presbyterian University Hospital. He is Director of the Internal Medicine House Staff Training Program, and Medical Director of the Pharmacodynamic Research Center. He has been involved in numerous clinical studies during his 16 years on the faculty.

Roslyn Stone, Ph.D. is Assistant Professor of Biostatistics at the Graduate School of Public Health. She has extensive experience in development and implementation of statistical methods in research studies.

Michael T. Lotze, M.D. is Professor of Surgery, Molecular Genetics, and Biochemistry. He is also Co-Director of the Biological Therapeutics at University of Pittsburgh Cancer Institute.

Janet A. Amico, M.D. is Professor of Medicine in the Division of Endocrinology. She is active in both clinical and research endeavors that focus on endocrinology.

APPENDIX A

LISTING OF LABORATORY TESTS FOR SCREENING SUBJECTS

Biochemical Profile:	BUN, creatinine, sodium, potassium, chloride, glucose, phosphorus, calcium, uric acid, cholesterol, triglycerides, total protein, albumin, total and direct bilirubin, LDH, AST, ALT and alkaline phosphatase, cortisol
Complete Blood Count:	hemoglobin, hematocrit, RBC count, RBC index (MCV, MCH, MCHC), platelets and WBC
Urinalysis:	Routine and Microscopic
Drug Screen:	Urine for drugs of abuse, blood alcohol concentration

EXCLUSION CRITERIA

Excluded will be those subjects who have:

1. Drug or alcohol dependence, or who abuse or consume, on average, more than 2 alcoholic beverages per day.
2. Seizure disorder reported in the medical history (i.e., seizure disorders that required chronic treatment into adolescence and adulthood).
3. A score of less than 25 on the MiniMental State Exam,³⁹ or history of any major psychiatric illness, or abnormal psychiatric examination as assessed by the Structured Clinical Interview for DSM-IV Diagnosis (SCID).⁴⁰
4. Renal, hepatic, collagen, vascular, or pulmonary disease; GI disturbances or history of malabsorption.
5. Endocrine diseases such as diabetes mellitus, Cushing's disease, Addison's disease, or thyroid conditions.
6. Cardiovascular disease that is symptomatic or clotting abnormalities.
7. Known hypersensitivity/allergy to alprazolam, other benzodiazepines or steroids.
8. History of benzodiazepine ingestion in the previous 6 months or chronic benzodiazepine use (greater than one week) within the last year, steroid ingestion in the previous 3 months or chronic steroid use (greater than one week) within the last year, participation as a blood donor in the past 2 months, or participation in a drug study in the past 6 months.
9. Saccade dysmetria, strabismus or nystagmus (assessed during SEM screening).

Elderly women who have taken hormone replacement therapy (estrogen or progesterone) during the three months prior to participation in the study will not be eligible. Young women must not be pregnant and must not have taken oral contraceptives for at least three months. Subjects should not have received any known enzyme inducing agents (barbiturates, rifampin, etc.) or any known enzyme inhibiting agents (cimetidine, erythromycin, etc.) for a period of 30 days prior to the study day.

APPENDIX B

Schematic of Study Participation for Each Subject

Within 3 months prior to the first week of study: Informed consent; laboratory, saccadic eye movement, and psychiatric screening for eligibility and psychomotor practice to plateau performance.

Within 1 month prior to the first week of study: Medical screening.

Schematic of study events for each of the four treatment days.

Time in h Clock Time	-1.0h 7:30a	0	1.0	2.0	2.5	3.0	3.5 12N	4.5	5.5	6.5	7.0	8.5	10.0 6:30p	11.5	12.5	16.0	20.0	23.0 7:30a
SEM & Psychomotor	X			x			x	x	x		x	x	x	x	x			
Dose (drug or placebo) [¶]		x			x					x								
DHEA conc & Sedation	X		x	x		x	x	x	x		x	x	x	x	x	x	x	x
Alprazolam conc Phase II	X					x	x	x	x		x	x	x	x	x	x	x	x
DHEA-S	X		x	x		x		x				x	x	x	x			x
Cortisol	X			x								x			x			x
Other assessments	*†§			§				†	†		†	‡						§

¶Dose administration schedule in Phase I: DHEA ≤150 mg at 0h (8:30am), DHEA ≤150 mg at 6.5h (3pm)—times are approximate.

Dose administration schedule in Phase II: DHEA at 0 h and at 6.5 h, an individualized dose not to exceed a total of 400 mg.; Alprazolam 2 mg at 2.5 h.

*Blood sample for progesterone

§ Blood sample for immunologic testing

†Randt Memory Test Administration

‡Hopkins Verbal Learning Test

Subjects will be discharged after the 23 h sample in Phases I and II. In the week after discharge, subjects will be phoned to assure continued participation.

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Approved: 8/1/00
Biomedical IRB
University of Pittsburgh

CONSENT TO ACT AS A SUBJECT IN AN EXPERIMENTAL STUDY

TITLE: DHEA & GABA-Receptor Mediated Responses in Aged Adults

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DESCRIPTION: The purpose of this study is to determine if the hormone dehydroepiandrosterone (DHEA) hastens recovery from the sedative effects (sleepiness, slowing of response time) that occur after taking the drug alprazolam (Xanax®). At least sixty-four healthy young and elderly men and women will complete all four treatments in this study. The treatment that I receive on each of the four days will be unknown to me. Each of the treatment days will require two overnight stays at the General Clinical Research Center at Montefiore University Hospital. I am being asked to participate in all four treatment days. I am being asked to participate in this study because I am between the ages of 20 and 79 years old and (*investigator circle one*) am healthy or have a stable medical or psychiatric condition.

This study is divided into Phase I and Phase II.

Phase I: This phase consists of two treatments given on two separate days with one week between each day. On one of the days I will receive two doses of a placebo and on the other day I will receive two doses of DHEA for a total dose of no greater than 300 mg. Neither I nor the investigators will know which treatment I receive

on each day until the study is completed. A sealed record of the treatment that I receive will be kept at the study site in the event that it is necessary to determine whether I have received the drug or a placebo.

I will begin Phase II one or two weeks after the second treatment day of Phase I.

Phase II: This phase consists of two treatments given on two separate days with one week between each day. On one of the days I will receive two doses of a placebo and a single dose of alprazolam (Xanax®, 2 mg). On the other day I will receive DHEA and alprazolam. The total DHEA dose will be no greater than 400 mg. Neither I, nor the investigators, will know which treatment I receive on each day until the study is completed.

DHEA is a naturally occurring steroid hormone that is being investigated for treatment of different conditions such as obesity, memory loss, and immune deficiencies. I understand that the DHEA tablet that I will receive is not yet approved by the FDA for general use. I will receive no more than 400 mg of DHEA in one day. DHEA has been given safely to patients in doses up to 2250 mg each day. Alprazolam tablets have been approved by the FDA and are available by prescription to treat anxiety disorders. I will receive 2 mg of alprazolam in one day. The maximum recommended daily dose used to treat anxiety or nervousness is 4 mg. Both DHEA and alprazolam will be given to me by mouth.

This study will require me to complete several tests and tasks throughout each treatment day. These tests include a card sorting task and a pen and paper test where I must draw symbols to match numbers and memory tests where I will be asked to remember some pictures and a series of words. Also, in order to measure my eye movements, I must wear a special pair of glasses with infrared sensors on them and follow a moving dot on a computer screen. In addition, small electrodes will be placed on the middle of my forehead, and above and below one of my eyes.

If I agree to participate, I understand that I will be expected to do the following:

- I will be required to have a physical exam and give information about my past medical, psychiatric and medication history. Psychologists from Western Psychiatric Institute and Clinic will conduct my psychiatric screening interview and a physician will perform my medical history, physical examination and laboratory screening at no cost to me or my third party payers.
- If I am determined to be suffering from psychological distress, a referral for treatment will be offered to me.
- My eyes will also be tested to determine if I have a condition, which might prevent me from properly responding to the eye movement test. These examinations and screenings will require several hours of my time and are not designed for the purpose of my personal health care, but only for qualification to enter the study. I will also complete some questionnaires and practice the tests described in the previous paragraph.
- I will be tested for drugs of abuse and alcohol at the time of screening and may be tested at other times.
- I will not take any over-the-counter and/or prescription medications for one week prior to the start of each treatment day or during the treatment day without knowledge of the study investigators.
- I will not have any beverages that contain alcohol or caffeine for 48 hours before each treatment day. Examples of caffeine containing beverages include coffee, tea, colas (e.g. Pepsi and Coke), and Mountain Dew.
- I will be admitted to the General Clinical Research Center at Montefiore Hospital in the afternoon before the treatment day, practice the manual tasks and other tests and be in bed by 11:00 p.m.
- I will not eat or drink anything other than water after 10:00 p.m. on the night prior to each treatment day.
- Before each treatment day, I will go to bed so that I obtain 8 hours or a normal night of sleep.

For each treatment day:

- I will arise by 7:00 a.m. and eat the light breakfast provided for me on the morning of the treatment day. An intravenous catheter will be placed in my forearm to be used for blood sampling.
- **For Phase I:** At approximately 8:30 a.m. on the treatment day, I will receive either placebo or DHEA (in a dose no greater than 150 mg). I will be given a second dose of either placebo or DHEA (in a dose no greater than 150 mg) at approximately 3:00 p.m. The total dose of DHEA that I will receive during

Phase I is 300 mg or less. I will receive all treatments by mouth. The treatment that I receive on each day will be unknown to me. During each treatment day of Phase I, 85.5ml (3 ounces, about 1/3 cup) of blood will be taken from the catheter in my arm. All of my urine will be collected from the time of the morning dose until the next morning.

- **For Phase II:** At approximately 8:30 a.m. on the treatment day, I will receive either placebo or DHEA. Approximately 2½ hours later, I will receive alprazolam (2 mg). At approximately 3:00 p.m. I will receive a second dose of either placebo or DHEA. The dose of DHEA that I receive during Phase II will not exceed 400 mg. I will receive all treatments by mouth. The treatment that I receive on each day will be unknown to me. During each treatment day of Phase II, 123 ml (4 ounces, about 1/2 cup) of blood will be taken from the catheter in my arm. All of my urine will be collected from the time of the morning dose until the next morning.
- After breakfast, I will be required to fast throughout the morning with only water permitted. I will be given a glass of juice or a liquid meal several times throughout the day at approximately 10:30 a.m., 12:30 p.m., and 2:30 p.m. Dinner will be served at approximately 5:30 p.m. Also, a snack will be served before I go to bed.
- On several occasions during the each of the four treatment days I will be requested to complete some manual tasks (for example, a pen and paper test), memory tests (for example, remembering words and pictures), and eye movement tests.
- I will remain in the study chair until 6 hours after the alprazolam dose (until about 5:00 p.m.); after this time, I will be able to walk around with supervision for 15 minutes.
- Breakfast will be provided on the morning after the treatment day and I will be discharged after the last blood sample (approximately 8:00 a.m.).
- The total amount of blood withdrawn for all four treatment days, including the screening labs will be approximately 395 ml (about 13 ounces or 1 and 1/2 cups). The amount of blood withdrawn when someone donates a unit of blood is approximately 480 ml (16 ounces or 2 cups).
- After each of the treatment days, prior to being discharged, I understand I must answer the question, "Since you received the study medication, have you noticed anything unusual?" During the week after each of the treatment days, I will receive a phone call from one of the study investigators and the same question will be asked.

RISK AND BENEFITS: I understand that I will not experience any personal benefits to my health as a result of my participation in these studies. The risks of participating in these studies include the discomfort and inconvenience of having an intravenous catheter placed in my arm and light-headedness from having blood samples collected. I understand that arm pain, swelling, bruising and/or infection may result from having the catheter placed and blood withdrawn.

I understand that I may feel drowsy or sleepy for a few hours after alprazolam is administered. Other side effects for alprazolam include: hiccups, dizziness, confusion, headache, inability to remember events that occur within 8 hours after drug administration, slowing of response time and interference when operating automobiles or other machinery, dry mouth, light-headedness, nausea, double vision, loss of coordination, and slurred speech. Studies have shown that oral administration of DHEA 50 to 2,250 mg each day over a long period (1 to 4 months) is well tolerated. One subject in a past study received DHEA 1600 mg each day for 28 days and experienced an elevation in liver enzymes. Liver enzymes returned to normal levels after the subject stopped taking DHEA. I will have a blood sample drawn prior to discharge after each of the two phases for the purpose of evaluating my liver enzymes.

In Phase II of the study, I will abstain from drinking alcohol or taking any sedatives the day I am discharged.

NEW INFORMATION: New information, whether good or bad, which comes to the attention of the investigators during the course of the research and which relate to my willingness to participate will be provided to me or my legal representative.

COSTS AND PAYMENTS: If I agree to participate, all procedures necessary for the completion of this study will be performed at no cost to me. Upon successful completion of all that is required for the four treatment periods I will be paid a total of \$600.00. There will be a partial payment of \$125.00 if I decide to withdraw from the study after the first treatment period, a total of \$250.00 if I decide to withdraw from the study after

the second treatment period, and a total of \$400.00 if I decide to withdraw from the study after the third treatment period. There will be partial payment dependent on the extent of my involvement in the study if the investigators require me to withdraw from the study prior to its completion.

CONFIDENTIALITY: I understand that any information about me obtained from this research, including answers to questionnaires, history, laboratory data, or test results will be kept confidential. It is now University policy that all research records be kept for a period of at least five years post termination. When the study results are published, they will be anonymous and/or my identity will not be revealed. I understand that my research records, just like hospital records, may be subpoenaed by court order, or reviewed by federal investigatory agents. The FDA may also need to have access to my medical records. With these exceptions, any research data released or published will not identify me by name. Therefore, I consent to such publication for scientific purposes.

RIGHT TO WITHDRAW: I understand that I am free to refuse to participate in this study or to withdraw at any time. My decision will not adversely affect my care at this institution or cause a loss of benefits to which I might otherwise be entitled. I also understand that the investigators may ask that I withdraw from the study if it is felt that the risks to my health outweigh the benefits to continue to be enrolled in this study.

COMPENSATION FOR ILLNESS OR INJURY: University of Pittsburgh investigators and their associates who provide services at the UPMC Health System (UPMC HS) recognize the important of your voluntary participation to their research studies. These individuals and their staffs will make reasonable efforts to minimize, control, and treat any injuries that may arise as a result of this research.

If you believe that you are injured as the result of the research procedures being performed, please contact immediately the Principal Investigator listed on the cover sheet of this form or the University of Pittsburgh Institutional Review board (412-692-4376). Emergency medical treatment for injured solely and directly relating to your participation in this research will be provided to you by hospitals of the UPMC HS may bill your insurance provider for the costs of this emergency treatment, but none of these costs will be charged directly to you. If your research-related injury requires medical care beyond this emergency treatment, you will be responsible for the costs of this follow-up care unless otherwise specifically stated below. You will not receive monetary payment for, or associated with, any injury that you suffer in relation to this research.

VOLUNTARY CONSENT: I certify that I have read the preceding or it has been read to me, and I understand its contents. Any questions I have pertaining to the research have been, and will continue to be answered by Dr. Patricia Kroboth (648-8430) or her associates. Any questions I have concerning my rights as a research subject will be answered by the Human Subjects Protection Advocate at the University of Pittsburgh IRB Office (412-692-4376). A copy of this consent form will be given to me. My signature below means that I have freely agreed to participate in this project.

Date

Subject Signature

Witness

I certify that I have explained to the above individual the nature and purpose, the potential benefits, and the possible risks associated with participating in this research study, have answered any questions that have been raised, and have witnessed the above signature.

Date

Investigator Signature

INITIAL AND RECORD ACTUAL TIME IN ALL BLANK AREAS

PHASE I (PAGE 1 OF 1)

Protocol Time	Actual Clock Time	NRSS / SRSS	Rand Memory score	DSST score	Card Sorting #cards/sec	Blood Sample Record actual clock time	SEM	Vital Signs	Meals other assessments
-1.0h									Breakfast; Collect baseline urine
-0.5h						4.5ml redtop 3ml greentop			Empty bladder POMS;
0h		Administer oral dose of DHEA ____mg or PLACEBO Administered by_____ Time of administration_____							
		Begin Urine Collection #1 (0h-12h)							
1.0h						4.5ml redtop			
2.0h						4.5ml redtop 3ml greentop			Juice
3.0h						4.5ml redtop			
3.5h						4.5ml redtop			
4.5h						4.5ml redtop			POMS, Liquid lunch
5.5h						4.5ml redtop			
6.5h		Administer oral dose of DHEA ____mg or PLACEBO Administered by_____ Time of administration_____							
7.0h						4.5ml redtop			Liquid Lunch
8.5h						4.5ml redtop			POMS, Hopkins
10.0h						4.5ml redtop			Dinner
11.5h						4.5ml redtop			End #1 urine collect Begin #2 (12h-23h)
12.5h						4.5ml redtop			POMS
16.0h						4.5ml redtop			
20.0h						4.5ml redtop			
23.0h						4.5ml redtop 3ml greentop			Discharge subject End urine collect #2

* Activity:

**Split redtop sample per orders, greentop goes in tube labelled 'LOTZE' AND INITIALS

Nurse Rated Sedation Score

- | | |
|--|---|
| 0 Wide Awake; Alert | 3 Sleeping; Awakened by Name |
| 1 Awake; Lethargic | 4 Sleeping; Responds to Strong Stimuli |
| 2 Eyes closed; Responds to Name AND/OR Unable to do Psychomotor Performance Tests | |

SIGNATURES

_____	_____
_____	_____
_____	_____

INITIAL AND RECORD ACTUAL TIME IN ALL BLANK AREAS

PHASE II (PAGE 1 OF 1)

Protocol Time	Actual Clock Time	NRS SRS	Randt Memory score	DSST score	Card Sorting #cards /sec	Blood Sample Record actual clock time	SEM	Vital Signs	Meals other assessments
-1.0h									Breakfast; Collect baseline urine
-0.5h						7ml redtop 3ml greentop			Empty bladder POMS
0h		Administer oral dose of DHEA _____mg or PLACEBO Administered by_____ Time of administration_____							
									Begin Urine Collection #1 (0h-12h)
1.0h						7ml redtop			
2.0h						7ml redtop 3ml greentop			Juice
2.5h		Administer oral dose of Alprazolam 2mg Administered by_____ Time of administration_____							
3.0h						7ml redtop			
3.5h						7ml redtop			
4.5h						7ml redtop			POMS, Liquid lunch
5.5h						7ml redtop			
6.5h		Administer oral dose of DHEA _____mg or PLACEBO Administered by_____ Time of administration_____							
7.0h						7ml redtop			Liquid Lunch
8.5h						7ml redtop			POMS, Hopkins
10.0h						7ml redtop			Dinner
11.5h						7ml redtop			End #1 urine collect Begin #2 (12h-23h)
12.5h						7ml redtop			POMS
16.0h						7ml redtop			
20.0h						7ml redtop			
23.0h						7ml redtop 3ml greentop			Discharge subject End urine collect #2

* Activity:

**Split redtop sample per orders, greentop goes in tube labelled 'LOTZE'

AND INITIALS

Nurse Rated Sedation Score

0 Wide Awake; Alert

3 Sleeping; Awakened by Name

1 Awake; Lethargic

4 Sleeping; Responds to Strong Stimuli

2 Eyes closed; Responds to Name AND/OR Unable to do Psychomotor Performance Tests

SIGNATURES

_____	_____
_____	_____
_____	_____

APPENDIX B

Saccadic Eye Movement Parameters

Velocity: 8 degree & 16 degree

Table B1. Velocity (msec) to 8 degree targets for young women during Placebo Treatment

Subject	Time (h)									
	0	2	3.5	4.5	5.5	7	8.5	10	11.5	12.5
1	349.02	348.58	362.78	365.75	366.12	368.72	351.72	354.80	377.92	360.42
3	276.22	274.08	285.71	285.92	273.84	274.72	272.65	283.68	262.07	258.58
4	298.14	311.97	282.68	267.74	288.44	294.13	312.24	275.33	284.18	274.02
5	283.78	308.12	291.60	261.64	250.96	239.16	256.03	269.99	248.28	272.20
7	236.93	241.05	239.01	257.94	260.42	252.70	245.70	255.48	257.23	244.41
8	246.06	245.22	235.31	247.48	245.13	235.22	230.86	257.68	275.01	260.33
9	309.36	283.26	281.99	295.58	308.14	298.41	269.94	295.86	283.73	319.46
10	284.14	274.43	276.83	247.04	259.50	245.01	252.32	245.89	255.44	241.82
12	269.45	214.14	236.45	258.55	251.09	261.23	259.78	258.11	273.50	268.78
14*	318.83	302.45	310.65	289.97	320.01	349.39	318.58	287.93	341.79	313.80
15*	247.04	237.55	215.49	233.44	225.29	236.50	229.48	230.48	243.48	241.42
16*	283.09	283.76	294.19	270.06	268.86	276.18	292.08	282.54	251.29	277.67
102	259.51	289.92	295.26	291.96	268.97	271.54	287.03	299.83	271.63	270.78
111	307.41	297.95	271.26	264.92	280.38	269.27	282.23	274.15	279.17	282.00
112	321.27	328.43	335.42	316.19	306.10	334.10	311.49	315.01	303.17	325.69
114*	263.52	252.46	268.21	260.77	268.10	252.45	302.69	268.79	287.06	280.52
206	335.75	323.39	306.21	331.27	297.19	315.35	338.26	296.57	305.47	339.79
213*	293.92	313.34	339.11	294.77	313.54	309.51	296.84	320.72	327.01	307.81
Mean	287.97	285.01	284.90	280.06	280.67	282.42	283.88	281.82	284.86	285.53
St. Dev.	31.65	36.01	38.49	32.96	33.51	39.88	35.01	29.60	35.32	34.67

*Minority Subjects

Table B2. Velocity (msec) to 8 degree targets for young men during Placebo Treatment

Subject	Time (h)									
	0	2	3.5	4.5	5.5	7	8.5	10	11.5	12.5
33	289.57	306.14	304.50	302.74	300.66	308.65	287.19	314.06	326.21	303.65
34	203.34	185.73	287.65	320.48	300.47	318.37	274.17	297.65	293.64	285.78
35	341.17	310.43	316.19	342.87	325.19	325.37	343.10	319.58	332.14	316.72
36	314.80	308.85	308.40	289.27	289.85	263.48	310.99	320.38	314.33	312.16
37	301.75	297.69	300.59	297.83	308.29	335.14	309.17	326.87	299.93	355.74
38	307.85	296.79	302.63	295.87	300.04	301.05	321.88	297.32	302.90	291.13
39	324.45	275.30	237.58	319.15	290.87	275.59	268.99	318.49	310.20	319.80
41	307.85	305.31	324.58	293.75	322.64	307.84	293.39	308.64	312.97	299.00
42	296.06	262.98	303.29	288.69	282.67	289.20	302.68	297.60	295.61	301.27
43	308.87	313.41	327.50	321.06	317.35	317.54	310.02	300.60	290.10	314.41
44	269.23	272.63	275.65	262.55	279.02	278.53	291.20	297.24	286.96	301.98
47*	330.08	295.95	320.33	289.81	310.88	292.52	314.28	293.48	298.31	302.85
48*	256.28	223.70	252.48	261.46	263.82	259.63	254.41	269.15	273.54	233.47
140	282.41	275.33	292.39	257.73	267.16	289.61	269.54	263.24	282.49	271.62
146*	249.83	239.80	259.12	241.04	257.11	245.13	218.89	247.58	253.90	258.81
245*	243.67	228.85	240.38	255.65	240.10	231.29	255.84	256.69	245.48	252.45
Mean	289.20	274.93	290.83	290.00	291.01	289.93	289.11	295.54	294.92	295.05
St. Dev.	36.59	37.69	29.42	28.28	24.61	29.52	30.99	24.24	23.42	29.71

*Minority Subjects

Table B3. Velocity (msec) to 8 degree targets for older women during Placebo Treatment

Subject	Time (h)									
	0	2	3.5	4.5	5.5	7	8.5	10	11.5	12.5
17	238.42	254.16	221.81	232.47	235.77	234.66	279.62	280.72	279.99	257.17
18	262.62	252.84	284.23	270.27	269.85	312.09	265.14	277.43	278.45	282.57
19	271.10	273.18	270.32	240.55	220.68	244.39	261.46	275.58	219.12	252.88
20*	235.60	245.28	218.90	233.77	251.87	244.63	228.50	256.35	216.84	249.44
21	276.92	270.97	253.12	235.44	246.34	327.34	270.50	252.75	236.76	278.28
22	268.77	267.01	258.07	267.79	260.82	258.14	261.82	274.85	255.56	251.75
23	271.45	238.53	291.79	269.38	233.27	249.48	221.95	223.16	249.17	230.99
24	326.95	294.41	309.32	294.70	151.81	319.48	315.92	287.36	331.64	287.02
25	289.35	282.69	267.22	301.90	295.54	275.58	282.23	271.30	307.79	278.76
26	219.04	196.45	204.35	221.34	189.09	203.98	247.98	221.17	249.33	235.21
27	252.01	301.40	250.76	253.81	276.73	256.43	277.96	252.79	265.49	259.89
28	291.07	287.71	273.03	277.23	280.73	265.20	277.49	255.21	267.52	270.71
29*	276.52	264.50	285.55	241.71	--	291.00	252.57	230.59	226.95	323.68
30*	276.01	230.53	242.26	270.21	259.19	274.16	268.36	258.45	258.04	235.00
31*	--	212.99	174.34	277.95	184.27	241.16	222.42	--	235.20	205.42
120	330.94	293.05	285.87	296.11	276.57	309.62	282.24	279.46	273.00	301.72
Mean	272.45	260.36	255.68	261.54	242.17	269.21	263.51	259.81	259.43	262.53
St. Dev.	30.44	30.02	35.98	25.16	40.66	34.70	24.76	21.25	31.03	29.48

*Minority Subjects

(--) Velocity not obtained

Table B4. Velocity (msec) to 8 degree targets for older men during Placebo Treatment

Subject	Time (h)									
	0	2	3.5	4.5	5.5	7	8.5	10	11.5	12.5
50	257.99	220.74	231.91	221.95	193.18	172.63	278.46	219.15	268.67	252.61
51	310.72	262.71	255.13	281.53	285.13	278.59	272.70	261.74	258.54	253.02
52	259.70	236.46	260.52	286.07	276.18	255.58	195.15	249.11	260.50	248.94
53	272.59	248.67	250.38	273.43	243.32	261.99	237.10	238.59	281.15	285.47
54	208.20	228.89	206.56	197.38	203.10	210.13	162.40	243.91	256.25	235.11
55	231.03	239.49	239.56	246.48	242.37	219.73	238.51	237.99	241.52	247.74
56	294.24	294.18	324.82	311.23	290.01	303.80	296.54	272.94	317.65	313.03
57	353.71	352.82	337.71	348.45	324.82	343.13	337.86	316.30	357.21	340.31
58	230.14	227.12	241.41	229.24	236.77	224.18	254.24	247.42	241.32	245.11
59	290.79	254.42	281.33	272.94	254.09	245.75	275.58	290.20	281.05	262.14
61*	–	281.84	273.62	299.01	284.39	289.14	303.42	286.18	287.58	297.25
149	284.45	313.83	289.52	330.13	292.61	272.94	286.71	298.43	298.79	307.78
160	313.22	305.16	273.52	236.21	241.81	230.08	194.74	277.36	264.26	298.67
Mean	275.57	266.64	266.61	271.85	259.06	254.44	256.42	264.56	278.04	275.94
St. Dev.	41.09	40.16	36.39	44.36	37.46	44.66	49.65	28.27	32.27	32.91

*Minority Subjects

(–) Velocity not obtained

Table B5. Velocity (msec) to 8 degree targets for young women during DHEA Treatment

Subject	Time (h)									
	0	2	3.5	4.5	5.5	7	8.5	10	11.5	12.5
1	349.43	296.67	349.10	252.11	341.20	358.20	357.53	358.45	290.92	344.88
3	237.01	245.39	260.89	287.06	271.58	277.17	292.76	298.94	282.84	266.98
4	300.52	276.76	274.24	285.11	290.89	278.01	273.50	284.92	295.38	281.32
5	291.83	272.16	288.09	256.81	256.40	274.17	293.52	273.18	281.82	266.53
7	269.90	256.34	258.75	228.35	245.24	251.14	249.40	258.41	267.51	239.41
8	237.46	265.07	260.06	263.24	263.78	257.64	265.54	268.03	271.91	278.47
9	301.65	295.93	321.39	301.74	283.37	269.88	267.55	287.43	302.51	299.60
10	311.55	290.34	260.72	252.13	248.48	299.19	253.39	261.44	256.61	276.21
12	276.59	239.36	231.48	262.50	229.84	251.81	269.72	253.76	274.51	245.81
14*	315.90	297.21	296.26	322.20	282.87	292.29	327.41	300.12	339.67	275.20
15*	242.08	256.36	225.14	232.33	215.41	212.31	251.95	248.88	257.94	227.09
16*	318.41	304.55	262.97	266.24	279.06	284.00	268.47	292.97	311.69	271.62
102	262.51	253.88	263.56	264.98	281.39	276.48	280.17	262.28	269.72	267.36
111	271.20	287.48	266.96	267.34	260.50	268.01	255.88	290.05	265.29	270.06
112	342.57	337.28	316.07	341.50	320.79	342.59	340.24	353.37	355.17	344.39
114*	260.42	259.42	262.17	272.01	260.96	278.54	277.95	243.03	267.82	262.48
206	314.25	302.47	303.04	306.56	--	311.76	306.86	329.03	309.37	328.39
213*	--	--	298.83	266.85	--	304.41	326.56	296.50	326.39	296.83
Mean	288.43	278.63	277.76	273.84	270.74	282.64	286.58	286.71	290.39	280.15
St. Dev.	34.88	25.88	31.57	29.27	31.31	33.49	32.54	33.30	28.61	32.55

*Minority Subjects

(--) Velocity not obtained

Table B6. Velocity (msec) to 8 degree targets for young men during DHEA Treatment

Subject	Time (h)									
	0	2	3.5	4.5	5.5	7	8.5	10	11.5	12.5
33	299.13	305.77	299.76	299.21	311.78	303.50	296.29	298.68	309.77	299.52
34	294.35	289.84	296.15	310.61	283.60	290.74	283.91	297.66	279.01	318.86
35	196.67	339.71	296.29	331.52	329.63	333.97	321.06	334.58	309.42	325.26
36	293.25	291.67	318.28	299.62	293.15	312.97	310.08	307.64	307.94	299.81
37	330.25	303.41	279.64	272.77	291.35	316.77	290.47	276.70	298.74	319.67
38	287.74	325.39	309.84	297.04	309.76	296.54	313.49	300.06	314.17	278.44
39	329.20	304.07	341.95	276.33	270.43	291.14	289.48	274.58	338.62	345.29
41	292.67	290.40	291.42	300.08	298.66	319.37	310.46	295.69	318.51	326.38
42	318.52	321.66	303.86	326.84	319.52	307.35	301.64	298.05	316.76	309.59
43	309.36	309.07	309.40	288.58	338.21	319.63	305.63	320.33	320.51	325.90
44	282.09	273.90	294.40	296.10	290.67	278.52	284.30	270.19	298.80	296.79
47*	314.09	307.35	318.80	296.54	306.16	318.28	330.43	318.82	292.70	308.78
48*	239.30	247.35	232.59	232.31	277.94	231.89	278.63	270.29	244.87	272.24
140	271.27	254.18	276.75	269.56	268.40	277.89	271.33	293.22	287.09	271.47
146*	232.64	223.50	238.03	253.41	244.92	215.26	243.74	238.93	225.57	231.84
245*	256.28	250.13	263.59	251.52	221.44	233.67	231.25	250.51	240.13	238.42
Mean	284.18	289.84	291.92	287.63	290.98	290.47	291.39	290.37	293.91	298.02
St. Dev.	37.08	32.03	28.75	26.93	30.26	35.27	26.46	25.50	31.85	32.04

*Minority Subjects

Table B7. Velocity (msec) to 8 degree targets for older women during DHEA Treatment

Subject	Time (h)									
	0	2	3.5	4.5	5.5	7	8.5	10	11.5	12.5
17	269.26	249.33	239.11	231.37	184.18	262.29	283.04	230.87	247.22	260.48
18	256.18	290.11	251.58	283.06	290.41	322.02	305.24	273.35	273.49	304.82
19	274.08	270.17	248.79	270.39	232.29	256.39	289.72	261.86	265.87	257.52
20*	214.41	221.77	214.75	226.60	217.08	230.04	245.33	272.83	204.04	218.14
21	265.40	264.51	280.39	296.14	253.13	277.46	281.48	264.06	282.95	276.44
22	292.85	269.26	287.65	274.10	270.27	282.50	283.97	298.31	279.64	302.70
23	227.83	236.24	269.34	226.93	233.10	265.29	269.27	259.98	241.48	225.42
24	285.62	287.42	318.81	274.57	319.45	324.53	326.28	320.13	294.17	294.82
25	285.09	251.78	290.94	300.37	284.23	270.98	277.81	269.75	256.57	302.68
26	203.52	180.43	235.29	216.42	212.85	178.76	205.45	205.04	237.98	196.80
27	--	297.90	288.68	248.43	281.85	237.62	238.11	255.94	238.99	223.87
28	288.26	277.43	272.69	270.64	268.03	291.01	271.47	258.81	274.37	299.77
29*	278.32	254.40	305.07	282.87	327.38	276.13	294.49	297.79	313.13	264.28
30*	251.27	231.25	303.83	284.97	232.20	259.14	229.10	315.48	268.72	284.71
31*	--	--	--	200.73	--	--	--	188.45	--	190.23
120	293.13	260.43	303.17	295.25	281.00	256.91	268.98	278.20	271.11	282.12
Mean	263.23	256.16	274.01	261.43	259.16	266.07	271.32	265.68	263.32	261.55
St. Dev.	29.30	30.22	30.27	31.66	40.35	35.52	30.94	35.47	26.64	39.09

*Minority Subjects

(--) Velocity not obtained

Table B8. Velocity (msec) to 8 degree targets for older men during DHEA Treatment

Subject	Time (h)									
	0	2	3.5	4.5	5.5	7	8.5	10	11.5	12.5
50	250.85	269.18	258.65	299.32	272.14	245.77	265.57	246.51	268.49	259.51
51	258.05	271.54	246.02	273.29	248.37	286.13	312.14	250.39	295.30	259.14
52	270.38	270.64	283.38	240.23	270.71	262.73	194.45	270.92	250.00	231.35
53	271.73	260.86	251.18	275.12	231.82	278.66	287.34	229.14	218.71	256.79
54	176.35	208.64	198.54	197.68	192.11	190.14	171.80	196.38	240.23	214.08
55	243.88	240.96	233.08	231.00	248.12	227.49	251.21	243.63	248.92	233.79
56	284.88	257.60	315.89	289.50	298.95	299.95	353.27	352.90	293.60	299.60
57	346.01	315.61	358.24	325.57	346.51	329.62	338.23	349.81	357.93	354.79
58	233.39	245.44	235.24	236.56	253.48	246.95	250.54	248.68	247.28	238.27
59	259.12	306.92	251.56	283.26	310.07	291.06	306.05	276.30	271.44	246.21
61*	233.07	238.69	270.21	242.93	283.20	258.78	310.95	278.60	277.03	292.73
149	308.17	327.38	279.28	275.24	295.45	317.86	288.35	286.74	309.92	311.22
160	272.23	214.08	236.41	287.03	170.17	234.11	260.54	275.71	230.63	253.31
Mean	262.16	263.66	262.90	265.90	263.16	266.87	276.19	269.67	269.96	265.45
St. Dev.	40.26	36.25	40.52	34.31	47.63	38.90	52.18	43.63	37.64	38.94

*Minority Subjects

Table B9. Velocity (msec) to 8 degree targets for young women during Alprazolam/Placebo Treatment

Subject	Time (h)									
	0	2	3.5	4.5	5.5	7	8.5	10	11.5	12.5
1	350.06	257.75	158.68	136.62	143.71	144.58	188.93	198.09	179.86	313.39
3	249.94	245.68	160.87	167.01	166.57	210.69	190.88	207.45	253.41	264.69
4	282.14	285.19	194.97	111.64	210.44	157.23	230.97	235.29	256.83	233.47
5	259.42	249.53	85.16	164.66	127.02	141.26	250.72	247.04	271.23	269.54
7	234.49	223.35	160.07	141.43	161.28	192.57	213.05	197.26	199.77	197.83
8	216.20	254.14	126.79	128.64	69.15	169.66	131.75	217.74	209.89	245.64
9	286.50	281.40	246.19	151.32	136.72	223.50	246.04	256.76	253.29	272.79
10	242.96	252.95	250.94	183.04	211.21	212.86	239.14	220.47	224.93	238.72
11	296.69	285.87	178.05	106.57	167.21	188.54	236.39	298.97	304.64	287.67
12	260.36	259.72	213.02	123.94	154.06	158.57	97.26	224.69	215.34	215.66
14*	314.33	319.82	262.99	163.47	168.75	218.23	283.35	271.93	240.72	309.60
15*	234.60	244.02	139.44	90.51	117.86	185.50	194.51	219.52	216.84	222.88
16*	276.14	239.13	242.87	232.81	203.00	215.44	220.49	248.48	248.68	267.56
102	267.06	260.97	151.93	102.42	132.86	175.61	213.45	252.74	227.16	263.66
111	257.20	284.97	231.08	120.84	124.26	180.41	224.14	238.41	226.96	253.12
112	348.96	314.11	191.33	200.71	167.14	238.64	211.99	263.08	295.26	297.49
114*	222.68	221.55	153.77	163.06	141.98	154.85	214.38	198.13	196.69	210.78
206	322.95	317.16	226.68	157.22	149.95	162.76	212.03	228.74	253.53	277.57
213*	279.97	283.04	174.24	184.80	186.79	220.59	239.31	238.32	279.48	279.97
Mean	273.82	267.39	186.79	148.98	154.73	186.92	212.57	234.90	239.71	259.05
St. Dev.	39.13	29.41	48.19	36.53	34.83	29.68	41.70	27.06	33.65	32.97

*Minority Subjects

Table B10. Velocity (msec) to 8 degree targets for young men during Alprazolam/Placebo Treatment

Subject	Time (h)									
	0	2	3.5	4.5	5.5	7	8.5	10	11.5	12.5
33	293.84	310.99	156.23	162.83	182.08	228.52	209.52	275.08	309.30	299.43
34	299.26	284.11	114.93	143.54	252.46	236.62	263.33	260.68	304.17	292.39
35	281.75	328.93	--	272.25	282.30	300.13	296.11	302.64	316.31	306.29
36	303.90	307.80	267.79	243.56	239.15	257.30	280.10	284.52	274.83	290.77
37	288.08	291.15	226.09	203.74	212.82	293.27	301.96	305.30	309.89	314.37
38	320.73	330.82	174.39	88.32	192.23	213.04	289.54	289.80	280.18	286.51
39	314.39	335.35	102.76	128.06	170.33	144.29	208.80	294.82	296.92	320.28
41	295.81	307.90	281.77	264.85	285.73	287.30	282.59	282.41	310.82	297.16
42	--	277.31	172.06	136.88	179.12	185.79	241.37	240.73	255.86	274.45
43	320.44	297.08	216.43	154.85	141.48	231.46	254.68	288.37	289.46	288.55
44	288.49	281.73	219.85	107.05	124.03	148.73	--	212.55	265.55	282.66
47*	325.01	297.57	184.61	195.94	218.55	203.78	212.95	278.36	261.46	239.09
48*	287.13	240.51	170.75	--	113.42	183.03	192.24	238.99	212.95	234.78
140	263.06	253.93	66.99	106.85	140.60	186.14	193.50	254.33	236.42	270.32
146*	243.98	232.43	156.63	141.06	106.91	169.84	161.60	208.89	221.85	238.56
245*	235.44	238.10	--	--	--	173.85	197.01	183.89	249.84	209.27
Mean	290.75	288.48	179.38	167.84	189.41	215.19	239.02	262.59	274.74	277.81
St. Dev.	26.61	33.08	60.37	59.42	58.44	49.85	45.26	36.37	33.05	31.67

*Minority Subjects
 (--) Velocity not obtained

Table B11. Velocity (msec) to 8 degree targets for older women during Alprazolam/Placebo Treatment

Subject	Time (h)									
	0	2	3.5	4.5	5.5	7	8.5	10	11.5	12.5
17	225.81	238.36	142.04	95.21	109.41	150.99	181.74	64.83	132.66	104.83
18	312.24	290.98	99.42	109.83	91.48	142.73	183.94	232.17	250.04	228.60
19	274.71	292.87	--	--	106.34	--	131.14	118.52	209.22	200.39
20*	262.67	246.74	215.87	155.76	129.21	129.80	122.97	161.30	152.27	174.33
21	289.99	266.46	--	94.78	139.54	208.95	219.65	238.52	252.01	263.91
22	234.17	271.03	171.98	65.58	94.60	88.88	92.28	171.23	176.08	194.31
23	--	236.81	--	151.74	162.06	189.32	172.92	199.18	231.79	185.57
24	321.34	312.97	192.18	138.40	178.46	251.57	274.70	259.65	303.78	--
25	279.23	312.56	229.95	137.79	145.76	263.23	231.65	222.06	232.80	263.17
26	231.54	212.76	--	--	129.51	140.09	103.68	141.87	95.07	143.69
27	287.64	306.05	--	--	--	--	--	--	192.72	179.07
28	293.26	282.38	--	174.88	129.01	--	--	178.18	240.79	197.46
29*	273.32	322.44	--	67.26	169.04	102.26	187.66	197.50	210.00	123.17
30*	225.08	280.06	--	--	185.50	118.98	267.99	189.91	236.26	273.47
31*	232.11	206.40	--	--	--	--	--	--	152.14	173.19
120	304.07	274.81	--	--	--	--	207.10	222.45	247.99	242.83
Mean	269.81	272.11	175.24	119.12	136.15	162.44	182.88	185.53	207.23	196.53
St. Dev.	32.92	35.46	48.56	38.07	31.03	58.30	58.35	52.13	53.81	50.81

*Minority Subjects

(--) Velocity not obtained

Table B12. Velocity (msec) to 8 degree targets for older men during Alprazolam/Placebo Treatment

Subject	Time (h)									
	0	2	3.5	4.5	5.5	7	8.5	10	11.5	12.5
50	238.76	267.08	96.65	73.12	161.02	181.00	136.29	201.37	203.28	217.79
51	284.48	261.60	103.58	150.44	101.30	193.91	199.00	205.38	242.38	236.76
52	259.60	191.89	--	--	--	--	152.61	123.15	195.20	180.31
53	298.71	266.33	145.73	143.22	193.62	124.40	190.85	243.39	260.20	228.58
54	196.75	217.62	116.34	111.76	93.92	91.14	159.03	202.94	154.99	191.34
55	260.16	198.17	198.17	146.60	202.91	184.28	195.42	233.11	236.21	238.34
56	339.21	290.24	--	116.12	120.25	169.96	198.29	252.89	289.30	197.34
57	322.89	325.93	194.71	212.50	152.84	217.20	280.01	268.70	317.24	325.51
58	233.38	246.22	194.86	188.48	171.83	201.89	211.93	201.70	206.72	226.65
59	275.37	291.98	--	108.26	151.81	240.17	250.31	215.77	243.10	203.09
61*	288.23	326.51	92.04	175.99	220.08	253.59	272.99	283.16	317.16	320.52
149	306.94	--	101.63	123.36	126.70	124.45	165.89	239.92	234.20	224.75
160	259.41	262.18	--	--	--	127.67	148.47	132.89	154.92	148.32
Mean	274.15	262.15	138.19	140.90	154.21	175.81	197.01	215.72	234.99	226.10
St. Dev.	38.86	43.90	46.00	40.23	41.20	50.28	46.72	46.99	52.78	49.87

*Minority Subjects

(--) Velocity not obtained

Table B13. Velocity (msec) to 8 degree targets for young women during Alprazolam/DHEA Treatment

Subject	Time (h)									
	0	2	3.5	4.5	5.5	7	8.5	10	11.5	12.5
1	344.47	282.96	152.83	145.35	225.17	204.92	228.24	263.93	316.00	318.99
3	270.85	288.93	170.95	175.85	151.57	184.84	207.13	270.75	246.22	275.56
4	295.54	275.28	183.55	127.69	154.17	174.32	232.44	267.06	245.63	249.07
5	264.70	262.13	97.99	139.39	123.49	185.91	229.37	245.52	226.51	265.01
7	243.43	235.22	146.76	141.39	136.44	172.42	161.29	200.68	213.46	205.10
8	264.68	257.64	239.82	143.58	160.37	178.43	169.73	209.84	214.15	246.48
9	319.21	265.51	240.52	205.22	179.23	217.03	224.62	268.19	275.65	289.92
10	262.10	269.12	173.12	217.58	164.44	226.40	235.13	251.20	269.65	262.14
11	310.04	279.90	223.21	176.14	171.74	244.37	271.87	258.46	285.27	314.48
12	268.85	236.72	163.18	135.84	146.59	166.35	209.97	243.38	223.68	212.83
14*	332.73	326.73	287.55	318.39	315.40	298.79	274.23	326.18	319.68	322.31
15*	222.73	233.11	152.56	101.64	118.39	131.80	192.75	200.31	212.88	189.74
16*	271.68	292.54	203.62	249.86	253.93	238.15	275.58	253.04	270.71	248.80
102	263.62	257.47	227.93	198.56	172.96	190.99	246.98	192.90	251.87	230.64
111	263.56	240.51	163.54	108.92	135.63	179.46	164.01	230.81	257.30	226.52
112	292.45	327.10	164.52	260.66	205.67	248.98	271.71	266.74	297.29	306.90
114*	250.98	262.11	198.21	145.44	197.24	209.84	248.66	238.55	226.32	234.30
206	309.07	333.66	234.93	--	164.21	174.68	189.89	257.67	266.55	285.16
213*	265.34	298.55	98.54	200.13	205.88	255.70	227.62	259.22	287.45	257.75
Mean	279.79	275.01	185.44	177.31	178.03	204.39	224.27	247.60	258.22	260.09
St. Dev.	31.53	30.76	49.00	57.38	48.21	39.91	36.70	31.43	33.71	39.14

*Minority Subjects
 (--) Velocity not obtained

Table B14. Velocity (msec) to 8 degree targets for young men during Alprazolam/DHEA Treatment

Subject	Time (h)									
	0	2	3.5	4.5	5.5	7	8.5	10	11.5	12.5
33	319.89	312.36	185.09	89.43	142.83	265.66	247.95	315.69	300.19	299.73
34	350.42	324.53	163.15	199.20	242.85	243.36	282.22	257.41	267.01	294.61
35	293.41	297.43	258.34	243.88	254.88	260.55	257.09	267.15	308.96	321.91
36	293.30	308.48	248.73	238.19	241.22	261.42	266.11	268.45	299.33	277.13
37	294.97	284.25	220.34	243.52	246.16	274.06	295.55	299.53	292.19	310.04
38	299.76	296.13	147.59	77.18	150.93	254.87	245.85	277.33	285.40	305.67
39	320.78	313.06	136.55	128.33	155.42	118.82	255.80	266.93	250.12	322.05
41	--	290.33	214.03	256.48	239.93	238.47	281.42	301.78	299.62	285.94
42	286.15	285.71	249.36	215.69	170.22	178.03	255.23	262.67	277.40	274.42
43	323.26	324.40	204.71	189.76	213.59	254.04	223.96	286.40	299.16	320.10
44	297.21	291.68	205.02	171.66	199.31	191.36	234.66	246.56	258.69	287.50
47*	302.92	309.72	195.39	204.56	207.23	217.39	265.49	273.99	285.40	265.87
48*	257.02	232.53	166.43	164.03	92.09	110.09	134.55	180.09	214.32	200.22
140	251.59	272.14	145.64	122.60	95.38	172.03	177.16	221.02	230.31	262.89
146*	240.61	247.66	217.46	176.34	154.79	216.83	265.06	252.16	252.06	259.42
245*	237.49	240.01	--	--	--	194.56	190.13	209.20	209.94	210.49
Mean	291.25	289.40	197.19	181.39	187.12	215.72	242.39	261.65	270.63	281.12
St. Dev.	32.41	28.51	39.20	56.53	54.25	51.12	42.56	35.09	31.80	36.07

*Minority Subjects

(--) Velocity not obtained

Table B15. Velocity (msec) to 8 degree targets for older women during Alprazolam/DHEA Treatment

Subject	Time (h)									
	0	2	3.5	4.5	5.5	7	8.5	10	11.5	12.5
17	246.05	242.22	--	--	--	--	187.95	178.05	189.17	163.77
18	269.42	301.03	131.59	140.64	97.94	158.72	138.45	177.29	237.40	217.61
19	275.09	270.44	--	--	--	--	136.24	182.06	173.94	185.73
20*	239.29	223.17	99.24	106.01	104.09	125.09	77.87	173.28	173.05	125.79
21	280.55	261.36	95.92	83.09	145.84	191.50	185.20	186.99	201.18	199.68
22	260.48	252.05	79.55	77.22	108.50	160.48	146.18	184.13	182.30	239.06
23	231.82	267.39	--	101.45	146.83	178.70	235.46	203.03	238.61	229.93
24	313.57	332.02	129.23	234.05	123.81	222.05	287.19	274.90	278.77	302.98
25	374.44	285.81	220.10	106.11	82.02	150.87	202.69	199.79	185.38	186.90
26	198.50	210.78	--	--	--	62.64	52.21	70.40	99.40	209.70
27	289.10	296.24	--	--	--	--	--	157.49	241.67	214.66
28	292.72	287.61	112.22	--	156.19	--	212.68	206.39	--	230.36
29*	252.26	270.52	--	--	--	--	--	--	259.40	245.99
30*	238.40	258.01	--	120.48	183.31	179.44	67.62	198.02	201.28	210.03
31*	235.10	242.68	--	--	--	--	--	174.47	219.16	208.75
120	297.55	282.29	--	--	--	170.38	135.15	195.18	233.67	237.54
Mean	268.40	267.73	123.98	121.13	127.61	159.99	158.84	184.10	207.63	213.03
St. Dev.	41.03	30.43	46.25	49.78	32.62	42.77	68.68	41.06	44.05	38.94

*Minority Subjects
 (--) Velocity not obtained

Table B16. Velocity (msec) to 8 degree targets for older men during Alprazolam/DHEA Treatment

Subject	Time (h)									
	0	2	3.5	4.5	5.5	7	8.5	10	11.5	12.5
50	252.95	257.76	--	--	--	--	198.92	194.86	141.36	198.42
51	256.48	268.65	--	--	--	--	197.07	216.87	240.38	191.56
52	245.77	218.25	--	--	130.25	65.91	65.64	113.30	141.48	62.61
53	251.86	160.68	242.53	157.09	125.68	150.77	178.14	212.98	162.38	206.81
54	148.52	214.05	76.34	70.94	80.05	111.92	118.34	164.83	182.79	199.07
55	252.02	235.71	157.05	190.71	211.27	187.47	196.04	204.67	208.07	216.75
56	314.67	330.29	164.55	198.55	167.79	189.35	122.28	167.87	207.67	237.05
57	341.24	325.23	170.72	162.37	221.69	247.90	253.54	281.62	321.46	295.31
58	235.61	245.13	150.55	130.01	185.56	166.84	202.09	224.92	231.46	212.75
59	260.37	252.15	--	167.51	117.40	214.95	224.98	245.90	218.86	167.88
61*	287.85	270.63	188.93	233.67	--	175.98	208.64	236.78	282.57	314.55
149	293.23	282.48	--	99.54	122.07	176.01	149.96	217.43	230.08	230.97
160	276.52	245.64	--	--	--	--	96.61	122.24	83.57	76.28
Mean	262.85	254.36	164.38	156.71	151.31	168.71	170.17	200.33	204.01	200.77
St. Dev.	45.69	44.98	49.58	50.39	47.67	51.00	55.12	47.77	62.91	70.89

*Minority Subjects

(--) Velocity not obtained

Table B17. Velocity (msec) to 16 degree targets for young women during Placebo Treatment

Subject	Time (h)									
	0	2	3.5	4.5	5.5	7	8.5	10	11.5	12.5
1	564.74	526.62	555.22	583.40	590.82	552.95	517.08	541.34	574.42	569.38
3	391.14	396.01	428.17	426.39	425.33	403.64	396.87	406.08	376.34	370.96
4	418.67	402.42	370.41	407.54	349.79	403.53	412.92	371.35	404.60	410.71
5	342.22	395.14	378.52	337.55	367.14	335.17	361.78	352.93	325.05	368.81
7	330.53	343.53	329.41	319.82	325.66	356.52	324.12	335.26	322.59	321.63
8	361.85	365.44	409.39	392.53	368.94	362.45	356.26	387.17	393.57	376.71
9	429.42	405.26	413.49	441.40	452.55	408.66	423.07	422.50	426.70	446.80
10	403.41	415.94	406.82	363.94	369.51	380.59	366.34	367.79	365.81	344.92
12	373.05	381.11	345.04	368.54	370.33	382.48	409.81	414.73	399.03	346.33
14*	421.56	415.57	416.22	458.67	445.65	402.29	450.81	344.40	431.52	463.50
15*	303.94	320.82	318.14	338.06	413.55	315.06	336.36	323.91	352.21	337.61
16*	385.69	385.77	411.16	371.43	380.70	395.43	401.81	383.73	377.75	388.06
102	329.97	359.32	351.22	346.27	340.89	459.39	320.55	337.56	341.27	351.12
111	440.85	490.80	374.00	358.94	345.87	379.86	396.91	352.91	381.41	373.04
112	450.96	422.14	433.84	422.93	440.47	453.35	439.81	455.11	451.18	477.54
114*	360.61	397.96	416.29	386.73	398.75	395.79	446.71	398.45	423.41	409.71
206	441.05	441.19	435.14	450.35	411.18	429.51	453.45	396.44	434.75	442.59
213*	419.79	429.02	460.97	396.59	435.11	433.27	414.59	426.45	454.99	420.91
Mean	398.30	405.23	402.97	398.39	401.79	402.77	401.63	389.90	402.03	401.13
St. Dev.	60.11	48.66	54.71	61.67	61.22	52.89	51.18	52.21	59.13	61.80

*Minority Subjects

Table B18. Velocity (msec) to 16 degree targets for young men during Placebo Treatment

Subject	Time (h)									
	0	2	3.5	4.5	5.5	7	8.5	10	11.5	12.5
33	467.18	429.00	458.17	439.66	417.10	415.09	398.74	442.53	419.14	427.26
34	323.68	307.87	479.91	417.81	456.49	438.37	435.22	464.15	437.24	427.26
35	506.04	459.38	447.08	440.71	462.39	446.47	463.85	436.56	419.12	434.89
36	449.68	436.08	430.80	429.90	395.14	412.36	456.02	446.76	453.78	428.47
37	408.61	403.53	381.05	419.01	449.16	434.91	393.11	404.51	412.77	437.34
38	424.18	420.89	428.13	431.13	408.35	418.62	415.06	421.17	434.29	420.41
39	475.97	435.19	385.53	462.59	430.73	420.31	391.62	435.25	466.87	421.39
41	492.13	440.33	465.37	422.52	434.76	439.56	446.74	435.09	461.67	417.14
42	363.64	357.47	364.54	355.95	346.79	354.54	418.61	434.58	487.26	408.94
43	446.98	438.38	431.99	445.91	382.49	389.13	444.29	425.84	436.66	442.59
44	347.07	323.75	370.25	380.40	376.69	389.34	391.43	396.50	387.99	395.76
47*	487.48	462.06	418.40	444.03	431.85	419.50	414.83	431.62	453.00	443.38
48*	381.11	392.74	437.89	335.05	394.48	388.86	403.50	392.98	317.88	323.87
140	347.24	342.67	306.90	330.03	350.81	339.10	353.58	349.29	360.04	346.37
146*	368.37	338.76	365.63	341.05	385.54	375.99	382.24	383.74	341.45	365.48
245*	341.69	321.52	332.81	334.50	356.37	342.62	369.95	355.11	352.76	334.61
Mean	414.44	394.35	406.53	401.89	404.95	401.55	411.17	415.98	415.12	404.70
St. Dev.	61.73	53.64	49.79	47.18	37.33	34.54	31.60	32.74	49.58	39.71

*Minority Subjects

Table B19. Velocity (msec) to 16 degree targets for older women during Placebo Treatment

Subject	Time (h)									
	0	2	3.5	4.5	5.5	7	8.5	10	11.5	12.5
17	420.69	396.43	324.81	356.90	359.46	396.24	380.36	357.29	381.01	370.86
18	458.85	426.94	458.27	449.55	430.33	386.83	369.34	399.20	406.01	438.69
19	385.00	480.24	335.61	391.66	347.84	365.82	343.07	346.46	367.90	383.93
20*	345.78	400.55	305.89	382.30	453.02	395.57	431.79	391.18	407.25	360.58
21	423.61	411.94	364.93	352.21	316.33	369.45	355.11	353.97	348.15	329.47
22	398.94	372.65	352.43	372.86	331.91	355.88	382.79	370.30	340.68	361.29
23	405.13	388.68	398.54	402.08	364.03	339.26	331.09	342.73	335.16	355.30
24	435.61	500.93	396.59	627.76	212.18	405.27	379.86	362.75	377.04	424.99
25	388.73	346.11	368.62	444.27	425.35	405.13	429.40	444.15	430.87	410.33
26	283.34	245.60	255.04	346.52	251.36	277.69	317.16	273.14	274.24	289.27
27	364.67	510.45	411.09	435.90	344.43	365.66	394.91	358.64	376.74	376.95
28	502.24	374.55	402.31	361.74	372.09	361.86	381.15	394.75	382.97	403.27
29*	314.97	438.68	361.80	313.26	--	384.78	422.91	314.79	353.66	524.23
30*	286.67	280.35	318.11	316.68	313.46	457.62	320.81	343.34	296.86	294.52
31*	--	297.29	302.16	386.30	354.47	406.46	314.51	--	344.63	264.48
120	423.30	413.30	377.24	395.20	373.24	377.82	438.56	399.09	372.10	420.37
Mean	389.17	392.79	358.34	395.95	349.97	378.21	374.55	363.45	362.20	375.53
St. Dev.	61.65	74.69	50.45	73.75	63.04	38.37	41.94	40.23	39.83	64.25

*Minority Subjects
 (--) Velocity not obtained

Table B20. Velocity (msec) to 16 degree targets for older men during Placebo Treatment

Subject	Time (h)									
	0	2	3.5	4.5	5.5	7	8.5	10	11.5	12.5
50	386.65	390.02	338.18	350.36	383.50	343.22	336.28	--	394.22	464.05
51	378.87	358.28	362.86	362.65	342.66	361.84	351.34	355.71	366.99	379.87
52	353.95	389.07	403.82	414.81	361.66	341.25	274.79	337.24	403.15	323.80
53	390.60	336.47	347.17	322.04	350.16	348.07	331.29	356.16	338.87	305.52
54	260.29	308.72	238.79	246.74	261.96	267.21	199.96	309.15	285.23	332.16
55	292.99	332.49	319.86	325.84	323.58	306.24	313.53	303.82	310.66	338.11
56	472.24	419.81	470.82	487.48	485.50	451.92	437.39	434.13	423.14	503.81
57	465.02	504.79	456.36	473.28	447.41	455.65	455.88	449.63	467.01	448.93
58	331.69	334.56	312.97	310.14	303.87	290.82	305.26	300.10	311.97	312.91
59	498.12	335.72	398.31	303.02	385.38	351.55	372.72	390.69	420.43	370.80
61*	--	445.46	444.81	392.41	448.41	411.36	432.08	438.50	458.53	464.41
149	458.46	422.47	412.60	449.14	425.09	405.53	425.62	438.01	435.08	428.22
160	378.03	350.00	344.61	339.65	304.80	310.96	281.50	363.81	369.34	365.38
Mean	388.91	379.07	373.17	367.50	371.08	357.36	347.51	373.08	383.43	387.54
St. Dev.	73.84	56.31	65.87	71.90	66.20	58.99	75.54	56.05	58.63	66.71

*Minority Subjects
 (--) Velocity not obtained

Table B21. Velocity (msec) to 16 degree targets for young women during DHEA Treatment

Subject	Time (h)									
	0	2	3.5	4.5	5.5	7	8.5	10	11.5	12.5
1	516.48	491.57	531.85	465.94	528.71	511.91	555.47	544.45	495.57	510.63
3	347.43	361.09	386.59	411.06	394.63	389.73	428.15	387.36	400.76	422.84
4	407.88	396.88	370.72	391.03	379.08	387.27	366.14	356.44	395.33	371.73
5	392.23	332.37	371.16	370.23	352.17	363.74	432.62	339.47	424.49	357.93
7	356.77	333.84	344.69	320.03	354.46	354.64	338.66	353.75	358.94	329.82
8	395.50	386.53	385.88	403.94	380.94	384.95	380.02	375.71	408.59	400.37
9	435.09	414.83	422.23	414.39	413.65	400.83	405.67	428.90	428.36	432.18
10	427.77	423.72	401.75	359.04	381.67	407.94	384.98	393.49	385.60	405.26
12	373.82	371.63	385.06	387.37	354.69	409.36	410.25	364.30	397.39	397.73
14*	398.05	385.99	407.76	516.27	518.21	370.91	380.94	382.08	388.08	375.80
15*	333.28	348.46	341.16	326.19	339.77	318.41	347.38	352.80	344.53	328.78
16*	425.36	423.58	389.59	381.53	404.73	388.52	370.10	367.15	443.72	375.23
102	343.81	301.87	318.71	274.57	450.28	385.89	356.67	312.42	308.02	347.15
111	362.80	392.24	351.76	348.55	361.02	365.60	347.64	362.17	368.46	356.56
112	486.17	456.13	495.41	498.42	446.63	478.44	476.14	490.95	484.36	438.73
114*	364.51	359.90	369.69	379.25	418.65	363.27	373.66	391.80	398.82	404.35
206	429.22	427.86	421.81	425.10	--	423.40	408.96	432.88	434.37	430.83
213*	--	--	392.79	383.86	--	434.54	413.40	458.45	432.99	422.95
Mean	399.77	388.73	393.81	392.04	404.96	396.63	398.71	394.14	405.47	394.94
St. Dev.	50.13	48.16	51.82	60.12	56.65	45.11	52.62	57.61	46.00	45.25

*Minority Subjects

(--) Velocity not obtained

Table B22. Velocity (msec) to 16 degree targets for young men during DHEA Treatment

Subject	Time (h)									
	0	2	3.5	4.5	5.5	7	8.5	10	11.5	12.5
33	426.10	398.95	408.72	444.57	416.53	425.06	401.15	434.09	416.17	421.95
34	465.46	466.42	455.71	442.78	442.69	423.74	440.00	455.71	418.99	373.66
35	327.40	466.78	436.92	454.74	460.74	447.67	417.27	424.95	388.36	435.37
36	421.55	404.73	403.85	421.47	394.38	441.44	422.09	416.54	432.75	448.61
37	424.69	424.84	393.08	405.94	396.45	399.09	383.90	389.88	411.04	388.61
38	447.32	435.92	372.11	418.60	449.14	438.55	426.21	422.77	441.99	436.01
39	478.07	387.75	438.86	422.24	408.63	420.08	352.15	395.02	457.73	484.41
41	472.02	430.03	439.70	425.09	448.94	476.72	443.25	482.26	444.47	470.15
42	443.39	475.58	371.24	452.84	419.34	374.22	418.91	400.02	416.99	421.94
43	450.78	432.69	420.83	417.66	450.72	424.89	447.27	453.58	466.34	442.02
44	386.54	375.83	376.21	385.06	375.49	384.56	388.96	400.35	395.08	377.96
47*	449.30	432.99	432.27	449.96	442.73	449.98	451.72	467.07	428.02	453.61
48*	424.34	452.87	380.65	495.61	429.06	463.77	474.00	447.59	385.63	453.95
140	307.46	343.04	338.62	345.82	326.78	320.77	355.94	335.52	346.96	321.68
146*	354.28	367.78	366.92	419.13	373.45	316.03	375.39	336.60	329.44	349.18
245*	374.57	353.63	358.54	367.07	316.46	342.76	325.27	354.21	337.70	354.79
Mean	415.83	415.61	399.64	423.04	409.47	409.33	407.72	413.51	407.35	414.62
St. Dev.	51.50	41.34	34.92	36.18	43.62	49.16	41.26	44.39	41.26	47.69

*Minority Subjects

Table B23. Velocity (msec) to 16 degree targets for older women during DHEA Treatment

Subject	Time (h)									
	0	2	3.5	4.5	5.5	7	8.5	10	11.5	12.5
17	386.42	368.12	353.62	286.69	285.89	367.45	406.35	343.36	374.54	386.66
18	438.26	575.51	457.09	474.77	477.81	409.82	444.31	445.41	401.29	396.75
19	313.37	382.92	319.08	349.78	350.54	346.32	319.43	435.89	327.69	371.01
20*	408.14	324.20	425.22	410.77	349.73	382.08	389.60	468.30	384.44	339.61
21	388.12	374.78	351.05	341.22	355.91	381.31	372.09	396.86	349.14	350.23
22	427.90	384.74	399.62	372.99	396.27	389.88	376.67	386.31	382.16	378.36
23	411.65	445.53	386.91	419.75	392.08	344.60	376.53	407.51	374.93	326.96
24	443.09	379.96	419.12	447.15	377.92	416.61	560.33	353.20	646.88	432.35
25	411.92	386.08	438.56	442.11	378.71	389.16	375.27	396.21	360.93	401.17
26	273.56	277.30	273.72	308.69	247.33	254.05	260.61	259.88	336.72	253.46
27	--	476.03	498.32	343.76	488.73	328.89	347.63	329.56	315.47	286.62
28	426.60	416.25	433.14	375.40	389.31	388.29	408.72	369.11	399.01	388.30
29*	374.04	372.37	317.90	366.40	449.28	356.21	436.05	342.36	343.81	389.50
30*	314.05	318.03	465.89	329.83	324.57	334.25	273.29	338.61	312.58	311.13
31*	--	--	--	284.61	--	--	--	401.75	--	218.17
120	377.63	353.37	386.83	442.10	398.25	348.56	378.41	398.77	394.63	379.91
Mean	385.34	389.01	395.07	374.75	377.49	362.50	381.69	379.57	380.28	350.64
St. Dev.	51.53	70.88	62.46	59.26	64.82	40.14	71.63	51.41	79.41	58.28

*Minority Subjects
 (--) Velocity not obtained

Table B24. Velocity (msec) to 16 degree targets for older men during DHEA Treatment

Subject	Time (h)									
	0	2	3.5	4.5	5.5	7	8.5	10	11.5	12.5
50	367.74	389.86	390.32	409.98	412.40	473.70	380.29	399.24	337.45	369.20
51	369.69	365.92	350.15	335.72	361.11	322.77	388.66	371.34	389.13	454.40
52	435.89	353.37	441.26	382.44	372.81	343.54	293.34	392.19	367.29	366.69
53	358.12	367.02	351.00	356.17	354.53	363.00	358.89	444.09	339.67	294.41
54	211.94	248.04	253.72	233.84	230.47	254.73	202.19	239.93	274.87	234.09
55	322.61	360.35	322.25	322.94	315.59	306.97	315.46	330.37	362.29	329.20
56	442.57	439.98	397.47	387.32	418.55	418.06	421.76	477.57	412.29	403.33
57	452.96	491.20	473.39	468.58	483.55	440.95	473.20	455.12	534.15	494.83
58	315.54	326.12	310.87	311.41	346.59	312.57	320.90	312.97	311.18	309.80
59	343.88	390.60	440.59	443.39	350.34	356.44	385.45	337.88	345.77	375.17
61*	407.13	414.81	389.30	433.76	452.59	420.37	448.10	488.83	443.81	422.42
149	416.50	436.88	416.58	429.21	375.66	450.39	419.32	398.65	401.69	392.14
160	340.94	292.00	275.37	405.66	347.60	286.14	345.09	329.98	314.93	317.81
Mean	368.12	375.09	370.17	378.49	370.91	365.36	365.59	382.94	371.89	366.42
St. Dev.	65.73	64.44	66.75	64.95	63.30	69.26	72.15	72.34	66.88	70.19

*Minority Subjects

Table B25. Velocity (msec) to 16 degree targets for young women during Alprazolam/Placebo Treatment

Subject	Time (h)									
	0	2	3.5	4.5	5.5	7	8.5	10	11.5	12.5
1	511.62	500.37	322.35	245.59	307.12	284.35	290.55	385.11	311.26	439.45
3	372.08	378.89	308.19	271.04	252.07	323.84	323.67	329.88	387.41	399.32
4	401.77	380.11	313.27	170.33	271.74	273.19	357.07	352.83	376.62	357.25
5	315.63	348.74	178.08	219.76	204.34	191.15	338.82	336.26	384.55	360.09
7	311.93	337.66	200.71	224.04	230.11	246.60	274.94	290.27	307.46	275.76
8	338.29	403.36	278.33	255.43	170.29	314.27	272.05	312.40	315.48	327.05
9	391.09	392.61	381.43	266.47	256.08	378.84	381.56	362.12	361.39	338.83
10	377.32	376.64	364.28	315.08	309.02	361.22	345.93	337.63	360.96	337.31
11	431.68	409.98	286.51	234.71	265.54	286.10	357.59	401.97	415.63	396.81
12	400.00	385.55	357.06	238.33	264.63	261.71	217.85	352.93	355.20	352.93
14*	431.22	464.92	352.66	219.85	236.73	272.27	282.94	334.41	353.46	435.85
15*	336.54	333.99	180.06	156.80	196.68	254.83	248.04	287.52	291.13	290.30
16*	367.74	388.06	307.65	305.27	342.60	361.50	309.36	355.34	318.95	355.55
102	292.87	337.46	266.48	203.81	205.18	233.30	299.28	324.69	307.22	320.28
111	352.37	344.17	292.44	186.56	165.93	233.58	313.31	309.84	313.42	331.06
112	482.40	456.48	299.15	316.47	306.71	300.49	334.75	374.07	403.14	427.77
114*	324.92	363.94	255.33	254.28	225.49	280.55	293.47	302.98	308.02	306.01
206	454.42	426.80	287.25	197.57	158.57	301.68	230.46	310.18	338.77	360.77
213*	384.06	394.17	300.74	284.64	312.60	333.95	332.46	348.55	408.28	366.51
Mean	383.05	390.73	291.16	240.32	246.39	289.13	305.48	337.31	348.33	356.78
St. Dev.	59.39	45.77	57.35	46.38	54.30	48.76	44.39	31.25	39.48	46.44

*Minority Subjects

Table B26. Velocity (msec) to 16 degree targets for young men during Alprazolam/Placebo Treatment

Subject	Time (h)									
	0	2	3.5	4.5	5.5	7	8.5	10	11.5	12.5
33	410.34	437.39	242.10	291.40	318.15	373.87	315.41	411.57	432.33	448.76
34	457.12	443.39	102.93	219.96	316.16	363.81	423.56	408.58	446.49	425.41
35	392.37	439.94	--	332.64	374.50	369.91	419.68	424.96	438.32	425.96
36	429.75	423.72	363.48	327.28	355.35	380.22	424.16	405.51	368.70	410.61
37	393.49	367.84	326.88	286.59	317.05	368.35	387.38	399.28	422.77	434.63
38	442.16	455.88	241.86	149.94	253.62	293.74	364.02	391.50	360.34	393.46
39	449.78	504.05	238.68	216.40	227.08	253.37	271.28	443.29	448.01	460.85
41	472.34	436.29	402.27	404.63	439.72	403.08	380.91	390.97	456.40	446.77
42	--	372.65	202.23	209.49	208.53	272.14	315.58	337.07	330.11	370.33
43	433.22	414.66	257.49	278.33	306.28	302.17	360.22	376.38	389.80	403.16
44	399.22	366.43	311.30	203.18	182.74	304.94	--	337.10	391.39	389.94
47*	423.23	407.08	314.98	322.05	294.15	329.76	400.24	429.68	372.49	345.86
48*	435.34	296.82	276.09	--	163.68	418.95	321.72	330.09	287.90	328.55
140	323.46	364.17	111.46	352.65	211.08	237.67	226.02	323.57	334.71	333.55
146*	399.76	350.44	236.27	253.05	191.90	243.03	286.42	320.69	318.93	335.45
245*	326.56	331.60	--	--	--	230.25	280.57	274.51	303.09	302.51
Mean	412.54	400.77	259.14	274.83	277.33	321.58	345.14	375.30	381.36	390.99
St. Dev.	42.79	53.50	84.61	69.92	79.80	62.58	62.22	48.48	55.55	49.50

*Minority Subjects
 (--) Velocity not obtained

Table B27. Velocity (msec) to 16 degree targets for older women during Alprazolam/Placebo Treatment

Subject	Time (h)									
	0	2	3.5	4.5	5.5	7	8.5	10	11.5	12.5
17	406.86	351.30	198.87	150.89	147.28	214.56	315.52	184.86	248.45	216.81
18	467.52	412.65	154.01	150.48	196.52	209.02	244.54	335.76	328.79	308.35
19	383.42	379.82	--	--	173.78	--	182.54	187.09	240.00	279.12
20*	479.89	394.19	403.65	230.32	202.57	167.54	197.72	227.41	384.47	294.81
21	377.22	344.49	--	170.26	198.42	266.58	270.19	305.72	334.26	305.53
22	357.93	380.47	208.52	132.47	123.95	199.80	177.67	232.35	273.41	297.98
23	--	362.39	--	193.06	212.09	303.50	312.06	358.33	380.40	263.62
24	559.64	404.70	239.22	284.94	228.13	327.54	337.73	361.92	366.57	417.92
25	421.82	440.33	249.56	160.18	161.92	262.84	308.65	291.20	283.33	351.01
26	300.23	296.64	--	--	200.45	174.96	122.89	159.59	189.53	197.24
27	404.66	417.88	--	--	--	--	--	--	297.36	300.32
28	494.40	376.16	--	190.09	195.33	--	--	278.83	307.29	292.43
29*	299.54	437.05	--	205.44	224.67	261.13	308.24	351.68	334.04	194.18
30*	291.68	355.96	--	--	320.84	180.86	394.27	298.80	422.78	380.52
31*	298.70	302.84	--	--	--	--	--	--	315.94	256.91
120	385.98	379.79	--	--	--	--	304.10	282.66	369.10	306.60
Mean	395.30	377.29	242.31	186.81	198.92	233.48	267.39	275.44	317.23	291.46
St. Dev.	80.34	41.62	85.93	45.30	47.33	53.95	77.24	67.47	61.13	60.19

*Minority Subjects
 (--) Velocity not obtained

Table B28. Velocity (msec) to 16 degree targets for older men during Alprazolam/Placebo Treatment

Subject	Time (h)									
	0	2	3.5	4.5	5.5	7	8.5	10	11.5	12.5
50	405.53	357.51	171.06	182.60	251.91	292.15	263.43	312.49	310.14	383.37
51	373.61	338.90	180.26	179.73	205.72	298.04	257.88	329.18	316.25	333.06
52	366.49	309.12	--	--	--	--	252.94	209.87	253.47	272.21
53	366.21	346.65	237.61	261.31	244.18	185.09	275.70	309.54	324.78	321.65
54	300.91	254.16	155.76	197.03	178.94	124.00	159.23	264.32	184.03	239.37
55	368.34	272.34	272.34	192.60	250.25	263.07	272.24	281.24	309.85	317.76
56	558.07	458.71	--	221.61	230.25	327.20	282.45	321.67	439.40	370.95
57	467.67	451.41	238.98	292.43	228.74	336.14	382.33	381.83	448.05	456.62
58	328.43	328.43	219.19	232.55	229.59	263.50	298.81	260.88	316.58	307.91
59	348.36	355.49	--	181.91	212.18	360.74	290.86	408.02	303.89	315.48
61*	472.68	502.02	166.14	275.92	337.29	337.93	446.97	442.88	412.06	418.55
149	444.36	--	174.12	153.34	141.39	226.87	308.14	363.46	330.93	329.97
160	354.27	369.43	--	--	--	205.58	223.80	178.70	237.14	246.36
Mean	396.53	362.01	201.72	215.55	228.22	268.36	285.75	312.62	322.04	331.79
St. Dev.	70.92	74.73	41.09	44.96	48.92	71.58	69.83	75.44	76.09	63.14

*Minority Subjects
 (--) Velocity not obtained

Table B29. Velocity (msec) to 16 degree targets for young women during Alprazolam/DHEA Treatment

Subject	Time (h)									
	0	2	3.5	4.5	5.5	7	8.5	10	11.5	12.5
1	553.13	503.97	255.50	311.72	368.50	292.56	411.24	387.99	507.29	502.27
3	435.82	412.56	282.71	193.75	147.10	276.74	317.47	359.60	414.44	400.62
4	394.70	379.53	273.42	258.80	225.28	237.82	325.80	336.48	339.64	307.24
5	369.80	356.99	194.63	215.76	208.78	275.51	325.41	330.73	361.33	339.49
7	341.37	327.96	227.10	219.02	269.66	245.71	268.27	281.96	299.33	281.79
8	290.46	362.56	274.41	280.06	286.75	279.84	281.28	345.22	324.49	353.70
9	451.64	417.53	367.20	370.03	326.02	360.66	373.94	348.36	364.78	378.95
10	365.70	389.13	363.89	270.03	243.78	319.25	343.50	372.82	379.77	383.63
11	469.50	433.95	265.46	292.13	312.69	409.31	413.76	369.70	390.52	472.62
12	363.29	335.81	247.29	183.69	251.74	279.28	326.81	328.33	356.86	358.16
14*	422.88	436.26	418.05	424.37	506.58	419.86	420.17	451.86	517.97	391.15
15*	330.99	324.00	198.67	150.01	176.00	174.14	258.73	292.92	301.08	274.97
16*	370.86	418.49	318.83	362.40	325.40	346.97	340.52	353.99	389.71	380.92
102	347.19	333.13	280.10	247.34	285.02	247.99	290.58	287.87	294.83	294.86
111	342.43	346.67	190.48	207.09	198.65	238.33	245.59	293.66	337.24	315.75
112	421.82	437.52	327.78	341.77	307.73	397.73	401.15	409.26	422.88	415.66
114*	388.55	387.61	338.75	227.85	299.75	299.51	327.32	355.99	337.07	310.87
206	447.75	432.58	320.92	-	220.28	367.28	229.74	322.38	333.26	373.94
213*	369.75	417.52	160.98	334.01	337.94	364.87	340.52	351.90	373.79	353.11
Mean	393.56	392.30	279.27	271.66	278.82	307.02	328.52	346.37	370.86	362.62
St. Dev.	60.73	48.35	68.09	74.15	80.94	67.13	57.40	42.73	61.73	60.24

*Minority Subjects
 (-) Velocity not obtained

Table B30. Velocity (msec) to 16 degree targets for young men during Alprazolam/DHEA Treatment

Subject	Time (h)									
	0	2	3.5	4.5	5.5	7	8.5	10	11.5	12.5
33	455.05	458.28	265.15	244.48	249.76	410.90	346.67	427.21	416.08	420.18
34	523.94	535.61	218.08	317.40	386.83	358.41	420.47	371.42	395.38	402.59
35	422.22	431.48	365.35	328.94	384.29	383.85	441.50	368.40	448.36	430.15
36	383.05	420.40	370.25	336.31	344.76	352.36	397.64	364.76	405.67	375.88
37	395.92	385.45	304.50	317.53	332.53	377.90	372.27	394.11	408.09	408.12
38	427.13	416.30	174.65	143.99	236.82	378.67	407.69	382.10	454.45	409.77
39	459.30	472.45	191.71	247.69	212.74	205.44	430.39	366.84	403.76	443.70
41	--	445.91	323.44	380.69	360.86	380.26	416.98	419.51	422.87	447.06
42	389.70	403.61	307.35	258.83	252.79	273.61	379.48	374.77	374.89	433.43
43	418.64	449.76	260.69	294.09	333.10	362.28	347.60	374.28	414.47	415.15
44	408.21	389.31	309.53	324.09	334.02	341.52	322.43	383.74	387.35	362.00
47*	426.80	380.24	240.31	279.88	297.54	315.98	350.84	364.51	408.53	361.11
48*	319.51	306.45	261.14	209.96	94.22	244.81	242.82	302.87	271.09	270.70
140	347.48	350.23	241.32	183.78	165.37	275.86	250.25	308.19	331.40	326.68
146*	362.45	358.62	326.82	285.90	282.09	337.30	377.67	399.24	350.00	373.06
245*	356.17	368.67	--	--	--	257.30	267.16	287.31	308.35	302.61
Mean	406.37	410.80	277.35	276.90	284.51	328.53	360.74	368.08	387.55	386.39
St. Dev.	51.16	55.42	58.78	63.22	83.33	59.72	62.85	38.91	49.69	51.53

*Minority Subjects

(--) Velocity not obtained

Table B31. Velocity (msec) to 16 degree targets for older women during Alprazolam/DHEA Treatment

Subject	Time (h)									
	0	2	3.5	4.5	5.5	7	8.5	10	11.5	12.5
17	345.11	408.41	--	--	--	--	324.13	360.36	399.73	425.17
18	425.05	445.59	227.28	165.59	205.15	251.16	231.67	305.04	321.27	342.57
19	364.76	338.11	--	--	--	--	245.91	348.50	321.65	321.88
20*	413.66	329.89	149.17	181.13	119.02	158.85	201.50	262.13	265.17	217.42
21	345.33	365.80	133.71	167.88	247.96	221.48	325.78	270.95	250.01	286.41
22	365.51	336.41	104.36	108.40	128.23	213.95	226.70	253.94	286.87	329.59
23	457.61	398.83	--	185.90	270.20	259.99	315.00	298.88	375.77	346.42
24	443.01	430.47	209.98	291.69	229.58	339.20	363.72	369.46	360.51	331.78
25	758.66	489.64	240.22	119.72	191.07	240.43	229.07	288.26	290.98	229.07
26	247.99	303.93	--	--	--	78.48	162.09	169.24	176.47	225.55
27	442.05	466.03	--	--	--	--	--	264.00	326.97	321.33
28	367.73	408.18	210.87	--	234.51	--	313.42	293.07	--	267.74
29*	446.58	491.21	--	--	--	--	--	--	415.97	348.96
30*	329.32	351.50	--	155.79	250.83	326.53	136.66	270.22	253.84	231.80
31*	393.98	302.91	--	--	--	--	--	190.92	331.31	426.74
120	410.43	421.01	--	--	--	251.68	274.95	326.35	348.38	334.11
Mean	409.80	393.00	182.23	172.01	208.51	234.18	257.74	284.75	314.99	311.66
St. Dev.	107.93	62.44	52.43	55.68	53.67	75.53	68.63	55.95	63.11	64.90

*Minority Subjects
 (--) Velocity not obtained

Table B32. Velocity (msec) to 16 degree targets for older men during Alprazolam/DHEA Treatment

Subject	Time (h)									
	0	2	3.5	4.5	5.5	7	8.5	10	11.5	12.5
50	365.52	371.15	--	--	--	--	301.29	347.00	219.18	317.04
51	345.03	336.64	--	--	--	--	272.06	320.83	323.02	275.13
52	389.45	332.38	--	--	213.29	143.66	172.79	159.76	202.04	136.70
53	356.11	209.07	339.80	236.03	241.11	197.08	239.80	255.83	279.56	277.79
54	224.61	273.31	85.08	139.33	109.73	147.73	156.03	231.21	219.05	251.35
55	323.80	321.15	217.67	308.53	275.16	257.22	264.09	293.79	298.69	297.03
56	560.25	401.09	278.23	291.95	230.87	276.48	334.76	250.22	303.45	429.20
57	466.54	451.60	250.20	298.47	315.10	344.30	325.64	382.36	417.04	503.82
58	326.57	324.26	170.80	182.76	263.53	257.50	273.75	299.27	309.68	301.37
59	352.43	390.32	--	141.94	204.45	364.26	372.17	334.44	347.23	252.25
61*	439.00	503.40	216.20	320.16	--	351.03	340.59	408.84	411.45	415.60
149	403.22	416.02	--	341.31	232.66	314.85	229.61	313.44	358.08	391.82
160	306.76	380.13	--	--	--	--	128.12	172.56	302.00	143.81
Mean	373.79	362.35	222.57	251.16	231.77	265.41	262.36	289.97	306.96	307.15
St. Dev.	82.60	76.13	80.88	78.60	56.91	81.21	75.33	74.41	67.60	106.65

*Minority Subjects
 (--) Velocity not obtained

APPENDIX C

Saccadic Eye Movement Parameters

Latency: 8 degree & 16 degree

Table C1. Latency (msec) to 8 degree targets for young women during Placebo Treatment

Subject	Time (h)									
	0	2	3.5	4.5	5.5	7	8.5	10	11.5	12.5
1	141	149	143	148	129	145	144	152	147	148
3	180	168	144	163	164	218	238	206	210	227
4	208	212	210	215	221	201	223	213	201	199
5	148	144	145	141	142	140	159	145	158	151
7	142	167	135	152	156	126	130	140	136	149
8	126	144	135	142	155	134	142	141	175	163
9	181	181	179	173	173	183	178	174	189	184
10	295	327	290	261	270	252	323	236	265	270
12	188	310	168	171	178	174	173	167	163	155
14*	156	159	149	149	165	149	158	153	154	165
15*	159	160	189	150	162	156	163	151	157	163
16*	162	171	164	173	165	157	150	156	169	158
102	143	146	153	147	173	140	150	167	161	158
111	185	210	198	223	196	203	173	179	172	168
112	128	125	127	128	134	124	131	131	134	139
114*	247	160	195	165	153	143	146	147	155	155
206	178	166	168	157	160	164	183	159	170	189
213*	144	143	147	153	150	149	150	162	156	163
Mean	172.83	180.11	168.83	167.28	169.22	164.33	173	165.50	170.67	172.44
St. Dev.	42.90	54.97	38.70	33.52	32.96	34.70	47.03	27.68	30.75	32.27

*Minority Subjects

Table C2. Latency (msec) to 8 degree targets for young men during Placebo Treatment

Subject	Time (h)									
	0	2	3.5	4.5	5.5	7	8.5	10	11.5	12.5
33	162	186	170	167	163	147	174	162	157	162
34	157	166	160	165	151	161	154	157	162	165
35	133	132	143	126	126	130	124	134	125	124
36	139	134	137	131	127	132	135	139	132	131
37	216	214	229	246	227	226	233	229	251	238
38	157	157	152	156	153	154	155	154	151	143
39	169	157	147	146	160	175	165	164	162	169
41	172	165	166	154	165	177	174	169	172	166
42	152	168	152	157	150	157	171	155	147	163
43	169	158	173	185	198	189	194	177	171	178
44	136	144	135	133	127	141	126	124	123	124
47*	143	150	162	152	155	154	150	147	153	152
48*	161	192	150	161	220	146	152	149	149	144
140	117	130	120	109	112	121	117	138	116	116
146*	131	137	129	138	136	133	136	127	129	128
245*	146	158	156	148	164	157	148	155	162	164
Mean	153.75	159.25	155.06	154.63	158.38	156.25	156.75	155	153.88	154.19
St. Dev.	22.84	23.10	24.63	30.45	32.67	26.12	29.13	24.66	31.26	29.48

*Minority Subjects

Table C3. Latency (msec) to 8 degree targets for older women during Placebo Treatment

Subject	Time (h)									
	0	2	3.5	4.5	5.5	7	8.5	10	11.5	12.5
17	185	215	250	207	218	207	181	223	194	188
18	197	172	179	211	184	191	228	210	220	193
19	176	170	185	186	170	166	170	158	171	160
20*	497	499	547	558	592	546	537	582	553	530
21	193	184	212	178	191	200	194	194	190	194
22	160	186	193	191	211	199	184	199	195	171
23	232	254	241	247	234	236	246	233	243	237
24	228	176	178	164	320	176	186	179	186	170
25	228	227	225	227	223	227	227	228	217	226
26	169	184	182	173	158	180	167	166	181	181
27	195	191	209	193	194	209	212	204	198	209
28	199	176	180	179	184	171	180	184	172	185
29*	164	181	181	176	--	193	171	185	166	176
30*	172	190	188	177	165	172	176	179	175	175
31*	--	171	208	223	246	195	175	--	173	201
120	195	200	219	194	196	203	202	191	200	209
Mean	212.67	211	223.56	217.75	232.40	216.94	214.75	221	214.63	212.81
St. Dev.	81.92	80.11	89.22	93.52	107.27	89.89	89.12	102.20	92.59	87.12

*Minority Subjects
 (--) Latency not obtained

Table C4. Latency (msec) to 8 degree targets for older men during Placebo Treatment

Subject	Time (h)									
	0	2	3.5	4.5	5.5	7	8.5	10	11.5	12.5
50	132	170	158	150	134	146	148	132	136	133
51	158	149	162	165	165	166	169	175	177	178
52	158	160	185	179	158	174	183	152	159	167
53	223	232	236	227	248	222	217	216	211	221
54	388	356	328	363	409	393	367	449	343	391
55	136	139	137	137	136	141	135	130	146	137
56	152	169	162	160	182	176	175	183	158	172
57	171	160	162	157	166	161	157	150	150	157
58	184	183	175	158	148	172	168	159	159	179
59	193	205	182	181	180	195	186	180	162	186
61*	–	138	132	134	144	152	151	134	141	154
149	147	181	170	170	185	175	172	175	174	173
160	188	214	207	203	186	205	213	189	181	197
Mean	185.83	188.92	184.31	183.38	187.77	190.62	187.77	186.46	176.69	188.08
St. Dev.	68.83	57.64	51.06	59.64	72.81	64.99	58.78	82.81	53.73	65.34

*Minority Subjects

(–) Latency not obtained

Table C5. Latency (msec) to 8 degree targets for young women during DHEA Treatment

Subject	Time (h)									
	0	2	3.5	4.5	5.5	7	8.5	10	11.5	12.5
1	159	162	166	140	164	152	148	149	155	149
3	212	203	173	156	162	169	175	156	170	177
4	199	202	201	234	220	226	201	217	198	198
5	148	139	132	150	148	150	149	138	148	159
7	131	152	147	137	141	143	163	146	176	162
8	125	141	131	129	140	136	173	180	182	173
9	177	166	169	180	193	177	176	167	170	172
10	226	242	290	347	254	199	254	245	291	233
12	169	187	214	193	196	183	173	179	158	164
14*	160	160	154	150	152	154	150	157	157	148
15*	174	189	160	164	189	157	157	153	159	162
16*	166	159	187	188	184	176	163	162	178	174
102	156	165	166	159	162	158	158	149	160	145
111	168	152	156	173	164	169	162	167	166	164
112	146	141	118	122	130	128	129	129	128	130
114*	183	175	184	170	151	157	155	165	163	159
206	167	156	155	166	--	147	160	156	168	147
213*	--	--	176	163	--	152	148	157	146	149
Mean	168.59	170.06	171.06	173.39	171.88	162.94	166.33	165.11	170.72	164.72
St. Dev.	26.21	27.14	38.21	50.51	32.63	23.39	26.73	27.52	33.70	22.87

*Minority Subjects
 (--) Latency not obtained

Table C6. Latency (msec) to 8 degree targets for young men during DHEA Treatment

Subject	Time (h)									
	0	2	3.5	4.5	5.5	7	8.5	10	11.5	12.5
33	192	181	210	195	191	180	203	175	171	178
34	157	158	154	159	157	163	154	156	151	146
35	135	135	133	123	127	131	136	139	167	135
36	137	128	124	138	136	136	137	130	121	126
37	236	242	234	234	234	230	213	220	218	229
38	156	165	146	150	151	169	169	172	157	158
39	168	176	167	157	166	162	157	162	158	158
41	152	156	164	160	161	150	156	155	154	162
42	154	178	173	178	160	168	166	163	158	155
43	176	161	158	181	169	182	188	159	160	170
44	129	120	125	134	136	132	139	151	129	130
47*	149	135	143	148	144	149	145	149	145	153
48*	188	195	162	194	176	171	173	173	173	163
140	111	139	123	110	124	114	119	121	115	122
146*	131	125	130	127	122	131	129	129	127	122
245*	160	168	145	161	175	176	157	151	163	161
Mean	158.19	160.13	155.69	159.31	158.06	159	158.81	156.56	154.19	154.25
St. Dev.	29.95	31.22	30.75	31.61	28.64	27.91	26.06	23.25	24.67	26.48

*Minority Subjects

Table C7. Latency (msec) to 8 degree targets for older women during DHEA Treatment

Subject	Time (h)									
	0	2	3.5	4.5	5.5	7	8.5	10	11.5	12.5
17	178	195	180	219	211	198	188	203	193	187
18	233	222	204	212	211	207	237	189	196	205
19	185	183	175	187	202	209	212	193	181	170
20*	625	603	593	608	639	645	612	549	586	570
21	209	192	189	193	188	173	200	178	194	179
22	179	173	197	185	188	190	213	189	177	198
23	197	193	203	200	204	206	192	189	196	211
24	232	229	208	213	212	211	207	224	230	218
25	232	218	223	210	224	215	236	225	227	230
26	163	189	164	172	172	154	178	177	179	181
27	--	207	202	220	198	206	201	211	205	222
28	181	170	166	170	163	161	166	167	163	168
29*	155	156	165	154	164	165	165	164	154	172
30*	170	182	179	166	176	168	178	161	157	168
31*	--	--	--	252	--	--	--	219	--	257
120	195	188	171	189	209	229	189	202	183	191
Mean	223.86	220	214.60	221.88	224.07	222.47	224.93	215	214.73	220.44
St. Dev.	118.23	107.80	106.23	105.89	116.32	119.09	109.26	91.37	105.04	96.65

*Minority Subjects

(--) Latency not obtained

Table C8. Latency (msec) to 8 degree targets for older men during DHEA Treatment

Subject	Time (h)									
	0	2	3.5	4.5	5.5	7	8.5	10	11.5	12.5
50	177	150	150	147	162	143	153	146	145	140
51	149	154	164	149	157	157	150	154	148	152
52	154	157	157	170	169	161	169	164	164	163
53	205	233	221	210	237	233	210	223	238	208
54	388	419	425	436	397	368	370	404	365	375
55	140	132	125	131	132	136	142	137	132	143
56	151	177	157	167	165	161	164	163	170	172
57	192	188	175	176	176	178	169	168	171	166
58	154	243	242	206	173	200	178	192	182	183
59	183	184	189	193	169	222	175	187	184	196
61*	147	156	159	150	148	148	145	159	156	145
149	189	184	174	182	182	183	191	206	182	191
160	191	200	204	197	185	190	194	189	191	172
Mean	186.15	198.23	195.54	193.38	188.62	190.77	185.38	191.69	186.77	185.08
St. Dev.	64.29	73.64	75.72	76.86	67.15	60.90	59	68.32	59.65	60.86

*Minority Subjects

Table C9. Latency (msec) to 8 degree targets for young women during Alprazolam/Placebo Treatment

Subject	Time (h)									
	0	2	3.5	4.5	5.5	7	8.5	10	11.5	12.5
1	134	139	199	200	204	162	179	152	163	167
3	212	195	287	276	253	261	238	199	171	181
4	237	239	218	292	270	225	192	218	204	214
5	139	153	175	193	183	167	168	146	146	145
7	122	118	183	238	250	210	168	148	154	159
8	132	133	208	240	322	248	225	168	168	132
9	167	175	178	193	180	185	174	179	179	177
10	247	229	215	207	223	234	230	223	208	191
11	150	149	193	241	190	181	169	162	149	150
12	176	174	177	173	173	169	172	171	170	171
14*	176	165	227	231	239	202	200	182	183	179
15*	155	151	182	189	184	154	159	153	165	154
16*	166	169	249	210	191	199	213	172	181	164
102	156	158	196	230	202	205	172	152	150	140
111	159	153	167	226	238	218	170	179	169	184
112	131	129	193	196	188	190	174	139	132	124
114*	141	145	193	189	211	172	173	171	162	157
206	162	171	232	214	227	219	215	220	192	195
213*	173	185	191	180	190	192	193	187	180	179
Mean	165	164.74	203.32	216.74	216.74	199.63	188.63	174.79	169.79	166.47
St. Dev.	34.31	31.18	29.54	31.63	38.18	29.59	24.38	25.44	19.46	22.82

*Minority Subjects

Table C10. Latency (msec) to 8 degree targets for young men during Alprazolam/Placebo Treatment

Subject	Time (h)									
	0	2	3.5	4.5	5.5	7	8.5	10	11.5	12.5
33	166	198	206	210	210	184	186	197	166	151
34	152	156	292	196	173	162	161	154	148	151
35	127	129	--	137	140	133	137	140	131	127
36	136	142	148	135	144	138	144	153	136	145
37	241	228	204	225	205	223	228	215	216	218
38	155	138	147	161	150	174	142	158	154	150
39	150	151	180	187	188	179	165	168	157	164
41	167	163	174	175	167	165	161	164	159	162
42	--	185	182	169	196	169	170	167	178	207
43	171	158	250	223	217	190	178	177	172	172
44	127	135	189	169	167	156	--	169	134	130
47*	146	146	204	245	224	183	150	192	141	159
48*	128	125	350	--	289	160	154	151	141	147
140	116	124	162	181	207	196	210	168	156	153
146*	127	129	157	162	163	136	139	137	140	143
245*	153	176	--	--	--	198	183	169	180	165
Mean	150.80	155.19	203.21	183.93	189.33	171.63	167.20	167.44	156.81	159
St. Dev.	30.16	29.17	57.99	32.72	38.66	24.53	26.31	20.45	22.06	24.12

*Minority Subjects
 (--) Latency not obtained

Table C11. Latency (msec) to 8 degree targets for older women during Alprazolam/Placebo Treatment

Subject	Time (h)									
	0	2	3.5	4.5	5.5	7	8.5	10	11.5	12.5
17	179	185	254	240	280	257	287	248	235	231
18	194	197	307	289	241	244	252	226	212	232
19	170	167	--	--	264	--	227	228	191	190
20*	530	574	600	521	312	646	630	597	602	641
21	165	180	--	231	205	209	216	207	207	222
22	180	191	302	292	333	264	242	213	209	205
23	--	195	--	276	238	250	231	239	215	218
24	167	170	258	228	210	191	189	190	174	--
25	200	192	258	242	218	257	274	230	239	284
26	157	170	--	--	304	255	247	244	218	201
27	183	183	--	--	--	--	--	--	226	223
28	163	160	--	260	247	--	--	214	203	202
29*	149	157	--	252	279	222	201	182	184	195
30*	161	162	--	--	223	188	189	180	191	183
31*	172	193	--	--	--	--	--	--	221	210
120	188	176	--	--	--	--	236	236	206	208
Mean	197.20	203.25	329.83	283.10	258	271.18	263.15	245.29	233.31	243
St. Dev.	93.13	99.74	134.43	86.64	41.20	127.29	114.11	103.61	99.89	112.67

*Minority Subjects

(--) Latency not obtained

Table C12. Latency (msec) to 8 degree targets for older men during Alprazolam/Placebo Treatment

Subject	Time (h)									
	0	2	3.5	4.5	5.5	7	8.5	10	11.5	12.5
50	132	138	223	213	185	166	168	174	168	192
51	150	149	219	244	238	210	179	178	179	168
52	167	155	--	--	--	--	206	207	167	178
53	215	225	276	217	228	218	224	207	206	230
54	430	484	553	401	487	435	553	411	418	433
55	131	161	161	168	154	153	153	145	146	145
56	144	147	--	238	224	168	185	199	177	210
57	172	172	211	201	183	178	167	183	183	167
58	145	152	176	179	182	173	165	174	166	166
59	197	199	--	372	320	205	231	199	194	222
61*	130	139	316	208	216	214	169	168	175	171
149	174	--	258	263	261	238	203	221	194	203
160	175	208	--	--	--	249	269	234	213	225
Mean	181.69	194.08	265.89	245.82	243.45	217.25	220.92	207.69	198.92	208.46
St. Dev.	79	95.60	117.92	74.99	92.59	74.92	105.05	65.59	68.22	72.55

*Minority Subjects
 (--) Latency not obtained

Table C13. Latency (msec) to 8 degree targets for young women during Alprazolam/DHEA Treatment

Subject	Time (h)									
	0	2	3.5	4.5	5.5	7	8.5	10	11.5	12.5
1	131	139	196	189	154	153	155	157	184	181
3	199	177	306	270	265	285	232	223	168	169
4	213	209	227	249	282	278	193	200	204	189
5	164	149	169	173	232	170	156	146	150	152
7	131	138	218	240	237	222	215	159	178	167
8	128	169	222	233	210	187	168	193	204	149
9	168	170	170	175	187	185	182	152	173	176
10	226	243	218	224	198	196	200	219	181	188
11	161	158	231	212	195	177	183	173	155	156
12	172	204	191	196	192	182	182	173	174	180
14*	150	161	149	176	155	187	154	169	164	161
15*	163	156	174	194	202	182	161	157	156	160
16*	163	166	217	197	216	174	178	170	159	164
102	148	155	145	190	211	198	169	185	150	148
111	160	162	190	216	202	189	187	180	170	165
112	131	128	199	133	162	137	132	135	137	137
114*	146	150	170	201	167	161	167	155	153	151
206	143	149	208	--	209	237	229	181	185	170
213*	167	164	189	176	189	180	190	190	184	186
Mean	161.26	165.63	199.42	202.44	203.42	193.68	180.68	174.58	169.95	165.74
St. Dev.	27.10	27.37	36.35	32.66	33.95	37.98	25.86	23.47	18.10	14.91

*Minority Subjects
 (-- Latency not obtained)

Table C14. Latency (msec) to 8 degree targets for young men during Alprazolam/DHEA Treatment

Subject	Time (h)									
	0	2	3.5	4.5	5.5	7	8.5	10	11.5	12.5
33	157	180	210	195	195	169	177	168	171	167
34	156	161	243	166	153	148	146	145	141	147
35	124	124	131	139	145	140	137	133	130	125
36	134	134	139	139	138	135	137	144	138	129
37	232	214	204	212	215	213	202	190	219	206
38	170	142	150	162	146	150	158	159	157	147
39	151	152	205	214	188	204	165	167	173	159
41	--	156	177	168	168	156	166	168	154	150
42	150	168	175	186	180	194	197	172	155	177
43	164	153	219	221	197	213	207	154	148	150
44	122	122	160	167	151	146	147	129	134	141
47*	140	142	253	185	157	176	150	152	140	141
48*	153	146	189	201	279	241	194	176	143	148
140	125	118	230	281	289	178	173	173	143	140
146*	134	128	137	154	162	139	140	141	139	129
245*	150	164	--	--	--	186	191	183	179	184
Mean	150.80	150.25	188.13	186	184.20	174.25	167.94	159.63	154	152.50
St. Dev.	26.86	24.57	39.44	36.96	46.24	31.92	24.35	17.90	22.52	21.73

*Minority Subjects
 (--) Latency not obtained

Table C15. Latency (msec) to 8 degree targets for older women during Alprazolam/DHEA Treatment

Subject	Time (h)									
	0	2	3.5	4.5	5.5	7	8.5	10	11.5	12.5
17	160	170	--	--	--	--	222	193	196	194
18	205	196	256	265	261	211	253	212	207	218
19	161	188	--	--	--	--	205	190	174	170
20*	616	660	551	501	574	606	523	570	612	515
21	171	182	211	252	206	209	220	215	224	216
22	189	188	349	354	268	208	206	195	194	190
23	192	190	--	383	244	220	206	212	204	214
24	182	168	345	221	308	194	207	181	184	175
25	228	204	296	257	282	274	274	267	222	262
26	158	161	--	--	--	356	301	267	220	206
27	177	194	--	--	--	--	--	291	218	220
28	160	167	255	--	219	--	202	228	--	220
29*	153	152	--	--	--	--	--	--	177	178
30*	168	167	--	200	198	202	220	198	182	185
31*	179	185	--	--	--	--	--	216	197	194
120	199	191	--	--	--	231	276	258	222	206
Mean	206.13	210.19	323.29	304.13	284.44	271.10	255	246.20	228.87	222.69
St. Dev.	111.15	120.82	112.20	101.20	114.44	127.26	86.94	95.47	107.38	81.19

*Minority Subjects

(--) Latency not obtained

TableC16. Latency (msec) to 8 degree targets for older men during Alprazolam/DHEA Treatment

Subject	Time (h)									
	0	2	3.5	4.5	5.5	7	8.5	10	11.5	12.5
50	132	130	--	--	--	--	158	158	165	152
51	142	150	--	--	--	--	187	190	188	188
52	170	151	--	--	197	264	287	270	196	290
53	201	278	218	245	264	241	235	219	230	230
54	330	440	307	340	490	365	380	413	349	420
55	126	141	142	138	147	158	149	147	148	152
56	149	168	196	198	178	221	202	208	178	196
57	164	156	259	224	190	172	174	172	165	173
58	132	160	201	177	162	175	162	155	164	168
59	211	204	--	305	269	192	205	204	217	212
61*	122	128	303	229	--	322	225	142	156	159
149	169	181	--	258	252	222	178	230	205	201
160	204	220	--	--	--	--	233	241	233	233
Mean	173.23	192.85	232.29	234.89	238.78	233.20	213.46	211.46	199.54	213.38
St. Dev.	56.02	85.06	60.48	62.10	104.27	67.52	63.06	72.13	52.86	73.32

*Minority Subjects

(--) Latency not obtained

Table C17. Mean Latency (sec) to 16 degree targets for young women during Placebo Treatment

Subject	Time (h)									
	0	2	3.5	4.5	5.5	7	8.5	10	11.5	12.5
1	145	154	157	148	147	164	148	162	156	153
3	186	165	143	164	143	233	235	211	203	231
4	209	230	211	227	232	230	232	217	216	218
5	147	146	144	156	149	156	156	151	164	149
7	161	173	152	152	149	153	137	151	150	154
8	137	146	147	166	166	162	154	151	160	157
9	175	172	178	168	170	174	172	174	186	179
10	335	356	307	286	302	262	322	263	271	295
12	171	252	165	177	180	168	175	178	178	166
14*	176	185	173	172	172	191	172	188	199	193
15*	164	164	195	169	169	162	162	161	159	171
16*	184	185	179	189	195	161	151	169	171	170
102	158	158	156	177	170	164	166	167	166	176
111	205	243	229	242	223	216	198	195	196	191
112	133	139	136	141	136	134	142	140	133	140
114*	307	149	210	159	144	146	141	143	160	147
206	178	166	171	172	164	173	185	171	194	200
213*	143	137	142	137	143	140	140	153	152	158
Mean	184.11	184.44	177.50	177.89	175.22	177.17	177.11	174.72	178.56	180.44
St. Dev.	54.41	54.81	41.93	37.84	41.35	35.34	46.21	30.99	31.78	37.90

*Minority Subjects

Table C18. Mean Latency (sec) to 16 degree targets for young men during Placebo Treatment

Subject	Time (h)									
	0	2	3.5	4.5	5.5	7	8.5	10	11.5	12.5
33	190	197	193	188	209	166	192	194	180	168
34	169	166	166	179	154	165	165	155	171	164
35	132	126	134	128	127	127	126	128	131	135
36	143	145	139	140	144	137	139	145	132	137
37	202	201	229	245	225	235	227	218	257	233
38	154	152	156	158	159	178	152	148	165	158
39	170	156	188	155	167	160	162	165	173	171
41	174	173	166	168	160	176	171	171	159	158
42	169	184	163	177	171	176	179	180	167	195
43	184	167	180	202	228	201	201	185	175	180
44	160	166	159	162	150	165	157	142	151	135
47*	150	159	169	146	150	145	155	152	162	156
48*	175	171	184	178	234	161	166	155	155	161
140	117	138	135	120	118	136	125	141	121	115
146*	138	143	144	141	145	141	144	132	129	148
245*	164	167	170	162	172	168	162	169	172	185
Mean	161.94	163.19	167.19	165.56	169.56	164.81	163.94	161.25	162.50	162.44
St. Dev.	22.24	20.26	24.58	30.48	35.73	26.71	26.67	24.12	31.26	27.88

*Minority Subjects

Table C19. Mean Latency (sec) to 16 degree targets for older women during Placebo Treatment

Subject	Time (h)									
	0	2	3.5	4.5	5.5	7	8.5	10	11.5	12.5
17	193	225	262	228	226	233	212	211	221	202
18	229	224	210	246	224	227	303	235	276	258
19	202	207	189	200	210	183	201	188	195	182
20*	542	548	569	577	627	577	551	579	545	509
21	215	226	231	212	238	229	223	218	218	215
22	203	231	235	241	253	237	251	234	219	229
23	277	282	266	263	250	235	261	225	251	243
24	229	228	201	206	383	223	217	221	229	209
25	278	261	310	250	263	278	246	281	261	273
26	211	234	220	224	218	200	221	227	213	252
27	207	211	209	221	202	211	201	222	205	203
28	180	178	194	191	180	195	200	192	182	185
29*	200	206	216	211	--	222	220	243	245	227
30*	219	228	210	209	196	197	228	199	246	205
31*	--	214	232	240	361	212	235	--	215	215
120	207	222	214	218	228	226	231	252	216	238
Mean	239.47	245.31	248	246.06	270.60	242.81	250.06	248.47	246.06	240.31
St. Dev.	88.06	83.92	90.96	90.42	113.57	91.80	84.43	94.43	83.39	76.10

*Minority Subjects
 (--) Latency not obtained

Table C20. Mean Latency (sec) to 16 degree targets for older men during Placebo Treatment

Subject	Time (h)									
	0	2	3.5	4.5	5.5	7	8.5	10	11.5	12.5
50	160	210	183	167	177	172	198	–	169	166
51	196	188	187	185	184	184	195	223	204	209
52	195	188	195	173	175	201	223	195	186	188
53	231	243	248	251	303	274	236	252	235	267
54	459	393	358	454	456	494	389	463	442	454
55	153	148	151	153	161	175	155	162	157	168
56	156	199	187	177	186	175	174	194	182	164
57	169	175	168	185	176	170	165	178	165	157
58	210	203	191	184	179	193	198	190	178	196
59	177	219	202	225	208	202	204	191	184	193
61*	–	191	183	188	205	205	178	197	185	169
149	184	195	196	203	198	193	199	209	203	197
160	207	223	214	225	206	214	214	199	196	231
Mean	208.08	213.46	204.85	213.08	216.46	219.38	209.85	221.08	206.62	212.23
St. Dev.	82.54	58.78	51.34	77.22	80.05	86.86	58.41	79.39	73.47	78.85

*Minority Subjects

(–) Latency not obtained

Table C21. Mean Latency (sec) to 16 degree targets for young women during DHEA Treatment

Subject	Time (h)									
	0	2	3.5	4.5	5.5	7	8.5	10	11.5	12.5
1	173	178	171	154	168	163	168	153	171	163
3	221	202	175	159	142	162	174	157	159	164
4	229	210	211	250	238	232	250	241	210	220
5	145	143	146	146	163	161	145	146	157	160
7	156	153	163	159	150	164	184	157	183	181
8	140	153	142	137	148	143	166	183	166	158
9	173	164	163	160	181	166	168	162	168	166
10	235	304	339	315	270	250	264	290	317	227
12	170	212	197	186	180	178	184	191	172	172
14*	201	209	180	177	188	200	172	215	200	166
15*	163	167	178	166	166	149	148	153	158	154
16*	191	167	204	207	186	174	168	195	175	191
102	170	197	171	191	163	178	188	178	155	160
111	176	168	176	186	178	186	182	178	177	180
112	154	150	121	133	135	139	138	140	135	136
114*	172	159	172	159	156	158	152	172	156	150
206	175	176	168	181	--	162	170	167	160	176
213*	--	--	157	154	--	156	133	142	140	130
Mean	179.06	183.06	179.67	178.89	175.75	173.39	175.22	178.89	175.50	169.67
St. Dev.	27.86	38.47	45.18	43.74	34.80	28.82	33.85	38.09	39.79	24.64

*Minority Subjects
 (--) Latency not obtained

Table C22. Mean Latency (sec) to 16 degree targets for young men during DHEA Treatment

Subject	Time (h)									
	0	2	3.5	4.5	5.5	7	8.5	10	11.5	12.5
33	215	209	236	202	199	200	242	187	201	183
34	167	162	163	165	160	162	162	156	154	156
35	140	131	133	136	136	133	131	136	183	137
36	136	143	134	137	145	143	142	139	131	137
37	230	257	254	243	235	249	203	201	211	230
38	164	160	145	164	150	155	163	174	162	156
39	170	169	159	164	161	169	156	160	164	152
41	166	160	172	169	181	158	174	160	148	160
42	174	190	215	195	185	187	183	167	170	173
43	180	174	170	172	178	205	191	162	166	178
44	129	133	128	131	130	142	147	169	148	141
47*	150	146	151	148	160	161	145	142	154	157
48*	195	196	164	188	176	185	172	183	200	178
140	127	137	145	134	134	121	126	120	141	112
146*	136	138	136	137	133	140	141	136	130	127
245*	176	173	160	167	177	172	175	171	172	173
Mean	165.94	167.38	166.56	165.75	165	167.63	165.81	160.19	164.69	159.38
St. Dev.	29.82	33.32	37.20	30.29	28.15	32.14	29.66	21.48	24.25	27.48

*Minority Subjects

TableC23. Mean Latency (sec) to 16 degree targets for older women during DHEA Treatment

Subject	Time (h)									
	0	2	3.5	4.5	5.5	7	8.5	10	11.5	12.5
17	205	206	197	213	248	190	184	192	195	203
18	255	290	238	226	210	236	262	210	240	282
19	231	224	238	223	246	230	226	207	215	239
20*	623	621	631	627	661	656	611	570	643	645
21	235	210	215	227	198	207	210	196	217	202
22	226	232	255	233	263	239	247	261	255	210
23	241	241	218	218	224	202	228	221	236	222
24	266	257	251	247	227	224	223	247	223	228
25	264	251	257	261	296	279	283	273	300	275
26	222	261	232	243	236	229	217	215	229	243
27	--	226	202	234	200	201	201	215	219	242
28	193	175	186	169	165	185	163	169	173	187
29*	187	191	189	201	187	204	207	226	221	224
30*	211	218	227	190	210	193	204	185	194	187
31*	--	--	--	290	--	--	--	245	--	331
120	201	224	212	199	213	276	235	228	210	209
Mean	254.29	255.13	249.87	250.06	252.27	250.07	246.73	241.25	251.33	258.06
St. Dev.	109.03	105.23	107.90	104.51	117.57	115.86	105.02	91.91	112.19	109.88

*Minority Subjects

(--) Latency not obtained

Table C24. Mean Latency (sec) to 16 degree targets for older men during DHEA Treatment

Subject	Time (h)									
	0	2	3.5	4.5	5.5	7	8.5	10	11.5	12.5
50	236	191	179	159	169	187	194	194	182	194
51	176	171	183	174	183	163	180	173	160	161
52	167	174	182	173	186	189	194	176	168	175
53	237	305	243	261	285	269	221	246	231	257
54	409	481	484	479	442	405	432	482	423	439
55	164	155	157	155	147	157	157	166	160	164
56	174	172	176	174	168	163	187	181	175	176
57	194	188	187	197	187	199	182	178	174	182
58	210	266	270	238	196	238	216	230	224	224
59	207	197	210	190	212	227	189	240	225	221
61*	191	189	166	204	222	243	188	201	224	182
149	215	227	216	208	215	207	222	223	214	223
160	208	206	198	225	228	196	206	185	206	193
Mean	214.46	224.77	219.31	218.23	218.46	218.69	212.92	221.15	212.77	214.69
St. Dev.	63.13	87.47	85.50	84.30	75.53	65.33	68.28	82.88	68.57	72.95

*Minority Subjects

Table C25. Mean Latency (sec) to 16 degree targets for young women during Alprazolam/Placebo Treatment

Subject	Time (h)									
	0	2	3.5	4.5	5.5	7	8.5	10	11.5	12.5
1	157	149	210	202	176	182	171	181	168	158
3	208	186	264	284	231	226	221	191	159	172
4	262	272	225	296	252	241	203	215	230	223
5	150	150	218	200	190	190	177	142	139	159
7	144	150	186	225	213	188	167	164	157	168
8	161	142	211	208	241	235	205	181	175	146
9	167	168	169	179	180	174	161	159	164	162
10	303	290	253	215	212	272	208	216	225	185
11	163	161	249	244	214	197	180	172	162	161
12	168	166	178	180	178	178	176	188	165	167
14*	201	197	234	285	299	233	225	209	233	227
15*	137	145	193	214	195	151	153	150	160	146
16*	171	187	242	233	199	210	215	166	190	175
102	159	163	193	205	205	180	172	165	153	146
111	169	166	185	235	221	224	194	185	184	196
112	142	144	166	173	165	163	161	147	141	137
114*	148	150	189	179	169	170	160	173	157	153
206	167	166	233	245	214	212	210	200	185	188
213*	156	168	179	168	178	177	199	171	163	159
Mean	175.42	174.74	209.32	219.47	206.95	200.16	187.26	177.63	174.21	169.89
St. Dev.	42.21	40.53	30.29	38.54	33.05	31.63	22.99	21.87	27.82	24.68

*Minority Subjects

Table C26. Mean Latency (sec) to 16 degree targets for young men during Alprazolam/Placebo Treatment

Subject	Time (h)									
	0	2	3.5	4.5	5.5	7	8.5	10	11.5	12.5
33	193	215	209	227	201	185	192	209	180	170
34	154	156	247	202	182	161	164	155	148	152
35	140	132	--	140	135	127	139	139	123	134
36	143	147	141	146	144	133	144	151	142	151
37	245	222	203	209	215	207	222	217	209	212
38	151	142	148	158	146	163	148	149	153	149
39	153	156	182	243	216	187	182	162	167	162
41	170	171	175	172	178	166	157	165	161	162
42	--	211	181	175	234	194	199	179	209	225
43	155	173	240	213	197	189	170	171	182	167
44	139	139	189	166	166	164	--	148	136	146
47*	136	153	197	253	195	164	173	202	148	186
48*	146	144	150	--	230	163	161	158	177	152
140	121	124	246	204	195	204	187	147	161	131
146*	133	141	158	156	160	148	148	146	158	148
245*	167	191	--	--	--	227	209	182	209	177
Mean	156.40	163.56	190.43	190.29	186.27	173.88	173	167.50	166.44	164
St. Dev.	30.01	30.80	35.76	36.29	31.18	27.02	25	24.07	26.30	25.80

*Minority Subjects

(--) Latency not obtained

Table C27. Mean Latency (sec) to 16 degree targets for older women during Alprazolam/Placebo Treatment

Subject	Time (h)									
	0	2	3.5	4.5	5.5	7	8.5	10	11.5	12.5
17	177	191	268	262	259	243	301	315	233	242
18	202	224	306	357	256	279	323	249	276	251
19	194	194	--	--	348	--	311	280	207	198
20*	561	595	631	558	378	709	691	689	621	651
21	198	209	--	273	231	233	232	221	222	235
22	214	231	348	382	384	349	284	289	267	259
23	--	208	--	420	282	313	266	258	225	213
24	204	194	295	270	238	212	235	241	203	328
25	236	244	305	332	279	277	326	281	312	309
26	204	206	--	--	453	344	298	289	254	249
27	190	187	--	--	--	--	--	--	212	220
28	162	172	--	253	250	--	--	210	202	215
29*	178	184	--	247	258	216	208	202	218	230
30*	193	187	--	--	290	241	224	219	223	225
31*	215	210	--	--	--	--	--	--	254	269
120	228	193	--	--	--	--	309	273	234	245
Mean	223.73	226.81	358.83	335.40	300.46	310.55	308.31	286.86	260.19	271.19
St. Dev.	95.26	99.95	135.80	98.61	68.44	140.55	121.76	120.64	100.78	106.82

*Minority Subjects

(--) Latency not obtained

Table C28. Mean Latency (sec) to 16 degree targets for older men during Alprazolam/Placebo Treatment

Subject	Time (h)									
	0	2	3.5	4.5	5.5	7	8.5	10	11.5	12.5
50	152	171	255	256	236	186	199	185	188	335
51	177	170	278	291	258	228	216	205	202	197
52	197	185	--	--	--	--	224	233	203	185
53	224	280	248	264	254	218	258	215	255	236
54	480	515	523	469	536	553	567	459	522	459
55	144	173	173	185	164	166	159	168	163	165
56	150	161	--	292	246	202	220	201	197	227
57	182	168	256	222	200	202	180	192	190	191
58	186	173	222	202	210	199	187	207	194	193
59	219	211	--	301	383	213	207	206	223	228
61*	159	164	349	234	193	211	190	178	175	177
149	189	--	276	292	317	256	236	215	222	219
160	224	221	--	--	--	315	303	218	227	225
Mean	206.38	216	286.67	273.45	272.45	245.75	242	221.69	227.77	233.62
St. Dev.	86.69	100.17	100.29	75.84	106.52	103.84	104.35	73.45	91.62	79.86

*Minority Subjects
 (--) Latency not obtained

Table C29. Mean Latency (sec) to 16 degree targets for young women during Alprazolam/DHEA Treatment

Subject	Time (h)									
	0	2	3.5	4.5	5.5	7	8.5	10	11.5	12.5
1	152	162	217	171	206	215	158	158	166	180
3	162	166	241	302	239	230	189	195	156	152
4	241	237	229	248	235	279	233	203	235	206
5	165	159	195	203	208	169	166	151	167	153
7	152	144	213	209	219	214	207	161	169	168
8	144	152	225	206	214	210	176	172	199	145
9	156	163	165	169	171	173	173	175	176	173
10	241	260	228	244	195	194	202	192	190	206
11	178	176	208	212	207	199	182	180	174	164
12	161	190	199	175	189	191	181	168	171	171
14*	195	181	180	200	179	250	191	192	191	199
15*	153	158	185	198	219	208	155	156	160	166
16*	176	158	255	192	196	180	172	176	156	165
102	160	153	154	170	189	171	167	175	159	158
111	185	173	210	205	215	197	198	192	181	183
112	136	137	202	135	157	150	136	145	148	141
114*	142	149	165	208	183	154	151	151	149	180
206	154	163	231	-	211	208	209	186	195	168
213*	156	158	191	170	170	171	177	171	165	171
Mean	168.89	170.47	204.89	200.94	200.11	198.05	180.16	173.63	174.05	171
St. Dev.	29.33	30.46	27.27	37.19	22.06	32.26	23.31	16.89	21.06	18.41

*Minority Subjects
 (-) Latency not obtained

Table C30. Mean Latency (sec) to 16 degree targets for young men during Alprazolam/DHEA Treatment

Subject	Time (h)									
	0	2	3.5	4.5	5.5	7	8.5	10	11.5	12.5
33	171	206	217	216	170	179	198	170	175	181
34	154	160	231	175	156	157	151	151	147	155
35	124	131	129	143	142	142	136	136	129	134
36	141	137	142	149	141	146	143	140	144	139
37	222	239	199	210	196	203	197	185	209	193
38	166	154	165	168	164	153	159	156	147	148
39	156	153	189	177	210	197	171	163	170	158
41	--	163	182	162	169	163	156	165	161	158
42	169	195	191	197	202	227	219	193	166	192
43	161	156	228	212	196	191	192	163	151	157
44	137	136	144	141	136	131	138	143	132	143
47*	145	152	244	173	166	169	150	152	144	142
48*	167	157	209	215	246	211	186	165	152	145
140	135	126	223	287	251	167	157	158	142	131
146*	142	135	146	152	159	145	140	140	141	142
245*	164	171	--	--	--	184	189	183	199	181
Mean	156.93	160.69	189.27	185.13	180.27	172.81	167.63	160.19	156.81	156.19
St. Dev.	23.02	30.12	36.90	38.71	35.74	27.52	25.80	16.81	22.43	20.11

*Minority Subjects
 (--) Latency not obtained

Table C31. Mean Latency (sec) to 16 degree targets for older women during Alprazolam/DHEA Treatment

Subject	Time (h)									
	0	2	3.5	4.5	5.5	7	8.5	10	11.5	12.5
17	166	193	--	--	--	--	205	198	196	217
18	257	213	341	334	303	237	321	304	248	238
19	183	212	--	--	--	--	223	215	188	193
20*	657	644	636	713	669	491	662	673	752	704
21	203	206	260	264	265	241	243	242	231	249
22	218	204	274	354	397	304	245	251	247	237
23	204	204	--	363	259	230	250	221	202	209
24	207	235	324	261	260	210	200	219	202	198
25	256	273	296	265	350	276	311	302	290	328
26	212	207	--	--	--	480	292	257	261	235
27	175	197	--	--	--	--	--	290	218	213
28	166	177	240	--	216	--	198	221	--	217
29*	168	193	--	--	--	--	--	--	192	224
30*	193	185	--	246	232	234	253	220	222	217
31*	201	206	--	--	--	--	--	261	222	217
120	233	214	--	--	--	247	291	288	268	225
Mean	231.19	235.19	338.71	350	327.89	295	284.15	277.47	262.60	257.56
St. Dev.	117.08	111.18	135.74	153.79	140.21	103.73	120.70	114.64	138.71	122.88

*Minority Subjects
 (--) Latency not obtained

Table C32. Mean Latency (sec) to 16 degree targets for older men during Alprazolam/DHEA Treatment

Subject	Time (h)									
	0	2	3.5	4.5	5.5	7	8.5	10	11.5	12.5
50	175	183	--	--	--	--	188	184	240	174
51	162	173	--	--	--	--	220	224	212	224
52	186	180	--	--	230	274	291	260	213	380
53	214	263	224	266	249	238	252	257	258	223
54	395	483	424	375	522	492	432	457	425	462
55	146	143	158	160	159	179	163	164	169	156
56	166	175	224	209	221	280	254	208	192	201
57	192	186	405	225	199	183	184	180	193	190
58	165	186	211	199	184	190	199	182	183	187
59	207	225	--	296	254	205	243	219	210	231
61*	151	165	274	216	--	306	219	170	187	194
149	197	195	--	289	274	249	231	225	228	218
160	206	207	--	--	--	--	301	247	297	257
Mean	197.08	212.62	274.29	248.33	254.67	259.60	244.38	229	231.31	238.23
St. Dev.	63.40	86.41	101.72	64.86	106.57	92.83	69.32	75.82	67.69	86.89

*Minority Subjects

(--) Latency not obtained

APPENDIX D

Saccadic Eye Movement Parameters

Duration: 8 degree & 16 degree

Table D1. Duration (msec) to 8 degree targets for young women during Placebo Treatment

Subject	Time (h)									
	0	2	3.5	4.5	5.5	7	8.5	10	11.5	12.5
1	50.00	51.00	49.00	49.00	49.00	50.00	49.00	49.00	48.00	49.00
3	57.00	58.00	56.00	58.00	58.00	60.00	60.00	59.00	58.00	61.00
4	54.00	55.00	56.00	58.00	57.00	57.00	57.00	56.00	58.00	56.00
5	57.00	55.00	57.00	59.00	61.00	62.00	59.00	58.00	62.00	60.00
7	64.00	64.00	66.00	61.00	61.00	63.00	63.00	63.00	63.00	64.00
8	61.00	61.00	61.00	62.00	60.00	61.00	59.00	62.00	59.00	59.00
9	61.00	65.00	57.00	61.00	59.00	58.00	63.00	56.00	54.00	53.00
10	57.00	64.00	65.00	64.00	69.00	68.00	66.00	66.00	64.00	63.00
12	56.00	62.00	60.00	61.00	63.00	62.00	61.00	60.00	61.00	60.00
14*	50.00	53.00	53.00	54.00	55.00	54.00	53.00	54.00	53.00	51.00
15*	57.00	59.00	62.00	60.00	61.00	62.00	60.00	60.00	59.00	59.00
16*	56.00	58.00	56.00	56.00	57.00	57.00	58.00	57.00	60.00	57.00
102	56.00	54.00	59.00	55.00	60.00	58.00	57.00	57.00	59.00	57.00
111	57.00	58.00	58.00	61.00	57.00	57.00	55.00	57.00	57.00	57.00
112	52.00	51.00	53.00	52.00	52.00	53.00	52.00	53.00	53.00	51.00
114*	67.00	60.00	61.00	62.00	61.00	64.00	58.00	60.00	62.00	61.00
206	51.00	53.00	54.00	53.00	53.00	54.00	52.00	53.00	53.00	51.00
213*	55.00	57.00	54.00	56.00	56.00	55.00	55.00	55.00	54.00	54.00
Mean	56.56	57.67	57.61	57.89	58.28	58.61	57.61	57.50	57.61	56.83
St. Dev.	4.55	4.42	4.38	4.09	4.52	4.53	4.39	4.06	4.30	4.48

*Minority Subjects

Table D2. Duration (msec) to 8 degree targets for young men during Placebo Treatment

Subject	Time (h)									
	0	2	3.5	4.5	5.5	7	8.5	10	11.5	12.5
33	55.00	55.00	55.00	54.00	55.00	55.00	57.00	54.00	53.00	56.00
34	71.00	74.00	55.00	54.00	62.00	56.00	58.00	54.00	57.00	55.00
35	54.00	54.00	53.00	52.00	53.00	52.00	53.00	54.00	52.00	53.00
36	54.00	51.00	50.00	51.00	56.00	59.00	52.00	52.00	53.00	52.00
37	57.00	55.00	59.00	58.00	54.00	57.00	55.00	55.00	58.00	54.00
38	61.00	64.00	59.00	69.00	57.00	61.00	57.00	59.00	58.00	62.00
39	50.00	60.00	81.00	56.00	59.00	63.00	75.00	57.00	53.00	50.00
41	53.00	56.00	55.00	57.00	55.00	55.00	56.00	53.00	56.00	55.00
42	54.00	59.00	53.00	54.00	55.00	54.00	55.00	52.00	54.00	54.00
43	56.00	53.00	52.00	53.00	54.00	52.00	52.00	54.00	53.00	52.00
44	55.00	56.00	60.00	58.00	58.00	56.00	53.00	55.00	56.00	58.00
47*	53.00	56.00	55.00	56.00	55.00	57.00	55.00	55.00	59.00	56.00
48*	62.00	61.00	60.00	59.00	57.00	60.00	59.00	60.00	58.00	61.00
140	53.00	56.00	54.00	54.00	54.00	54.00	54.00	56.00	54.00	54.00
146*	60.00	60.00	64.00	62.00	63.00	64.00	65.00	63.00	64.00	62.00
245*	60.00	62.00	61.00	62.00	71.00	62.00	61.00	59.00	61.00	62.00
Mean	56.75	58.25	57.88	56.81	57.38	57.31	57.31	55.75	56.19	56.00
St. Dev.	5.08	5.47	7.24	4.58	4.62	3.79	5.84	3.09	3.37	3.90

*Minority Subjects

TableD3. Duration (msec) to 8 degree targets for older women during Placebo Treatment

Subject	Time (h)									
	0	2	3.5	4.5	5.5	7	8.5	10	11.5	12.5
17	60.00	61.00	61.00	65.00	60.00	60.00	58.00	58.00	58.00	61.00
18	52.00	60.00	77.00	63.00	61.00	56.00	57.00	57.00	62.00	55.00
19	59.00	62.00	61.00	65.00	69.00	60.00	59.00	61.00	62.00	59.00
20*	56.00	59.00	60.00	60.00	62.00	64.00	68.00	63.00	62.00	61.00
21	57.00	57.00	58.00	59.00	58.00	60.00	58.00	58.00	61.00	58.00
22	56.00	58.00	59.00	57.00	59.00	58.00	60.00	56.00	57.00	59.00
23	59.00	62.00	59.00	60.00	64.00	64.00	64.00	63.00	62.00	64.00
24	52.00	57.00	50.00	52.00	57.00	50.00	52.00	53.00	50.00	51.00
25	57.00	58.00	58.00	57.00	58.00	58.00	58.00	58.00	55.00	60.00
26	68.00	67.00	65.00	64.00	66.00	68.00	62.00	62.00	63.00	62.00
27	71.00	65.00	83.00	75.00	64.00	63.00	75.00	73.00	87.00	75.00
28	76.00	62.00	61.00	61.00	62.00	60.00	63.00	64.00	62.00	62.00
29*	50.00	65.00	58.00	58.00	--	66.00	56.00	53.00	55.00	52.00
30*	70.00	68.00	70.00	64.00	67.00	68.00	64.00	65.00	66.00	70.00
31*	--	64.00	76.00	61.00	68.00	63.00	63.00	--	62.00	62.00
120	58.00	57.00	58.00	57.00	58.00	56.00	58.00	60.00	58.00	58.00
Mean	60.07	61.38	63.38	61.13	62.20	60.88	60.94	60.27	61.38	60.56
St. Dev.	7.68	3.63	8.71	5.12	3.97	4.77	5.38	5.12	7.90	5.94

*Minority Subjects

(--) Duration not obtained

Table D4. Duration (msec) to 8 degree targets for older men during Placebo Treatment

Subject	Time (h)									
	0	2	3.5	4.5	5.5	7	8.5	10	11.5	12.5
50	66.00	73.00	65.00	74.00	86.00	124.00	60.00	60.00	58.00	60.00
51	56.00	57.00	58.00	57.00	57.00	57.00	58.00	57.00	57.00	58.00
52	56.00	58.00	81.00	58.00	57.00	63.00	92.00	66.00	59.00	62.00
53	58.00	64.00	72.00	66.00	63.00	63.00	72.00	72.00	59.00	60.00
54	86.00	71.00	72.00	71.00	80.00	81.00	106.00	61.00	62.00	83.00
55	63.00	66.00	66.00	64.00	64.00	68.00	64.00	66.00	70.00	61.00
56	54.00	56.00	56.00	60.00	63.00	59.00	60.00	62.00	58.00	55.00
57	49.00	48.00	50.00	50.00	49.00	50.00	49.00	50.00	48.00	48.00
58	61.00	62.00	62.00	60.00	62.00	63.00	61.00	60.00	60.00	61.00
59	49.00	70.00	52.00	57.00	57.00	56.00	52.00	51.00	49.00	53.00
61*	–	56.00	51.00	53.00	54.00	53.00	57.00	58.00	55.00	57.00
149	54.00	58.00	54.00	54.00	55.00	54.00	56.00	55.00	53.00	53.00
160	57.00	56.00	58.00	74.00	76.00	92.00	90.00	64.00	59.00	56.00
Mean	59.08	61.15	61.31	61.38	63.31	67.92	67.46	60.15	57.46	59.00
St. Dev.	9.87	7.29	9.47	7.89	10.94	20.51	17.54	6.16	5.62	8.26

*Minority Subjects

(–) Duration not obtained

Table D5. Duration (msec) to 8 degree targets for young women during DHEA Treatment

Subject	Time (h)									
	0	2	3.5	4.5	5.5	7	8.5	10	11.5	12.5
1	47.00	52.00	50.00	64.00	50.00	51.00	47.00	48.00	62.00	48.00
3	59.00	62.00	63.00	57.00	59.00	58.00	57.00	55.00	58.00	57.00
4	55.00	56.00	58.00	56.00	58.00	59.00	56.00	57.00	56.00	57.00
5	54.00	55.00	57.00	56.00	63.00	58.00	56.00	57.00	57.00	60.00
7	59.00	62.00	63.00	62.00	63.00	62.00	62.00	60.00	60.00	64.00
8	59.00	61.00	60.00	60.00	60.00	60.00	61.00	61.00	61.00	60.00
9	57.00	55.00	56.00	59.00	59.00	60.00	59.00	60.00	58.00	57.00
10	55.00	58.00	66.00	67.00	65.00	59.00	65.00	60.00	65.00	59.00
12	56.00	58.00	64.00	63.00	67.00	63.00	60.00	60.00	59.00	65.00
14*	52.00	54.00	53.00	53.00	55.00	52.00	52.00	53.00	53.00	54.00
15*	61.00	63.00	65.00	60.00	61.00	60.00	60.00	58.00	60.00	61.00
16*	54.00	55.00	60.00	52.00	75.00	55.00	54.00	55.00	54.00	57.00
102	55.00	57.00	58.00	58.00	57.00	54.00	57.00	59.00	58.00	58.00
111	57.00	56.00	57.00	57.00	58.00	57.00	57.00	58.00	58.00	57.00
112	50.00	50.00	50.00	51.00	52.00	51.00	50.00	50.00	50.00	50.00
114*	61.00	58.00	61.00	60.00	57.00	58.00	58.00	58.00	61.00	60.00
206	52.00	53.00	53.00	53.00	--	54.00	56.00	54.00	52.00	52.00
213*	--	--	56.00	59.00	--	56.00	55.00	56.00	54.00	55.00
Mean	55.47	56.76	58.33	58.17	59.94	57.06	56.78	56.61	57.56	57.28
St. Dev.	3.83	3.68	4.86	4.31	5.97	3.59	4.32	3.60	3.84	4.39

*Minority Subjects

(--) Duration not obtained

Table D6. Duration (msec) to 8 degree targets for young men during DHEA Treatment

Subject	Time (h)									
	0	2	3.5	4.5	5.5	7	8.5	10	11.5	12.5
33	57.00	56.00	56.00	55.00	55.00	56.00	55.00	55.00	55.00	55.00
34	71.00	58.00	58.00	66.00	55.00	59.00	57.00	61.00	62.00	58.00
35	70.00	51.00	53.00	53.00	52.00	52.00	52.00	53.00	53.00	52.00
36	56.00	54.00	52.00	52.00	52.00	52.00	52.00	52.00	50.00	52.00
37	56.00	55.00	57.00	56.00	56.00	58.00	58.00	57.00	55.00	55.00
38	55.00	56.00	63.00	56.00	56.00	58.00	60.00	57.00	59.00	62.00
39	50.00	54.00	54.00	65.00	67.00	57.00	59.00	66.00	54.00	52.00
41	54.00	54.00	55.00	55.00	55.00	55.00	56.00	55.00	55.00	54.00
42	54.00	51.00	52.00	53.00	52.00	54.00	52.00	53.00	53.00	54.00
43	53.00	53.00	54.00	57.00	53.00	52.00	54.00	53.00	50.00	51.00
44	52.00	53.00	55.00	54.00	54.00	56.00	55.00	59.00	54.00	54.00
47*	55.00	56.00	56.00	56.00	56.00	53.00	56.00	57.00	56.00	56.00
48*	59.00	64.00	58.00	64.00	57.00	59.00	64.00	59.00	62.00	59.00
140	52.00	56.00	56.00	52.00	62.00	54.00	53.00	53.00	54.00	53.00
146*	63.00	63.00	69.00	63.00	63.00	66.00	61.00	63.00	68.00	62.00
245*	60.00	63.00	60.00	63.00	66.00	67.00	64.00	63.00	63.00	63.00
Mean	57.31	56.06	56.75	57.50	56.94	56.75	56.75	57.25	56.44	55.75
St. Dev.	6.09	4.06	4.36	4.93	4.88	4.51	3.97	4.27	5.01	3.91

*Minority Subjects

Table D7. Duration (msec) to 8 degree targets for older women during DHEA Treatment

Subject	Time (h)									
	0	2	3.5	4.5	5.5	7	8.5	10	11.5	12.5
17	61.00	61.00	61.00	71.00	79.00	60.00	57.00	62.00	59.00	59.00
18	61.00	76.00	78.00	77.00	59.00	56.00	56.00	61.00	55.00	54.00
19	60.00	58.00	61.00	57.00	66.00	63.00	57.00	62.00	61.00	58.00
20*	63.00	60.00	66.00	64.00	78.00	67.00	69.00	61.00	65.00	76.00
21	58.00	57.00	57.00	59.00	61.00	59.00	60.00	59.00	63.00	59.00
22	59.00	55.00	57.00	55.00	58.00	64.00	60.00	63.00	58.00	57.00
23	76.00	91.00	69.00	67.00	63.00	66.00	60.00	59.00	62.00	69.00
24	54.00	54.00	50.00	53.00	51.00	51.00	53.00	51.00	53.00	52.00
25	58.00	57.00	58.00	59.00	57.00	58.00	56.00	59.00	56.00	55.00
26	63.00	66.00	67.00	70.00	72.00	71.00	63.00	67.00	62.00	65.00
27	--	67.00	66.00	63.00	57.00	62.00	63.00	76.00	66.00	84.00
28	62.00	60.00	60.00	62.00	61.00	66.00	60.00	61.00	61.00	60.00
29*	54.00	54.00	54.00	53.00	49.00	58.00	57.00	58.00	54.00	54.00
30*	65.00	71.00	69.00	65.00	66.00	75.00	69.00	60.00	68.00	59.00
31*	--	--	--	69.00	--	--	--	73.00	--	70.00
120	57.00	58.00	58.00	58.00	57.00	62.00	59.00	58.00	58.00	58.00
Mean	60.79	63.00	62.07	62.63	62.27	62.53	59.93	61.88	60.07	61.81
St. Dev.	5.45	10.04	7.11	6.94	8.74	6.03	4.54	5.94	4.46	8.82

*Minority Subjects

(--) Duration not obtained

Table D8. Duration (msec) to 8 degree targets for older men during DHEA Treatment

Subject	Time (h)									
	0	2	3.5	4.5	5.5	7	8.5	10	11.5	12.5
50	56.00	60.00	59.00	55.00	62.00	56.00	58.00	60.00	58.00	56.00
51	57.00	57.00	67.00	60.00	62.00	57.00	58.00	59.00	58.00	62.00
52	61.00	56.00	60.00	59.00	58.00	63.00	79.00	58.00	58.00	58.00
53	58.00	64.00	64.00	64.00	65.00	63.00	62.00	79.00	72.00	60.00
54	90.00	75.00	77.00	79.00	90.00	92.00	96.00	81.00	63.00	66.00
55	75.00	66.00	69.00	71.00	67.00	65.00	69.00	63.00	67.00	63.00
56	59.00	57.00	55.00	58.00	55.00	57.00	57.00	53.00	53.00	54.00
57	48.00	50.00	54.00	54.00	48.00	51.00	51.00	49.00	48.00	48.00
58	59.00	62.00	63.00	61.00	62.00	60.00	59.00	60.00	61.00	60.00
59	55.00	48.00	54.00	56.00	51.00	51.00	53.00	48.00	50.00	49.00
61*	53.00	55.00	52.00	53.00	54.00	49.00	53.00	53.00	54.00	52.00
149	56.00	67.00	59.00	54.00	65.00	80.00	70.00	54.00	52.00	51.00
160	72.00	89.00	88.00	55.00	103.00	87.00	61.00	56.00	95.00	81.00
Mean	61.46	62.00	63.15	59.92	64.77	63.92	63.54	59.46	60.69	58.46
St. Dev.	11.21	10.89	10.25	7.59	15.42	13.88	12.51	10.11	12.34	8.78

*Minority Subjects

Table D9. Duration (msec) to 8 degree targets for young women during Alprazolam/Placebo Treatment

Subject	Time (h)									
	0	2	3.5	4.5	5.5	7	8.5	10	11.5	12.5
1	51.00	64.00	157.00	169.00	190.00	131.00	118.00	103.00	166.00	63.00
3	57.00	60.00	74.00	77.00	59.00	62.00	66.00	65.00	59.00	63.00
4	55.00	56.00	79.00	136.00	72.00	75.00	63.00	63.00	61.00	61.00
5	63.00	60.00	149.00	146.00	138.00	124.00	71.00	60.00	60.00	58.00
7	58.00	63.00	106.00	108.00	133.00	87.00	73.00	73.00	74.00	81.00
8	65.00	65.00	73.00	109.00	119.00	82.00	141.00	65.00	67.00	66.00
9	57.00	57.00	67.00	100.00	109.00	82.00	71.00	67.00	67.00	65.00
10	65.00	62.00	70.00	88.00	87.00	76.00	73.00	69.00	67.00	65.00
11	55.00	60.00	126.00	121.00	104.00	95.00	72.00	57.00	58.00	59.00
12	61.00	62.00	63.00	175.00	150.00	114.00	223.00	69.00	65.00	79.00
14*	55.00	55.00	60.00	84.00	80.00	58.00	57.00	60.00	59.00	58.00
15*	58.00	59.00	102.00	158.00	155.00	68.00	68.00	66.00	66.00	64.00
16*	58.00	64.00	71.00	86.00	80.00	107.00	82.00	61.00	60.00	63.00
102	57.00	60.00	94.00	194.00	130.00	85.00	69.00	63.00	61.00	61.00
111	57.00	57.00	61.00	127.00	148.00	83.00	67.00	64.00	63.00	62.00
112	51.00	52.00	88.00	82.00	110.00	78.00	83.00	57.00	55.00	53.00
114*	65.00	70.00	92.00	102.00	113.00	102.00	73.00	74.00	76.00	65.00
206	53.00	54.00	67.00	109.00	126.00	141.00	92.00	66.00	72.00	58.00
213*	56.00	57.00	80.00	82.00	75.00	69.00	65.00	61.00	58.00	58.00
Mean	57.74	59.84	88.37	118.58	114.63	90.47	85.63	66.47	69.16	63.26
St. Dev.	4.33	4.36	28.57	35.44	33.96	23.54	38.88	10.01	24.14	6.77

*Minority Subjects

Table D10. Duration (msec) to 8 degree targets for young men during Alprazolam/Placebo Treatment

Subject	Time (h)									
	0	2	3.5	4.5	5.5	7	8.5	10	11.5	12.5
33	54.00	55.00	92.00	102.00	96.00	61.00	86.00	57.00	56.00	54.00
34	66.00	56.00	162.00	165.00	132.00	87.00	86.00	67.00	58.00	59.00
35	56.00	50.00	--	55.00	58.00	55.00	52.00	53.00	55.00	53.00
36	51.00	52.00	53.00	56.00	56.00	59.00	63.00	56.00	59.00	55.00
37	58.00	56.00	74.00	65.00	81.00	59.00	57.00	57.00	56.00	55.00
38	57.00	57.00	100.00	191.00	87.00	83.00	61.00	57.00	57.00	55.00
39	52.00	53.00	158.00	152.00	97.00	140.00	81.00	62.00	61.00	57.00
41	54.00	55.00	59.00	67.00	60.00	61.00	62.00	58.00	57.00	56.00
42	--	59.00	88.00	111.00	77.00	70.00	61.00	60.00	57.00	55.00
43	53.00	54.00	97.00	116.00	117.00	61.00	62.00	59.00	57.00	56.00
44	54.00	53.00	63.00	171.00	188.00	120.00	--	72.00	60.00	56.00
47*	54.00	55.00	75.00	70.00	76.00	61.00	62.00	61.00	60.00	60.00
48*	55.00	59.00	109.00	--	143.00	68.00	68.00	63.00	66.00	66.00
140	54.00	58.00	96.00	128.00	108.00	102.00	82.00	62.00	59.00	59.00
146*	63.00	67.00	98.00	109.00	184.00	92.00	92.00	68.00	66.00	64.00
245*	61.00	64.00	--	--	--	74.00	63.00	64.00	65.00	67.00
Mean	56.13	56.44	94.57	111.29	104.00	78.31	69.20	61.00	59.31	57.94
St. Dev.	4.22	4.34	32.43	45.48	42.04	24.59	12.54	4.98	3.55	4.30

*Minority Subjects

(--) Duration not obtained

Table D11. Duration (msec) to 8 degree targets for older women during Alprazolam/Placebo Treatment

Subject	Time (h)									
	0	2	3.5	4.5	5.5	7	8.5	10	11.5	12.5
17	61.00	64.00	118.00	169.00	163.00	129.00	99.00	263.00	129.00	223.00
18	56.00	56.00	136.00	112.00	105.00	138.00	82.00	60.00	58.00	63.00
19	60.00	60.00	--	--	182.00	--	120.00	113.00	93.00	92.00
20*	56.00	58.00	71.00	109.00	87.00	144.00	118.00	89.00	128.00	96.00
21	55.00	56.00	--	146.00	126.00	70.00	69.00	60.00	60.00	62.00
22	57.00	57.00	178.00	145.00	220.00	124.00	127.00	68.00	71.00	64.00
23	--	62.00	--	163.00	153.00	57.00	96.00	94.00	65.00	67.00
24	49.00	53.00	76.00	112.00	76.00	53.00	58.00	60.00	52.00	--
25	59.00	57.00	59.00	157.00	133.00	65.00	64.00	64.00	63.00	67.00
26	63.00	65.00	--	--	64.00	81.00	76.00	65.00	125.00	62.00
27	73.00	64.00	--	--	--	--	--	--	76.00	77.00
28	60.00	59.00	--	83.00	73.00	--	--	93.00	66.00	76.00
29*	58.00	53.00	--	161.00	117.00	135.00	76.00	91.00	66.00	139.00
30*	71.00	62.00	--	--	107.00	139.00	95.00	92.00	103.00	86.00
31*	65.00	64.00	--	--	--	--	--	--	68.00	69.00
120	58.00	58.00	--	--	--	--	80.00	78.00	68.00	61.00
Mean	60.07	59.25	106.33	135.70	123.54	103.18	89.23	92.14	80.69	86.93
St. Dev.	6.10	3.91	45.96	29.35	46.19	37.38	22.14	51.93	26.31	42.83

*Minority Subjects

(--) Duration not obtained

Table D12. Duration (msec) to 8 degree targets for older men during Alprazolam/Placebo Treatment

Subject	Time (h)									
	0	2	3.5	4.5	5.5	7	8.5	10	11.5	12.5
50	65.00	55.00	151.00	172.00	68.00	60.00	70.00	63.00	66.00	75.00
51	56.00	58.00	91.00	74.00	100.00	58.00	60.00	57.00	62.00	61.00
52	59.00	69.00	--	--	--	--	77.00	95.00	68.00	72.00
53	59.00	64.00	91.00	74.00	74.00	93.00	62.00	62.00	63.00	61.00
54	78.00	73.00	118.00	135.00	126.00	147.00	193.00	65.00	92.00	86.00
55	64.00	76.00	76.00	90.00	74.00	71.00	73.00	68.00	66.00	69.00
56	58.00	55.00	--	168.00	126.00	83.00	77.00	79.00	65.00	81.00
57	51.00	51.00	51.00	53.00	59.00	55.00	53.00	53.00	51.00	52.00
58	62.00	60.00	74.00	73.00	76.00	69.00	65.00	66.00	64.00	65.00
59	48.00	50.00	--	107.00	57.00	54.00	54.00	56.00	54.00	52.00
61*	53.00	54.00	85.00	60.00	62.00	59.00	57.00	54.00	55.00	56.00
149	52.00	--	120.00	132.00	142.00	130.00	109.00	58.00	73.00	59.00
160	59.00	79.00	--	--	--	165.00	128.00	138.00	141.00	133.00
Mean	58.77	62.00	95.22	103.45	87.64	87.00	82.92	70.31	70.77	70.92
St. Dev.	7.69	10.03	29.92	42.38	30.60	38.88	39.64	23.35	23.41	21.44

*Minority Subjects

(--) Duration not obtained

Table D13. Duration (msec) to 8 degree targets for young women during Alprazolam/DHEA Treatment

Subject	Time (h)									
	0	2	3.5	4.5	5.5	7	8.5	10	11.5	12.5
1	49.00	56.00	121.00	149.00	114.00	151.00	77.00	67.00	51.00	52.00
3	59.00	58.00	87.00	69.00	113.00	74.00	71.00	64.00	61.00	59.00
4	56.00	56.00	69.00	84.00	74.00	68.00	64.00	61.00	61.00	63.00
5	61.00	58.00	138.00	130.00	142.00	81.00	69.00	65.00	74.00	65.00
7	59.00	63.00	119.00	133.00	121.00	94.00	87.00	73.00	70.00	71.00
8	59.00	62.00	69.00	86.00	79.00	78.00	74.00	69.00	68.00	62.00
9	57.00	63.00	66.00	80.00	104.00	86.00	72.00	58.00	63.00	61.00
10	60.00	62.00	84.00	101.00	105.00	68.00	66.00	67.00	62.00	62.00
11	55.00	57.00	92.00	114.00	104.00	63.00	66.00	60.00	57.00	56.00
12	60.00	71.00	147.00	191.00	164.00	125.00	77.00	68.00	65.00	68.00
14*	52.00	53.00	55.00	56.00	54.00	54.00	56.00	53.00	53.00	53.00
15*	60.00	60.00	69.00	97.00	147.00	111.00	67.00	69.00	69.00	73.00
16*	59.00	55.00	99.00	67.00	92.00	66.00	65.00	59.00	59.00	58.00
102	58.00	59.00	61.00	70.00	84.00	86.00	62.00	69.00	60.00	61.00
111	56.00	58.00	90.00	132.00	133.00	74.00	105.00	63.00	58.00	59.00
112	52.00	50.00	78.00	58.00	64.00	55.00	53.00	56.00	53.00	54.00
114*	60.00	59.00	93.00	121.00	77.00	74.00	66.00	63.00	67.00	63.00
206	53.00	55.00	66.00	--	99.00	87.00	79.00	57.00	61.00	57.00
213*	56.00	55.00	155.00	84.00	67.00	66.00	64.00	60.00	57.00	58.00
Mean	56.89	58.42	92.53	101.22	101.95	82.16	70.53	63.21	61.53	60.79
St. Dev.	3.38	4.59	30.08	36.03	30.20	24.31	11.58	5.36	6.19	5.67

*Minority Subjects

(--) Duration not obtained

Table D14. Duration (msec) to 8 degree targets for young men during Alprazolam/DHEA Treatment

Subject	Time (h)									
	0	2	3.5	4.5	5.5	7	8.5	10	11.5	12.5
33	54.00	55.00	104.00	205.00	118.00	58.00	72.00	55.00	56.00	56.00
34	63.00	61.00	105.00	119.00	94.00	74.00	66.00	72.00	62.00	60.00
35	53.00	52.00	54.00	54.00	58.00	54.00	56.00	55.00	55.00	52.00
36	56.00	53.00	53.00	55.00	58.00	58.00	57.00	56.00	60.00	56.00
37	57.00	56.00	66.00	68.00	70.00	59.00	58.00	56.00	58.00	56.00
38	57.00	57.00	115.00	199.00	97.00	64.00	65.00	55.00	57.00	56.00
39	50.00	55.00	65.00	106.00	106.00	219.00	68.00	62.00	67.00	66.00
41	--	56.00	67.00	62.00	69.00	65.00	61.00	58.00	57.00	57.00
42	54.00	55.00	55.00	69.00	78.00	70.00	59.00	58.00	58.00	57.00
43	54.00	52.00	79.00	114.00	88.00	67.00	74.00	58.00	54.00	55.00
44	59.00	55.00	70.00	81.00	74.00	60.00	81.00	63.00	57.00	58.00
47*	55.00	55.00	66.00	67.00	61.00	61.00	60.00	61.00	59.00	58.00
48*	59.00	63.00	90.00	90.00	140.00	151.00	115.00	73.00	69.00	70.00
140	54.00	55.00	125.00	233.00	162.00	97.00	95.00	76.00	78.00	58.00
146*	61.00	64.00	69.00	91.00	119.00	76.00	66.00	66.00	68.00	64.00
245*	62.00	62.00	--	--	--	66.00	65.00	65.00	67.00	66.00
Mean	56.53	56.63	78.87	107.53	92.80	81.19	69.88	61.81	61.38	59.06
St. Dev.	3.66	3.79	23.25	58.22	31.22	43.57	15.68	6.88	6.60	4.88

*Minority Subjects
 (--) Duration not obtained

Table D15. Duration (msec) to 8 degree targets for older women during Alprazolam/DHEA Treatment

Subject	Time (h)									
	0	2	3.5	4.5	5.5	7	8.5	10	11.5	12.5
17	74.00	62.00	--	--	--	--	91.00	88.00	112.00	93.00
18	59.00	58.00	96.00	100.00	117.00	82.00	91.00	83.00	63.00	76.00
19	57.00	61.00	--	--	--	--	98.00	117.00	80.00	75.00
20*	65.00	64.00	120.00	99.00	151.00	125.00	153.00	110.00	110.00	164.00
21	58.00	57.00	143.00	164.00	113.00	80.00	73.00	72.00	73.00	67.00
22	56.00	57.00	127.00	177.00	169.00	73.00	74.00	66.00	67.00	64.00
23	58.00	59.00	--	69.00	87.00	85.00	65.00	71.00	71.00	63.00
24	51.00	51.00	92.00	61.00	98.00	55.00	69.00	53.00	55.00	53.00
25	72.00	57.00	64.00	194.00	226.00	139.00	79.00	74.00	132.00	110.00
26	66.00	62.00	--	--	--	210.00	284.00	147.00	232.00	60.00
27	59.00	90.00	--	--	--	--	--	79.00	70.00	83.00
28	60.00	60.00	93.00	--	88.00	--	77.00	88.00	--	79.00
29*	69.00	79.00	--	--	--	--	--	--	69.00	54.00
30*	67.00	63.00	--	125.00	92.00	103.00	222.00	83.00	79.00	83.00
31*	63.00	68.00	--	--	--	--	--	79.00	65.00	70.00
120	57.00	58.00	--	--	--	81.00	140.00	87.00	63.00	72.00
Mean	61.94	62.88	105.00	123.63	126.78	103.30	116.62	86.47	89.40	79.13
St. Dev.	6.35	9.46	26.55	50.01	46.94	44.98	67.26	23.04	45.00	26.90

*Minority Subjects

(--) Duration not obtained

Table D16. Duration (msec) to 8 degree targets for older men during Alprazolam/DHEA Treatment

Subject	Time (h)									
	0	2	3.5	4.5	5.5	7	8.5	10	11.5	12.5
50	58.00	60.00	--	--	--	--	64.00	65.00	83.00	70.00
51	58.00	58.00	--	--	--	--	59.00	62.00	60.00	60.00
52	57.00	69.00	--	--	127.00	106.00	101.00	106.00	103.00	130.00
53	58.00	88.00	62.00	89.00	94.00	80.00	70.00	65.00	66.00	62.00
54	91.00	70.00	181.00	181.00	284.00	212.00	244.00	110.00	88.00	73.00
55	67.00	69.00	83.00	69.00	66.00	77.00	66.00	69.00	67.00	64.00
56	56.00	55.00	94.00	77.00	101.00	104.00	106.00	90.00	77.00	70.00
57	50.00	50.00	54.00	60.00	72.00	65.00	53.00	54.00	53.00	48.00
58	60.00	61.00	71.00	81.00	72.00	74.00	66.00	66.00	66.00	66.00
59	51.00	52.00	--	68.00	72.00	54.00	54.00	50.00	61.00	84.00
61*	51.00	54.00	76.00	73.00	--	86.00	78.00	59.00	57.00	58.00
149	54.00	54.00	--	146.00	152.00	74.00	101.00	69.00	65.00	74.00
160	68.00	71.00	--	--	--	--	199.00	173.00	209.00	222.00
Mean	59.92	62.38	88.71	93.78	115.56	93.20	97.00	79.85	81.15	83.15
St. Dev.	10.84	10.64	42.76	41.31	69.51	44.66	58.78	33.61	40.87	46.12

*Minority Subjects

(--) Duration not obtained

Table D17. Duration (msec) to 16 degree targets for young women during Placebo Treatment

Subject	Time (h)									
	0	2	3.5	4.5	5.5	7	8.5	10	11.5	12.5
1	57.00	59.00	60.00	65.00	62.00	62.00	59.00	59.00	65.00	58.00
3	76.00	72.00	70.00	71.00	73.00	76.00	78.00	73.00	77.00	79.00
4	71.00	74.00	75.00	76.00	81.00	73.00	75.00	76.00	70.00	73.00
5	74.00	71.00	72.00	72.00	74.00	79.00	72.00	75.00	77.00	75.00
7	81.00	79.00	84.00	80.00	82.00	83.00	88.00	84.00	85.00	85.00
8	76.00	75.00	75.00	78.00	75.00	75.00	74.00	76.00	84.00	76.00
9	79.00	81.00	71.00	72.00	74.00	74.00	79.00	81.00	70.00	69.00
10	73.00	83.00	81.00	78.00	79.00	78.00	79.00	81.00	82.00	85.00
12	72.00	72.00	80.00	76.00	77.00	78.00	73.00	76.00	69.00	78.00
14*	63.00	65.00	64.00	67.00	67.00	66.00	67.00	68.00	69.00	64.00
15*	73.00	68.00	78.00	75.00	69.00	72.00	72.00	71.00	75.00	74.00
16*	71.00	74.00	73.00	73.00	72.00	70.00	71.00	71.00	76.00	71.00
102	77.00	77.00	77.00	81.00	79.00	76.00	79.00	79.00	80.00	78.00
111	72.00	71.00	74.00	80.00	78.00	74.00	73.00	74.00	74.00	73.00
112	64.00	66.00	65.00	68.00	66.00	64.00	65.00	65.00	66.00	64.00
114*	87.00	73.00	75.00	77.00	76.00	83.00	78.00	74.00	73.00	73.00
206	66.00	68.00	69.00	68.00	69.00	69.00	67.00	70.00	66.00	72.00
213*	68.00	67.00	66.00	68.00	69.00	69.00	71.00	68.00	68.00	69.00
Mean	72.22	71.94	72.72	73.61	73.44	73.39	73.33	73.39	73.67	73.11
St. Dev.	7.03	5.98	6.32	5.00	5.55	5.94	6.54	6.15	6.28	6.91

*Minority Subjects

Table D18. Duration (msec) to 16 degree targets for young men during Placebo Treatment

Subject	Time (h)									
	0	2	3.5	4.5	5.5	7	8.5	10	11.5	12.5
33	68.00	71.00	70.00	68.00	75.00	74.00	74.00	71.00	69.00	71.00
34	84.00	84.00	70.00	69.00	73.00	69.00	71.00	71.00	71.00	68.00
35	66.00	66.00	67.00	66.00	68.00	67.00	67.00	67.00	66.00	69.00
36	64.00	66.00	66.00	64.00	73.00	71.00	65.00	67.00	70.00	68.00
37	76.00	71.00	78.00	79.00	76.00	76.00	74.00	77.00	76.00	73.00
38	73.00	72.00	77.00	73.00	72.00	71.00	69.00	69.00	75.00	71.00
39	63.00	72.00	77.00	71.00	67.00	70.00	78.00	71.00	66.00	69.00
41	71.00	76.00	73.00	74.00	74.00	74.00	71.00	70.00	70.00	71.00
42	73.00	74.00	71.00	73.00	78.00	73.00	74.00	72.00	65.00	69.00
43	67.00	69.00	66.00	65.00	70.00	68.00	68.00	69.00	67.00	66.00
44	77.00	77.00	86.00	82.00	75.00	74.00	71.00	76.00	76.00	73.00
47*	69.00	68.00	67.00	68.00	70.00	70.00	67.00	67.00	71.00	67.00
48*	75.00	79.00	80.00	79.00	77.00	78.00	82.00	81.00	81.00	87.00
140	66.00	71.00	72.00	84.00	67.00	81.00	72.00	71.00	67.00	73.00
146*	73.00	76.00	79.00	76.00	77.00	79.00	85.00	76.00	86.00	77.00
245*	73.00	74.00	75.00	77.00	79.00	75.00	77.00	76.00	77.00	76.00
Mean	71.13	72.88	73.38	73.00	73.19	73.13	72.81	71.94	72.06	71.75
St. Dev.	5.50	4.80	5.81	6.13	3.89	4.03	5.53	4.12	5.96	5.11

*Minority Subjects

Table D19. Duration (msec) to 16 degree targets for older women during Placebo Treatment

Subject	Time (h)									
	0	2	3.5	4.5	5.5	7	8.5	10	11.5	12.5
17	76.00	77.00	77.00	79.00	76.00	74.00	77.00	73.00	72.00	77.00
18	65.00	69.00	62.00	75.00	68.00	65.00	78.00	66.00	74.00	71.00
19	74.00	79.00	78.00	80.00	85.00	76.00	79.00	76.00	74.00	78.00
20*	74.00	75.00	78.00	74.00	80.00	78.00	81.00	78.00	79.00	83.00
21	84.00	80.00	77.00	87.00	81.00	93.00	81.00	80.00	81.00	84.00
22	87.00	72.00	77.00	75.00	85.00	86.00	81.00	75.00	78.00	76.00
23	78.00	79.00	74.00	76.00	79.00	84.00	83.00	84.00	79.00	84.00
24	68.00	65.00	64.00	60.00	67.00	70.00	68.00	65.00	61.00	67.00
25	81.00	73.00	72.00	72.00	67.00	76.00	79.00	77.00	69.00	73.00
26	101.00	113.00	109.00	96.00	108.00	98.00	97.00	98.00	97.00	91.00
27	113.00	83.00	81.00	70.00	90.00	109.00	84.00	89.00	75.00	87.00
28	75.00	73.00	71.00	73.00	76.00	77.00	77.00	82.00	76.00	78.00
29*	68.00	73.00	77.00	76.00	--	81.00	70.00	66.00	65.00	65.00
30*	79.00	99.00	105.00	84.00	102.00	85.00	89.00	102.00	95.00	95.00
31*	--	84.00	119.00	85.00	108.00	75.00	83.00	--	79.00	80.00
120	73.00	74.00	77.00	74.00	75.00	75.00	97.00	75.00	79.00	80.00
Mean	79.73	79.25	81.13	77.25	83.13	81.38	81.50	79.07	77.06	79.31
St. Dev.	12.75	11.82	15.88	8.14	13.62	11.07	7.87	10.83	9.20	8.11

*Minority Subjects

(--) Duration not obtained

Table D20. Duration (msec) to 16 degree targets for older men during Placebo Treatment

Subject	Time (h)									
	0	2	3.5	4.5	5.5	7	8.5	10	11.5	12.5
50	80.00	109.00	88.00	86.00	85.00	92.00	79.00	--	77.00	82.00
51	72.00	73.00	75.00	76.00	72.00	71.00	73.00	74.00	71.00	69.00
52	76.00	84.00	82.00	71.00	71.00	72.00	134.00	82.00	71.00	79.00
53	91.00	95.00	93.00	89.00	81.00	87.00	93.00	92.00	79.00	86.00
54	120.00	108.00	110.00	116.00	118.00	122.00	161.00	87.00	95.00	114.00
55	79.00	85.00	83.00	86.00	83.00	83.00	82.00	89.00	84.00	86.00
56	74.00	74.00	84.00	67.00	69.00	79.00	79.00	81.00	71.00	64.00
57	58.00	59.00	61.00	67.00	66.00	64.00	63.00	64.00	58.00	62.00
58	82.00	87.00	82.00	83.00	80.00	86.00	80.00	84.00	79.00	81.00
59	58.00	83.00	70.00	61.00	68.00	75.00	65.00	65.00	59.00	72.00
61*	--	68.00	66.00	68.00	68.00	73.00	70.00	70.00	64.00	67.00
149	67.00	69.00	69.00	67.00	72.00	69.00	68.00	68.00	70.00	67.00
160	81.00	87.00	80.00	91.00	102.00	102.00	104.00	87.00	79.00	90.00
Mean	78.17	83.15	80.23	79.08	79.62	82.69	88.54	78.58	73.62	78.38
St. Dev.	16.35	14.89	12.81	14.94	15.21	15.78	28.99	9.91	10.19	14.15

*Minority Subjects

(--) Duration not obtained

Table D21. Duration (msec) to 16 degree targets for young women during DHEA Treatment

Subject	Time (h)									
	0	2	3.5	4.5	5.5	7	8.5	10	11.5	12.5
1	56.00	61.00	58.00	66.00	63.00	59.00	58.00	58.00	70.00	59.00
3	78.00	82.00	78.00	74.00	74.00	74.00	72.00	74.00	73.00	72.00
4	73.00	75.00	75.00	74.00	78.00	76.00	77.00	76.00	72.00	74.00
5	68.00	69.00	73.00	69.00	70.00	76.00	62.00	72.00	69.00	75.00
7	78.00	81.00	88.00	83.00	83.00	82.00	83.00	81.00	82.00	82.00
8	74.00	75.00	75.00	79.00	75.00	79.00	77.00	78.00	76.00	76.00
9	73.00	73.00	70.00	75.00	72.00	74.00	72.00	76.00	70.00	70.00
10	69.00	74.00	74.00	79.00	78.00	74.00	78.00	76.00	81.00	75.00
12	75.00	74.00	78.00	74.00	76.00	73.00	72.00	75.00	74.00	75.00
14*	65.00	72.00	70.00	67.00	68.00	69.00	68.00	66.00	68.00	67.00
15*	72.00	75.00	69.00	77.00	78.00	76.00	77.00	71.00	79.00	79.00
16*	70.00	67.00	73.00	58.00	74.00	70.00	70.00	72.00	68.00	69.00
102	75.00	80.00	80.00	81.00	78.00	79.00	75.00	84.00	80.00	78.00
111	75.00	73.00	74.00	74.00	76.00	74.00	75.00	75.00	76.00	76.00
112	61.00	64.00	59.00	64.00	66.00	64.00	63.00	64.00	64.00	64.00
114*	74.00	76.00	79.00	72.00	72.00	73.00	73.00	72.00	73.00	76.00
206	71.00	70.00	68.00	71.00	--	70.00	78.00	70.00	67.00	67.00
213*	--	--	67.00	66.00	--	69.00	63.00	66.00	66.00	65.00
Mean	71.00	73.00	72.67	72.39	73.81	72.83	71.83	72.56	72.67	72.17
St. Dev.	5.85	5.61	7.21	6.48	5.15	5.48	6.71	6.24	5.41	5.98

*Minority Subjects

(--) Duration not obtained

Table D22. Duration (msec) to 16 degree targets for young men during DHEA Treatment

Subject	Time (h)									
	0	2	3.5	4.5	5.5	7	8.5	10	11.5	12.5
33	73.00	75.00	77.00	70.00	70.00	70.00	76.00	69.00	68.00	68.00
34	76.00	68.00	72.00	77.00	72.00	77.00	74.00	89.00	92.00	79.00
35	82.00	68.00	67.00	67.00	68.00	68.00	68.00	69.00	68.00	67.00
36	67.00	69.00	67.00	69.00	64.00	64.00	66.00	66.00	70.00	65.00
37	73.00	72.00	75.00	74.00	81.00	77.00	79.00	74.00	75.00	75.00
38	69.00	71.00	87.00	69.00	69.00	79.00	74.00	72.00	72.00	79.00
39	62.00	70.00	68.00	74.00	77.00	75.00	80.00	77.00	67.00	65.00
41	66.00	67.00	72.00	69.00	75.00	69.00	72.00	70.00	69.00	70.00
42	66.00	67.00	69.00	66.00	66.00	70.00	71.00	71.00	67.00	70.00
43	65.00	67.00	68.00	71.00	67.00	68.00	67.00	66.00	64.00	66.00
44	74.00	77.00	78.00	73.00	80.00	73.00	73.00	72.00	70.00	72.00
47*	67.00	69.00	72.00	67.00	67.00	64.00	68.00	65.00	67.00	68.00
48*	80.00	72.00	78.00	71.00	78.00	73.00	77.00	76.00	80.00	70.00
140	69.00	70.00	72.00	79.00	74.00	77.00	68.00	67.00	67.00	62.00
146*	81.00	77.00	78.00	80.00	76.00	85.00	78.00	83.00	84.00	84.00
245*	73.00	76.00	77.00	77.00	97.00	79.00	78.00	75.00	77.00	77.00
Mean	71.44	70.94	73.56	72.06	73.81	73.00	73.06	72.56	72.31	71.06
St. Dev.	6.07	3.57	5.44	4.40	8.11	5.85	4.67	6.47	7.54	6.14

*Minority Subjects

Table D23. Duration (msec) to 16 degree targets for older women during DHEA Treatment

Subject	Time (h)									
	0	2	3.5	4.5	5.5	7	8.5	10	11.5	12.5
17	74.00	75.00	81.00	95.00	93.00	77.00	73.00	73.00	75.00	76.00
18	85.00	72.00	82.00	88.00	69.00	71.00	75.00	76.00	72.00	74.00
19	79.00	74.00	78.00	75.00	89.00	78.00	78.00	81.00	86.00	77.00
20*	89.00	85.00	86.00	83.00	87.00	88.00	81.00	79.00	85.00	85.00
21	84.00	92.00	83.00	85.00	82.00	85.00	83.00	80.00	84.00	78.00
22	78.00	73.00	78.00	77.00	77.00	76.00	82.00	77.00	83.00	88.00
23	89.00	84.00	97.00	92.00	82.00	84.00	84.00	80.00	83.00	86.00
24	69.00	69.00	69.00	67.00	72.00	67.00	66.00	74.00	71.00	64.00
25	71.00	73.00	70.00	68.00	68.00	70.00	70.00	73.00	76.00	71.00
26	106.00	99.00	103.00	123.00	133.00	117.00	109.00	101.00	90.00	107.00
27	--	71.00	70.00	85.00	70.00	85.00	85.00	84.00	92.00	134.00
28	72.00	71.00	76.00	77.00	75.00	81.00	76.00	76.00	75.00	76.00
29*	64.00	65.00	66.00	74.00	62.00	68.00	70.00	72.00	67.00	72.00
30*	86.00	98.00	87.00	88.00	100.00	96.00	99.00	88.00	96.00	87.00
31*	--	--	--	88.00	--	--	--	83.00	--	88.00
120	73.00	77.00	75.00	76.00	77.00	87.00	77.00	75.00	80.00	76.00
Mean	79.93	78.53	80.07	83.81	82.40	82.00	80.53	79.50	81.00	83.69
St. Dev.	10.84	10.62	10.29	13.28	17.37	12.73	11.19	7.27	8.28	16.66

*Minority Subjects

(--) Duration not obtained

Table D24. Duration (msec) to 16 degree targets for older men during DHEA Treatment

Subject	Time (h)									
	0	2	3.5	4.5	5.5	7	8.5	10	11.5	12.5
50	76.00	74.00	84.00	70.00	73.00	76.00	72.00	75.00	76.00	73.00
51	71.00	73.00	80.00	76.00	81.00	79.00	73.00	81.00	74.00	69.00
52	76.00	75.00	73.00	81.00	80.00	92.00	107.00	77.00	74.00	76.00
53	78.00	83.00	80.00	83.00	87.00	94.00	83.00	83.00	89.00	93.00
54	141.00	110.00	112.00	124.00	117.00	121.00	142.00	121.00	97.00	114.00
55	86.00	84.00	83.00	90.00	83.00	80.00	88.00	82.00	80.00	86.00
56	74.00	74.00	71.00	70.00	71.00	72.00	71.00	73.00	74.00	73.00
57	62.00	59.00	64.00	69.00	59.00	75.00	62.00	60.00	56.00	59.00
58	81.00	83.00	84.00	83.00	77.00	81.00	82.00	82.00	82.00	82.00
59	72.00	70.00	69.00	69.00	69.00	65.00	63.00	58.00	59.00	61.00
61*	68.00	62.00	59.00	64.00	66.00	70.00	63.00	69.00	67.00	68.00
149	69.00	75.00	73.00	70.00	70.00	72.00	71.00	72.00	73.00	63.00
160	100.00	122.00	140.00	87.00	96.00	132.00	82.00	97.00	114.00	106.00
Mean	81.08	80.31	82.46	79.69	79.15	85.31	81.46	79.23	78.08	78.69
St. Dev.	20.31	17.64	21.57	15.59	14.92	20.11	21.99	16.16	15.39	17.05

*Minority Subjects

Table D25. Duration (msec) to 16 degree targets for young women during Alprazolam/Placebo Treatment

Subject	Time (h)									
	0	2	3.5	4.5	5.5	7	8.5	10	11.5	12.5
1	60.00	72.00	130.00	134.00	94.00	92.00	108.00	117.00	159.00	98.00
3	76.00	76.00	109.00	114.00	124.00	86.00	89.00	83.00	76.00	82.00
4	75.00	75.00	94.00	201.00	91.00	100.00	83.00	83.00	81.00	83.00
5	82.00	75.00	141.00	126.00	154.00	174.00	93.00	81.00	77.00	82.00
7	80.00	80.00	151.00	164.00	149.00	108.00	102.00	96.00	96.00	98.00
8	80.00	76.00	102.00	110.00	164.00	107.00	114.00	86.00	93.00	87.00
9	77.00	72.00	87.00	116.00	109.00	99.00	86.00	82.00	84.00	79.00
10	78.00	78.00	81.00	100.00	117.00	90.00	94.00	85.00	84.00	81.00
11	67.00	74.00	154.00	185.00	121.00	109.00	95.00	78.00	78.00	76.00
12	74.00	76.00	81.00	171.00	155.00	143.00	203.00	78.00	81.00	104.00
14*	72.00	75.00	80.00	109.00	125.00	92.00	86.00	89.00	86.00	84.00
15*	73.00	74.00	131.00	150.00	159.00	89.00	86.00	83.00	83.00	81.00
16*	73.00	70.00	96.00	82.00	121.00	102.00	125.00	84.00	83.00	74.00
102	86.00	84.00	94.00	135.00	138.00	121.00	105.00	84.00	84.00	85.00
111	75.00	74.00	87.00	157.00	183.00	127.00	89.00	91.00	86.00	84.00
112	64.00	64.00	96.00	102.00	109.00	113.00	88.00	80.00	76.00	79.00
114*	86.00	91.00	114.00	118.00	140.00	105.00	101.00	91.00	90.00	86.00
206	68.00	70.00	107.00	220.00	141.00	136.00	135.00	106.00	101.00	80.00
213*	69.00	71.00	94.00	107.00	95.00	89.00	83.00	76.00	71.00	73.00
Mean	74.47	75.11	106.79	136.89	131.00	109.58	103.42	87.00	87.84	84.00
St. Dev.	6.92	5.69	23.70	37.45	25.77	22.49	28.08	10.12	18.72	8.11

*Minority Subjects

Table D26. Duration (msec) to 16 degree targets for young men during Alprazolam/Placebo Treatment

Subject	Time (h)									
	0	2	3.5	4.5	5.5	7	8.5	10	11.5	12.5
33	73.00	71.00	120.00	108.00	98.00	92.00	107.00	77.00	71.00	69.00
34	87.00	77.00	309.00	175.00	132.00	140.00	113.00	91.00	74.00	82.00
35	69.00	66.00	--	82.00	78.00	75.00	85.00	72.00	73.00	70.00
36	64.00	65.00	78.00	88.00	77.00	77.00	81.00	71.00	77.00	69.00
37	78.00	82.00	93.00	104.00	99.00	90.00	81.00	81.00	79.00	75.00
38	70.00	71.00	131.00	193.00	136.00	118.00	93.00	72.00	80.00	71.00
39	65.00	61.00	159.00	182.00	156.00	168.00	140.00	79.00	83.00	68.00
41	69.00	70.00	79.00	80.00	80.00	80.00	80.00	76.00	70.00	72.00
42	--	81.00	159.00	144.00	156.00	139.00	91.00	91.00	80.00	79.00
43	66.00	68.00	135.00	116.00	105.00	88.00	79.00	71.00	74.00	70.00
44	69.00	80.00	92.00	187.00	208.00	132.00	--	97.00	77.00	76.00
47*	65.00	73.00	86.00	90.00	89.00	81.00	81.00	79.00	76.00	86.00
48*	71.00	80.00	116.00	--	184.00	90.00	92.00	82.00	93.00	86.00
140	66.00	69.00	251.00	118.00	159.00	118.00	119.00	77.00	86.00	82.00
146*	74.00	80.00	123.00	136.00	172.00	141.00	103.00	88.00	89.00	86.00
245*	74.00	77.00	--	--	--	84.00	82.00	83.00	83.00	84.00
Mean	70.67	73.19	137.93	128.79	128.60	107.06	95.13	80.44	79.06	76.56
St. Dev.	6.03	6.52	66.74	40.97	42.49	29.30	17.93	7.88	6.46	6.91

*Minority Subjects

(--) Duration not obtained

Table D27. Duration (msec) to 16 degree targets for older women during Alprazolam/Placebo Treatment

Subject	Time (h)									
	0	2	3.5	4.5	5.5	7	8.5	10	11.5	12.5
17	73.00	82.00	162.00	196.00	215.00	159.00	145.00	181.00	142.00	181.00
18	65.00	69.00	200.00	188.00	177.00	197.00	139.00	97.00	93.00	98.00
19	76.00	77.00	--	--	164.00	--	168.00	134.00	131.00	140.00
20*	72.00	83.00	88.00	110.00	114.00	162.00	142.00	134.00	132.00	125.00
21	71.00	74.00	--	156.00	165.00	100.00	94.00	93.00	93.00	101.00
22	77.00	74.00	80.00	157.00	185.00	125.00	165.00	98.00	105.00	91.00
23	--	81.00	--	121.00	136.00	131.00	115.00	121.00	91.00	92.00
24	62.00	69.00	94.00	105.00	121.00	71.00	74.00	88.00	74.00	70.00
25	82.00	82.00	101.00	179.00	207.00	121.00	97.00	99.00	111.00	103.00
26	90.00	100.00	--	--	141.00	147.00	214.00	154.00	177.00	141.00
27	79.00	72.00	--	--	--	--	--	--	87.00	92.00
28	74.00	76.00	--	171.00	140.00	--	--	123.00	103.00	108.00
29*	77.00	67.00	--	130.00	159.00	169.00	150.00	99.00	99.00	165.00
30*	97.00	88.00	--	--	137.00	226.00	140.00	138.00	116.00	135.00
31*	94.00	84.00	--	--	--	--	--	--	95.00	104.00
120	77.00	82.00	--	--	--	--	102.00	122.00	81.00	96.00
Mean	77.73	78.75	120.83	151.30	158.54	146.18	134.23	120.07	108.13	115.13
St. Dev.	9.76	8.36	48.62	32.96	31.18	43.57	37.61	26.68	26.39	29.97

*Minority Subjects

(--) Duration not obtained

Table D28. Duration (msec) to 16 degree targets for older men during Alprazolam/Placebo Treatment

Subject	Time (h)									
	0	2	3.5	4.5	5.5	7	8.5	10	11.5	12.5
50	79.00	76.00	112.00	126.00	127.00	97.00	119.00	88.00	90.00	85.00
51	75.00	79.00	124.00	118.00	105.00	81.00	81.00	79.00	80.00	79.00
52	74.00	82.00	--	--	--	--	117.00	130.00	105.00	111.00
53	82.00	84.00	112.00	111.00	118.00	154.00	96.00	87.00	91.00	88.00
54	103.00	114.00	177.00	147.00	185.00	247.00	126.00	106.00	133.00	136.00
55	81.00	103.00	103.00	112.00	96.00	92.00	94.00	96.00	88.00	94.00
56	68.00	68.00	--	122.00	139.00	103.00	100.00	94.00	77.00	100.00
57	61.00	64.00	99.00	76.00	72.00	74.00	63.00	63.00	65.00	62.00
58	80.00	76.00	94.00	88.00	93.00	90.00	83.00	92.00	81.00	83.00
59	61.00	61.00	--	145.00	67.00	67.00	72.00	70.00	66.00	68.00
61*	65.00	70.00	119.00	85.00	79.00	89.00	73.00	75.00	72.00	72.00
149	64.00	--	157.00	236.00	188.00	130.00	103.00	85.00	94.00	81.00
160	85.00	94.00	--	--	--	171.00	150.00	195.00	162.00	146.00
Mean	75.23	80.92	121.89	124.18	115.36	116.25	98.23	96.92	92.62	92.69
St. Dev.	11.81	15.91	27.70	43.58	41.65	51.98	24.80	33.94	27.48	25.14

*Minority Subjects

(--) Duration not obtained

Table D29. Duration (msec) to 16 degree targets for young women during Alprazolam/DHEA Treatment

Subject	Time (h)									
	0	2	3.5	4.5	5.5	7	8.5	10	11.5	12.5
1	57.00	65.00	209.00	90.00	84.00	122.00	89.00	91.00	61.00	62.00
3	72.00	70.00	105.00	151.00	223.00	105.00	94.00	87.00	74.00	76.00
4	75.00	75.00	110.00	119.00	116.00	112.00	83.00	83.00	82.00	88.00
5	78.00	76.00	139.00	134.00	156.00	111.00	90.00	87.00	89.00	91.00
7	82.00	83.00	131.00	169.00	128.00	124.00	114.00	98.00	93.00	97.00
8	73.00	75.00	86.00	97.00	95.00	86.00	104.00	88.00	88.00	81.00
9	71.00	74.00	80.00	91.00	110.00	96.00	89.00	77.00	81.00	78.00
10	77.00	75.00	99.00	117.00	119.00	87.00	82.00	84.00	78.00	78.00
11	66.00	71.00	136.00	132.00	110.00	79.00	76.00	78.00	73.00	69.00
12	75.00	76.00	165.00	231.00	182.00	142.00	95.00	109.00	99.00	94.00
14*	70.00	69.00	75.00	73.00	70.00	72.00	71.00	72.00	72.00	76.00
15*	74.00	77.00	85.00	119.00	182.00	147.00	90.00	90.00	85.00	91.00
16*	72.00	67.00	120.00	84.00	120.00	79.00	78.00	73.00	72.00	71.00
102	78.00	81.00	92.00	111.00	111.00	100.00	92.00	92.00	85.00	83.00
111	75.00	75.00	154.00	147.00	146.00	111.00	108.00	86.00	81.00	84.00
112	65.00	64.00	96.00	83.00	91.00	72.00	85.00	77.00	77.00	81.00
114*	70.00	72.00	105.00	140.00	99.00	90.00	85.00	78.00	80.00	80.00
206	68.00	70.00	95.00	--	124.00	92.00	150.00	98.00	90.00	80.00
213*	70.00	70.00	191.00	112.00	87.00	85.00	82.00	78.00	76.00	77.00
Mean	72.00	72.89	119.63	122.22	123.84	100.63	92.47	85.58	80.84	80.89
St. Dev.	5.62	4.97	37.90	37.86	38.84	21.93	17.57	9.51	8.88	8.75

*Minority Subjects

(--) Duration not obtained

Table D30. Duration (msec) to 16 degree targets for young men during Alprazolam/DHEA Treatment

Subject	Time (h)									
	0	2	3.5	4.5	5.5	7	8.5	10	11.5	12.5
33	69.00	69.00	139.00	144.00	117.00	73.00	95.00	71.00	72.00	73.00
34	69.00	66.00	170.00	145.00	138.00	118.00	119.00	91.00	90.00	90.00
35	66.00	67.00	80.00	97.00	112.00	95.00	79.00	97.00	71.00	71.00
36	68.00	69.00	72.00	87.00	84.00	85.00	76.00	86.00	81.00	70.00
37	74.00	74.00	105.00	92.00	97.00	80.00	78.00	74.00	74.00	82.00
38	69.00	73.00	186.00	254.00	157.00	83.00	87.00	78.00	75.00	75.00
39	65.00	68.00	107.00	132.00	213.00	227.00	81.00	93.00	86.00	73.00
41	--	72.00	90.00	86.00	88.00	85.00	81.00	75.00	74.00	71.00
42	74.00	75.00	93.00	114.00	128.00	102.00	85.00	86.00	87.00	84.00
43	67.00	66.00	110.00	124.00	100.00	94.00	84.00	76.00	74.00	72.00
44	76.00	72.00	113.00	101.00	90.00	96.00	104.00	84.00	85.00	79.00
47*	64.00	66.00	95.00	110.00	95.00	86.00	86.00	84.00	78.00	76.00
48*	84.00	80.00	126.00	124.00	247.00	149.00	114.00	93.00	92.00	97.00
140	72.00	72.00	158.00	158.00	200.00	113.00	146.00	87.00	79.00	78.00
146*	74.00	79.00	88.00	103.00	129.00	91.00	82.00	80.00	85.00	81.00
245*	73.00	78.00	--	--	--	81.00	80.00	80.00	82.00	81.00
Mean	70.93	71.63	115.47	124.73	133.00	103.63	92.31	83.44	80.31	78.31
St. Dev.	5.16	4.67	33.93	42.08	50.23	37.77	19.26	7.63	6.66	7.46

*Minority Subjects

(--) Duration not obtained

Table D31. Duration (msec) to 16 degree targets for older women during Alprazolam/DHEA Treatment

Subject	Time (h)									
	0	2	3.5	4.5	5.5	7	8.5	10	11.5	12.5
17	80.00	77.00	--	--	--	--	104.00	88.00	101.00	110.00
18	69.00	75.00	179.00	200.00	207.00	107.00	154.00	107.00	108.00	91.00
19	73.00	84.00	--	--	--	--	136.00	109.00	114.00	102.00
20*	81.00	86.00	151.00	141.00	124.00	136.00	158.00	115.00	142.00	161.00
21	71.00	74.00	172.00	179.00	124.00	128.00	106.00	98.00	112.00	96.00
22	77.00	77.00	128.00	218.00	207.00	108.00	112.00	100.00	103.00	88.00
23	76.00	76.00	--	135.00	110.00	102.00	96.00	96.00	82.00	88.00
24	66.00	65.00	94.00	74.00	101.00	78.00	89.00	75.00	74.00	86.00
25	99.00	75.00	95.00	223.00	218.00	160.00	139.00	106.00	133.00	179.00
26	98.00	94.00	--	--	--	205.00	156.00	242.00	190.00	126.00
27	98.00	80.00	--	--	--	--	--	101.00	85.00	93.00
28	73.00	75.00	144.00	--	149.00	--	106.00	130.00	--	106.00
29*	101.00	74.00	--	--	--	--	--	--	98.00	89.00
30*	87.00	85.00	--	189.00	162.00	151.00	212.00	119.00	109.00	112.00
31*	74.00	89.00	--	--	--	--	--	112.00	102.00	86.00
120	74.00	77.00	--	--	--	116.00	126.00	118.00	99.00	92.00
Mean	81.06	78.94	137.57	169.88	155.78	129.10	130.31	114.40	110.13	106.56
St. Dev.	11.76	7.08	33.97	50.34	45.17	36.05	34.01	37.76	28.21	27.38

*Minority Subjects

(--) Duration not obtained

Table D32. Duration (msec) to 16 degree targets for older men during Alprazolam/DHEA Treatment

Subject	Time (h)									
	0	2	3.5	4.5	5.5	7	8.5	10	11.5	12.5
50	81.00	88.00	--	--	--	--	88.00	95.00	127.00	97.00
51	76.00	78.00	--	--	--	--	80.00	85.00	81.00	85.00
52	74.00	83.00	--	--	128.00	142.00	109.00	163.00	119.00	182.00
53	81.00	121.00	90.00	98.00	141.00	116.00	102.00	100.00	84.00	102.00
54	115.00	101.00	327.00	272.00	217.00	269.00	249.00	142.00	117.00	110.00
55	85.00	89.00	104.00	89.00	83.00	107.00	93.00	95.00	92.00	87.00
56	68.00	75.00	121.00	100.00	138.00	123.00	122.00	112.00	104.00	86.00
57	62.00	65.00	79.00	66.00	81.00	77.00	79.00	63.00	66.00	53.00
58	78.00	80.00	95.00	104.00	92.00	94.00	91.00	85.00	85.00	86.00
59	70.00	65.00	--	128.00	134.00	66.00	58.00	68.00	77.00	90.00
61*	65.00	62.00	119.00	106.00	--	109.00	100.00	74.00	72.00	69.00
149	68.00	68.00	--	87.00	121.00	97.00	148.00	91.00	86.00	78.00
160	101.00	96.00	--	--	--	--	205.00	222.00	182.00	198.00
Mean	78.77	82.38	133.57	116.67	126.11	120.00	117.23	107.31	99.38	101.77
St. Dev.	14.91	16.85	86.63	60.59	41.49	56.74	54.10	44.46	31.21	41.77

*Minority Subjects

(--) Duration not obtained

APPENDIX E

Saccadic Eye Movement Parameters

Accuracy: 8 degree & 16 degree

Table E1. Accuracy (msec) to 8 degree targets for young women during Placebo Treatment

Subject	Time (h)									
	0	2	3.5	4.5	5.5	7	8.5	10	11.5	12.5
1	101.70	103.90	100.90	105.00	100.90	103.50	101.40	99.20	105.40	99.70
3	94.20	95.30	96.00	98.60	97.10	99.30	98.40	101.60	95.70	96.70
4	101.60	102.40	98.60	95.00	99.60	101.50	102.30	97.60	100.00	96.00
5	95.40	102.40	99.90	93.80	94.40	94.40	98.90	96.60	97.10	99.50
7	89.90	91.80	95.20	96.50	97.80	97.80	93.90	97.30	98.60	97.00
8	91.50	93.10	92.60	96.10	91.10	89.90	95.20	96.70	96.10	94.90
9	97.60	99.70	97.40	103.10	105.70	101.70	100.80	100.70	98.90	106.90
10	97.20	96.80	103.40	96.60	101.30	101.00	98.50	97.50	97.90	94.70
12	93.20	92.40	88.10	95.90	97.70	93.50	94.00	92.40	97.90	96.80
14*	94.30	93.00	96.50	92.40	97.60	100.10	99.60	92.40	104.50	94.90
15*	89.40	90.00	85.50	93.10	86.00	90.00	88.50	90.60	92.00	89.60
16*	93.60	96.20	101.00	91.70	94.20	95.40	102.50	95.50	94.30	97.20
102	88.10	91.90	99.80	96.20	96.40	94.70	97.50	98.70	95.70	95.40
111	104.50	101.90	99.50	100.30	99.30	96.70	96.60	94.10	97.70	97.00
112	97.90	103.30	102.60	97.30	94.70	104.50	97.20	97.10	94.10	96.00
114*	98.90	92.80	97.50	100.20	97.90	92.00	103.80	96.50	104.10	100.90
206	99.50	99.20	96.30	100.70	92.80	100.40	101.30	92.80	96.30	101.30
213*	96.40	104.50	105.70	97.80	104.30	100.10	99.20	103.30	106.50	98.00
Mean	95.83	97.26	97.58	97.24	97.16	97.58	98.31	96.70	98.49	97.36
St. Dev.	4.39	4.79	4.91	3.50	4.54	4.34	3.65	3.28	4.02	3.48

*Minority Subjects

Table E2. Accuracy (msec) to 8 degree targets for young men during Placebo Treatment

Subject	Time (h)									
	0	2	3.5	4.5	5.5	7	8.5	10	11.5	12.5
33	95.60	99.00	96.30	100.90	97.60	99.30	97.90	99.40	99.20	98.60
34	87.30	85.00	91.60	98.10	96.90	97.30	90.70	94.00	94.80	88.10
35	100.50	98.20	96.70	100.20	100.10	97.30	103.20	100.00	98.30	96.60
36	93.60	91.60	92.60	90.50	93.50	91.30	94.00	96.30	97.70	92.80
37	94.40	96.90	97.80	102.10	97.80	108.50	98.40	103.60	102.10	109.70
38	91.50	91.90	95.70	96.00	94.50	94.80	101.70	95.90	95.60	96.20
39	95.60	96.60	88.20	96.90	94.50	90.80	92.70	98.10	94.30	93.60
41	98.30	99.10	107.00	95.00	108.20	101.10	98.20	98.20	103.30	97.70
42	92.10	90.00	92.70	92.60	91.50	93.30	94.80	89.80	95.10	94.10
43	97.60	98.80	97.70	100.50	101.50	97.20	94.80	94.90	91.70	96.30
44	88.00	89.20	93.90	93.70	92.50	95.60	93.50	98.10	95.20	97.50
47*	103.50	101.80	103.60	97.40	100.10	93.70	100.80	95.20	95.80	101.60
48*	92.80	85.40	95.50	95.80	95.20	96.00	93.10	98.70	96.90	89.30
140	90.60	91.30	93.90	85.00	86.00	94.90	87.30	87.30	90.90	87.30
146*	89.90	87.40	97.00	91.00	99.40	94.30	89.60	96.70	96.70	95.30
245*	92.00	88.20	93.50	98.40	100.00	91.40	97.20	94.80	93.70	96.00
Mean	93.96	93.15	95.86	95.88	96.83	96.05	95.49	96.31	96.33	95.67
St. Dev.	4.43	5.45	4.50	4.52	5.03	4.37	4.44	3.89	3.31	5.37

*Minority Subjects

Table E3. Accuracy (msec) to 8 degree targets for older women during Placebo Treatment

Subject	Time (h)									
	0	2	3.5	4.5	5.5	7	8.5	10	11.5	12.5
17	92.00	95.50	85.20	91.30	90.40	88.00	96.20	101.30	98.20	94.60
18	84.70	78.60	93.30	96.80	93.80	99.00	88.80	90.00	92.50	93.30
19	89.90	98.50	94.20	86.80	89.10	90.40	96.10	95.90	82.90	89.20
20*	83.90	89.70	82.20	86.60	91.40	94.30	89.30	94.00	85.30	92.40
21	92.10	92.90	91.80	91.60	89.80	94.30	91.90	90.30	91.50	98.00
22	89.50	95.80	94.10	91.80	93.60	92.60	91.80	94.50	90.00	90.80
23	94.60	96.50	101.70	97.90	91.60	98.90	90.90	92.50	97.30	92.70
24	97.70	91.00	92.00	100.40	60.70	94.10	93.80	88.10	91.10	96.70
25	102.20	98.40	97.60	105.70	106.30	103.10	101.50	103.70	110.90	107.40
26	86.30	81.60	86.10	86.20	82.40	86.60	90.30	86.40	95.10	87.60
27	93.10	95.40	93.30	92.00	101.90	96.60	97.10	91.40	91.60	95.30
28	100.00	102.30	98.70	97.60	101.20	93.30	103.40	98.10	100.00	98.70
29*	83.00	93.00	95.80	92.80	--	94.70	88.90	82.80	84.80	110.00
30*	100.00	91.40	92.80	99.70	95.90	96.00	98.80	95.20	92.60	96.20
31*	--	87.10	85.40	93.20	77.50	94.10	89.60	--	90.90	86.10
120	113.90	101.10	101.40	101.10	98.50	101.10	100.50	101.80	96.10	101.40
Mean	93.53	93.05	92.85	94.47	90.94	94.82	94.31	93.73	93.18	95.65
St. Dev.	8.28	6.50	5.75	5.68	11.12	4.39	4.86	5.89	6.73	6.53

*Minority Subjects

(--) Accuracy not obtained

Table E4. Accuracy (msec) to 8 degree targets for older men during Placebo Treatment

Subject	Time (h)									
	0	2	3.5	4.5	5.5	7	8.5	10	11.5	12.5
50	83.30	83.90	79.60	83.50	87.40	83.80	96.10	76.30	91.10	92.20
51	98.10	92.50	92.60	97.80	97.60	95.10	94.10	91.00	91.80	90.90
52	88.70	84.10	94.40	95.70	95.90	94.20	96.30	91.70	87.70	91.30
53	97.90	96.10	99.20	100.70	92.60	96.40	92.90	94.70	96.80	102.20
54	95.10	95.30	91.00	85.10	90.40	92.20	88.40	92.40	93.40	102.40
55	89.50	88.70	92.70	94.30	93.90	86.20	95.40	92.70	92.30	91.00
56	99.50	100.90	106.60	108.00	99.80	101.50	102.70	98.70	98.30	102.60
57	98.40	102.60	97.10	100.50	94.00	100.90	95.60	93.40	103.80	95.70
58	87.50	89.00	93.60	86.80	94.20	90.70	95.90	92.90	91.20	92.40
59	82.80	84.10	85.60	82.70	81.00	78.80	84.30	88.80	83.70	82.10
61*	–	90.80	82.40	91.80	91.40	91.80	96.80	91.70	89.50	92.20
149	91.10	100.10	93.20	103.40	95.50	91.30	96.40	94.00	95.30	93.30
160	95.20	97.40	91.80	85.80	90.40	97.80	84.20	92.90	96.30	90.90
Mean	92.26	92.73	92.29	93.55	92.62	92.36	93.78	91.63	93.17	93.78
St. Dev.	5.93	6.58	7.00	8.30	4.79	6.54	5.24	5.14	5.09	5.78

*Minority Subjects

(–) Accuracy not obtained

Table E5. Accuracy (msec) to 8 degree targets for young women during DHEA Treatment

Subject	Time (h)									
	0	2	3.5	4.5	5.5	7	8.5	10	11.5	12.5
1	93.60	85.00	102.90	86.80	101.10	104.80	98.40	99.20	106.10	95.60
3	86.30	96.60	96.10	100.40	96.20	96.60	99.20	99.80	96.10	94.50
4	99.80	94.50	98.40	98.40	102.10	98.90	96.70	96.70	99.40	96.80
5	93.90	91.90	98.00	91.10	97.90	95.90	93.80	95.90	98.40	100.80
7	95.00	94.90	99.30	88.10	94.50	94.50	93.50	92.50	95.90	92.70
8	89.20	95.50	95.30	95.00	98.40	96.40	99.00	98.30	100.10	100.10
9	103.70	96.60	104.70	103.30	99.40	96.90	97.40	103.70	99.50	99.90
10	101.20	98.90	99.60	99.30	101.20	101.60	95.60	97.10	97.40	98.20
12	93.90	85.90	92.30	98.10	94.30	95.30	96.40	95.40	96.20	97.00
14*	93.60	95.30	94.00	98.80	98.40	91.20	99.40	93.10	103.90	89.70
15*	89.50	97.30	84.50	86.00	81.50	84.90	95.20	88.20	92.50	86.30
16*	101.50	100.40	105.30	92.80	95.70	94.80	92.50	98.50	100.00	92.80
102	87.60	89.30	92.70	94.00	96.00	88.50	94.20	92.20	96.80	93.60
111	97.70	97.60	92.80	94.30	95.90	98.00	92.90	103.10	96.50	97.50
112	103.80	100.60	92.10	102.40	97.70	104.10	100.90	105.30	104.40	102.30
114*	97.40	93.00	96.40	102.10	92.00	96.20	96.00	88.90	99.20	98.10
206	96.00	94.50	94.50	96.10	--	98.00	95.20	102.20	96.40	100.50
213*	--	--	101.40	98.10	--	101.80	104.70	98.00	104.60	97.30
Mean	95.51	94.58	96.68	95.84	96.39	96.58	96.72	97.12	99.08	96.32
St. Dev.	5.40	4.47	5.16	5.27	4.82	5.01	3.14	4.86	3.65	4.14

*Minority Subjects

(--) Accuracy not obtained

Table E6. Accuracy (msec) to 8 degree targets for young men during DHEA Treatment

Subject	Time (h)									
	0	2	3.5	4.5	5.5	7	8.5	10	11.5	12.5
33	98.30	100.00	99.10	97.90	96.60	101.00	98.80	97.30	99.40	97.40
34	90.60	90.90	95.70	99.30	91.40	97.00	93.10	95.80	92.10	102.70
35	86.50	98.30	92.20	100.40	99.70	98.90	95.40	100.60	95.50	98.80
36	95.90	93.00	96.60	93.10	93.00	95.10	95.10	94.30	96.40	94.10
37	99.50	100.00	98.00	94.40	97.70	103.20	100.10	91.70	97.10	102.80
38	90.80	98.10	98.00	95.80	96.70	96.70	97.50	96.20	98.30	92.40
39	96.50	93.80	104.60	93.80	89.70	95.40	96.60	93.80	102.60	102.00
41	93.40	93.10	96.70	97.70	98.10	99.50	103.80	94.50	102.40	102.80
42	93.30	95.60	90.80	100.10	93.50	96.80	90.90	90.60	95.70	97.00
43	96.10	97.00	98.90	97.00	102.70	96.70	96.10	96.10	95.00	98.20
44	92.10	90.20	95.80	95.80	96.50	94.60	93.50	92.50	96.50	94.60
47*	102.00	101.20	103.50	98.90	100.90	100.00	107.50	104.50	97.70	103.70
48*	88.20	93.30	83.50	92.00	97.60	92.30	100.00	100.00	97.20	95.90
140	83.50	83.50	86.10	84.50	85.20	88.40	85.70	91.60	91.50	87.10
146*	89.70	86.20	92.40	97.00	94.30	89.00	88.60	93.90	90.70	89.40
245*	90.60	98.90	97.00	99.10	93.50	100.60	92.80	97.30	95.60	95.50
Mean	92.94	94.57	95.56	96.05	95.44	96.58	95.97	95.67	96.48	97.15
St. Dev.	4.94	5.08	5.56	3.98	4.40	4.13	5.47	3.69	3.35	4.96

*Minority Subjects

Table E7. Accuracy (msec) to 8 degree targets for older women during DHEA Treatment

Subject	Time (h)									
	0	2	3.5	4.5	5.5	7	8.5	10	11.5	12.5
17	98.40	94.50	89.00	94.80	81.10	96.40	93.30	86.30	88.80	88.90
18	84.50	95.20	99.00	108.00	94.80	102.20	91.20	87.20	93.90	95.30
19	94.80	94.60	93.20	94.20	91.90	93.30	96.90	85.80	95.90	92.60
20*	83.30	84.50	84.50	86.70	88.10	94.30	97.00	94.30	81.60	87.10
21	94.60	94.70	96.10	98.30	95.90	95.40	98.40	94.00	95.20	99.60
22	94.80	89.80	94.20	92.30	93.70	99.10	91.80	98.10	93.50	98.30
23	91.20	92.10	98.20	90.90	92.20	102.00	98.70	91.90	93.10	93.50
24	92.70	94.10	94.00	90.70	96.60	95.20	102.90	92.60	93.60	91.10
25	100.30	95.20	109.90	108.90	101.00	101.80	97.70	98.60	90.70	102.70
26	81.10	77.30	90.70	86.20	80.90	78.20	83.10	88.40	93.40	81.80
27	--	101.00	100.80	90.90	96.20	87.50	94.20	97.00	91.10	87.20
28	105.20	99.40	96.00	98.10	95.40	101.50	94.80	94.70	99.10	108.30
29*	90.90	83.10	94.80	89.80	93.10	100.20	100.00	101.90	98.10	94.40
30*	95.70	94.70	107.20	101.40	92.50	100.70	97.90	99.30	100.30	102.50
31*	--	--	--	92.20	--	--	--	80.70	--	87.40
120	103.70	92.50	100.60	101.90	98.60	95.30	93.50	101.60	96.10	100.70
Mean	93.66	92.18	96.55	95.33	92.80	96.21	95.43	93.28	93.63	94.46
St. Dev.	7.19	6.24	6.54	6.88	5.67	6.48	4.67	6.19	4.56	7.16

*Minority Subjects

(--) Accuracy not obtained

Table E8. Accuracy (msec) to 8 degree targets for older men during DHEA Treatment

Subject	Time (h)									
	0	2	3.5	4.5	5.5	7	8.5	10	11.5	12.5
50	82.80	85.30	85.70	91.10	91.50	82.60	83.20	89.10	90.00	85.10
51	88.10	94.60	91.40	94.20	90.20	93.90	99.40	89.10	92.40	87.60
52	98.00	91.70	97.70	87.80	96.10	95.10	94.10	90.80	89.20	84.80
53	100.00	95.10	96.20	100.20	93.40	101.30	102.80	90.50	88.50	94.10
54	88.70	92.50	91.10	91.80	95.50	93.60	90.40	91.40	90.40	91.40
55	92.10	92.20	90.50	90.40	93.60	91.90	96.00	90.40	96.90	86.10
56	96.90	93.80	103.30	95.30	98.70	100.80	102.30	101.00	95.80	95.70
57	97.00	90.90	107.50	97.00	96.20	98.80	98.20	100.10	105.30	99.80
58	85.20	95.40	92.70	90.10	95.90	93.20	93.10	92.50	92.70	89.00
59	72.90	84.30	72.80	81.70	92.80	88.30	88.60	73.40	79.60	69.80
61*	68.70	76.90	83.10	76.30	91.90	80.10	94.20	86.00	89.30	90.20
149	96.00	94.30	89.70	87.30	87.80	99.50	94.60	93.20	92.50	92.00
160	105.50	95.90	96.40	94.80	91.00	98.80	90.40	92.60	93.70	93.10
Mean	90.15	90.99	92.16	90.62	93.43	93.68	94.41	90.78	92.02	89.13
St. Dev.	10.67	5.57	8.82	6.39	2.99	6.69	5.54	6.67	5.82	7.26

*Minority Subjects

Table E9. Accuracy (msec) to 8 degree targets for young women during Alprazolam/Placebo Treatment

Subject	Time (h)									
	0	2	3.5	4.5	5.5	7	8.5	10	11.5	12.5
1	102.80	87.20	72.80	68.60	79.70	88.30	85.80	86.70	92.40	95.00
3	87.40	89.30	66.30	66.90	59.50	81.80	76.70	86.40	92.90	102.30
4	98.40	99.30	87.30	72.00	88.20	74.60	93.40	95.50	100.10	88.90
5	96.70	92.90	63.70	91.90	82.80	87.50	107.90	91.50	101.90	96.80
7	83.10	87.40	91.80	95.30	113.90	98.30	92.60	90.60	96.00	99.20
8	89.80	99.20	61.20	79.10	52.20	87.30	88.70	89.30	88.80	99.20
9	94.70	95.30	96.70	85.50	83.20	101.70	105.10	105.20	107.40	111.70
10	94.00	95.70	97.60	92.70	105.90	97.50	103.30	95.30	93.30	95.60
11	97.60	96.70	102.90	65.70	82.00	91.00	95.70	103.80	101.30	100.70
12	96.80	97.80	90.90	79.10	90.10	82.30	80.30	91.70	88.70	98.40
14*	98.10	101.20	94.50	68.70	78.50	75.40	93.90	97.00	87.30	103.20
15*	89.90	93.30	72.00	70.20	85.50	83.40	84.40	94.90	95.10	91.40
16*	97.30	89.90	96.80	95.50	102.40	112.20	101.40	96.90	96.40	95.80
102	89.00	93.70	79.40	82.20	86.70	90.30	92.30	95.60	86.60	95.80
111	91.60	101.70	90.50	74.80	85.80	90.70	95.70	96.80	92.90	100.60
112	105.80	97.40	76.60	75.60	76.40	89.60	82.90	86.00	95.60	93.40
114*	90.30	90.50	81.20	92.90	88.50	90.40	94.60	87.70	91.70	89.00
206	99.30	98.90	79.30	60.50	72.70	74.90	82.60	82.80	94.10	95.50
213*	93.10	96.30	82.20	88.20	82.50	90.90	95.10	89.70	97.60	96.50
Mean	94.51	94.93	83.35	79.23	84.03	88.85	92.23	92.81	94.74	97.32
St. Dev.	5.57	4.47	12.37	11.20	14.25	9.42	8.62	5.92	5.34	5.29

*Minority Subjects

Table E10. Accuracy (msec) to 8 degree targets for young men during Alprazolam/Placebo Treatment

Subject	Time (h)									
	0	2	3.5	4.5	5.5	7	8.5	10	11.5	12.5
33	94.60	99.70	76.50	77.40	84.60	84.30	88.60	92.70	100.80	95.20
34	94.10	90.70	66.00	93.80	109.30	91.10	92.60	81.70	97.30	93.00
35	87.90	97.00	--	79.60	86.10	93.40	89.10	93.20	99.60	94.60
36	94.10	94.40	83.30	78.40	79.90	84.10	92.10	92.80	92.10	94.10
37	96.30	97.00	85.40	74.20	84.00	96.90	99.90	100.50	102.40	101.10
38	99.00	106.80	76.20	81.00	86.10	84.70	91.50	89.90	90.90	87.60
39	94.60	98.10	56.70	56.90	68.60	68.00	82.50	95.10	97.40	98.40
41	98.00	101.10	98.50	98.00	100.90	105.30	102.20	99.10	101.20	98.30
42	--	93.30	70.80	67.40	71.10	68.60	81.90	87.50	88.10	88.30
43	97.60	94.30	90.00	83.50	86.30	84.00	92.30	95.20	95.10	92.10
44	92.40	89.60	81.80	76.80	80.30	81.40	--	82.70	89.70	91.90
47*	100.90	98.20	69.50	78.50	84.70	78.10	81.80	103.70	95.00	87.00
48*	96.70	90.70	49.50	--	73.50	83.20	85.50	92.60	91.40	93.10
140	85.90	87.30	43.10	72.30	76.00	80.30	88.20	89.70	85.60	89.10
146*	93.20	94.60	78.00	85.00	83.30	90.40	85.10	88.80	93.80	92.40
245*	89.90	97.40	--	--	--	81.90	84.20	83.30	100.30	92.30
Mean	94.35	95.64	73.24	78.77	83.65	84.73	89.17	91.78	95.04	93.03
St. Dev.	4.11	4.86	15.45	10.15	10.51	9.47	6.14	6.27	5.10	3.97

*Minority Subjects

(--) Accuracy not obtained

Table E11. Accuracy (msec) to 8 degree targets for older women during Alprazolam/Placebo Treatment

Subject	Time (h)									
	0	2	3.5	4.5	5.5	7	8.5	10	11.5	12.5
17	83.90	90.10	85.60	75.90	84.70	96.40	103.10	90.10	91.80	99.10
18	97.30	97.90	55.10	66.20	51.50	79.00	70.50	79.10	86.90	78.70
19	92.60	99.10	--	--	75.60	--	64.60	59.30	80.40	78.60
20*	92.90	89.20	83.00	65.00	56.70	73.20	70.30	75.50	86.10	78.40
21	93.70	93.80	--	71.30	72.50	84.80	94.10	88.50	88.80	94.20
22	85.50	93.50	88.40	50.80	74.80	58.20	59.60	66.90	79.20	76.50
23	--	93.30	--	96.50	88.40	71.60	78.30	85.30	90.10	80.00
24	98.00	99.20	74.00	72.50	75.10	81.50	85.40	86.10	95.70	--
25	101.40	111.10	83.60	80.60	80.00	92.40	84.60	85.60	85.10	93.60
26	93.90	88.20	--	--	47.30	49.60	48.00	56.70	55.80	57.90
27	96.50	101.70	--	--	--	--	--	--	90.70	91.40
28	103.00	98.50	--	64.20	44.50	--	--	81.50	92.90	83.50
29*	80.70	100.20	--	50.20	74.50	55.30	63.10	81.70	70.40	62.20
30*	94.30	104.80	--	--	100.20	75.50	100.70	93.10	112.80	105.90
31*	100.00	86.40	--	--	--	--	--	--	67.40	78.60
120	111.80	96.20	--	--	--	--	84.50	94.00	97.00	95.60
Mean	95.03	96.45	78.28	69.32	71.22	74.32	77.45	80.24	85.69	83.61
St. Dev.	7.84	6.50	12.35	13.69	16.68	14.97	16.58	11.79	13.27	13.20

*Minority Subjects

(--) Accuracy not obtained

Table E12. Accuracy (msec) to 8 degree targets for older men during Alprazolam/Placebo Treatment

Subject	Time (h)									
	0	2	3.5	4.5	5.5	7	8.5	10	11.5	12.5
50	81.70	86.60	52.70	50.40	58.50	61.40	55.80	71.70	69.80	83.10
51	98.40	93.70	43.80	60.70	54.20	67.30	71.90	69.70	80.90	82.40
52	94.00	82.50	--	--	--	--	72.40	64.90	83.00	75.90
53	102.30	103.70	61.70	61.00	78.00	59.50	74.50	92.70	99.90	88.90
54	88.20	95.40	71.40	73.20	74.10	68.80	95.70	79.40	90.30	90.20
55	92.40	86.60	86.60	72.80	89.30	81.80	87.70	91.70	87.60	96.90
56	110.20	97.00	--	70.60	75.20	70.10	82.70	91.60	100.60	82.40
57	96.90	96.20	54.90	60.90	45.50	66.60	86.30	83.20	94.10	96.60
58	91.20	93.50	82.90	87.50	85.20	89.90	90.70	84.90	89.20	97.90
59	75.70	82.30	--	58.70	60.70	74.70	73.60	73.50	76.10	63.60
61*	90.00	96.50	43.90	59.60	69.50	82.40	85.30	88.10	100.70	99.10
149	93.70	--	71.00	72.70	74.40	73.70	82.50	82.70	86.20	78.70
160	91.30	96.60	--	--	--	82.20	82.20	71.80	90.20	82.90
Mean	92.77	92.55	63.21	66.19	69.51	73.20	80.10	80.45	88.35	86.05
St. Dev.	8.63	6.58	15.79	10.21	13.41	9.32	10.35	9.35	9.40	10.29

*Minority Subjects

(--) Accuracy not obtained

Table E13. Accuracy (msec) to 8 degree targets for young women during Alprazolam/DHEA Treatment

Subject	Time (h)									
	0	2	3.5	4.5	5.5	7	8.5	10	11.5	12.5
1	101.90	89.00	67.80	84.60	82.20	88.90	88.40	89.00	94.20	96.00
3	97.20	101.00	80.40	66.20	86.40	84.30	92.90	100.30	94.10	99.10
4	103.80	96.30	81.80	68.70	70.00	71.80	96.30	102.60	95.10	98.80
5	99.90	95.20	65.00	84.20	70.00	89.20	96.50	97.20	100.60	102.90
7	89.00	92.20	96.00	98.40	92.60	103.70	93.50	92.30	97.70	92.90
8	104.50	97.40	88.60	74.40	71.90	79.00	72.10	86.80	88.10	95.50
9	106.00	99.70	97.00	98.10	93.80	108.20	98.60	96.00	106.30	107.90
10	97.30	98.70	92.30	97.00	90.10	94.60	95.60	94.90	102.70	98.20
11	101.20	94.70	86.00	87.50	84.10	90.50	103.90	89.50	97.00	102.70
12	92.70	95.20	77.20	94.10	89.30	82.50	85.30	90.20	87.60	87.20
14*	102.50	99.50	97.20	106.70	96.80	104.80	94.30	99.50	111.00	97.00
15*	85.90	92.70	63.80	61.00	65.40	81.30	82.40	88.50	93.30	87.90
16*	95.80	97.10	103.30	99.40	103.70	97.00	100.30	98.90	100.00	92.80
102	93.00	90.40	83.70	84.80	83.90	99.50	93.40	82.30	90.50	87.30
111	91.10	89.20	77.80	71.00	90.80	84.00	85.20	93.20	95.20	87.90
112	90.80	95.10	57.60	84.20	73.10	81.40	86.30	84.80	95.20	95.60
114*	94.90	95.10	97.60	92.90	88.60	91.70	98.90	94.30	95.00	91.10
206	98.70	104.10	83.00	--	70.50	78.40	76.80	86.70	93.10	94.10
213*	89.10	95.30	79.80	90.20	83.00	100.20	91.00	94.40	96.90	89.80
Mean	96.59	95.68	82.94	85.74	83.48	90.05	91.14	92.71	96.51	94.98
St. Dev.	5.90	3.96	12.84	12.94	10.66	10.19	8.19	5.63	5.78	5.81

*Minority Subjects

(--) Accuracy not obtained

Table E14. Accuracy (msec) to 8 degree targets for young men during Alprazolam/DHEA Treatment

Subject	Time (h)									
	0	2	3.5	4.5	5.5	7	8.5	10	11.5	12.5
33	99.80	98.40	80.70	78.90	72.20	90.00	94.00	100.80	99.00	99.00
34	99.80	94.60	66.40	87.30	91.80	86.70	96.00	90.90	92.00	96.50
35	90.30	91.80	81.20	74.20	80.60	79.00	80.90	82.70	96.50	97.80
36	95.70	96.10	75.40	75.90	82.60	87.10	87.40	89.30	100.80	92.90
37	98.10	93.40	77.00	87.10	92.90	92.30	98.50	98.60	99.30	100.70
38	92.60	95.00	78.20	74.70	81.80	89.20	85.80	84.80	92.10	95.20
39	91.90	94.80	46.70	57.30	63.20	77.10	85.00	90.00	84.40	100.40
41	--	98.70	85.70	99.10	100.00	98.70	103.90	105.40	102.60	95.60
42	89.10	91.30	75.00	73.40	69.10	72.00	88.70	90.50	92.70	93.00
43	100.30	99.40	79.50	84.30	92.80	95.60	93.60	96.70	93.90	100.80
44	95.70	95.90	78.60	76.50	78.40	74.10	87.70	88.00	89.50	93.60
47*	98.20	102.40	71.80	80.80	81.90	80.80	92.30	100.70	101.70	92.30
48*	96.40	91.30	87.80	93.20	66.90	75.00	87.10	85.80	94.50	91.80
140	85.60	90.20	82.60	107.70	68.80	80.60	84.80	93.90	91.30	91.40
146*	89.30	96.70	92.30	83.00	87.70	91.70	98.30	97.00	100.10	101.30
245*	89.30	93.00	--	--	--	86.40	81.90	89.70	92.60	92.60
Mean	94.14	95.19	77.26	82.23	80.71	84.77	90.37	92.80	95.19	95.93
St. Dev.	4.72	3.38	10.56	12.00	11.01	8.05	6.55	6.48	5.06	3.60

*Minority Subjects

(--) Accuracy not obtained

Table E15. Accuracy (msec) to 8 degree targets for older women during Alprazolam/DHEA Treatment

Subject	Time (h)									
	0	2	3.5	4.5	5.5	7	8.5	10	11.5	12.5
17	101.30	90.00	--	--	--	--	96.40	93.60	100.80	74.50
18	90.10	98.50	52.80	64.70	62.70	70.40	60.90	70.20	87.40	81.60
19	93.60	91.00	--	--	--	--	61.80	74.70	68.00	73.90
20*	91.30	88.40	53.40	46.20	58.40	56.70	58.80	83.10	65.70	83.30
21	98.10	93.00	71.10	67.10	76.70	86.40	88.80	88.90	95.70	87.20
22	88.90	88.90	52.00	65.60	64.00	66.50	64.50	75.10	78.80	88.00
23	85.50	93.20	--	32.60	68.30	85.60	88.10	82.60	92.60	91.50
24	95.90	99.90	69.20	79.20	60.10	73.70	86.90	92.50	84.60	92.40
25	107.20	100.30	79.10	71.70	72.60	75.20	77.50	80.80	92.20	87.90
26	83.10	83.40	--	--	--	42.00	63.70	46.40	69.30	76.50
27	96.90	97.10	--	--	--	--	--	83.90	92.70	87.20
28	103.90	101.90	53.10	--	67.70	--	90.50	96.40	--	101.70
29*	91.50	95.50	--	--	--	--	--	--	90.70	85.40
30*	92.60	104.20	--	78.60	93.30	94.40	67.20	89.70	92.20	94.50
31*	91.80	96.20	--	--	--	--	--	71.60	91.70	87.30
120	103.40	97.60	--	--	--	81.50	79.00	86.90	92.80	97.00
Mean	94.69	94.94	61.53	63.21	69.31	73.24	75.70	81.09	86.35	86.87
St. Dev.	6.77	5.62	11.28	16.10	10.73	15.45	13.39	12.52	10.85	7.78

*Minority Subjects

(--) Accuracy not obtained

Table E16. Accuracy (msec) to 8 degree targets for older men during Alprazolam/DHEA Treatment

Subject	Time (h)									
	0	2	3.5	4.5	5.5	7	8.5	10	11.5	12.5
50	85.70	87.00	--	--	--	--	72.40	70.70	72.90	74.70
51	91.20	95.30	--	--	--	--	69.60	79.40	78.60	69.40
52	86.70	90.10	--	--	71.60	44.20	38.10	57.60	68.00	54.50
53	92.30	67.30	92.70	65.00	59.40	65.50	76.80	82.80	68.20	80.80
54	84.50	91.40	66.10	60.60	77.50	65.40	95.80	90.80	92.50	87.10
55	88.80	94.20	74.70	82.70	84.10	77.50	77.10	86.90	80.50	82.60
56	100.50	103.00	72.90	72.50	75.20	87.10	55.10	75.30	91.60	85.50
57	101.20	95.80	51.30	54.30	73.50	79.40	78.50	87.00	97.50	91.20
58	87.80	92.30	52.60	75.00	82.70	83.80	84.20	94.90	97.10	89.20
59	77.10	77.40	--	57.80	45.00	68.70	70.60	71.50	78.60	56.70
61*	89.20	81.50	70.30	77.30		80.60	82.20	79.10	88.40	94.30
149	91.10	91.70	--	68.80	68.50	68.40	70.80	84.90	88.70	91.50
160	97.00	91.60	--	--	--	--	76.70	77.20	69.70	71.90
Mean	90.24	89.12	68.66	68.22	70.83	72.06	72.92	79.85	82.48	79.18
St. Dev.	6.61	9.16	14.15	9.54	12.20	12.51	14.04	9.83	10.80	12.99

*Minority Subjects

(-) Accuracy not obtained

Table E17. Accuracy (msec) to 16 degree targets for young women during Placebo Treatment

Subject	Time (h)									
	0	2	3.5	4.5	5.5	7	8.5	10	11.5	12.5
1	96.30	92.30	95.10	94.70	95.40	95.30	89.70	93.20	97.30	96.70
3	97.40	92.80	93.40	94.40	97.70	99.60	97.60	98.10	95.70	96.80
4	98.40	94.80	92.60	103.50	88.10	95.80	102.10	93.70	100.00	98.30
5	82.20	90.60	91.60	88.80	93.70	91.70	91.80	87.60	91.30	93.10
7	93.40	92.20	93.60	90.70	93.20	96.90	92.10	93.30	92.10	91.30
8	90.60	92.70	98.70	96.40	92.60	90.80	93.30	98.30	96.00	92.60
9	92.20	92.00	93.10	96.10	100.60	91.40	97.70	97.10	91.90	96.50
10	96.00	100.10	98.20	94.50	95.30	96.30	95.00	96.80	93.60	96.60
12	88.40	91.80	83.00	92.50	96.20	90.50	97.60	97.50	90.10	89.60
14*	84.70	88.80	87.80	94.00	92.90	91.50	92.70	81.10	95.30	91.80
15*	81.20	81.70	88.70	91.90	88.90	83.80	85.80	87.60	92.10	91.90
16*	90.00	90.40	96.40	91.00	91.10	91.80	93.60	91.00	95.60	92.20
102	85.80	92.60	89.70	91.50	93.70	98.50	85.00	88.80	89.50	91.40
111	92.60	104.80	94.20	96.90	94.10	96.10	98.50	90.10	97.60	93.40
112	90.10	90.10	90.10	91.60	88.90	93.00	90.30	96.20	92.90	91.00
114*	95.30	93.40	97.00	99.00	95.50	94.00	99.50	95.00	101.40	99.20
206	91.30	90.80	89.30	93.40	87.90	92.00	94.60	89.90	89.80	93.10
213*	90.10	91.90	94.40	92.10	94.70	95.30	91.70	91.90	99.60	94.80
Mean	90.89	92.43	92.61	94.06	93.36	93.57	93.81	92.62	94.54	93.91
St. Dev.	5.01	4.62	4.01	3.47	3.41	3.66	4.56	4.59	3.64	2.80

*Minority Subjects

Table E18. Accuracy (msec) to 16 degree targets for young men during Placebo Treatment

Subject	Time (h)									
	0	2	3.5	4.5	5.5	7	8.5	10	11.5	12.5
33	95.60	92.00	95.70	93.70	93.60	94.00	95.50	95.30	89.10	92.40
34	86.70	82.10	88.20	82.80	87.90	88.50	88.80	90.20	89.10	82.00
35	96.70	94.90	91.40	92.50	95.80	92.60	93.60	89.20	89.10	92.50
36	87.40	86.70	87.20	86.80	90.10	88.10	90.40	91.10	90.50	88.80
37	92.80	88.50	95.30	100.30	91.70	105.20	90.50	96.20	92.40	97.00
38	87.60	86.80	90.20	87.20	85.60	92.00	87.90	90.50	90.90	90.60
39	85.10	87.00	81.00	89.20	85.10	84.40	84.00	85.00	85.30	85.30
41	100.60	101.80	103.90	93.90	99.70	99.00	98.00	94.30	100.00	92.40
42	82.70	84.90	84.70	86.90	86.00	84.10	94.80	94.90	95.60	91.10
43	92.40	93.60	91.30	91.90	88.00	86.00	92.00	92.10	94.00	91.60
44	82.60	82.60	88.60	91.70	88.80	89.90	90.20	90.80	92.10	90.70
47*	96.40	94.30	89.20	93.00	91.20	88.10	87.50	90.40	91.70	94.80
48*	93.10	94.00	97.90	89.30	101.00	90.60	97.40	98.00	85.80	103.10
140	75.50	79.50	69.90	80.00	78.40	84.80	85.50	80.30	82.50	82.00
146*	83.40	84.40	93.50	83.90	92.30	91.40	92.90	89.70	88.20	85.00
245*	84.20	84.00	85.90	89.50	94.20	87.80	93.20	89.50	90.80	87.30
Mean	88.93	88.57	89.62	89.54	90.59	90.41	91.39	91.09	90.44	90.41
St. Dev.	6.72	5.97	7.63	4.98	5.70	5.55	4.05	4.33	4.17	5.46

*Minority Subjects

Table E19. Accuracy (msec) to 16 degree targets for older women during Placebo Treatment

Subject	Time (h)									
	0	2	3.5	4.5	5.5	7	8.5	10	11.5	12.5
17	88.10	101.20	88.20	93.10	92.10	95.80	96.70	90.90	93.30	90.10
18	92.00	79.80	81.50	94.40	89.60	80.30	91.90	90.30	91.50	97.30
19	82.60	105.70	81.00	87.20	87.00	88.00	84.40	89.40	83.00	96.80
20*	84.80	92.60	82.40	89.80	97.80	92.00	96.30	96.60	91.60	91.60
21	94.50	98.10	93.40	88.10	87.60	93.00	95.40	93.20	94.20	94.10
22	94.20	88.80	89.70	89.40	91.30	93.00	93.40	92.60	87.20	91.40
23	92.60	95.00	93.60	103.20	91.40	93.20	96.10	95.40	97.30	84.60
24	91.10	99.50	82.00	103.00	61.10	88.90	86.20	83.10	83.10	93.40
25	93.00	88.10	92.30	101.60	98.80	91.80	99.70	99.10	96.90	100.30
26	90.90	91.50	92.60	95.90	90.70	95.40	94.80	90.80	91.80	90.70
27	85.90	98.80	86.10	87.60	92.10	90.20	94.30	90.70	93.30	93.20
28	103.50	87.10	91.40	88.00	93.30	88.30	92.10	94.50	91.90	95.30
29*	71.00	87.00	85.00	77.70	--	83.80	85.80	70.00	78.60	102.80
30*	79.80	80.20	93.70	90.90	92.40	99.30	80.60	91.40	86.10	92.80
31*	--	90.20	90.70	92.70	82.80	94.10	90.60	--	95.20	76.70
120	100.10	95.30	94.80	94.40	92.90	94.60	95.80	92.90	89.80	96.90
Mean	89.61	92.43	88.65	92.31	89.39	91.36	92.13	90.73	90.30	93.00
St. Dev.	8.06	7.28	4.93	6.62	8.75	4.72	5.29	6.79	5.34	6.10

*Minority Subjects

(--) Latency not obtained

Table E20. Accuracy (msec) to 16 degree targets for older men during Placebo Treatment

Subject	Time (h)									
	0	2	3.5	4.5	5.5	7	8.5	10	11.5	12.5
50	83.10	103.00	80.60	90.80	90.30	88.50	82.20	--	92.90	90.50
51	90.50	84.30	87.90	91.00	85.30	83.90	83.30	84.20	85.20	82.50
52	82.30	91.00	101.30	91.90	87.80	79.10	90.30	90.40	88.70	86.60
53	99.20	92.00	97.30	86.20	90.60	94.70	90.90	92.90	88.30	84.80
54	92.20	98.10	86.80	90.50	90.60	93.40	94.80	87.70	87.80	96.60
55	80.50	90.50	89.80	89.30	91.30	88.00	87.40	87.70	85.90	90.50
56	100.00	98.10	108.50	95.80	97.80	100.00	100.30	101.00	95.20	95.10
57	80.70	89.30	86.10	87.20	83.30	83.30	80.60	84.00	81.70	80.70
58	91.40	87.50	87.60	87.40	83.10	87.80	85.90	85.90	84.30	84.30
59	87.60	78.00	78.20	56.10	80.20	72.60	74.20	76.70	75.90	74.20
61*	--	90.50	89.00	84.10	93.90	87.60	92.50	92.40	88.30	89.60
149	93.50	91.80	91.80	90.90	93.70	88.60	97.20	91.70	90.60	92.90
160	89.90	87.50	85.90	90.10	87.20	85.10	82.40	89.10	84.00	90.80
Mean	89.24	90.89	90.06	87.02	88.85	87.12	87.85	88.64	86.83	87.62
St. Dev.	6.65	6.38	8.20	9.74	4.99	6.91	7.38	5.96	4.95	6.25

*Minority Subjects

(--) Latency not obtained

Table E21. Accuracy (msec) to 16 degree targets for young women during DHEA Treatment

Subject	Time (h)									
	0	2	3.5	4.5	5.5	7	8.5	10	11.5	12.5
1	84.70	83.40	91.20	88.30	105.30	92.80	91.20	93.10	93.90	91.20
3	92.00	97.70	97.20	98.00	97.50	95.40	98.50	97.00	98.10	98.10
4	94.90	99.40	93.10	93.80	98.10	100.80	97.60	93.40	94.80	96.50
5	89.90	77.40	87.70	89.70	86.30	93.00	86.80	83.70	97.60	88.10
7	91.30	92.80	91.70	88.50	95.60	94.40	94.80	91.30	92.50	90.90
8	95.90	94.50	94.40	98.00	94.80	95.20	96.20	97.60	98.30	97.20
9	98.70	94.30	95.10	98.60	95.00	96.80	95.80	102.60	93.90	93.60
10	94.60	99.60	96.30	95.60	97.90	99.30	96.70	98.60	96.30	97.40
12	81.60	86.20	94.90	92.70	88.90	90.40	94.50	88.50	92.30	93.20
14*	84.80	85.80	84.40	87.30	85.00	87.60	89.80	89.60	94.00	92.40
15*	81.40	91.80	87.10	83.80	90.40	87.30	95.20	94.20	95.10	89.80
16*	86.00	88.50	89.00	77.80	85.60	90.40	88.20	87.40	94.00	87.30
102	85.20	83.80	87.10	74.60	96.60	95.40	90.50	83.60	84.60	92.50
111	97.30	95.20	89.40	88.60	96.10	94.90	91.00	94.40	94.90	93.40
112	93.30	89.50	91.80	96.80	86.80	94.00	93.70	96.30	96.70	89.30
114*	88.90	91.10	96.20	93.00	95.70	92.00	92.60	92.80	101.80	99.50
206	92.40	92.60	89.30	93.40	--	91.60	92.20	94.10	90.80	91.60
213*	--	--	84.00	78.70	--	91.00	89.80	93.00	89.40	86.80
Mean	90.17	90.80	91.11	89.84	93.48	93.46	93.06	92.84	94.39	92.71
St. Dev.	5.42	6.07	4.10	7.23	5.70	3.57	3.34	4.95	3.81	3.80

*Minority Subjects

(--) Latency not obtained

Table E22. Accuracy (msec) to 16 degree targets for young men during DHEA Treatment

Subject	Time (h)									
	0	2	3.5	4.5	5.5	7	8.5	10	11.5	12.5
33	93.30	89.90	94.90	93.30	88.90	90.80	96.60	94.70	92.80	90.80
34	86.40	86.90	90.10	91.90	91.10	91.90	91.50	96.30	93.90	83.10
35	85.30	93.50	90.30	90.90	95.60	92.70	88.90	88.20	88.90	89.70
36	90.50	88.60	90.80	92.50	86.50	89.80	90.20	88.40	90.60	90.20
37	95.90	93.30	93.20	95.40	92.50	95.30	93.50	92.00	94.90	91.90
38	90.70	88.80	88.00	88.90	94.50	94.50	89.50	89.80	91.00	92.30
39	85.60	79.30	87.20	87.00	88.90	86.70	80.60	84.80	89.60	91.20
41	94.60	91.80	96.80	93.90	99.10	98.00	98.40	101.40	97.50	99.20
42	90.30	95.90	82.20	94.90	89.30	90.20	98.60	87.90	87.30	89.30
43	90.40	90.40	90.80	89.20	93.70	91.70	95.60	92.50	92.00	89.70
44	86.70	86.80	87.70	90.20	87.40	90.70	90.90	90.80	89.00	88.00
47*	93.80	94.00	91.10	93.20	92.10	96.30	94.90	93.10	88.60	91.20
48*	86.70	94.10	96.20	94.20	93.50	95.60	99.30	95.40	99.10	91.70
140	70.90	78.20	78.90	80.40	76.10	77.60	85.00	74.90	78.50	68.60
146*	82.80	87.30	87.10	98.00	88.20	86.60	90.00	85.30	85.20	89.50
245*	88.20	92.90	91.90	94.70	90.80	91.90	86.20	89.50	86.30	92.50
Mean	88.26	89.48	89.83	91.79	90.51	91.27	91.86	90.31	90.33	89.31
St. Dev.	5.94	5.05	4.72	4.13	5.08	4.85	5.29	5.93	4.97	6.37

*Minority Subjects

TableE23. Accuracy (msec) to 16 degree targets for older women during DHEA Treatment

Subject	Time (h)									
	0	2	3.5	4.5	5.5	7	8.5	10	11.5	12.5
17	94.00	90.00	95.10	90.00	85.00	93.60	93.90	90.20	90.00	91.00
18	77.90	92.50	90.20	99.10	88.60	88.10	88.80	86.20	85.30	90.30
19	81.80	89.70	81.20	89.10	90.10	82.00	80.50	87.50	86.20	88.60
20*	93.60	85.90	99.10	98.40	87.90	97.00	92.90	91.10	87.60	90.60
21	94.80	95.60	91.90	95.20	97.00	98.00	97.20	98.50	96.20	91.70
22	95.70	90.50	95.10	92.60	94.10	92.60	93.10	92.40	93.00	94.70
23	89.60	98.00	95.00	95.30	95.00	97.10	99.60	99.90	97.80	91.30
24	88.80	87.30	89.00	92.70	84.00	89.50	109.20	81.10	95.10	83.70
25	97.70	93.40	101.30	98.00	93.10	93.90	88.60	91.50	91.00	93.60
26	93.50	86.60	91.00	97.70	94.50	98.10	92.10	89.70	91.10	90.10
27	--	92.10	92.40	86.30	90.80	89.00	95.20	85.50	82.80	82.40
28	94.30	96.60	100.60	91.40	93.10	98.10	96.10	90.10	93.40	95.30
29*	78.50	80.20	68.10	87.10	92.40	79.50	95.40	75.80	76.40	83.10
30*	83.80	95.50	93.60	94.10	99.50	89.40	92.40	90.90	92.00	90.20
31*	--	--	--	87.10	--	--	--	90.80	--	68.80
120	91.00	87.70	94.60	101.20	94.80	94.30	95.60	94.40	94.40	93.20
Mean	89.64	90.77	91.88	93.46	91.99	92.01	94.04	89.73	90.15	88.66
St. Dev.	6.56	4.78	8.24	4.69	4.29	5.77	6.15	5.89	5.67	6.57

*Minority Subjects

(--) Latency not obtained

Table E24. Accuracy (msec) to 16 degree targets for older men during DHEA Treatment

Subject	Time (h)									
	0	2	3.5	4.5	5.5	7	8.5	10	11.5	12.5
50	82.90	83.00	89.80	88.60	89.20	94.80	86.60	91.40	81.50	91.00
51	88.40	86.40	82.50	81.40	90.60	77.10	88.60	87.10	90.10	94.50
52	90.90	83.80	103.00	92.80	89.20	92.20	93.50	87.10	86.70	88.10
53	91.20	97.30	90.50	93.40	90.70	99.80	93.50	97.70	93.50	82.80
54	87.00	91.50	91.60	90.90	88.90	96.80	89.30	89.70	88.40	89.80
55	85.70	91.60	87.90	90.00	85.10	88.00	91.20	89.90	92.40	89.20
56	100.30	99.50	88.40	91.90	94.70	98.00	95.10	100.70	96.50	96.30
57	79.90	86.30	87.50	89.60	85.00	85.70	86.60	83.70	86.80	86.00
58	87.00	92.00	89.70	89.20	92.90	90.10	89.80	87.30	86.90	86.70
59	64.60	72.10	89.30	80.20	68.00	73.30	76.80	63.50	67.20	72.90
61*	81.10	77.40	72.00	83.80	85.70	90.10	86.30	92.00	87.30	91.70
149	89.90	87.70	91.90	92.30	85.70	98.50	94.70	90.10	89.60	91.30
160	92.80	89.70	96.90	101.40	91.10	95.40	85.30	90.40	87.70	90.60
Mean	86.28	87.56	89.31	89.65	87.45	90.75	89.02	88.51	87.28	88.53
St. Dev.	8.43	7.49	7.13	5.54	6.58	8.14	4.98	8.74	7.08	5.87

*Minority Subjects

Table E25. Accuracy (msec) to 16 degree targets for young women during Alprazolam/Placebo Treatment

Subject	Time (h)									
	0	2	3.5	4.5	5.5	7	8.5	10	11.5	12.5
1	90.60	97.60	75.60	59.30	71.20	70.50	76.40	89.00	91.20	94.00
3	91.50	93.90	78.70	86.40	86.10	91.90	93.20	95.20	94.10	100.70
4	99.50	94.40	100.20	73.90	87.90	94.00	99.30	102.20	97.60	96.80
5	86.60	89.40	65.70	79.30	74.00	80.90	105.60	91.60	95.60	96.90
7	84.00	87.20	89.70	99.20	105.30	93.60	91.90	94.80	98.20	93.90
8	87.70	95.80	84.50	78.80	72.50	90.00	91.70	89.60	95.60	96.20
9	93.90	94.80	93.90	89.00	89.70	101.40	105.20	101.40	102.00	91.70
10	97.80	97.30	95.20	90.00	96.20	98.00	101.90	92.10	95.60	92.00
11	91.80	93.60	93.40	101.40	81.40	90.20	103.30	94.00	94.00	92.00
12	94.30	90.80	89.10	81.40	88.10	91.80	93.00	89.00	90.00	95.80
14*	92.80	101.00	84.20	76.10	82.40	84.00	86.70	89.50	101.00	104.30
15*	85.60	86.50	64.80	66.10	70.00	83.30	77.80	88.90	92.50	85.90
16*	90.40	97.30	93.00	80.30	109.00	92.60	107.30	94.90	90.80	93.20
102	83.90	93.40	80.50	78.30	86.00	86.40	94.50	93.30	91.00	91.90
111	89.60	89.60	91.50	87.80	83.60	95.30	97.20	94.50	94.60	97.30
112	97.70	95.00	79.80	85.90	88.00	88.60	85.40	86.00	92.70	94.50
114*	90.10	94.10	86.60	90.60	100.70	97.30	95.80	91.00	92.50	92.00
206	94.40	93.00	77.60	72.10	55.00	83.60	76.10	82.30	89.00	88.70
213*	85.80	88.90	82.60	89.10	85.00	92.10	91.10	89.90	88.90	86.90
Mean	90.95	93.35	84.56	82.37	84.85	89.76	93.34	92.06	94.05	93.93
St. Dev.	4.64	3.81	9.56	10.48	12.96	7.15	9.60	4.75	3.74	4.43

*Minority Subjects

Table E26. Accuracy (msec) to 16 degree targets for young men during Alprazolam/Placebo Treatment

Subject	Time (h)									
	0	2	3.5	4.5	5.5	7	8.5	10	11.5	12.5
33	95.00	94.80	86.70	85.10	87.00	95.70	100.70	96.20	94.10	95.00
34	87.50	89.60	64.40	85.80	91.30	100.10	98.10	86.00	88.70	91.50
35	81.00	91.40	--	68.50	75.30	85.00	83.30	89.50	95.80	93.40
36	89.80	89.40	82.90	78.30	83.50	84.90	94.70	92.30	85.80	89.20
37	93.30	91.90	88.80	86.50	92.50	98.50	94.70	98.00	97.30	100.60
38	91.40	95.40	81.20	82.00	89.70	93.10	90.10	86.30	86.90	84.80
39	84.70	89.70	77.10	79.20	75.20	84.70	79.60	90.10	92.20	90.00
41	100.50	96.60	97.80	100.00	101.00	100.40	96.50	95.40	95.40	97.90
42	--	91.40	80.30	70.90	81.50	91.10	85.10	92.60	84.00	88.30
43	89.50	90.40	86.70	95.80	106.80	92.30	96.70	90.20	93.70	93.80
44	89.40	86.10	80.30	79.60	81.50	89.60	--	91.80	89.20	90.60
47*	83.20	87.20	79.60	89.50	81.40	84.30	94.60	99.10	88.50	89.00
48*	94.60	84.10	80.80	--	90.20	87.00	97.90	84.40	89.10	94.50
140	72.70	82.00	57.20	93.40	76.90	79.10	73.20	81.00	87.80	83.10
146*	88.40	89.40	78.90	86.90	88.60	88.90	89.50	88.30	88.60	94.60
245*	83.40	90.30	--	--	--	78.70	84.20	85.10	89.10	90.30
Mean	88.29	89.98	80.19	84.39	86.83	89.59	90.59	90.39	90.39	91.66
St. Dev.	6.73	3.88	9.87	8.86	9.02	6.82	7.94	5.14	3.88	4.51

*Minority Subjects

(--) Latency not obtained

TableE27. Accuracy (msec) to 16 degree targets for older women during Alprazolam/Placebo Treatment

Subject	Time (h)									
	0	2	3.5	4.5	5.5	7	8.5	10	11.5	12.5
17	91.00	90.30	88.90	79.00	86.10	96.70	96.90	84.60	95.20	89.60
18	90.00	86.90	66.40	74.10	80.20	100.30	92.80	94.80	90.40	90.80
19	84.80	90.60	--	--	72.50	--	66.40	62.60	75.40	77.20
20*	92.90	90.90	88.50	74.30	62.10	71.00	75.70	70.90	103.70	94.80
21	97.30	94.50	--	69.30	68.30	89.60	91.60	92.70	91.40	90.10
22	92.30	91.10	51.00	54.20	68.00	76.80	77.60	79.90	91.50	86.50
23	--	97.80	--	72.70	69.90	85.10	88.20	92.10	83.50	79.80
24	89.70	88.00	68.70	73.40	71.90	75.60	80.60	88.90	85.60	89.90
25	101.00	108.00	75.30	66.60	77.90	85.90	84.20	84.30	82.80	86.70
26	95.80	90.00	--	--	80.50	75.70	71.90	70.10	81.40	87.40
27	93.70	93.20	--	--	--	--	--	--	89.80	92.60
28	95.50	89.30	--	75.30	73.90	--	--	92.80	89.00	87.40
29*	74.70	87.60	--	62.60	72.00	82.60	74.40	86.60	80.30	81.00
30*	92.30	94.00	--	--	90.20	82.30	82.80	90.30	94.60	98.20
31*	91.90	86.00	--	--	--	--	--	--	93.30	94.90
120	98.30	93.60	--	--	--	--	94.50	102.00	91.10	92.90
Mean	92.08	91.99	73.13	70.15	74.88	83.78	82.89	85.19	88.69	88.74
St. Dev.	6.21	5.29	14.45	7.30	7.81	9.10	9.51	10.92	6.93	5.72

*Minority Subjects
 (--) Latency not obtained

Table E28. Accuracy (msec) to 16 degree targets for older men during Alprazolam/Placebo Treatment

Subject	Time (h)									
	0	2	3.5	4.5	5.5	7	8.5	10	11.5	12.5
50	86.30	87.60	56.00	60.80	75.50	75.40	81.60	80.20	83.50	86.70
51	92.60	89.80	63.40	67.20	64.50	75.70	71.50	77.80	76.70	82.40
52	92.30	84.50	--	--	--	--	82.80	84.90	84.80	89.80
53	96.00	92.90	77.20	81.10	82.50	76.60	87.20	88.10	94.00	90.90
54	99.30	94.10	81.70	80.50	90.20	77.50	62.60	92.00	96.40	96.60
55	99.70	83.80	83.80	73.80	84.60	86.70	86.80	95.00	86.70	97.50
56	103.20	93.00	--	59.70	68.70	73.90	80.80	83.00	95.50	97.20
57	87.20	85.50	46.40	56.40	42.30	62.80	73.70	74.20	87.20	84.20
58	89.20	85.60	70.70	77.80	78.60	80.80	84.10	83.00	88.50	85.60
59	67.40	69.30	--	64.20	61.10	74.10	63.60	87.00	61.40	71.10
61*	92.20	98.30	54.00	71.10	78.90	83.70	92.40	90.10	91.00	88.50
149	88.20	--	65.50	71.60	68.20	80.80	89.10	94.00	92.10	83.80
160	88.00	88.00	--	--	--	82.00	81.00	80.10	83.30	86.90
Mean	90.89	87.70	66.52	69.47	72.28	77.50	79.78	85.34	86.24	87.78
St. Dev.	8.84	7.30	12.96	8.52	13.36	6.14	9.34	6.40	9.30	7.18

*Minority Subjects

(--) Latency not obtained

Table E29. Accuracy (msec) to 16 degree targets for young women during Alprazolam/DHEA Treatment

Subject	Time (h)									
	0	2	3.5	4.5	5.5	7	8.5	10	11.5	12.5
1	94.80	92.40	78.40	76.40	77.30	74.50	89.10	88.90	94.00	95.30
3	96.00	93.20	95.70	76.40	74.20	89.50	94.30	94.60	98.00	99.30
4	98.40	96.40	88.90	86.70	84.80	87.50	93.90	95.50	93.90	93.30
5	92.30	93.20	76.90	81.80	85.10	94.00	91.10	92.50	94.10	95.20
7	93.30	91.90	98.70	98.60	106.10	102.10	106.10	95.60	95.80	95.10
8	72.90	94.70	76.70	79.80	76.70	80.60	88.00	93.30	94.00	94.90
9	99.20	94.90	92.00	97.60	102.10	103.50	107.10	90.90	102.00	96.10
10	93.70	98.20	107.00	92.40	85.90	92.80	94.60	99.50	100.50	94.70
11	97.10	94.40	85.20	83.60	98.50	94.70	98.90	92.00	96.70	103.60
12	84.70	84.90	79.30	88.20	89.60	91.40	84.20	83.40	94.50	88.90
14*	93.00	92.80	96.50	92.60	101.70	89.80	92.80	97.50	108.70	90.40
15*	91.90	89.20	59.10	57.70	74.70	73.90	80.10	91.60	87.40	90.60
16*	90.80	92.20	106.10	101.20	95.40	94.90	98.50	96.50	94.80	93.90
102	87.60	89.80	83.50	81.60	87.10	85.90	86.90	92.90	86.60	88.30
111	88.00	92.10	86.50	97.90	92.40	89.70	94.00	92.10	95.80	91.20
112	88.00	89.60	75.00	78.80	79.30	88.90	91.50	91.70	93.80	94.00
114*	90.70	94.50	105.20	88.50	93.30	92.00	94.90	90.20	89.70	85.00
206	93.70	94.20	82.20	–	74.50	86.80	75.90	84.90	83.80	93.80
213*	84.40	91.60	73.80	104.50	89.40	97.20	89.50	90.10	90.30	88.70
Mean	91.08	92.64	86.67	86.91	87.79	89.98	92.18	92.30	94.44	93.28
St. Dev.	6.08	2.94	12.70	11.40	10.06	7.74	7.69	3.96	5.70	4.22

*Minority Subjects

(–) Latency not obtained

Table E30. Accuracy (msec) to 16 degree targets for young men during Alprazolam/DHEA Treatment

Subject	Time (h)									
	0	2	3.5	4.5	5.5	7	8.5	10	11.5	12.5
33	94.10	94.90	85.90	88.10	81.20	91.80	93.60	91.70	94.30	94.40
34	91.50	95.10	60.20	93.90	98.10	91.30	101.40	88.90	89.70	91.00
35	86.00	88.60	81.30	80.40	89.10	90.10	90.10	88.10	95.60	92.30
36	84.60	89.50	81.50	80.70	84.70	85.90	89.50	89.70	92.90	85.60
37	90.50	90.10	84.60	87.00	94.70	94.40	93.50	94.10	96.90	99.70
38	89.30	92.40	78.90	88.30	90.70	88.50	95.40	87.20	97.00	89.90
39	87.10	88.10	46.00	65.30	68.00	79.70	88.20	87.40	89.90	90.10
41	--	97.20	95.80	100.70	99.00	99.80	104.50	101.00	101.10	97.50
42	87.60	92.50	82.40	80.70	85.10	82.10	92.70	91.70	87.90	95.20
43	92.70	91.40	84.80	98.90	100.30	97.30	92.50	93.60	96.60	92.60
44	91.60	87.80	81.90	83.20	84.40	81.20	84.40	91.00	89.10	87.30
47*	86.50	83.50	69.90	81.30	84.10	85.10	86.80	93.10	98.50	87.90
48*	93.70	85.30	85.10	87.30	66.70	88.50	91.20	90.50	91.60	94.30
140	79.80	82.30	92.40	69.90	75.70	83.00	90.20	85.50	85.60	81.00
146*	85.10	90.60	92.60	86.30	91.90	96.90	94.20	94.80	89.70	94.30
245*	87.30	91.50	--	--	--	77.70	82.80	84.60	92.30	87.80
Mean	88.49	90.05	80.22	84.80	86.25	88.33	91.94	90.81	93.04	91.31
St. Dev.	3.93	4.10	12.90	9.41	10.34	6.67	5.56	4.07	4.31	4.74

*Minority Subjects
 (--) Latency not obtained

Table E31. Accuracy (msec) to 16 degree targets for older women during Alprazolam/DHEA Treatment

Subject	Time (h)									
	0	2	3.5	4.5	5.5	7	8.5	10	11.5	12.5
17	91.70	98.50	--	--	--	--	94.60	95.60	98.40	89.20
18	90.90	95.80	73.80	71.00	83.10	80.80	90.60	89.50	97.00	93.10
19	88.20	85.10	--	--	--	--	79.70	72.90	85.00	85.50
20*	98.40	88.90	65.30	65.80	48.80	57.70	61.90	79.10	83.30	78.60
21	93.00	93.90	67.70	70.80	78.70	82.50	92.80	88.10	86.90	92.60
22	92.60	89.20	48.60	73.10	59.90	80.30	82.30	88.40	98.10	90.40
23	100.10	99.40	--	40.80	91.90	84.30	83.90	95.40	95.10	97.00
24	95.40	89.90	65.30	70.10	61.60	77.80	85.70	90.10	83.70	82.60
25	100.60	108.20	73.10	61.30	71.40	76.30	72.80	80.90	92.30	80.30
26	92.50	86.30	--	--	--	45.80	76.90	85.60	80.60	82.90
27	100.20	101.20	--	--	--	--	--	93.20	90.20	93.80
28	86.40	96.60	79.40	--	101.90	--	94.30	99.20	--	89.20
29*	90.80	86.70	--	--	--	--	--	--	88.00	75.90
30*	93.40	97.70	--	71.40	95.10	99.00	78.10	80.50	92.50	85.80
31*	95.00	86.30	--	--	--	--	--	69.70	95.90	103.40
120	94.90	96.00	--	--	--	87.00	88.60	105.10	101.70	94.40
Mean	94.01	93.73	67.60	65.54	76.93	77.15	83.25	87.55	91.25	88.42
St. Dev.	4.20	6.56	9.83	10.69	17.91	15.05	9.47	9.69	6.45	7.33

*Minority Subjects

(--) Latency not obtained

Table E32. Accuracy (msec) to 16 degree targets for older men during Alprazolam/DHEA Treatment

Subject	Time (h)									
	0	2	3.5	4.5	5.5	7	8.5	10	11.5	12.5
50	85.30	89.20	--	--	--	--	80.60	87.30	85.30	88.00
51	87.70	88.30	--	--	--	--	75.90	85.30	78.10	78.90
52	90.20	92.10	--	--	76.80	65.60	51.50	77.70	78.80	67.60
53	93.40	60.30	94.10	64.10	92.90	70.20	74.90	80.10	82.70	88.90
54	91.50	92.00	75.60	86.60	76.00	83.00	96.70	92.00	90.10	94.60
55	89.30	85.80	74.80	83.40	79.90	81.80	86.00	85.10	87.90	84.90
56	101.30	94.20	68.50	68.80	78.00	86.40	87.30	82.90	87.70	93.20
57	89.50	87.40	50.80	52.90	55.60	67.80	67.30	73.30	82.10	76.20
58	85.40	87.50	50.40	68.60	80.80	82.00	84.30	86.60	86.80	86.60
59	74.00	77.60	--	48.00	70.20	76.90	52.00	72.00	77.10	68.80
61*	88.10	90.50	63.20	85.90	--	79.30	93.60	92.90	91.00	91.10
149	86.10	91.30	--	80.50	79.10	88.20	94.60	82.10	91.90	90.80
160	90.20	94.90	--	--	--	--	71.30	71.20	87.30	69.70
Mean	88.62	87.01	68.20	70.98	76.59	78.12	78.15	82.19	85.14	83.02
St. Dev.	6.06	9.15	15.35	14.25	9.90	7.83	14.77	7.09	4.97	9.66

*Minority Subjects

(-) Latency not obtained

APPENDIX F

Digit Symbol Substitution Test (DSST)
Card Sorting (CS)

Table F1. DSST scores for young women during Placebo Treatment

Subject	Time (h)									
	0	2	3.5	4.5	5.5	7	8.5	10	11.5	12.5
1	55	56	52	51	57	51	60	62	55	60
2	64	76	77	73	81	79	72	77	80	74
3	87	90	82	96	91	90	93	90	91	94
4	71	77	86	68	83	78	92	88	76	86
5	80	82	77	86	71	77	81	79	80	85
6	--	--	--	--	--	--	--	--	--	--
7	71	67	71	71	69	70	70	69	69	71
8	49	52	62	66	72	70	61	73	57	63
9	90	94	90	95	97	95	87	95	82	80
10	73	80	73	62	74	72	69	73	71	71
11	78	67	67	74	72	76	67	81	74	77
12	63	60	57	56	59	69	61	65	67	74
13	63	64	64	64	62	59	62	43	65	58
14*	60	61	66	60	61	63	60	58	58	60
15*	67	64	72	79	77	68	79	74	75	76
16*	76	83	90	89	74	83	91	86	90	91
66	73	75	74	69	69	74	72	71	69	73
102	87	108	103	98	97	96	100	106	100	88
106	91	80	85	90	93	82	98	88	97	91
111	73	81	84	88	84	75	75	77	79	75
112	84	75	97	93	89	94	96	90	92	99
113	65	51	68	63	65	59	62	69	64	64
114*	71	89	88	80	83	82	82	75	77	79
206	75	75	76	74	81	75	81	70	75	64

213*	73	61	69	66	64	65	73	68	72	77
Mean	72.46	73.67	76.25	75.46	76.04	75.08	76.83	76.13	75.63	76.25
St. Dev.	10.77	13.96	12.53	13.68	11.94	11.60	13.17	13.27	12.13	11.45

*Minority Subjects

(-) DSST score not obtained

Table F2. DSST scores for young men during Placebo Treatment

Subject	Time (h)									
	0	2	3.5	4.5	5.5	7	8.5	10	11.5	12.5
33	81	87	88	87	88	91	70	90	87	80
34	68	68	66	71	69	70	70	69	68	73
35	65	52	62	68	59	63	66	68	65	68
36	63	71	70	69	69	71	65	72	76	74
37	66	67	68	65	63	66	65	73	66	72
38	78	74	75	73	75	77	80	75	76	81
39	75	81	76	84	86	81	66	83	81	75
40	66	64	61	63	60	61	73	61	66	67
41	76	76	85	85	82	75	82	79	83	83
42	73	61	66	72	68	68	73	64	72	72
43	68	69	77	72	73	71	70	83	80	71
44	60	59	53	60	59	61	66	58	59	63
45	53	58	71	60	61	59	66	63	64	66
46	62	68	69	67	68	69	60	70	69	67
47*	79	76	68	74	69	76	80	76	70	69
48*	82	84	89	92	88	79	86	82	91	89
140	79	89	84	97	90	94	90	88	82	85
145	42	48	45	39	44	37	35	47	43	45
146*	67	65	73	70	77	69	66	66	65	72
245*	49	53	59	54	55	45	48	60	58	55
Mean	67.60	68.50	70.25	71.10	70.15	69.15	68.85	71.35	71.05	71.35
St. Dev.	10.87	11.55	11.35	13.45	12.39	13.35	12.42	10.97	11.32	10.11

*Minority Subjects

Table F3. DSST scores for older women during Placebo Treatment

Subject	Time (h)									
	0	2	3.5	4.5	5.5	7	8.5	10	11.5	12.5
17	38	35	43	39	43	45	39	40	41	39
18	52	53	50	51	51	52	51	52	46	54
19	44	43	45	47	48	49	45	44	49	47
20*	29	32	34	29	32	32	37	32	35	36
21	47	51	45	50	49	47	44	45	48	50
22	43	39	43	40	43	40	40	42	43	40
23	53	58	55	48	57	53	59	57	58	58
24	62	60	64	57	65	65	68	62	62	71
25	45	46	45	47	42	45	49	43	49	48
26	37	42	43	45	40	43	40	40	42	41
27	51	48	49	51	43	47	42	49	45	48
28	47	46	45	40	40	43	48	48	40	44
29*	59	46	53	43	48	51	53	46	47	43
30*	45	47	32	47	48	50	47	50	54	48
31*	46	42	45	42	46	45	44	48	52	52
120	43	34	42	36	34	34	34	24	31	29
Mean	46.31	45.13	45.81	44.50	45.56	46.31	46.25	45.13	46.38	46.75
St. Dev.	8.14	7.99	7.60	6.80	8.08	7.72	8.61	9.00	7.97	9.66

*Minority Subjects

Table F4. DSST scores for older men during Placebo Treatment

Subject	Time (h)									
	0	2	3.5	4.5	5.5	7	8.5	10	11.5	12.5
49	--	--	--	--	--	--	--	--	--	--
50	32	35	29	34	33	30	35	32	32	31
51	45	44	45	46	43	49	47	43	44	46
52	34	32	35	33	35	39	37	35	35	33
53	42	43	45	49	45	48	46	48	43	46
54	45	48	49	43	48	48	51	49	45	47
55	41	39	40	41	41	40	40	35	41	40
56	45	46	46	44	45	44	45	45	49	47
57	57	54	61	60	55	60	61	54	60	58
58	61	61	63	67	67	61	59	70	61	67
59	47	50	49	46	45	49	49	53	44	54
60	54	32	32	29	36	31	35	36	38	40
61*	33	44	37	45	42	39	42	37	37	40
149	45	42	48	47	50	44	46	46	47	48
160	41	39	37	36	40	40	40	36	35	36
Mean	44.43	43.50	44	44.29	44.64	44.43	45.21	44.21	43.64	45.21
St. Dev.	8.57	8.16	9.95	10.18	8.75	9.08	8.00	10.33	8.68	9.80

*Minority Subjects

(--) DSST score not obtained

Table F5. DSST scores for young women during DHEA Treatment

Subject	Time (h)									
	0	2	3.5	4.5	5.5	7	8.5	10	11.5	12.5
1	70	42	31	32	34	43	35	47	55	54
2	--	--	--	--	--	--	--	--	--	--
3	95	98	64	52	63	60	71	58	91	88
4	86	72	75	38	46	38	45	65	58	60
5	77	91	28	51	34	66	68	81	80	84
6	--	--	--	--	--	--	--	--	--	--
7	76	70	77	49	57	52	50	70	64	71
8	77	64	63	47	53	53	28	47	52	44
9	90	90	100	80	76	85	70	75	83	97
10	93	94	42	26	33	65	86	70	60	85
11	77	76	7	44	21	57	48	44	64	71
12	69	62	50	41	42	38	45	64	60	62
13	--	--	--	--	--	--	--	--	--	--
14*	70	68	60	62	62	57	63	62	65	62
15*	81	83	40	28	28	37	47	61	72	75
16*	93	94	28	46	61	68	67	80	90	81
66	73	72	26	33	36	39	44	46	59	51
102	107	110	108	83	84	66	88	84	106	109
106	--	--	--	--	--	--	--	--	--	--
111	85	86	75	60	53	69	62	64	77	79
112	92	86	45	66	60	67	68	60	82	76
113	71	72	56	43	34	44	49	56	47	58
114*	94	85	80	59	72	74	89	84	86	88
206	84	83	73	26	40	56	43	63	70	69

213*	78	78	45	43	53	60	56	61	77	79
Mean	82.76	79.81	55.86	48.05	49.62	56.86	58.19	63.90	71.33	73.48
St. Dev.	10.36	14.88	25.52	16.01	16.85	13.29	17.08	12.21	15.02	15.93

*Minority Subjects

(-) DSST Score not obtained

Table F6. DSST scores for young men during DHEA Treatment

Subject	Time (h)									
	0	2	3.5	4.5	5.5	7	8.5	10	11.5	12.5
33	66	66	73	75	83	75	76	70	83	80
34	74	71	74	73	70	73	72	69	71	71
35	58	53	47	60	56	62	64	62	52	65
36	73	74	71	79	78	75	79	72	81	78
37	71	70	69	70	68	74	75	73	72	74
38	78	79	81	85	84	82	81	81	89	86
39	67	63	72	67	72	64	78	78	79	77
40	59	63	69	61	67	61	62	58	63	69
41	75	72	69	69	75	76	81	78	79	73
42	49	53	58	60	65	67	57	62	68	67
43	75	78	73	80	85	79	60	82	75	75
44	56	57	68	72	57	60	69	60	65	66
45	69	73	73	72	69	72	73	75	76	75
46	61	58	65	58	60	62	61	66	64	65
47*	72	74	81	77	80	84	80	80	78	84
48*	75	80	77	80	83	81	82	82	84	79
140	77	85	90	78	84	88	81	92	83	84
145	41	46	48	45	46	46	47	44	46	48
146*	57	67	70	58	59	63	65	74	63	66
245*	50	55	50	55	59	57	52	56	56	59
Mean	65.15	66.85	68.90	68.70	70	70.05	69.75	70.70	71.35	72.05
St. Dev.	10.68	10.59	11.01	10.40	11.40	10.59	10.65	11.30	11.54	9.26

*Minority Subjects

Table F7. DSST scores for older women during DHEA Treatment

Subject	Time (h)									
	0	2	3.5	4.5	5.5	7	8.5	10	11.5	12.5
17	46	40	41	45	42	42	43	40	44	40
18	47	39	45	45	43	45	44	44	44	46
19	35	42	41	39	43	38	41	44	45	44
20*	37	40	38	42	40	45	27	40	32	33
21	47	47	53	49	57	53	51	40	51	53
22	43	42	40	39	40	41	39	39	39	40
23	56	50	59	57	59	58	58	51	58	56
24	57	44	53	58	54	53	54	55	56	54
25	49	54	52	50	44	52	49	48	48	48
26	37	30	34	35	36	39	38	37	38	33
27	48	41	47	43	44	44	44	44	44	44
28	51	45	49	48	41	50	48	48	54	52
29*	53	49	52	50	58	48	50	54	49	54
30*	60	57	57	57	58	55	55	53	54	63
31*	45	44	37	46	43	43	43	44	42	43
120	45	46	44	48	40	42	40	45	44	41
Mean	47.25	44.38	46.38	46.94	46.38	46.75	45.25	45.38	46.38	46.50
St. Dev.	7.19	6.39	7.52	6.67	7.85	6.08	7.72	5.63	7.07	8.38

*Minority Subjects

Table F8. DSST scores for older men during DHEA Treatment

Subject	Time (h)									
	0	2	3.5	4.5	5.5	7	8.5	10	11.5	12.5
49	45	36	43	44	35	39	26	37	46	48
50	32	28	30	30	30	29	29	28	31	27
51	51	47	47	50	48	50	48	46	45	39
52	42	39	42	36	30	38	35	37	40	35
53	42	44	45	42	42	37	45	46	41	46
54	52	49	47	52	48	50	47	48	54	54
55	40	40	41	35	39	32	42	39	38	37
56	46	48	50	48	50	50	52	48	48	48
57	50	62	58	58	57	57	60	53	54	61
58	53	53	54	57	57	61	60	60	62	61
59	60	52	56	63	48	55	49	50	45	57
60	43	41	45	38	45	45	41	42	39	46
61*	35	29	33	35	35	35	34	33	33	32
149	46	42	52	44	40	41	46	41	45	43
160	43	41	46	42	40	44	41	44	38	44
Mean	45.33	43.40	45.93	44.93	42.93	44.20	43.67	43.47	43.93	45.20
St. Dev.	7.17	8.95	7.74	9.62	8.54	9.47	9.93	8.11	8.28	10.19

*Minority Subjects

Table F9. DSST scores for young women during Alprazolam/Placebo Treatment

Subject	Time (h)									
	0	2	3.5	4.5	5.5	7	8.5	10	11.5	12.5
1	58	49	30	33	33	43	32	30	38	37
2	--	--	--	--	--	--	--	--	--	--
3	87	91	41	51	62	65	66	79	84	87
4	78	76	64	35	48	47	37	66	56	73
5	92	87	35	25	36	45	54	79	87	85
6	--	--	--	--	--	--	--	--	--	--
7	76	76	68	49	48	51	58	64	71	71
8	72	66	60	26	33	35	23	49	51	68
9	84	90	88	67	64	70	59	59	77	91
10	90	82	77	22	40	47	55	51	54	70
11	60	67	51	11	22	49	40	46	64	75
12	64	65	63	56	45	46	42	52	63	53
13	--	--	--	--	--	--	--	--	--	--
14*	60	60	56	40	36	44	42	56	56	57
15*	87	82	40	32	26	66	64	74	70	79
16*	95	84	52	60	47	28	47	83	90	88
66	71	69	53	54	58	52	51	58	68	59
102	113	119	98	42	76	76	86	90	104	110
106	--	--	--	--	--	--	--	--	--	--
111	77	82	83	36	43	51	70	65	75	76
112	90	96	32	29	53	53	44	60	83	80
113	67	59	63	38	44	42	53	40	55	58
114*	93	97	45	64	66	78	65	87	85	79
206	88	79	77	38	43	58	58	62	65	66

213*	81	86	31	41	63	65	66	66	73	75
Mean	80.14	79.14	57.48	40.43	46.95	52.90	52.95	62.67	69.95	73.19
St. Dev.	13.94	15.70	19.55	14.54	14.01	13.01	14.49	15.53	15.64	15.58

*Minority Subjects

(-) DSST score not obtained

Table F10. DSST scores for young men during Alprazolam/Placebo Treatment

Subject	Time (h)									
	0	2	3.5	4.5	5.5	7	8.5	10	11.5	12.5
33	80	92	37	38	36	53	31	45	77	82
34	73	48	5	26	39	43	45	46	74	71
35	62	74	23	26	38	38	35	42	43	57
36	84	75	57	56	61	55	57	66	74	76
37	70	73	65	50	60	60	74	70	69	73
38	86	91	67	41	67	65	65	78	80	83
39	73	83	71	22	46	37	65	65	70	48
40	--	--	--	--	--	--	--	--	--	--
41	88	84	70	67	77	71	78	74	85	79
42	68	73	23	17	36	74	60	58	44	60
43	72	64	24	9	40	41	65	75	75	76
44	58	64	22	15	37	45	46	53	52	54
45	81	84	11	53	68	51	78	76	79	79
46	66	69	29	42	31	53	51	47	58	60
47*	83	84	41	54	64	56	62	61	73	57
48*	90	95	7	15	24	53	59	72	75	76
140	89	89	44	32	50	80	22	83	90	94
145	45	49	14	6	26	22	43	31	47	48
146*	79	74	54	56	41	49	60	70	80	75
245*	60	49	42	42	30	48	45	46	58	52
Mean	74.05	74.42	37.16	35.11	45.84	52.32	54.79	60.95	68.58	68.42
St. Dev.	12.18	14.55	21.97	18.17	15.75	13.92	15.53	14.76	14.05	13.40

*Minority Subjects
 (--) DSST score not obtained

Table F11. DSST scores for older women during Alprazolam/Placebo Treatment

Subject	Time (h)									
	0	2	3.5	4.5	5.5	7	8.5	10	11.5	12.5
17	51	45	11	22	20	24	32	25	13	37
18	58	54	14	40	37	46	43	46	53	52
19	48	42	5	13	12	--	30	14	40	30
20*	32	36	34	22	11	24	26	16	33	16
21	58	54	--	19	31	27	39	36	48	32
22	41	45	21	25	26	27	24	26	35	32
23	63	56	32	8	16	25	22	25	40	47
24	68	63	4	17	45	45	41	51	65	64
25	48	49	49	25	34	37	33	39	43	34
26	44	42	2	9	14	22	24	25	27	33
27	54	48	29	8	15	9	19	26	39	38
28	46	47	10	9	21	35	26	39	40	43
29*	59	60	--	46	44	31	35	46	53	57
30*	57	55	32	--	33	35	45	20	41	43
31*	51	39	--	4	1	5	8	23	40	43
120	58	52	10	25	24	21	23	33	45	43
Mean	52.25	49.19	19.46	19.47	24.00	27.53	29.38	30.63	40.94	40.25
St. Dev.	9.01	7.59	14.51	11.95	12.53	11.39	9.83	11.14	11.61	11.53

*Minority Subjects

(--) DSST score not obtained

Table F12. DSST scores for older men during Alprazolam/Placebo Treatment

Subject	Time (h)									
	0	2	3.5	4.5	5.5	7	8.5	10	11.5	12.5
49	--	--	--	--	--	--	--	--	--	--
50	36	31	14	16	24	21	21	21	29	22
51	52	49	32	32	31	29	38	38	42	42
52	47	45	--	3	22	19	32	19	37	37
53	51	47	46	42	41	41	43	36	45	45
54	47	49	22	26	34	33	24	40	45	43
55	39	43	19	18	25	33	25	27	37	33
56	41	46	12	24	24	33	39	30	43	37
57	57	56	23	16	30	34	50	40	45	57
58	67	69	25	47	52	55	62	56	55	54
59	60	60	7	16	38	47	46	47	54	53
60	42	43	16	19	31	34	28	39	34	37
61*	43	45	15	26	24	27	21	35	37	37
149	52	46	23	29	21	37	21	37	38	46
160	50	48	--	4	5	19	25	27	39	40
Mean	48.86	48.36	21.17	22.71	28.71	33.00	33.93	35.14	41.43	41.64
St. Dev.	8.58	8.84	10.28	12.47	10.98	10.19	12.75	9.88	7.18	9.20

*Minority Subjects

(--) DSST score not obtained

Table F13. DSST scores for young women during Alprazolam/DHEA Treatment

Subject	Time (h)									
	0	2	3.5	4.5	5.5	7	8.5	10	11.5	12.5
1	70	42	31	32	34	43	35	47	55	54
2	--	--	--	--	--	--	--	--	--	--
3	95	98	64	52	63	60	71	58	91	88
4	86	72	75	38	46	38	45	65	58	60
5	77	91	28	51	34	66	68	81	80	84
6	--	--	--	--	--	--	--	--	--	--
7	76	70	77	49	57	52	50	70	64	71
8	77	64	63	47	53	53	28	47	52	44
9	90	90	100	80	76	85	70	75	83	97
10	93	94	42	26	33	65	86	70	60	85
11	77	76	7	44	21	57	48	44	64	71
12	69	62	50	41	42	38	45	64	60	62
13	--	--	--	--	--	--	--	--	--	--
14*	70	68	60	62	62	57	63	62	65	62
15*	81	83	40	28	28	37	47	61	72	75
16*	93	94	28	46	61	68	67	80	90	81
66	73	72	26	33	36	39	44	46	59	51
102	107	110	108	83	84	66	88	84	106	109
106	--	--	--	--	--	--	--	--	--	--
111	85	86	75	60	53	69	62	64	77	79
112	92	86	45	66	60	67	68	60	82	76
113	71	72	56	43	34	44	49	56	47	58
114*	94	85	80	59	72	74	89	84	86	88
206	84	83	73	26	40	56	43	63	70	69

213*	78	78	45	43	53	60	56	61	77	79
Mean	82.76	79.81	55.86	48.05	49.62	56.86	58.19	63.90	71.33	73.48
St. Dev.	10.36	14.88	25.52	16.01	16.85	13.29	17.08	12.21	15.02	15.93

*Minority Subjects
 (-) DSST Score not obtained

Table F14. DSST scores for young men during Alprazolam/DHEA Treatment

Subject	Time (h)									
	0	2	3.5	4.5	5.5	7	8.5	10	11.5	12.5
33	77	79	25	29	39	45	58	80	48	88
34	70	72	3	38	55	53	29	72	72	76
35	52	46	30	37	39	33	24	40	52	54
36	76	78	40	46	53	54	70	66	73	68
37	79	75	68	56	68	33	23	--	74	73
38	84	83	67	52	72	68	65	68	82	80
39	79	77	20	3	26	33	23	41	54	44
40	--	--	--	--	--	--	--	--	--	--
41	84	91	58	74	67	71	65	83	81	81
42	77	59	51	43	29	45	74	51	52	74
43	80	79	31	17	31	53	62	78	77	88
44	70	62	22	37	38	44	44	43	51	59
45	73	69	72	59	64	49	67	68	81	71
46	61	67	32	50	52	51	56	58	60	68
47*	82	87	48	63	65	61	57	63	82	76
48*	92	83	68	39	18	35	39	56	86	74
140	87	91	57	50	73	81	86	88	90	89
145	51	52	23	6	13	23	37	32	44	35
146*	72	81	84	66	61	76	76	79	79	83
245*	53	59	44	33	26	40	41	51	43	49
Mean	73.63	73.16	44.37	42.00	46.79	49.89	52.42	62.06	67.42	70.00
St. Dev.	11.84	12.82	21.81	19.06	19.36	15.93	19.51	16.55	15.76	15.35

*Minority Subjects

(--) DSST Score not obtained

Table F15. DSST scores for older women during Alprazolam/DHEA Treatment

Subject	Time (h)									
	0	2	3.5	4.5	5.5	7	8.5	10	11.5	12.5
17	54	48	18	18	23	25	41	44	48	45
18	55	46	23	17	39	36	43	40	46	52
19	51	48	19	7	--	--	27	33	40	43
20*	40	32	24	17	11	22	9	15	28	14
21	53	48	10	17	31	29	38	39	32	32
22	40	40	25	28	26	30	32	27	31	34
23	62	55	11	13	31	32	34	36	51	46
24	68	72	14	39	15	41	50	50	52	61
25	46	50	16	10	21	39	28	24	38	38
26	48	45	4	5	9	22	26	25	15	25
27	50	50	30	9	8	23	16	31	41	43
28	50	60	25	16	20	31	39	28	34	23
29*	63	60	35	5	19	40	57	50	57	47
30*	48	58	--	33	39	34	43	34	43	45
31*	46	39	--	5	33	31	32	31	39	40
120	53	49	23	25	22	30	26	34	41	43
Mean	51.69	50.00	19.79	16.50	23.13	31.00	33.81	33.81	39.75	39.44
St. Dev.	7.71	9.56	8.33	10.28	10.03	6.26	12.13	9.39	10.39	11.65

*Minority Subjects
 (--) DSST score not obtained

Table F16. DSST scores for older men during Alprazolam/DHEA Treatment

Subject	Time (h)									
	0	2	3.5	4.5	5.5	7	8.5	10	11.5	12.5
49	--	--	--	--	--	--	--	--	--	--
50	37	38	14	12	24	22	32	30	31	35
51	55	52	16	28	34	34	43	45	47	42
52	40	41	5	5	18	21	13	12	30	14
53	51	46	25	41	42	41	36	40	45	41
54	50	49	25	15	33	31	31	31	41	44
55	44	44	35	34	31	32	25	29	28	38
56	46	49	22	22	32	26	27	26	40	45
57	53	62	2	19	41	40	44	52	63	43
58	70	60	62	34	41	54	56	54	61	59
59	63	65	--	42	46	45	51	46	54	52
60	50	44	8	22	28	24	35	33	37	39
61*	41	45	13	28	23	28	24	26	37	37
149	51	48	6	27	31	31	37	36	43	41
160	45	44	--	6	10	20	13	22	34	34
Mean	49.71	49.07	19.42	23.93	31.00	32.07	33.36	34.43	42.21	40.29
St. Dev.	8.90	8.04	16.59	11.76	9.97	9.94	12.67	11.88	10.96	10.04

*Minority Subjects

(--) DSST score not obtained

Table F17. Card Sorting scores for young women during Placebo Treatment

Subject	Time (h)									
	0	2	3.5	4.5	5.5	7	8.5	10	11.5	12.5
1	1.49	0.98	1.27	1.33	1.49	1.44	1.41	1.18	1.41	1.49
2	1.00	1.00	1.00	1.00	1.00	1.00	1.00	1.00	1.00	1.00
3	1.58	1.58	1.53	1.49	1.44	1.53	1.44	1.63	1.37	1.58
4	1.32	1.63	1.58	1.63	1.55	1.37	1.43	1.63	1.53	1.49
5	1.27	1.27	1.27	1.30	1.27	1.18	1.37	1.27	1.33	1.27
6	1.68	1.68	1.73	1.68	1.79	1.79	1.79	1.49	1.58	1.68
7	0.98	1.30	1.33	1.27	1.41	1.27	1.44	1.41	1.41	1.30
8	1.63	1.53	1.49	1.63	1.63	1.37	1.41	1.41	1.41	1.46
9	1.58	1.33	1.44	1.44	1.53	1.49	1.58	1.53	1.68	1.58
10	1.21	1.30	1.21	1.16	1.11	1.27	1.18	1.08	1.30	1.30
11	1.18	1.16	1.27	1.21	1.30	1.00	1.21	1.24	1.30	1.06
12	1.33	1.41	1.41	1.49	1.44	1.30	1.44	1.44	1.33	1.53
13	1.00	1.00	1.00	1.00	1.00	1.00	1.00	1.00	1.00	1.00
14*	0.79	0.83	0.90	1.00	1.06	0.90	0.91	0.90	0.85	1.08
15*	1.16	1.11	1.11	1.18	0.98	1.13	1.11	1.13	1.13	1.24
16*	1.13	1.06	1.06	1.08	1.13	1.06	1.06	1.13	1.13	1.08
66	1.27	1.19	1.49	1.41	1.41	1.44	1.37	1.41	1.37	1.37
102	1.24	1.44	1.44	1.37	1.44	1.33	1.49	1.41	1.44	1.58
106	0.98	1.68	1.85	1.93	2.00	2.00	1.93	2.00	1.79	2.17
111	1.37	1.30	1.21	1.27	1.24	1.21	1.30	1.30	1.27	1.18
112	1.44	1.41	1.44	1.53	1.49	1.53	1.33	1.49	1.53	1.53
113	1.08	0.90	0.95	1.11	1.00	1.04	1.04	1.04	0.96	1.02
114*	1.49	1.49	1.41	1.44	1.44	1.37	1.49	1.49	1.68	1.53
206	1.41	1.53	1.49	1.44	1.44	1.44	1.53	1.49	1.53	1.58

213*	1.49	1.41	1.49	1.49	1.49	1.44	1.44	1.53	1.49	1.49
Mean	1.28	1.30	1.33	1.35	1.36	1.32	1.35	1.34	1.35	1.38
St. Dev.	0.23	0.25	0.24	0.23	0.26	0.26	0.24	0.25	0.24	0.27

*Minority Subjects

Table F18. Card Sorting scores for young men during Placebo Treatment

Subject	Time (h)									
	0	2	3.5	4.5	5.5	7	8.5	10	11.5	12.5
33	1.79	2.08	1.93	2.08	1.59	1.86	1.53	2.08	2.08	1.93
34	1.41	1.41	1.18	1.30	1.41	1.27	1.49	1.18	1.18	1.41
35	1.41	1.18	1.18	1.27	1.24	1.27	1.41	1.16	1.33	1.41
36	1.44	1.58	1.63	1.63	1.53	1.49	1.63	1.58	1.63	1.63
37	1.27	1.27	1.24	1.27	1.21	1.18	1.33	1.41	1.37	1.41
38	1.68	1.63	1.68	1.53	1.44	1.44	1.44	1.41	1.63	1.00
39	1.41	1.58	1.38	1.53	1.53	1.53	1.37	1.44	1.53	1.49
40	1.18	1.27	1.21	1.24	1.24	1.18	1.30	1.30	1.41	1.41
41	1.44	1.53	1.49	1.49	1.53	1.49	1.41	1.41	1.49	1.53
42	1.63	1.33	1.41	1.58	1.58	1.58	1.63	1.79	1.86	1.53
43	1.53	1.41	1.44	1.49	1.44	1.27	1.37	1.27	1.33	1.41
44	1.44	1.37	1.49	1.33	1.58	1.49	1.53	1.41	1.49	1.49
45	1.30	1.44	1.24	1.73	1.53	1.41	1.53	1.73	1.49	1.68
46	1.63	1.73	1.68	1.58	1.58	1.65	1.63	1.73	1.73	1.63
47*	1.53	1.37	1.44	1.58	1.24	1.27	1.41	1.37	1.33	1.33
48*	1.30	1.24	1.33	1.24	1.28	1.21	1.27	1.06	1.41	1.49
140	1.13	1.18	1.30	1.30	1.24	1.41	1.27	1.13	1.21	1.16
145	0.81	1.00	0.95	0.96	0.95	1.06	1.13	1.16	1.11	1.06
146*	1.33	1.21	1.33	1.24	1.30	1.19	1.41	1.41	1.20	1.33
245*	0.72	0.62	0.63	0.85	0.70	0.68	0.81	0.87	0.78	0.84
Mean	1.37	1.37	1.36	1.41	1.36	1.34	1.39	1.39	1.43	1.41
St. Dev.	0.26	0.30	0.28	0.27	0.23	0.25	0.19	0.28	0.28	0.25

*Minority Subjects

Table F19. Card Sorting scores for older women during Placebo Treatment

Subject	Time (h)									
	0	2	3.5	4.5	5.5	7	8.5	10	11.5	12.5
17	1.11	1.02	1.02	1.02	0.98	1.00	0.84	0.91	1.04	0.84
18	1.30	1.13	1.08	1.11	1.13	1.04	1.13	1.24	1.08	1.30
19	1.02	0.88	1.02	0.90	1.02	1.00	0.93	0.91	0.91	0.98
20*	1.16	0.93	1.13	1.08	1.13	1.16	1.13	0.98	1.13	1.04
21	1.13	1.18	1.21	1.00	1.16	1.24	1.13	1.16	1.18	1.21
22	1.13	1.11	1.08	1.18	1.11	1.04	1.13	1.13	1.16	1.24
23	1.04	1.11	1.02	1.02	1.08	1.16	0.93	0.93	1.06	1.04
24	1.27	1.21	1.30	0.93	1.30	1.21	1.27	1.37	1.21	0.98
25	0.83	0.90	0.91	0.83	0.98	0.88	0.95	0.87	0.88	0.88
26	1.08	1.16	1.18	1.16	1.11	1.11	1.13	1.16	1.08	1.18
27	1.41	1.41	1.37	1.37	1.33	1.33	1.33	1.41	1.30	1.37
28	1.00	1.04	0.88	0.98	1.02	0.85	0.96	0.96	0.95	0.96
29*	1.44	1.24	1.41	1.37	1.18	1.58	1.53	1.30	1.27	1.33
30*	1.27	1.11	1.04	1.24	1.06	0.98	1.06	1.17	1.24	1.27
31*	1.06	0.96	0.81	0.96	0.96	1.06	0.90	0.93	1.18	0.95
120	0.81	0.76	0.81	0.70	0.58	0.68	0.70	0.58	0.61	0.56
Mean	1.13	1.07	1.08	1.05	1.07	1.08	1.07	1.06	1.08	1.07
St. Dev.	0.18	0.16	0.18	0.18	0.17	0.21	0.20	0.22	0.18	0.22

*Minority Subjects

Table F20. Card Sorting scores for older men during Placebo Treatment

Subject	Time (h)									
	0	2	3.5	4.5	5.5	7	8.5	10	11.5	12.5
49	1.00	1.00	1.00	1.00	1.00	1.00	1.00	1.00	1.00	1.00
50	0.80	0.65	0.74	0.70	0.67	0.68	0.61	0.68	0.66	0.73
51	1.13	1.08	1.27	1.04	1.18	1.18	1.04	1.21	0.93	1.16
52	1.18	1.16	1.13	1.30	1.30	1.30	1.24	1.18	1.24	1.04
53	1.18	1.06	1.04	1.13	1.08	1.13	1.21	1.16	1.11	1.11
54	1.24	1.16	1.27	1.13	1.16	1.13	1.11	1.08	1.11	1.13
55	1.11	1.00	0.98	1.06	0.98	1.04	1.00	1.00	1.06	1.02
56	1.24	1.21	1.21	1.16	1.27	1.13	1.18	1.30	1.27	1.21
57	1.53	1.63	1.68	1.63	1.49	1.53	1.68	1.73	1.63	1.73
58	1.49	1.58	1.37	1.41	1.41	1.41	1.49	1.44	1.37	1.44
59	1.41	1.37	1.30	1.33	1.30	1.24	1.37	1.18	1.27	1.27
60	0.98	1.06	1.08	1.02	1.00	0.76	1.00	1.04	0.96	1.16
61*	1.30	1.30	1.13	1.04	1.08	1.06	1.21	1.13	1.18	1.21
149	1.16	1.13	1.13	1.16	0.98	1.16	1.21	1.11	1.13	1.16
160	0.71	0.93	0.90	0.87	1.04	0.95	0.81	0.95	0.93	0.83
Mean	1.16	1.15	1.15	1.13	1.13	1.11	1.14	1.15	1.12	1.15
St. Dev.	0.23	0.25	0.22	0.22	0.20	0.22	0.26	0.24	0.22	0.24

*Minority Subjects

Table F21. Card Sorting scores for young women during DHEA Treatment

Subject	Time (h)									
	0	2	3.5	4.5	5.5	7	8.5	10	11.5	12.5
1	1.27	1.33	0.98	1.18	1.30	1.24	1.13	1.33	1.27	1.44
2	1.37	1.44	1.41	1.53	1.16	1.53	1.49	1.37	1.63	1.27
3	1.63	1.58	1.53	1.63	1.49	1.73	1.58	1.58	1.49	1.79
4	1.33	1.49	1.53	1.44	1.73	1.30	1.73	1.67	1.73	1.68
5	1.16	1.27	1.21	1.13	1.27	1.24	1.27	1.21	0.62	1.33
6	1.00	1.00	1.00	1.00	1.00	1.00	1.00	1.00	1.00	1.00
7	1.18	1.13	1.13	1.13	1.24	1.30	1.27	1.41	1.24	1.24
8	1.16	1.16	1.00	0.98	1.44	1.44	1.41	1.21	1.13	1.41
9	1.68	1.49	1.53	1.53	1.58	1.63	1.53	1.49	1.53	1.68
10	1.27	1.21	1.37	1.18	1.33	1.24	1.00	1.30	1.11	1.24
11	1.30	1.30	1.11	1.21	1.33	1.41	1.44	1.30	1.27	1.37
12	1.37	1.21	1.41	1.33	1.37	1.18	1.37	1.41	1.30	1.37
13	1.27	1.21	1.18	1.18	1.13	1.08	1.18	1.21	1.16	1.04
14	1.04	1.13	1.13	0.93	1.27	0.96	1.11	1.18	1.04	1.16
15	1.04	0.96	1.24	1.13	1.00	1.08	1.13	1.06	1.08	1.11
16	1.16	1.11	1.08	1.13	1.11	0.98	0.90	0.86	1.13	1.13
66	1.33	1.37	1.18	1.33	1.30	1.18	1.27	1.44	1.49	1.30
102	1.30	1.44	1.41	1.41	1.41	1.33	1.53	1.44	1.41	1.49
106	1.73	2.17	2.08	1.79	1.79	1.67	1.79	1.93	1.93	1.86
111	1.41	1.16	1.33	1.24	1.30	1.37	1.37	1.33	1.44	1.33
112	1.37	1.37	1.58	1.63	1.53	1.49	1.58	1.53	1.58	1.49
113	1.06	0.96	1.08	1.02	0.96	0.95	1.00	1.00	1.04	1.11
114	1.53	1.63	1.41	1.41	1.44	1.37	1.63	1.49	1.41	1.49
206	1.63	1.73	1.68	1.68	1.63	1.73	1.86	1.79	1.79	1.93

213*	1.41	1.13	1.33	1.37	1.30	1.41	1.37	1.37	1.49	1.41
Mean	1.32	1.32	1.32	1.30	1.34	1.31	1.36	1.36	1.33	1.39
St. Dev.	0.20	0.27	0.25	0.24	0.22	0.23	0.26	0.24	0.29	0.25

*Minority Subjects

Table F22. Card Sorting scores for young men during DHEA Treatment

Subject	Time (h)									
	0	2	3.5	4.5	5.5	7	8.5	10	11.5	12.5
33	1.73	1.79	1.73	1.86	1.86	1.58	1.63	1.49	1.68	2.00
34	1.33	1.30	1.33	1.28	1.21	1.28	1.30	1.41	1.37	1.37
35	1.13	1.08	1.04	1.30	1.27	1.21	1.21	1.18	1.24	1.30
36	1.58	1.73	1.63	1.63	1.68	1.73	1.68	1.68	1.86	1.93
37	1.41	1.16	1.33	1.33	1.33	1.41	1.27	1.41	1.41	1.33
38	1.58	1.63	1.68	1.41	1.44	1.58	1.58	1.58	1.53	1.73
39	1.16	1.27	1.27	1.41	1.33	1.37	1.49	1.41	1.41	1.44
40	1.11	1.18	1.27	1.37	1.33	1.21	1.27	1.21	1.27	1.27
41	1.33	1.33	1.28	1.30	1.13	1.41	1.41	1.41	1.33	1.41
42	1.53	1.63	1.68	1.34	1.53	1.53	1.44	1.63	1.53	1.79
43	1.41	1.53	1.41	1.27	1.58	1.58	1.33	1.49	1.49	1.37
44	1.79	1.49	1.63	1.58	1.68	1.68	1.86	1.53	1.53	1.20
45	1.53	1.70	1.73	1.68	1.33	1.93	1.86	1.68	1.73	1.73
46	1.30	1.38	1.37	1.41	1.44	1.41	1.41	1.44	1.41	1.44
47*	1.49	1.37	1.27	1.30	1.41	1.30	1.33	1.30	1.44	1.33
48*	1.13	1.21	1.30	1.21	1.06	1.06	1.25	1.30	1.21	1.16
140	1.13	1.13	1.27	1.27	1.33	1.37	1.41	1.18	1.33	1.27
145	0.95	0.98	1.11	1.11	1.06	1.06	1.13	1.27	1.24	1.18
146*	1.27	1.30	1.33	1.33	1.49	1.41	1.44	1.33	1.37	1.37
245*	0.87	1.02	0.90	1.00	0.87	0.87	0.91	0.96	0.98	0.98
Mean	1.34	1.36	1.38	1.37	1.37	1.40	1.41	1.39	1.42	1.43
St. Dev.	0.25	0.24	0.23	0.19	0.24	0.25	0.23	0.18	0.20	0.27

*Minority Subjects

Table F23. Card Sorting scores for older women during DHEA Treatment

Subject	Time (h)									
	0	2	3.5	4.5	5.5	7	8.5	10	11.5	12.5
17	1.13	1.11	1.18	1.08	0.95	0.98	0.87	0.88	0.91	0.91
18	1.08	0.95	1.06	1.02	0.98	1.06	1.08	1.04	0.98	1.08
19	1.08	1.04	0.93	0.84	0.87	0.72	0.76	0.86	0.84	0.83
20*	1.24	1.18	1.13	1.16	1.16	1.11	1.06	1.18	1.08	1.21
21	1.41	1.13	1.21	1.24	1.21	1.18	1.27	1.16	1.21	1.24
22	1.02	1.16	1.06	1.08	1.11	1.04	1.13	1.13	1.08	1.11
23	1.06	1.02	1.04	1.02	1.04	1.02	0.91	1.11	1.06	1.04
24	1.18	1.13	1.18	1.30	1.16	1.18	1.13	1.11	1.11	1.27
25	1.08	1.06	1.08	1.24	1.06	1.24	1.06	1.00	0.95	0.95
26	1.11	1.04	1.06	1.04	1.02	1.06	1.08	1.08	1.04	1.11
27	1.18	1.13	1.13	1.18	1.16	1.16	1.16	1.16	1.13	1.21
28	1.00	0.79	0.96	0.93	1.00	1.13	0.96	0.98	0.98	0.98
29*	1.37	1.44	1.49	1.41	1.41	1.38	1.11	1.21	1.24	1.11
30*	1.24	1.16	1.02	0.98	0.81	1.00	0.90	1.21	0.93	1.27
31*	0.91	0.91	0.95	0.76	0.81	0.87	0.78	0.85	0.88	1.06
120	0.85	0.78	0.88	0.84	0.84	0.72	0.74	0.83	0.84	0.80
Mean	1.12	1.06	1.09	1.07	1.04	1.05	1.00	1.05	1.02	1.07
St. Dev.	0.15	0.16	0.14	0.18	0.16	0.17	0.16	0.13	0.12	0.15

*Minority Subjects

Table F24. Card Sorting scores for older men during DHEA Treatment

Subject	Time (h)									
	0	2	3.5	4.5	5.5	7	8.5	10	11.5	12.5
49	1.18	1.11	1.18	1.11	1.08	1.16	1.18	0.98	1.08	1.13
50	0.68	0.71	0.68	0.73	0.63	0.67	0.73	0.68	0.71	0.65
51	1.37	1.24	1.21	1.21	1.30	1.21	1.21	1.21	1.21	1.21
52	1.33	1.37	1.18	1.33	1.02	1.27	1.11	1.06	1.06	1.06
53	1.02	1.04	1.16	1.18	1.11	1.13	1.11	1.13	1.13	1.24
54	1.18	1.16	1.16	1.13	1.16	1.27	1.13	1.18	1.16	1.21
55	1.02	1.24	0.90	0.96	1.02	0.90	1.00	1.00	0.91	1.00
56	1.27	1.37	1.27	1.21	1.24	1.21	1.37	1.33	1.44	1.37
57	1.68	1.58	1.63	1.53	1.58	1.53	1.63	1.53	1.53	1.37
58	1.58	1.41	1.44	1.44	1.49	1.49	1.11	1.30	1.30	1.37
59	1.53	1.37	1.49	1.09	1.31	1.41	1.27	1.31	1.30	1.41
60	1.08	0.86	0.95	1.11	1.08	0.88	0.96	1.02	0.98	0.96
61*	1.16	1.04	1.30	1.11	1.16	1.21	1.16	1.18	1.02	1.06
149	1.16	1.02	1.04	1.11	1.06	1.11	1.08	1.13	1.13	1.02
160	0.88	0.96	0.88	0.93	0.88	0.88	0.84	0.93	1.02	0.95
Mean	1.21	1.16	1.16	1.15	1.14	1.15	1.13	1.13	1.13	1.13
St. Dev.	0.27	0.23	0.25	0.20	0.23	0.24	0.21	0.20	0.21	0.21

*Minority Subjects

Table F25. Card Sorting scores for young women during Alprazolam/Placebo Treatment

Subject	Time (h)									
	0	2	3.5	4.5	5.5	7	8.5	10	11.5	12.5
1	1.30	1.18	0.98	0.91	0.91	0.93	0.96	0.85	1.02	1.04
2	1.00	1.00	1.00	1.00	1.00	1.00	1.00	1.00	1.00	1.00
3	1.53	1.68	1.11	1.24	1.30	1.27	1.24	1.33	1.49	1.58
4	1.53	1.53	1.13	0.62	0.81	0.87	0.80	1.08	1.27	1.49
5	1.38	1.41	0.33	0.51	0.61	0.72	0.88	1.33	1.24	1.37
6	1.00	1.00	1.00	1.00	1.00	1.00	1.00	1.00	1.00	1.00
7	1.37	1.33	1.02	1.02	0.98	0.90	0.88	1.21	1.21	1.06
8	1.53	1.49	1.33	0.67	0.96	1.06	0.87	1.11	1.49	1.68
9	1.58	1.68	1.44	1.13	1.18	1.13	1.16	1.21	1.30	1.41
10	1.27	1.30	1.13	0.65	0.81	0.95	0.93	0.81	0.93	1.13
11	1.41	1.37	0.88	0.59	0.74	0.87	0.84	1.00	1.30	1.33
12	1.30	1.37	1.27	1.00	0.78	1.08	1.08	1.11	1.24	1.33
13	1.00	1.00	1.00	1.00	1.00	1.00	1.00	1.00	1.00	1.00
14*	1.18	1.02	1.06	0.68	0.68	0.79	0.83	0.64	1.04	1.00
15*	1.24	1.11	0.68	0.67	0.75	0.64	0.87	0.96	0.98	0.98
16*	1.08	1.08	0.63	0.72	0.76	0.70	0.63	0.90	1.04	0.96
66	1.41	1.30	1.02	1.00	1.06	1.04	1.08	1.11	1.41	1.30
102	1.44	1.86	1.30	0.91	1.16	1.08	1.16	1.33	1.41	1.58
106	1.00	1.00	1.00	1.00	1.00	1.00	1.00	1.00	1.00	1.00
111	1.49	1.41	1.27	0.71	0.87	0.73	1.04	1.18	1.30	1.30
112	1.27	1.53	0.47	0.49	0.76	0.68	0.65	0.83	1.16	1.24
113	1.08	1.04	0.96	0.68	0.82	0.74	0.78	0.71	0.83	0.80
114*	1.63	1.68	1.00	0.79	0.74	0.96	1.33	1.49	1.30	1.27
206	1.53	1.73	1.53	0.88	0.88	1.13	1.21	1.27	1.58	1.49

213*	1.49	1.58	1.11	1.06	1.19	1.24	1.33	1.41	1.37	1.53
Mean	1.32	1.35	1.03	0.84	0.91	0.94	0.98	1.07	1.19	1.23
St. Dev.	0.20	0.27	0.28	0.21	0.17	0.17	0.19	0.22	0.20	0.24

*Minority Subjects

Table F26. Card Sorting scores for young men during Alprazolam/Placebo Treatment

Subject	Time (h)									
	0	2	3.5	4.5	5.5	7	8.5	10	11.5	12.5
33	1.93	2.08	1.21	1.41	1.53	1.53	1.53	1.49	1.68	1.79
34	1.30	1.37	0.58	0.93	0.90	0.76	1.04	1.06	1.21	1.53
35	1.44	1.24	0.69	0.81	0.78	1.06	0.93	1.00	0.90	1.27
36	1.79	1.86	1.49	1.44	1.49	1.37	1.33	1.68	1.63	1.73
37	1.44	1.44	1.16	0.96	1.13	1.16	1.30	1.27	1.30	1.24
38	1.58	1.53	1.24	1.11	1.28	1.44	1.37	1.49	1.68	1.53
39	1.49	1.58	1.16	0.93	0.87	0.91	1.08	1.24	1.44	1.13
40	1.00	1.00	1.00	1.00	1.00	1.00	1.00	1.00	1.00	1.00
41	1.41	1.49	1.16	1.27	1.18	1.27	1.13	1.18	1.27	1.37
42	1.41	1.53	0.77	1.08	1.13	1.41	1.33	1.37	1.30	1.53
43	1.37	1.53	0.57	0.60	0.85	1.04	1.18	1.30	1.63	1.63
44	1.63	1.73	0.71	0.60	0.84	1.33	1.41	1.24	1.41	1.44
45	1.93	1.58	0.46	1.00	1.14	1.24	1.24	1.49	1.73	1.33
46	1.44	1.68	1.13	0.96	1.24	1.37	1.24	1.33	1.59	1.63
47*	1.58	1.41	0.91	0.93	1.13	1.08	1.16	1.11	1.41	1.24
48*	1.13	1.18	0.30	0.36	0.68	0.82	1.04	1.27	1.02	1.24
140	1.41	1.41	0.75	0.58	0.90	1.13	0.76	1.21	1.30	1.41
145	1.41	1.41	0.79	0.33	0.72	0.79	0.91	1.06	1.21	1.44
146*	1.22	1.49	1.08	1.18	1.16	1.16	1.30	1.33	1.37	1.53
245*	1.02	0.93	0.83	0.65	0.50	0.76	0.85	0.85	0.98	0.85
Mean	1.45	1.47	0.90	0.91	1.02	1.13	1.16	1.25	1.35	1.39
St. Dev.	0.25	0.27	0.30	0.31	0.26	0.24	0.20	0.20	0.25	0.24

*Minority Subjects

Table F27. Card Sorting scores for older women during Alprazolam/Placebo Treatment

Subject	Time (h)									
	0	2	3.5	4.5	5.5	7	8.5	10	11.5	12.5
17	1.24	0.96	0.36	0.70	0.70	0.56	0.67	0.83	0.60	0.72
18	1.18	1.24	0.62	0.85	0.74	0.93	0.98	0.91	1.11	1.11
19	1.16	0.95	0.72	0.71	1.00	1.00	0.57	0.48	0.74	0.66
20*	1.21	1.13	0.91	0.64	0.39	0.71	0.64	0.63	1.00	0.65
21	1.41	1.24	0.15	0.44	0.62	0.79	0.93	0.84	1.00	1.04
22	1.13	1.13	0.44	0.63	0.72	0.71	0.75	0.74	0.93	0.83
23	1.13	1.06	0.62	0.28	0.49	0.57	0.56	0.57	0.76	0.87
24	1.27	1.18	0.88	0.93	0.87	1.00	0.90	1.08	1.16	1.30
25	1.27	1.24	1.06	0.41	0.67	0.84	0.90	0.75	0.95	0.79
26	1.21	1.21	0.13	0.22	0.35	0.50	0.68	0.91	0.80	0.87
27	1.44	1.49	1.02	0.81	0.72	0.47	0.93	0.87	1.21	1.02
28	1.06	1.02	0.29	0.18	0.54	0.71	0.74	0.76	0.90	0.78
29*	1.68	1.37	1.00	0.91	0.95	0.81	0.80	1.13	1.18	0.96
30*	1.18	1.06	0.65	1.00	0.69	0.63	0.63	0.61	0.95	0.95
31*	0.90	0.81	1.00	0.15	1.00	0.13	0.26	0.31	0.90	0.87
120	0.96	0.98	0.08	0.32	0.37	0.42	0.40	0.50	0.73	0.75
Mean	1.21	1.13	0.62	0.58	0.68	0.67	0.71	0.75	0.93	0.88
St. Dev.	0.19	0.17	0.34	0.29	0.21	0.23	0.20	0.22	0.18	0.17

*Minority Subjects

Table F28. Card Sorting scores for older men during Alprazolam/Placebo Treatment

Subject	Time (h)									
	0	2	3.5	4.5	5.5	7	8.5	10	11.5	12.5
49	1.00	1.00	1.00	1.00	1.00	1.00	1.00	1.00	1.00	1.00
50	0.74	0.68	0.33	0.38	0.34	0.53	0.50	0.50	0.56	0.51
51	1.41	1.24	0.80	0.70	0.78	0.88	0.85	0.98	1.08	0.96
52	1.27	1.33	1.00	0.34	1.00	0.68	0.93	0.62	1.16	1.13
53	1.16	1.16	0.63	0.95	0.93	0.95	1.04	1.00	1.08	1.04
54	1.16	1.24	0.70	0.78	0.90	0.79	0.78	0.91	0.95	0.91
55	1.11	1.04	0.87	0.65	0.68	0.82	0.76	0.69	0.90	0.91
56	1.27	1.18	0.49	0.53	0.68	0.71	0.93	0.68	0.95	0.90
57	1.68	1.58	0.58	0.69	0.83	0.94	0.98	1.08	1.16	1.24
58	1.58	1.68	0.95	1.11	1.06	1.21	1.18	1.08	1.04	1.21
59	1.53	1.53	0.27	0.65	0.81	1.06	1.11	1.04	1.33	1.22
60	1.11	1.16	0.46	0.70	0.65	0.76	0.62	0.80	0.75	0.90
61*	1.27	1.11	0.45	0.85	0.73	0.72	0.62	0.90	0.84	0.95
149	1.27	1.11	0.65	0.63	0.71	0.76	0.73	0.90	1.02	1.00
160	1.06	0.98	1.00	0.16	1.00	0.50	0.53	0.58	0.70	0.74
Mean	1.24	1.20	0.68	0.67	0.81	0.82	0.84	0.85	0.97	0.97
St. Dev.	0.24	0.25	0.25	0.25	0.19	0.19	0.21	0.19	0.20	0.19

*Minority Subjects

Table F29. Card Sorting scores for young women during Alprazolam/DHEA Treatment

Subject	Time (h)									
	0	2	3.5	4.5	5.5	7	8.5	10	11.5	12.5
1	1.37	1.44	0.96	0.96	1.08	1.16	1.13	1.11	1.37	1.58
2	1.00	1.00	1.00	1.00	1.00	1.00	1.00	1.00	1.00	1.00
3	1.53	1.49	1.24	1.11	1.30	1.21	1.21	1.04	1.53	1.73
4	1.49	1.58	1.49	0.72	0.79	0.74	0.80	1.28	1.16	1.53
5	1.37	1.53	0.42	0.80	0.57	0.95	1.00	1.13	1.04	1.30
6	1.00	1.00	1.00	1.00	1.00	1.00	1.00	1.00	1.00	1.00
7	1.37	1.33	1.24	0.78	0.98	0.91	0.98	1.13	1.30	1.41
8	1.68	1.37	1.27	1.08	0.96	1.13	1.00	0.98	1.16	1.44
9	1.63	1.44	1.73	1.27	1.24	1.21	1.27	1.18	1.44	1.68
10	1.30	1.41	0.78	0.55	0.57	1.16	1.24	1.21	1.24	1.37
11	1.24	1.33	0.90	0.87	0.94	1.00	0.98	1.11	1.18	1.16
12	1.08	1.44	0.98	0.88	0.93	0.96	1.02	1.30	1.18	1.30
13	1.00	1.00	1.00	1.00	1.00	1.00	1.00	1.00	1.00	1.00
14*	1.11	1.21	0.95	1.27	1.11	1.13	1.00	1.02	1.18	1.11
15*	1.16	1.08	0.76	0.79	0.66	0.69	0.69	0.95	1.08	1.00
16*	1.16	1.06	0.41	0.71	0.71	0.76	0.78	0.93	0.98	1.02
66	1.44	1.44	0.65	0.69	0.63	0.58	0.95	0.87	1.13	1.13
102	1.41	1.53	1.33	1.04	1.02	0.95	1.13	1.08	1.49	1.58
106	1.00	1.00	1.00	1.00	1.00	1.00	1.00	1.00	1.00	1.00
111	1.33	1.37	1.04	0.95	0.88	0.96	0.94	1.04	1.30	1.24
112	1.33	1.41	0.65	0.79	0.76	0.84	0.74	0.87	1.18	1.11
113	1.06	1.02	0.78	0.71	0.66	0.67	0.72	0.85	0.84	0.95
114*	1.58	1.44	1.27	0.93	1.02	1.30	1.49	1.30	1.18	1.24
206	1.58	1.68	1.37	0.62	0.95	0.96	1.18	1.30	1.38	1.37

213*	1.44	1.53	1.00	0.91	1.13	1.08	1.11	1.09	1.37	1.44
Mean	1.31	1.33	1.01	0.90	0.92	0.97	1.01	1.07	1.19	1.27
St. Dev.	0.21	0.21	0.31	0.18	0.20	0.18	0.18	0.14	0.18	0.24

*Minority Subjects

Table F30. Card Sorting scores for young men during Alprazolam/DHEA Treatment

Subject	Time (h)									
	0	2	3.5	4.5	5.5	7	8.5	10	11.5	12.5
33	1.79	1.79	1.16	1.21	1.41	1.41	1.63	1.79	1.41	1.73
34	1.30	1.33	0.53	0.95	1.18	1.24	0.95	1.33	1.11	1.53
35	1.00	1.18	0.85	0.91	0.85	0.84	0.69	0.85	0.88	1.16
36	1.73	1.79	1.37	1.13	1.44	1.41	1.73	1.68	1.58	1.63
37	1.49	1.37	1.21	1.13	1.08	1.13	1.08	1.30	1.41	1.41
38	1.49	1.68	1.30	1.27	1.30	1.24	1.37	1.41	1.44	1.53
39	1.58	1.49	0.70	0.67	0.75	0.85	0.76	0.98	1.21	1.00
40	1.00	1.00	1.00	1.00	1.00	1.00	1.00	1.00	1.00	1.00
41	1.44	1.44	1.13	1.18	1.24	1.16	1.18	1.30	1.30	1.41
42	1.68	1.58	1.21	1.18	1.49	1.49	1.41	1.37	1.24	1.93
43	1.63	1.53	0.88	0.72	0.69	0.80	1.06	1.53	1.53	1.49
44	2.00	1.73	0.84	1.13	0.96	1.16	1.13	1.27	1.44	1.16
45	2.08	2.08	1.68	1.73	1.41	1.53	1.49	1.49	1.58	1.73
46	1.63	1.68	1.06	1.16	1.33	1.37	1.58	1.63	1.44	1.68
47*	1.68	1.53	1.11	1.16	1.18	1.21	1.30	1.33	1.41	1.49
48*	1.33	1.30	0.76	0.90	0.62	0.57	0.73	0.80	1.21	1.08
140	1.37	1.49	0.93	0.78	1.06	1.21	1.18	1.30	1.19	1.37
145	1.18	1.21	0.67	0.19	0.58	0.73	0.81	0.81	0.95	0.81
146*	1.44	1.58	1.27	1.30	1.27	1.44	1.44	1.41	1.58	1.53
245*	1.00	0.96	0.66	0.55	0.50	0.76	0.85	0.80	0.87	0.95
Mean	1.49	1.49	1.02	1.01	1.07	1.13	1.17	1.27	1.29	1.38
St. Dev.	0.31	0.28	0.29	0.33	0.31	0.28	0.32	0.30	0.23	0.31

*Minority Subjects

Table F31. Card Sorting scores for older women during Alprazolam/DHEA Treatment

Subject	Time (h)									
	0	2	3.5	4.5	5.5	7	8.5	10	11.5	12.5
17	0.96	1.06	0.44	0.47	0.59	0.64	0.69	0.76	0.88	0.75
18	1.24	1.24	0.59	0.81	0.93	0.87	0.96	1.02	1.02	0.95
19	1.02	1.02	0.35	0.37	1.00	1.00	0.66	0.62	0.74	0.93
20*	1.08	0.95	0.63	0.65	0.71	0.61	0.54	0.66	0.84	0.58
21	1.24	1.16	0.40	0.51	0.54	0.69	0.83	0.79	0.90	0.70
22	1.13	1.13	0.66	0.73	0.80	0.78	0.83	0.90	1.04	1.04
23	1.13	1.04	0.44	0.29	0.70	0.63	0.69	0.67	0.88	0.74
24	1.21	1.11	0.40	0.87	0.93	0.96	1.02	1.04	1.02	1.13
25	1.13	1.21	0.43	0.28	0.51	0.63	0.63	0.69	0.76	0.72
26	1.21	1.18	0.32	0.20	0.26	0.24	0.79	0.70	0.74	0.74
27	1.33	1.41	0.95	0.75	0.42	0.72	0.64	0.85	1.30	1.18
28	1.04	1.13	0.51	0.54	0.46	0.66	0.83	0.71	0.79	0.74
29*	1.73	1.53	0.76	1.00	0.81	1.11	1.08	1.18	1.21	1.27
30*	0.98	1.18	1.00	0.35	0.68	0.71	0.58	0.80	0.75	1.08
31*	1.11	0.76	1.00	0.26	0.26	0.48	0.78	0.76	0.85	0.87
120	0.91	0.84	0.28	0.33	0.38	0.51	0.45	0.43	0.69	0.59
Mean	1.15	1.12	0.57	0.53	0.62	0.70	0.75	0.79	0.90	0.88
St. Dev.	0.19	0.19	0.24	0.25	0.24	0.21	0.17	0.18	0.17	0.21

*Minority Subjects

Table F32. Card Sorting scores for older men during Alprazolam/DHEA Treatment

Subject	Time (h)									
	0	2	3.5	4.5	5.5	7	8.5	10	11.5	12.5
49	1.00	1.00	1.00	1.00	1.00	1.00	1.00	1.00	1.00	1.00
50	0.70	0.74	0.37	0.35	0.39	0.47	0.53	0.27	0.54	0.56
51	1.44	1.21	0.74	0.68	0.85	0.85	0.88	0.91	1.13	1.08
52	1.33	1.18	1.00	0.33	0.54	0.65	0.60	0.67	1.06	0.98
53	1.16	1.13	0.67	0.81	0.87	0.96	0.93	1.02	1.11	1.11
54	1.27	1.16	0.70	0.78	0.76	0.84	0.81	0.90	1.00	1.04
55	1.13	1.08	0.76	0.81	0.96	0.63	0.82	0.88	0.81	0.79
56	1.30	1.30	0.64	0.68	0.83	0.72	0.67	0.80	0.96	1.08
57	1.58	1.53	0.28	0.88	1.18	1.16	1.24	1.24	1.46	1.73
58	1.49	1.68	1.44	0.96	1.13	1.06	1.06	1.16	1.37	0.93
59	1.68	1.49	1	0.85	0.90	1.11	1.33	1.28	1.44	1.41
60	1.24	1.04	0.30	0.39	0.70	0.79	0.72	0.68	0.83	0.67
61*	1.30	1.21	0.50	0.63	0.61	0.80	0.70	0.68	1.11	0.98
149	1.21	1.16	0.26	0.59	0.62	0.75	0.83	0.83	0.91	0.96
160	0.86	0.93	1.00	1.00	1.00	0.39	0.26	0.50	0.67	0.57
Mean	1.25	1.19	0.71	0.72	0.82	0.81	0.83	0.85	1.03	0.99
St. Dev.	0.26	0.24	0.34	0.22	0.22	0.22	0.27	0.27	0.26	0.30

*Minority Subjects

APPENDIX G

Alprazolam Concentration

Table G1. Alprazolam Concentrations (msec) for young women during Alprazolam/Placebo Treatment

Subject	Time (h)												
	0	3	3.5	4.5	5.5	7	8.5	10	11.5	12.5	16	20	23
1	0.00	23.21	25.73	27.76	26.88	21.53	21.17	19.20	16.21	14.69	11.08	8.03	8.00
3	0.00	26.49	45.39	24.02	22.55	19.39	16.00	16.92	15.32	12.98	9.54	8.09	7.04
4	0.00	10.72	25.38	48.05	31.63	29.09	27.80	24.61	24.41	20.70	17.08	14.87	12.35
5	0.00	16.65	32.01	29.57	25.45	22.93	16.48	23.79	17.95	11.46	8.92	6.09	6.81
7	0.00	0.68	16.32	26.85	25.26	18.86	13.16	13.89	11.87	8.24	9.60	3.72	3.21
8	0.00	4.19	15.44	31.90	34.68	26.32	23.82	19.93	19.37	15.75	11.13	8.15	8.41
9	0.00	2.92	7.03	24.61	21.19	22.57	25.56	20.13	16.43	15.04	10.65	8.80	7.97
10	0.00	2.82	5.96	29.58	31.48	25.20	20.00	18.03	19.27	20.69	11.82	10.96	11.09
11	0.00	4.12	27.35	29.45	29.45	28.41	25.53	18.73	19.87	18.45	9.65	9.77	9.53
12	0.00	6.57	9.10	41.94	24.03	24.64	19.35	18.40	15.50	15.44	11.80	8.52	6.36
14*	0.00	0.29	1.20	32.44	40.66	32.10	26.26	26.39	22.92	21.20	15.23	11.84	13.23
15*	0.00	18.03	23.52	27.21	23.63	23.42	18.92	20.57	17.38	17.88	12.51	10.46	7.97
16*	0.00	19.74	24.89	23.81	22.82	22.18	19.99	19.30	16.59	14.16	13.02	11.62	10.10
66	0.00	4.89	29.39	30.74	22.42	21.57	20.50	18.53	16.33	15.70	16.56	12.34	13.32
102	0.00	8.08	17.86	32.19	27.00	28.54	19.99	18.64	15.24	16.66	13.12	7.25	7.23
111	0.00	3.79	6.06	31.37	24.10	22.47	20.26	20.01	15.93	14.54	11.94	10.41	10.36
112	0.00	15.31	30.87	27.29	22.56	21.18	18.79	17.61	17.20	13.68	11.85	10.45	9.50
113	0.00	3.93	10.76	29.10	33.27	26.97	25.76	25.74	19.93	19.25	13.45	13.21	11.84
114*	0.00	22.08	23.13	28.37	28.42	25.78	22.51	20.35	17.87	16.41	10.68	8.66	8.75
206	0.00	1.47	11.49	26.72	35.80	33.20	27.88	27.08	25.46	24.96	19.70	16.30	14.03
213*	0.00	24.08	25.10	26.32	22.65	17.33	17.41	13.50	11.84	10.60	6.54	5.80	5.44
Mean	0.00	10.48	19.71	29.97	27.42	24.46	21.29	20.06	17.76	16.12	12.18	9.78	9.17
St. Dev.	0.00	8.83	10.98	5.69	5.35	4.20	4.06	3.66	3.48	3.91	3.02	3.02	2.80

*Minority Subjects

Table G2. Alprazolam Concentrations (msec) for young men during Alprazolam/Placebo Treatment

Subject	Time (h)												
	0	3	3.5	4.5	5.5	7	8.5	10	11.5	12.5	16	20	23
33	0.00	10.43	25.26	31.12	24.14	21.34	22.01	18.76	16.27	15.23	11.26	9.19	8.54
34	0.00	25.21	21.40	20.03	18.52	16.46	14.66	14.69	12.44	12.24	9.51	7.32	6.36
35	0.00	27.98	26.24	22.34	21.69	23.30	17.93	16.37	16.65	14.74	13.31	10.66	9.12
36	0.00	11.03	18.57	32.46	30.97	26.35	20.87	18.27	18.23	17.87	13.68	11.46	6.90
37	0.00	10.16	19.80	26.26	24.47	20.36	19.38	18.69	16.37	14.80	9.19	7.64	7.48
38	0.00	26.14	23.79	31.17	31.01	22.47	20.76	18.21	18.53	14.47	8.50	7.27	8.10
39	0.00	11.06	27.05	27.81	28.93	26.87	22.84	22.90	22.28	21.40	16.55	15.79	12.94
41	0.00	21.04	30.66	34.61	26.63	25.78	24.53	22.32	16.62	16.06	11.41	8.59	8.69
42	0.00	23.25	23.78	33.30	26.14	24.85	20.19	15.48	14.91	13.57	9.61	7.52	7.45
43	0.00	16.08	18.10	23.80	29.41	21.68	20.97	19.78	18.25	14.91	11.62	9.83	9.43
44	0.00	24.57	27.20	26.94	24.73	22.70	20.99	19.64	18.26	17.16	16.75	13.08	10.56
45	0.00	36.36	26.64	20.70	17.09	16.05	14.84	13.92	11.38	11.04	9.05	7.09	7.31
46	0.00	32.98	33.46	45.68	29.14	24.27	25.33	22.28	22.70	19.91	15.91	15.49	14.36
47*	0.00	29.76	29.34	26.67	23.86	21.12	19.33	19.87	16.87	16.11	12.66	11.97	10.58
48*	0.00	17.89	24.85	27.98	27.56	22.87	21.58	20.51	20.21	17.83	16.10	12.39	11.09
140	0.00	2.15	30.89	26.25	22.57	23.44	22.95	17.01	16.86	18.19	12.39	9.54	8.71
145	0.00	11.55	13.35	20.33	15.32	13.83	12.72	12.25	12.15	11.81	11.02	8.10	7.42
146*	0.00	17.09	16.50	21.09	16.47	16.36	16.63	14.01	13.62	9.68	8.59	8.11	7.75
245*	0.00	3.79	11.31	12.42	14.25	12.53	11.91	10.60	10.35	10.31	8.33	6.50	5.99
Mean	0.00	18.87	23.59	26.89	23.84	21.19	19.50	17.66	16.47	15.12	11.86	9.87	8.88
St. Dev.	0.00	9.71	6.06	7.17	5.35	4.22	3.81	3.47	3.41	3.20	2.87	2.81	2.19

*Minority Subjects

Table G3. Alprazolam Concentrations (msec) for older women during Alprazolam/Placebo Treatment

Subject	Time (h)												
	0	3	3.5	4.5	5.5	7	8.5	10	11.5	12.5	16	20	23
17	0.00	33.26	39.58	29.13	30.62	24.84	21.93	22.04	20.98	19.93	17.01	15.14	14.03
18	0.00	34.73	24.31	29.08	23.97	23.90	18.92	19.39	18.26	16.15	14.29	13.50	12.39
19	0.00	18.04	26.34	39.93	34.88	31.26	27.32	23.17	23.11	20.05	17.36	14.51	14.34
20*	0.00	9.16	11.20	25.64	25.67	25.23	23.07	21.35	21.21	20.35	19.11	17.02	15.92
21	0.00	55.50	42.11	23.92	23.04	21.69	18.87	19.07	17.93	17.98	14.30	13.62	13.28
22	0.00	45.38	37.37	33.39	30.30	22.96	19.56	20.05	19.79	19.43	15.61	15.13	12.45
23	0.00	7.63	45.63	56.29	39.73	29.12	26.55	24.92	23.80	21.07	16.50	15.18	13.95
24	0.00	30.83	36.42	35.05	26.67	23.11	24.07	22.17	19.56	17.87	13.35	13.06	11.60
25	0.00	13.08	23.66	43.44	36.41	30.46	28.13	26.63	25.32	25.07	19.80	16.95	18.12
26	0.00	61.43	35.79	44.54	35.48	31.44	29.88	28.35	27.41	25.92	19.92	18.92	18.12
27	0.00	1.37	15.72	21.97	24.70	20.07	17.67	15.91	14.11	14.47	11.30	10.02	10.40
28	0.00	40.55	34.75	31.13	23.13	22.68	22.43	21.64	19.27	18.40	18.14	18.30	17.78
29*	0.00	26.74	43.09	38.07	35.46	28.51	21.43	22.17	21.50	18.22	14.52	11.44	10.97
30*	0.00	15.60	32.40	28.99	24.46	18.60	17.05	15.30	14.82	13.30	11.20	9.24	9.85
31*	0.00	40.08	33.08	28.64	25.80	21.46	21.06	18.75	17.08	17.19	13.51	10.46	10.69
120	0.00	50.58	34.51	34.33	28.36	23.38	21.72	21.08	16.53	17.14	12.67	9.68	7.97
Mean	0.00	30.25	32.25	33.97	29.29	24.92	22.48	21.37	20.04	18.91	15.54	13.89	13.24
St. Dev.	0.00	18.16	9.67	8.86	5.49	4.05	3.83	3.45	3.67	3.31	2.84	3.08	3.06

*Minority Subjects

Table G4. Alprazolam Concentrations (msec) for older men during Alprazolam/Placebo Treatment

Subject	Time (h)												
	0	3	3.5	4.5	5.5	7	8.5	10	11.5	12.5	16	20	23
50	0.00	11.64	17.68	23.16	26.80	22.54	18.35	20.61	16.30	16.12	14.35	13.07	12.22
51	0.00	11.68	18.10	20.11	23.79	22.39	19.46	19.36	18.00	17.56	14.42	14.14	15.12
52	0.00	22.20	36.50	28.83	22.68	21.74	22.80	21.26	18.75	19.37	15.05	13.99	13.40
53	0.00	7.34	19.10	18.47	25.42	21.86	19.91	21.39	17.84	15.59	13.64	12.31	10.78
54	0.00	22.42	21.72	23.23	23.06	15.87	16.14	15.21	12.70	12.83	9.68	7.46	6.69
55	0.00	18.52	24.31	29.20	28.98	23.40	22.39	20.45	22.05	20.90	18.68	14.55	12.67
56	0.00	32.63	30.28	23.14	23.01	20.35	18.07	21.37	14.96	15.95	12.77	12.09	12.03
57	0.00	17.03	31.09	23.90	22.54	20.88	19.35	17.29	14.94	16.88	15.33	14.25	12.38
58	0.00	58.25	31.11	24.06	17.73	15.96	17.92	15.66	13.01	12.67	10.04	9.23	9.05
59	0.00	64.28	41.26	26.63	21.26	18.53	18.36	15.06	15.23	13.76	10.38	9.13	7.40
60	0.00	29.45	21.54	20.28	18.25	--	12.84	14.56	12.94	12.84	6.78	7.66	6.04
61*	0.00	5.25	40.23	25.31	23.66	22.27	20.88	20.61	18.28	18.80	13.70	14.04	14.29
149	0.00	25.55	20.17	25.43	19.01	18.98	17.73	17.48	14.81	13.78	11.90	9.96	9.79
160	0.00	33.84	35.49	30.43	30.90	23.41	23.00	22.03	21.68	20.32	14.81	15.34	15.51
Mean	0.00	25.72	27.76	24.44	23.36	20.63	19.09	18.74	16.54	16.24	12.97	11.94	11.24
St. Dev.	0.00	17.49	8.40	3.52	3.79	2.57	2.73	2.75	3.02	2.85	2.99	2.72	3.06

*Minority Subjects

(-- Alprazolam concentration not obtained)

Table G5. Alprazolam Concentrations (msec) for young women during Alprazolam/DHEA Treatment

Subject	Time (h)												
	0	3	3.5	4.5	5.5	7	8.5	10	11.5	12.5	16	20	23
1	0.00	28.74	25.45	27.21	28.37	21.74	21.40	16.98	15.79	14.10	11.02	8.92	8.20
3	0.00	19.77	15.95	26.43	20.31	19.39	18.28	14.07	12.18	12.28	8.13	6.91	5.23
4	0.00	4.78	14.71	32.83	34.37	31.12	23.76	22.94	21.79	21.73	15.04	14.67	12.73
5	0.00	40.10	29.31	30.87	24.29	22.93	18.28	16.06	16.58	13.03	9.16	7.13	8.48
7	0.00	3.59	7.46	29.36	18.17	16.74	17.27	12.19	10.50	11.44	6.43	4.64	4.07
8	0.00	9.56	22.63	30.22	28.96	23.96	25.54	21.02	16.42	15.48	11.00	9.16	8.10
9	0.00	0.90	3.77	17.06	18.15	21.44	21.49	18.08	14.77	13.53	10.95	8.25	7.14
10	0.00	35.45	27.98	28.74	21.26	23.42	21.07	20.05	19.85	12.82	10.36	9.50	8.58
11	0.00	7.90	30.56	31.29	34.36	41.06	38.56	23.79	23.39	18.33	15.78	9.54	4.71
12	0.00	16.93	20.31	29.65	29.06	26.18	20.39	19.08	16.42	13.00	10.50	11.40	9.36
14*	0.00	3.35	5.83	5.89	5.33	4.79	3.97	3.85	2.89	3.00	2.52	2.85	2.88
15*	0.00	18.17	25.66	31.51	29.70	19.38	18.91	18.23	14.45	15.09	12.52	10.89	11.24
16*	0.00	24.64	24.81	24.52	22.45	25.14	22.53	20.98	18.40	18.20	13.94	12.72	11.31
66	0.00	19.38	18.34	25.55	24.52	19.77	19.80	18.76	16.31	15.93	13.84	12.10	12.65
102	0.00	1.02	19.03	22.72	23.67	26.64	21.94	17.96	18.23	14.37	10.60	7.55	6.04
111	0.00	19.31	20.14	25.03	22.97	22.17	21.23	17.45	17.07	15.85	13.17	10.91	10.85
112	0.00	0.69	39.48	23.48	19.24	18.02	15.55	14.76	13.74	12.55	12.26	10.12	7.66
113	0.00	13.47	30.51	35.76	31.98	25.93	25.69	20.91	20.57	20.30	14.45	9.04	9.91
114*	0.00	1.05	5.72	25.61	24.01	20.88	19.72	18.10	15.81	13.38	10.09	8.58	7.62
206	0.00	8.40	12.96	38.91	35.84	36.10	34.72	35.84	24.51	23.21	20.99	18.36	15.34
213*	0.00	18.83	32.22	24.27	22.52	19.55	15.91	15.16	14.76	11.18	8.20	5.83	4.67
Mean	0.00	14.09	20.61	27.00	24.74	23.16	21.24	18.39	16.40	14.71	11.47	9.48	8.42
St. Dev.	0.00	11.60	9.77	6.82	6.98	7.26	6.82	5.83	4.65	4.27	3.78	3.40	3.21

*Minority Subjects

Table G6. Alprazolam Concentrations (msec) for young men during Alprazolam/ DHEA Treatment

Subject	Time (h)												
	0	3	3.5	4.5	5.5	7	8.5	10	11.5	12.5	16	20	23
33	0.00	21.05	31.59	29.09	24.41	24.49	21.08	18.42	16.26	15.56	11.45	9.79	7.72
34	0.00	10.87	17.77	17.86	17.28	16.05	15.93	13.59	11.29	11.05	9.47	7.15	7.04
35	0.00	24.12	15.78	26.06	24.74	22.65	17.29	18.07	16.34	17.05	14.73	12.19	13.43
36	0.00	20.18	33.69	37.68	45.71	26.65	22.89	23.20	18.00	16.57	11.21	10.23	7.00
37	0.00	21.52	32.63	25.21	22.61	19.07	17.06	16.60	13.58	13.14	9.66	9.05	7.29
38	0.00	25.20	43.14	31.61	26.96	23.67	23.21	19.57	18.85	14.38	9.89	9.75	7.06
39	0.00	30.54	33.20	28.22	25.61	25.24	22.48	23.80	21.03	18.99	18.08	13.95	13.42
41	0.00	15.89	28.02	33.51	30.92	28.01	23.69	20.40	16.73	15.17	10.70	7.92	7.89
42	0.00	10.01	28.39	38.12	27.73	22.63	21.98	18.27	16.45	15.40	9.60	5.84	5.47
43	0.00	10.12	14.56	19.65	17.45	15.81	14.85	13.98	11.92	12.32	8.76	8.68	7.07
44	0.00	51.05	38.69	25.46	22.52	22.87	20.67	19.86	17.89	16.76	15.03	11.35	9.75
45	0.00	11.59	31.49	28.14	20.37	17.94	16.38	15.06	14.17	13.31	9.34	7.13	7.88
46	0.00	52.27	34.91	31.81	29.98	29.02	23.58	21.79	18.42	17.81	16.13	13.44	12.44
47*	0.00	42.68	28.47	27.08	20.71	20.59	19.11	19.03	16.89	16.24	13.23	11.35	9.91
48*	0.00	2.92	19.36	33.86	33.02	23.01	20.96	24.30	18.24	18.75	12.04	11.30	9.50
140	0.00	30.95	27.94	29.99	27.65	26.92	27.07	20.18	17.73	13.56	12.68	10.32	7.44
145	0.00	9.43	10.30	20.46	14.62	14.19	13.88	12.09	11.61	10.23	6.46	7.48	7.62
146*	0.00	2.05	4.81	18.44	21.22	18.40	15.23	15.58	11.66	11.58	10.67	8.20	7.24
245*	0.00	4.23	12.60	16.45	13.31	12.42	12.25	10.15	11.01	10.22	7.31	6.14	5.33
Mean	0.00	20.88	25.65	27.30	24.57	21.56	19.45	18.10	15.69	14.63	11.39	9.54	8.45
St. Dev.	0.00	15.14	10.51	6.49	7.44	4.81	4.05	3.95	3.03	2.75	3.00	2.34	2.39

*Minority Subjects

Table G7. Alprazolam Concentrations (msec) for older women during Alprazolam/DHEA Treatment

Subject	Time (h)												
	0	3	3.5	4.5	5.5	7	8.5	10	11.5	12.5	16	20	23
17	0.00	28.13	25.75	22.94	18.73	19.36	18.37	18.32	18.77	15.62	13.91	12.47	12.88
18	0.00	29.39	19.46	25.04	23.44	23.03	18.73	17.79	17.51	15.75	13.84	12.19	11.65
19	0.00	17.59	27.15	33.79	33.21	28.51	24.09	23.94	19.48	19.73	15.76	13.45	11.43
20*	0.00	2.74	21.16	21.64	26.77	29.96	22.04	22.19	23.64	19.32	19.57	17.67	16.59
21	0.00	41.66	32.74	36.22	27.02	22.16	20.24	18.52	17.33	17.69	18.16	15.19	14.44
22	0.00	11.85	32.91	32.79	28.82	29.57	999.00	22.12	22.03	22.52	16.24	15.19	15.38
23	0.00	59.47	38.14	41.52	35.60	29.82	27.17	24.47	23.44	19.79	16.72	14.13	14.17
24	0.00	29.01	34.60	32.15	26.35	24.12	24.12	21.15	18.36	16.52	12.12	11.15	11.45
25	0.00	33.19	28.35	40.29	29.35	28.42	29.38	29.08	28.35	25.48	25.26	21.76	15.71
26	0.00	26.35	40.93	42.05	35.84	31.57	29.74	27.78	26.73	24.47	20.61	19.43	18.54
27	0.00	8.13	14.17	25.40	27.02	20.59	18.37	18.05	16.59	13.76	11.24	9.00	8.88
28	0.00	27.93	31.31	27.10	21.74	21.33	21.06	19.66	18.04	18.25	17.23	15.58	17.22
29*	0.00	39.94	34.13	35.50	27.20	26.75	25.69	25.17	20.41	19.01	15.78	13.52	11.90
30*	0.00	60.24	40.11	26.08	24.01	19.73	20.34	16.71	14.71	13.44	10.37	10.03	8.92
31*	0.00	27.61	32.42	27.34	26.57	22.11	20.92	19.52	17.05	15.91	13.61	9.06	9.59
120	0.00	32.75	35.97	31.55	27.23	23.68	22.10	19.36	17.04	13.99	12.09	9.84	9.35
Mean	0.00	29.75	30.58	31.34	27.43	25.04	-41.04	21.49	19.97	18.20	15.78	13.73	13.01
St. Dev.	0.00	15.85	7.52	6.58	4.58	4.12	255.48	3.70	3.86	3.64	3.88	3.69	3.10

*Minority Subjects

Table G8. Alprazolam Concentrations (msec) for older men during Alprazolam/DHEA Treatment

Subject	Time (h)												
	0	3	3.5	4.5	5.5	7	8.5	10	11.5	12.5	16	20	23
50	0.00	27.53	29.34	24.70	23.59	21.35	21.57	21.40	19.49	16.62	13.95	11.61	11.10
51	0.00	23.92	27.43	20.69	22.48	22.56	20.73	19.74	20.22	17.30	14.00	14.98	14.29
52	0.00	49.86	31.85	27.13	24.71	23.27	19.56	19.99	17.49	16.01	15.26	13.61	14.95
53	0.00	33.19	25.26	22.92	20.92	20.84	18.74	19.49	15.61	14.82	11.97	11.72	10.02
54	0.00	27.58	21.31	22.48	20.18	20.45	18.09	16.48	13.90	14.20	9.48	7.66	5.46
55	0.00	9.36	18.40	16.88	14.79	23.88	27.90	16.54	22.38	19.80	18.41	13.52	15.08
56	0.00	23.48	23.28	28.13	23.64	21.65	20.33	18.92	17.37	15.88	14.35	13.86	11.24
57	0.00	39.82	30.73	23.70	21.79	18.74	18.06	17.52	16.04	14.74	13.01	12.65	10.24
58	0.00	0.23	50.54	25.19	20.62	18.25	16.71	15.62	13.77	13.26	10.53	9.92	8.57
59	0.00	60.13	24.83	20.72	19.24	17.59	18.90	16.68	15.08	14.02	11.14	9.18	8.93
60	0.00	30.33	24.24	20.42	18.08	19.08	15.04	13.10	14.30	13.41	9.22	8.89	7.04
61*	0.00	47.13	30.46	25.15	25.19	24.59	21.80	22.60	19.70	19.64	16.90	16.45	14.05
149	0.00	36.60	25.08	23.44	21.96	18.09	18.41	15.22	13.74	13.39	11.66	10.08	9.22
160	0.00	48.24	39.07	31.14	26.27	25.55	22.33	21.50	17.50	17.70	15.78	16.04	13.85
Mean	0.00	32.67	28.70	23.76	21.68	21.13	19.87	18.20	16.90	15.77	13.26	12.15	11.00
St. Dev.	0.00	16.13	8.10	3.61	3.05	2.58	3.07	2.75	2.74	2.20	2.76	2.75	3.06

*Minority Subjects

APPENDIX H

DHEA

DHEA-S

CORTISOL

Table H1. DHEA concentrations (ng/ml) for young women during Placebo Treatment

Subject	Time (h)														
	0	1	2	3	3.5	4.5	5.5	7	8.5	10	11.5	12.5	16	20	23
1	10.66	6.22	6.85	15.38	16.15	11.34	13.17	10.70	12.28	12.98	10.28	11.36	7.74	10.42	9.36
3	13.87	6.59	6.45	7.26	6.60	6.48	7.53	8.47	5.96	7.80	5.51	4.79	4.63	11.09	10.47
4	19.43	12.73	13.43	14.51	10.46	8.04	11.44	10.73	9.21	7.50	8.85	8.32	7.88	8.79	16.60
5	20.71	8.61	8.34	7.66	10.60	9.35	11.39	8.49	7.07	10.82	6.19	6.41	4.83	18.11	22.51
7	12.99	4.13	4.21	6.26	5.95	7.80	4.99	5.19	3.98	2.52	3.85	2.76	2.21	7.71	8.14
8	19.98	10.62	14.74	8.13	7.65	7.84	10.14	6.91	8.64	5.64	9.70	5.21	5.54	4.77	14.28
9	12.67	9.56	7.29	6.77	6.92	6.39	6.07	6.05	6.67	8.54	5.78	5.05	3.15	2.98	12.11
10	19.06	11.73	12.48	13.76	12.48	15.06	12.31	12.26	11.65	10.23	8.78	8.78	8.72	8.79	19.16
11	13.46	7.81	14.52	15.52	15.97	14.33	14.13	15.72	12.24	15.85	13.57	11.98	9.51	10.19	17.36
12	15.52	8.27	10.29	10.98	15.69	18.15	14.93	10.40	14.76	16.83	12.14	8.26	8.66	5.94	10.24
14*	11.10	5.25	5.26	6.52	6.80	7.15	5.67	5.59	7.07	5.14	6.06	3.82	3.80	5.96	8.04
15*	2.60	1.07	1.27	1.32	1.44	1.25	1.11	1.76	1.11	1.10	0.93	1.09	0.91	1.25	1.77
16*	4.08	6.62	7.57	7.20	6.09	6.26	4.89	5.10	5.40	6.14	6.12	4.43	3.43	4.23	9.58
66	18.98	11.14	13.28	16.26	16.43	12.26	12.25	11.18	9.06	13.15	9.41	7.34	10.37	10.83	15.62
102	17.62	8.37	10.71	10.75	13.85	12.48	10.68	10.56	9.41	8.65	8.38	7.46	6.78	5.32	14.50
111	15.22	8.58	14.87	19.56	13.64	7.87	6.80	8.83	7.50	7.36	6.06	5.36	5.08	11.01	13.41
112	9.31	13.57	8.31	5.94	8.02	6.71	6.92	5.99	10.01	8.67	4.63	6.88	4.75	2.33	14.03
113	20.23	10.41	9.47	12.79	15.39	18.63	17.23	12.31	12.80	11.12	13.74	8.37	6.12	12.84	16.61
114*	8.52	4.99	4.72	4.25	5.72	5.64	5.92	5.32	5.50	4.88	3.66	3.52	2.94	4.91	9.63
206	8.04	5.74	7.02	5.79	4.62	3.83	4.90	3.48	2.83	3.90	3.77	3.93	2.80	4.17	4.03
213*	14.59	6.25	6.25	6.05	6.82	6.57	6.40	6.77	7.13	8.16	5.51	5.52	5.41	6.22	15.93
Mean	13.74	8.01	8.92	9.65	9.87	9.21	8.99	8.18	8.11	8.43	7.28	6.22	5.49	7.52	12.54
St. Dev.	5.26	3.07	3.85	4.74	4.55	4.51	4.14	3.41	3.46	4.08	3.38	2.72	2.58	4.06	4.98

*Minority Subjects

Table H2. DHEA concentrations (ng/ml) for young men during Placebo Treatment

Subject	Time (h)														
	0	1	2	3	3.5	4.5	5.5	7	8.5	10	11.5	12.5	16	20	23
33	9.22	4.98	6.19	5.30	7.28	6.56	4.92	4.76	3.82	4.99	4.52	3.55	3.99	4.37	10.35
34	10.15	4.27	7.13	6.98	5.83	5.91	5.73	5.31	4.97	7.16	5.35	5.45	2.70	3.89	7.76
35	9.07	4.90	4.71	5.32	6.81	6.44	4.41	6.24	7.27	4.00	3.17	2.83	3.64	3.62	7.11
36	9.51	8.77	8.25	8.47	8.55	6.99	7.77	9.59	7.82	8.07	5.96	5.47	4.39	8.06	10.75
37	11.33	8.97	9.61	8.31	9.71	8.88	7.53	8.06	10.13	8.69	5.84	3.95	3.42	5.53	14.33
38	12.76	9.08	11.02	10.19	8.94	10.62	8.21	9.12	9.33	8.67	7.50	5.70	3.78	7.65	11.22
39	20.46	8.37	8.41	7.06	9.14	10.69	8.16	9.84	7.34	8.23	4.84	5.41	4.82	6.09	13.71
41	17.08	9.10	10.32	12.91	10.74	10.15	10.05	12.82	12.01	11.69	7.76	4.99	10.92	7.82	16.68
42	6.94	12.76	9.24	10.53	9.26	13.08	11.35	8.15	9.85	9.20	9.34	6.44	5.87	4.29	13.99
43	16.44	9.76	13.61	9.79	10.34	11.40	12.05	13.13	9.15	9.16	7.24	5.92	6.36	13.53	13.72
44	11.90	6.48	6.13	8.65	9.51	8.59	10.20	9.16	10.41	12.34	7.61	6.67	5.13	4.37	11.51
45	17.73	12.55	14.09	10.46	12.99	12.83	14.19	12.53	10.60	8.62	7.21	6.10	5.64	9.64	15.11
46	21.39	10.38	12.48	14.01	10.94	18.73	18.03	15.95	10.16	15.11	11.91	6.49	5.39	15.68	21.76
47*	16.05	5.41	5.70	6.32	9.87	7.40	6.44	4.95	13.43	5.92	4.35	4.00	3.94	7.63	14.29
48*	15.32	8.04	11.66	9.55	9.66	11.40	9.10	7.28	9.90	9.53	6.66	7.31	5.97	15.91	12.97
140	6.16	5.77	8.77	11.13	8.54	9.06	6.92	10.36	7.81	7.01	7.65	5.60	3.99	2.30	7.36
145	18.05	12.20	14.46	12.01	12.82	12.25	11.80	11.07	13.27	12.23	11.81	17.49	12.38	10.05	13.60
146*	15.05	7.10	8.09	7.00	9.10	9.67	7.18	8.14	7.10	6.42	5.97	5.17	5.31	9.02	15.68
245*	19.78	6.49	9.66	10.39	10.46	13.20	9.49	7.99	9.58	8.71	6.97	5.32	6.30	4.40	15.18
Mean	13.92	8.18	9.45	9.18	9.50	10.20	9.13	9.18	9.16	8.72	6.93	5.99	5.47	7.57	13.00
St. Dev.	4.65	2.61	2.88	2.46	1.78	3.11	3.34	2.99	2.48	2.70	2.28	3.00	2.43	4.00	3.53

*Minority Subjects

-Concentration not obtained

Table H3. DHEA concentrations (ng/ml) for older women during Placebo Treatment

Subject	Time (h)														
	0	1	2	3	3.5	4.5	5.5	7	8.5	10	11.5	12.5	16	20	23
17	4.23	1.91	2.06	0.86	1.98	1.71	2.28	1.56	4.08	1.35	1.23	1.25	1.00	1.99	10.60
18	4.26	2.10	2.15	1.80	2.04	2.95	1.63	2.61	1.93	2.07	1.58	1.78	1.05	1.84	2.24
19	9.78	4.06	3.81	5.48	6.20	4.84	3.80	6.24	4.43	3.45	3.46	2.95	2.13	2.41	6.37
20*	5.45	2.14	2.68	2.55	2.75	2.63	2.51	2.20	2.33	2.31	2.96	2.53	1.62	2.50	3.04
21	7.80	7.97	4.66	6.33	8.82	14.44	5.63	5.38	6.11	3.99	7.29	4.34	4.97	3.79	6.02
22	8.45	3.94	5.88	4.49	5.31	5.05	4.15	3.73	3.54	2.69	3.32	3.31	1.99	4.58	7.28
23	2.03	1.79	1.61	1.81	2.82	2.11	1.88	1.77	1.68	1.96	1.73	1.37	1.35	2.32	2.81
24	4.01	1.71	1.80	2.21	1.97	2.11	2.29	2.19	1.59	2.22	1.93	1.51	1.28	2.07	4.13
25	4.83	2.79	2.97	2.36	3.22	3.72	2.61	3.26	2.37	2.99	2.58	2.01	1.95	3.52	6.96
26	5.18	1.66	2.22	1.61	1.82	1.55	1.89	1.74	--	1.88	1.52	1.34	1.22	3.20	2.77
27	2.92	1.50	1.20	1.21	1.16	1.30	1.26	1.43	1.40	1.38	--	1.48	0.99	0.93	2.73
28	1.33	1.03	1.40	1.33	1.23	1.03	1.60	1.24	1.38	1.49	1.11	1.23	0.91	1.30	1.51
29*	1.33	1.02	0.98	1.01	1.48	1.43	1.33	1.07	1.27	1.02	0.91	1.07	0.78	1.86	2.22
30*	2.29	2.14	1.97	2.07	2.13	1.56	1.69	1.81	1.54	1.62	1.64	1.44	0.81	1.01	4.40
31*	0.63	1.33	1.45	0.89	0.89	0.88	1.39	0.75	0.86	0.96	0.78	0.74	1.00	0.72	1.32
120	10.32	3.26	3.49	2.88	3.25	3.35	5.67	3.58	3.23	4.19	2.40	1.74	1.98	2.28	5.02
Mean	4.68	2.52	2.52	2.43	2.94	3.17	2.60	2.54	2.52	2.22	2.30	1.88	1.56	2.27	4.34
St. Dev.	3.03	1.72	1.35	1.64	2.13	3.27	1.44	1.55	1.47	1.00	1.62	0.95	1.02	1.08	2.55

*Minority Subjects

--Concentration not obtained

Table H4. DHEA concentrations (ng/ml) for older men during Placebo Treatment

Subject	Time (h)														
	0	1	2	3	3.5	4.5	5.5	7	8.5	10	11.5	12.5	16	20	23
50	4.48	3.37	5.26	4.14	3.88	3.39	3.70	2.59	2.75	3.64	2.66	2.35	2.20	3.64	6.94
51	4.12	2.42	2.48	2.28	2.49	2.77	2.35	2.10	2.43	2.32	1.72	2.00	3.49	4.28	2.71
52	6.76	2.17	3.17	2.10	2.33	2.41	2.10	2.31	2.15	1.99	1.97	1.77	1.74	5.51	7.73
53	4.07	3.12	7.58	4.77	3.71	3.04	3.26	3.76	4.09	3.50	3.01	2.88	2.91	2.92	7.59
54	5.12	3.28	4.89	3.53	3.22	4.15	3.20	4.46	3.79	2.99	3.06	2.50	1.93	2.52	3.99
55	4.65	3.24	4.24	3.63	3.56	3.97	3.35	2.65	2.22	3.03	2.20	2.71	1.36	6.91	4.01
56	3.36	2.41	2.80	2.33	2.63	2.54	2.46	2.86	2.52	2.61	1.92	1.99	1.63	1.90	3.16
57	4.44	2.46	3.61	3.53	2.40	2.37	2.07	2.52	2.97	3.42	1.89	2.16	1.88	4.31	4.86
58	1.53	1.37	1.46	1.42	1.57	1.87	1.45	1.55	1.29	1.20	1.48	1.04	1.27	1.03	2.02
59	7.49	4.79	6.01	6.30	5.42	7.06	4.97	6.18	4.76	8.13	4.69	3.91	2.65	3.44	10.61
60	5.73	4.44	4.07	3.55	3.93	3.31	3.17	4.37	3.45	3.15	2.85	3.03	2.41	2.43	3.87
61*	12.10	5.50	4.70	4.97	5.75	7.02	5.22	5.47	5.49	5.35	4.57	3.73	3.74	7.08	12.20
149	4.18	3.06	3.05	2.92	3.47	3.37	3.14	2.88	2.48	2.79	2.58	2.39	2.20	3.37	4.65
160	4.81	2.39	2.46	2.23	2.95	2.96	2.48	2.07	2.18	2.22	2.54	1.79	1.85	1.85	2.79
Mean	5.20	3.14	3.98	3.41	3.38	3.59	3.07	3.27	3.04	3.31	2.65	2.45	2.23	3.66	5.51
St. Dev.	2.44	1.12	1.62	1.33	1.16	1.59	1.06	1.38	1.15	1.68	0.97	0.77	0.74	1.82	3.08

*Minority Subjects

-Concentration not obtained

Table H5. DHEA concentrations (ng/ml) for young women during DHEA Treatment

Subject	Time (h)														
	0	1	2	3	3.5	4.5	5.5	7	8.5	10	11.5	12.5	16	20	23
1	16.77	18.04	17.31	15.59	20.17	16.97	13.76	12.76	16.19	16.74	14.86	11.82	10.09	9.97	16.89
3	15.92	9.75	17.33	16.07	17.57	17.65	16.18	14.79	17.41	16.81	15.00	15.25	10.23	15.84	17.05
4	14.41	11.16	13.40	16.55	14.51	15.09	15.13	13.48	16.66	14.06	13.12	12.00	11.23	7.39	20.62
5	17.92	19.06	19.30	15.78	15.37	11.59	10.26	12.56	15.44	14.41	13.57	11.70	7.20	10.72	18.58
7	13.22	12.46	13.63	15.43	13.71	12.60	14.03	9.98	12.23	13.21	11.94	10.21	6.25	12.94	13.31
8	18.42	16.57	14.49	14.03	13.02	16.95	10.81	12.03	14.36	14.51	11.21	8.77	6.90	4.74	17.87
9	12.49	10.31	13.70	16.40	15.25	14.78	11.93	11.15	14.03	--	18.14	11.79	11.98	11.38	14.26
10	21.35	15.59	16.21	15.68	14.63	14.35	16.32	21.49	17.12	14.37	13.51	13.00	10.67	11.28	24.43
11	14.44	7.50	9.93	15.05	15.95	17.53	15.24	16.28	17.59	15.48	12.94	13.00	11.93	10.11	13.10
12	18.19	13.92	17.18	19.77	20.04	19.34	23.70	16.63	22.41	22.36	19.78	16.95	13.13	9.85	8.02
14*	10.39	6.10	15.28	14.83	16.54	12.61	12.94	13.62	17.39	13.43	17.07	12.38	8.15	9.54	12.84
15*	1.70	1.74	13.92	13.07	11.33	8.25	7.60	8.71	11.28	11.83	10.28	10.37	9.67	9.40	9.98
16*	7.12	17.24	14.48	12.06	11.72	11.28	8.05	10.54	13.06	11.81	10.85	8.60	6.38	8.01	13.40
66	19.42	21.66	23.32	20.13	20.88	19.28	12.16	18.11	20.82	21.52	15.15	13.85	14.60	17.63	17.65
102	14.91	15.94	16.14	15.34	17.70	17.48	14.28	13.20	12.35	13.77	15.78	12.94	10.76	9.48	18.57
111	14.69	9.16	13.91	13.46	15.01	12.45	10.90	12.47	11.72	17.94	18.14	13.11	9.73	11.92	13.24
112	14.25	10.14	16.44	11.59	11.14	9.86	9.63	9.67	11.82	13.02	8.92	8.88	8.10	8.42	8.75
113	19.89	9.96	19.98	19.39	19.13	16.86	16.77	15.74	18.63	17.12	12.34	12.09	12.87	9.15	17.78
114*	8.21	12.65	12.88	12.81	11.42	9.12	11.04	15.45	13.63	10.90	9.40	6.97	6.76	8.75	11.07
206	8.02	10.23	15.99	15.12	11.73	14.67	13.18	13.78	16.81	16.11	16.94	15.17	13.61	13.56	12.67
213*	18.26	16.22	19.05	16.38	16.82	15.05	13.99	15.35	13.48	17.56	16.34	13.72	11.22	12.43	16.40
Mean	14.29	12.64	15.90	15.45	15.41	14.46	13.23	13.70	15.45	15.35	14.06	12.03	10.07	10.60	15.07
St. Dev.	4.92	4.78	2.94	2.29	3.08	3.26	3.54	3.04	3.06	3.01	3.04	2.44	2.51	2.86	4.06

*Minority Subjects; (--) Concentration not obtained

Table H6. DHEA concentrations (ng/ml) for young men during DHEA Treatment

Subject	Time (h)														
	0	1	2	3	3.5	4.5	5.5	7	8.5	10	11.5	12.5	16	20	23
33	8.39	8.43	13.34	12.97	12.78	11.02	9.91	8.71	14.29	13.59	9.76	7.77	6.28	5.80	10.59
34	10.58	10.68	12.52	12.67	13.63	12.53	9.94	11.29	13.41	12.80	12.79	9.87	8.04	7.52	10.67
35	12.59	7.87	13.07	15.71	14.58	14.54	8.94	8.51	13.10	11.49	8.62	7.98	6.02	6.23	11.71
36	10.13	9.35	21.97	21.07	19.22	18.34	14.68	13.29	17.93	20.83	17.04	13.95	10.72	10.16	9.19
37	13.69	18.66	18.24	13.45	12.52	12.05	10.41	12.76	17.14	14.36	11.47	9.96	8.02	8.87	15.25
38	10.33	15.52	17.05	13.62	12.49	14.52	11.41	10.24	14.57	13.85	10.71	8.82	4.85	6.87	11.22
39	20.34	9.39	15.55	15.45	13.76	12.70	10.59	15.41	14.69	10.46	8.87	8.28	6.04	10.98	14.43
41	19.17	12.14	17.10	16.81	14.92	15.61	15.07	15.12	15.30	13.26	9.35	8.87	9.64	11.66	15.23
42	17.15	8.25	17.08	15.63	14.90	14.88	14.33	11.18	16.16	15.02	15.88	13.16	7.43	15.69	11.62
43	13.11	10.32	18.34	15.81	16.30	15.66	12.53	15.11	15.78	14.08	10.72	9.77	8.43	14.07	14.34
44	8.90	9.86	10.94	14.63	12.15	13.41	17.48	10.75	16.42	15.55	14.44	12.18	12.48	12.09	7.93
45	16.62	15.99	18.89	14.94	14.01	12.55	11.73	21.03	16.32	12.71	8.20	9.19	7.77	7.04	15.60
46	18.86	12.76	17.30	16.77	15.63	16.14	17.45	21.77	12.68	16.29	14.76	15.23	9.19	19.77	24.55
47*	15.55	13.38	13.57	12.86	11.90	12.82	10.56	8.30	13.06	13.74	12.21	9.31	6.90	8.57	11.93
48*	16.24	9.34	20.39	19.28	16.96	14.37	14.87	15.57	14.70	20.28	16.94	14.03	13.36	11.46	19.14
140	17.71	8.32	16.11	17.77	15.53	14.55	14.78	15.32	15.12	17.97	14.95	11.05	7.60	4.69	13.91
145	15.12	17.12	21.55	21.17	18.42	16.58	15.00	15.10	18.53	17.05	17.41	19.37	13.49	13.88	16.03
146*	15.31	17.91	15.87	13.84	13.19	13.67	12.44	11.80	11.63	14.05	12.99	10.53	7.47	13.38	15.80
245*	20.46	22.90	23.33	20.87	18.72	16.33	16.03	15.16	18.23	17.75	15.53	11.79	10.65	6.42	20.07
Mean	14.75	12.54	16.96	16.07	14.82	14.33	13.06	13.50	15.21	15.01	12.77	11.11	8.65	10.27	14.17
St. Dev.	3.82	4.33	3.38	2.81	2.26	1.84	2.66	3.75	1.95	2.76	3.08	2.97	2.50	3.95	4.03

*Minority Subjects

Table H7. DHEA concentrations (ng/ml) for older women during DHEA Treatment

Subject	Time (h)														
	0	1	2	3	3.5	4.5	5.5	7	8.5	10	11.5	12.5	16	20	23
17	2.51	20.34	22.13	19.40	18.56	16.81	14.32	12.75	15.77	14.94	11.21	9.51	10.59	9.10	9.36
18	5.85	15.23	15.05	14.95	14.39	13.78	11.85	15.96	19.75	16.36	14.62	12.34	8.99	8.90	12.77
19	8.69	3.93	16.99	15.98	16.95	14.05	11.75	11.29	16.89	13.53	12.10	10.03	9.81	8.16	13.16
20*	4.66	1.25	4.07	13.16	11.80	16.77	15.30	12.23	13.53	12.37	13.31	13.53	9.83	9.48	10.63
21	11.82	17.99	19.90	15.59	14.96	16.62	10.23	9.35	9.13	16.61	12.98	13.87	8.85	11.57	10.83
22	6.92	3.34	10.21	13.37	13.81	12.34	10.82	11.81	15.08	13.80	12.44	11.81	8.81	7.66	12.41
23	4.73	16.13	14.10	12.05	11.55	11.47	9.92	11.52	12.73	18.12	14.54	12.79	9.44	8.25	11.64
24	2.33	18.07	18.65	12.38	11.27	11.12	9.17	16.50	14.76	12.36	10.86	8.10	5.45	7.12	6.10
25	3.76	3.00	12.10	13.61	12.62	12.23	9.29	12.62	16.32	17.97	16.07	13.06	12.55	11.65	11.39
26	3.82	17.04	22.74	20.05	18.82	15.54	15.37	19.88	23.44	20.12	14.82	12.63	11.07	9.87	11.54
27	2.98	2.28	12.21	14.50	14.54	13.11	11.27	9.69	10.46	16.62	15.25	15.38	9.55	9.18	9.48
28	1.56	2.37	13.47	11.38	10.99	9.12	6.49	6.25	11.94	14.31	11.92	11.09	6.91	6.35	7.90
29*	0.88	9.98	20.34	18.25	16.51	16.04	12.96	10.05	10.33	15.76	11.29	8.58	6.55	6.67	6.32
30*	2.84	3.88	11.80	9.33	8.94	8.00	7.83	7.52	8.41	12.97	11.16	10.93	7.75	6.52	10.17
31*	0.93	9.94	11.94	9.70	11.51	11.19	8.87	8.22	13.02	13.34	11.10	9.61	5.44	6.36	6.23
120	11.64	3.59	12.25	12.74	12.24	12.62	11.90	9.87	14.11	12.72	10.75	10.54	9.32	16.11	14.25
Mean	4.75	9.27	14.87	14.15	13.72	13.18	11.08	11.59	14.10	15.12	12.78	11.49	8.81	8.93	10.26
St. Dev.	3.45	7.05	4.96	3.14	2.87	2.70	2.55	3.51	3.90	2.34	1.77	2.04	1.97	2.55	2.54

*Minority Subjects

Table H8. DHEA concentrations (ng/ml) for older men during DHEA Treatment

Subject	Time (h)														
	0	1	2	3	3.5	4.5	5.5	7	8.5	10	11.5	12.5	16	20	23
49	23.09	21.11	22.56	20.81	17.52	14.49	17.35	14.26	12.87	12.08	12.24	11.44	10.29	15.95	16.11
50	3.75	23.95	23.94	19.67	18.88	15.77	14.71	11.08	12.36	15.10	11.34	10.61	8.58	9.08	8.27
51	2.51	19.92	22.17	20.77	18.54	17.91	16.72	14.54	13.70	14.41	14.21	12.42	9.85	9.06	9.63
52	6.15	2.31	7.11	10.18	11.79	7.34	5.96	6.08	9.18	10.62	13.25	11.77	6.24	6.56	9.46
53	4.06	10.50	14.88	13.35	11.32	9.55	9.20	9.26	13.31	11.59	9.85	8.61	7.11	8.80	9.14
54	3.48	9.69	13.73	10.85	10.81	10.28	6.94	4.96	4.91	12.32	4.67	6.87	4.53	2.54	3.87
55	7.12	3.74	4.82	7.90	10.80	9.86	8.83	8.71	7.67	9.72	9.43	10.01	6.10	5.41	5.82
56	3.13	3.00	16.66	18.16	15.12	12.55	10.72	14.63	16.53	14.43	10.42	9.61	8.01	6.83	7.66
57	5.02	2.70	4.63	6.10	6.08	6.08	5.18	5.74	6.95	8.53	5.67	5.24	4.50	3.97	8.66
58	1.66	2.46	8.77	13.36	14.80	11.82	9.30	13.29	16.28	12.89	9.21	7.92	5.26	3.96	6.08
59	11.10	13.25	13.58	12.42	12.33	11.47	3.89	4.00	8.52	13.36	11.23	9.57	5.91	7.87	9.45
60	4.82	11.57	11.60	8.65	8.40	8.31	6.68	8.36	10.24	10.02	8.11	6.61	5.79	6.37	7.46
61*	11.35	8.82	16.23	18.44	19.25	15.91	12.83	12.73	13.61	16.76	16.26	11.13	8.99	9.26	11.51
149	4.40	2.66	12.64	10.80	10.36	9.53	7.66	8.04	11.94	10.44	9.18	7.77	6.92	6.93	9.21
160	3.44	2.24	12.69	12.40	11.13	9.96	8.38	14.43	18.45	14.10	10.98	8.83	8.66	6.36	10.32
Mean	6.34	9.19	13.73	13.59	13.14	11.39	9.62	10.01	11.77	12.42	10.40	9.23	7.12	7.26	8.84
St. Dev.	5.43	7.53	6.02	4.84	4.02	3.38	4.10	3.81	3.83	2.30	3.01	2.08	1.86	3.15	2.79

*Minority Subjects

Table H9. DHEA concentrations (ng/ml) for young women during Alprazolam/Placebo Treatment

Subject	Time (h)														
	0	1	2	3	3.5	4.5	5.5	7	8.5	10	11.5	12.5	16	20	23
1	13.99	13.43	14.51	13.58	12.74	11.38	12.85	13.57	15.77	10.96	12.54	11.51	9.35	14.88	9.07
3	16.21	7.81	8.15	7.58	7.32	6.04	5.39	8.40	9.80	6.89	5.99	4.48	4.37	6.64	13.65
4	17.43	8.50	11.17	8.46	8.25	7.40	9.39	8.55	7.79	7.11	8.47	7.15	5.60	7.11	10.55
5	20.73	9.44	13.75	11.90	9.23	6.90	7.96	10.82	8.82	7.10	9.83	7.19	5.78	7.60	10.05
7	14.01	4.76	5.23	7.49	4.73	3.80	3.67	3.68	3.63	8.20	2.93	2.61	2.86	2.98	8.09
8	18.24	6.72	7.17	14.81	9.38	7.94	6.86	7.31	8.05	6.83	9.64	6.23	5.28	3.93	15.09
9	10.52	4.94	8.52	6.23	6.29	5.95	3.86	5.13	9.02	5.83	6.00	4.90	3.44	4.73	7.60
10	22.46	12.65	12.12	12.38	11.17	9.65	9.17	9.25	9.94	8.19	9.95	8.92	10.08	13.52	25.66
11	8.54	7.83	10.96	11.01	8.24	6.51	5.83	6.31	11.67	7.74	8.04	6.24	3.07	5.14	10.98
12	10.06	14.68	16.65	14.15	10.35	9.23	7.47	14.02	8.43	5.71	9.45	7.08	7.71	4.55	5.91
14*	15.72	6.59	6.65	9.20	8.81	6.30	6.18	6.16	5.56	5.98	7.24	5.49	4.55	5.80	10.88
15*	3.07	2.85	1.14	1.20	1.00	0.71	0.80	0.75	0.58	0.90	0.77	0.72	0.67	0.85	1.42
16*	3.34	4.34	4.58	4.41	3.53	2.80	2.53	5.32	3.76	4.65	3.12	2.38	2.38	2.75	3.59
66	15.87	15.40	15.01	11.17	10.69	9.94	9.97	9.30	9.24	12.58	16.19	10.43	7.50	9.97	15.19
102	13.79	6.66	10.86	9.96	8.46	6.86	6.78	7.53	9.57	9.27	8.50	6.77	6.07	4.29	11.62
111	17.15	9.23	8.53	11.25	9.21	7.34	6.13	7.53	9.52	8.17	6.53	5.72	4.51	7.80	16.97
112	12.15	10.84	10.19	8.56	6.64	6.85	5.65	6.57	7.49	6.49	11.15	6.49	4.95	4.87	8.99
113	18.88	8.60	8.63	12.81	10.50	7.98	7.20	16.03	10.78	8.56	8.42	7.27	5.34	11.28	12.16
114*	7.35	3.70	3.65	3.45	3.41	2.84	3.32	3.92	4.50	3.56	4.35	3.21	4.30	3.25	9.95
206	10.31	6.93	10.19	12.35	9.21	6.36	5.77	5.96	5.78	6.63	5.40	4.86	4.80	4.35	8.08
213*	10.49	6.65	7.88	8.00	8.30	7.12	7.33	6.75	14.48	7.22	7.48	8.26	6.10	7.75	19.66
Mean	13.35	8.22	9.31	9.52	7.97	6.66	6.39	7.76	8.29	7.07	7.71	6.09	5.18	6.38	11.20
St. Dev.	5.23	3.52	3.91	3.62	2.87	2.53	2.73	3.61	3.55	2.43	3.47	2.60	2.22	3.58	5.38

*Minority subject

Subjects Table H10. DHEA concentrations (ng/ml) for young men during Alprazolam/Placebo Treatment

Subject	Time (h)														
	0	1	2	3	3.5	4.5	5.5	7	8.5	10	11.5	12.5	16	20	23
33	6.34	7.12	7.44	6.58	5.77	5.47	5.40	7.84	5.43	5.52	5.65	4.74	4.64	5.79	7.70
34	9.34	7.39	7.88	5.50	5.53	4.97	5.06	7.10	5.02	5.82	4.75	3.75	3.09	3.07	4.87
35	11.86	3.56	11.53	5.46	4.45	3.72	3.24	5.63	4.43	3.93	3.35	3.25	5.29	2.97	6.36
36	9.28	8.52	9.12	7.90	7.38	5.77	4.40	5.63	5.83	7.21	5.45	4.89	3.88	5.35	9.69
37	10.38	10.85	10.90	11.08	8.83	6.57	6.23	6.70	6.62	8.03	5.70	4.09	3.40	4.50	14.98
38	12.72	9.98	11.21	8.76	7.61	7.35	6.59	6.33	6.86	8.25	8.90	6.00	5.38	4.74	13.98
39	22.21	9.16	11.56	8.75	8.03	9.13	6.31	12.94	8.00	7.31	6.72	5.44	4.48	11.48	12.37
41	19.12	8.74	13.39	14.92	10.48	7.53	6.10	7.73	11.92	7.34	8.21	5.97	7.32	6.48	15.87
42	11.31	7.68	8.35	10.23	7.80	5.91	4.77	5.56	5.06	6.16	5.61	4.06	4.89	5.09	5.96
43	15.78	9.98	10.51	10.74	10.14	8.63	8.57	7.11	9.33	12.38	7.37	6.80	5.56	5.61	10.24
44	12.33	7.56	7.20	7.44	6.21	5.90	6.71	12.73	9.06	10.46	10.37	8.78	5.79	15.00	6.31
45	17.83	6.83	8.60	9.69	8.33	7.69	6.57	7.62	10.52	6.75	5.61	5.36	6.85	5.84	6.04
46	23.12	8.65	16.05	10.67	9.54	7.80	9.64	14.17	7.86	10.51	5.42	5.48	5.83	16.33	22.76
47*	10.55	6.51	6.62	6.46	5.24	4.70	4.18	4.72	10.83	5.10	4.15	3.45	3.80	7.20	14.71
48*	15.51	8.70	9.67	11.08	8.33	7.09	7.58	8.69	9.38	11.53	8.56	7.71	5.95	17.46	12.61
140	14.33	5.78	14.13	12.57	7.95	6.92	4.67	5.57	6.12	10.74	8.09	5.93	4.85	3.98	11.35
145	14.99	13.69	14.08	12.66	12.38	12.12	11.35	12.15	12.74	11.35	10.69	14.22	8.65	8.30	12.70
146*	15.72	7.78	9.37	8.30	8.42	6.80	6.41	7.33	9.79	11.22	7.05	5.25	5.34	12.19	17.11
245*	18.37	11.14	13.56	12.49	10.44	11.23	9.00	9.70	11.23	12.39	10.27	7.63	6.10	4.87	4.75
Mean	14.27	8.40	10.59	9.54	8.05	7.12	6.46	8.17	8.21	8.53	6.94	5.94	5.32	7.70	11.07
St. Dev.	4.49	2.21	2.70	2.64	2.03	2.10	2.05	2.84	2.56	2.68	2.15	2.50	1.37	4.52	4.88

*Minority Subjects

Table H11. DHEA concentrations (ng/ml) for older women during Alprazolam/Placebo Treatment

Subject	Time (h)														
	0	1	2	3	3.5	4.5	5.5	7	8.5	10	11.5	12.5	16	20	23
17	3.88	3.44	3.98	2.66	2.38	2.52	2.16	1.96	2.43	2.66	2.22	2.36	4.00	6.37	6.10
18	4.91	2.04	1.98	1.73	1.64	1.73	2.06	2.22	1.46	1.73	1.38	1.47	2.94	1.00	3.94
19	10.90	2.71	2.61	2.23	2.37	2.10	1.95	0.99	4.67	2.09	2.00	1.89	1.58	2.78	4.97
20*	7.21	2.89	2.96	2.83	3.09	2.78	2.34	2.53	2.04	2.45	2.98	2.52	2.12	3.29	2.61
21	10.52	4.17	5.95	3.63	3.23	2.32	1.52	4.50	3.06	2.66	2.86	3.05	2.33	12.48	4.88
22	8.65	4.32	3.11	2.68	3.21	2.58	2.52	2.80	4.46	2.61	2.60	2.50	1.71	4.33	8.19
23	2.72	1.91	1.64	1.59	1.59	1.58	1.74	1.98	1.88	1.57	1.94	1.67	1.33	2.89	2.38
24	3.65	1.96	1.82	1.73	1.75	1.86	1.39	1.61	1.63	1.69	2.03	1.55	1.22	1.46	2.70
25	3.02	2.18	2.71	3.08	2.65	2.06	1.88	1.77	3.06	2.50	2.78	1.94	1.50	2.12	2.49
26	2.40	1.62	1.93	2.33	1.94	1.64	1.62	1.54	1.59	5.40	1.83	1.72	1.22	4.73	1.48
27	1.59	1.36	1.52	1.22	1.10	0.89	1.03	1.10	0.86	0.98	2.41	1.25	1.28	1.91	2.11
28	0.92	0.81	2.06	0.92	1.02	0.91	0.83	0.83	0.85	0.82	1.03	0.90	1.42	0.82	1.36
29*	2.09	0.98	0.91	1.01	0.78	0.78	0.85	0.78	1.02	0.74	0.89	0.73	0.62	0.75	0.73
30*	2.43	1.25	1.96	1.55	1.55	1.42	1.86	1.49	3.14	1.54	1.30	1.18	0.94	1.34	3.16
31*	0.85	1.00	1.15	0.85	0.78	0.70	0.61	0.73	0.74	0.72	0.74	0.78	0.63	0.96	0.89
120	7.36	2.13	2.21	2.09	1.96	1.71	1.82	2.84	1.76	1.56	1.47	1.26	1.04	3.86	5.86
Mean	4.57	2.17	2.41	2.01	1.94	1.72	1.64	1.85	2.17	1.98	1.90	1.67	1.62	3.19	3.37
St. Dev.	3.32	1.08	1.22	0.82	0.82	0.66	0.56	0.99	1.22	1.15	0.72	0.67	0.88	2.96	2.12

*Minority Subjects

Table H12. DHEA concentrations (ng/ml) for older men during Alprazolam/Placebo Treatment

Subject	Time (h)														
	0	1	2	3	3.5	4.5	5.5	7	8.5	10	11.5	12.5	16	20	23
50	5.35	3.30	4.49	2.90	2.83	2.62	4.02	2.79	2.19	2.55	2.28	2.43	4.15	4.82	2.86
51	2.49	2.58	2.42	2.27	2.40	2.27	2.30	1.92	1.74	2.16	1.65	1.89	3.22	2.74	2.88
52	2.95	2.18	2.67	2.31	2.06	2.69	1.87	1.89	2.22	2.17	1.81	1.82	1.64	4.13	3.48
53	5.59	4.05	7.12	4.06	4.13	4.00	3.26	4.07	3.30	3.53	3.20	3.02	2.50	3.84	3.48
54	3.30	4.36	2.76	1.78	2.50	2.77	2.77	2.73	1.91	2.66	2.17	2.13	1.35	1.63	4.63
55	3.80	2.92	3.06	2.64	2.54	2.62	2.55	3.30	2.37	2.03	2.31	2.06	1.92	2.20	5.69
56	3.18	1.88	2.24	1.97	2.04	1.89	1.75	2.16	1.84	2.02	1.20	1.57	1.37	2.06	2.83
57	4.53	1.92	4.61	2.06	1.78	1.72	1.55	1.74	1.13	1.78	1.65	1.61	1.50	1.93	1.98
58	1.50	1.55	1.74	1.62	1.53	1.53	1.28	0.68	1.63	1.64	1.30	1.16	1.05	1.29	1.66
59	9.35	5.20	5.55	4.53	4.51	4.24	4.61	5.62	5.26	4.47	4.59	3.97	3.21	8.79	8.28
60	5.32	2.54	2.80	2.42	2.61	2.20	2.08	0.70	2.36	2.53	2.15	2.50	1.56	3.15	3.46
61*	10.81	5.97	5.48	4.49	3.73	4.45	4.15	4.29	4.77	4.78	4.21	3.60	2.96	4.88	7.54
149	4.08	2.26	2.37	2.42	3.11	2.84	2.67	3.26	3.72	3.13	2.87	2.40	2.65	3.77	4.86
160	6.38	2.02	2.35	2.90	2.34	2.59	2.54	2.64	2.72	2.69	2.32	1.92	1.78	1.95	3.36
Mean	4.90	3.05	3.55	2.74	2.72	2.75	2.67	2.70	2.65	2.72	2.41	2.29	2.20	3.37	4.07
St. Dev.	2.58	1.35	1.61	0.96	0.87	0.90	1.01	1.36	1.20	0.95	1.01	0.78	0.92	1.96	1.95

*Minority Subjects

Table H13. DHEA concentrations (ng/ml) for young women during Alprazolam/DHEA Treatment

Subject	Time (h)														
	0	1	2	3	3.5	4.5	5.5	7	8.5	10	11.5	12.5	16	20	23
1	13.32	17.79	16.43	17.39	14.90	14.22	13.36	19.85	18.39	16.45	14.23	12.79	11.70	9.08	8.82
3	12.78	9.01	16.42	16.53	15.14	13.50	12.11	14.75	17.88	19.98	16.16	14.95	11.52	10.39	16.46
4	19.04	7.47	16.49	16.17	15.05	15.31	13.66	14.42	12.35	17.58	18.59	15.00	9.76	14.51	12.43
5	19.99	22.46	21.53	17.04	14.10	12.33	10.63	13.27	12.25	23.33	18.18	14.95	10.35	10.80	13.72
7	12.63	12.33	13.51	12.56	9.28	8.85	6.59	6.64	13.52	11.62	7.48	6.04	4.28	5.79	10.83
8	16.26	11.99	16.09	19.52	13.54	12.54	10.11	12.97	12.34	17.00	13.34	11.04	4.68	5.50	16.05
9	10.92	6.13	19.69	19.24	19.50	16.25	17.20	13.36	14.92	16.38	18.65	17.77	13.22	12.95	16.54
10	13.71	11.44	16.08	15.74	14.69	13.67	13.41	13.42	16.99	15.63	14.56	9.58	10.16	9.55	17.06
11	15.70	8.76	18.07	14.77	12.51	11.35	11.15	11.55	16.68	15.52	14.65	13.04	9.56	11.79	11.26
12	11.79	11.22	18.15	24.12	18.47	14.59	14.10	19.92	16.68	22.06	14.83	15.45	11.15	10.37	10.39
14*	9.17	6.66	8.39	10.69	11.54	20.11	17.74	12.23	19.96	17.20	13.18	11.55	8.44	10.58	13.17
15*	2.95	8.60	12.39	10.44	9.73	7.55	7.12	6.01	8.42	13.36	11.46	9.90	8.35	8.01	8.20
16*	4.63	15.53	12.42	11.58	9.66	7.95	7.16	11.35	12.84	10.64	10.43	8.63	5.93	4.81	8.25
66	13.30	9.86	18.35	17.79	15.75	13.84	11.80	10.40	11.66	17.81	17.25	14.36	10.39	10.64	16.22
102	15.59	16.83	14.42	16.49	17.02	14.44	14.96	14.58	14.27	17.53	20.71	17.60	13.34	15.75	18.06
111	13.58	8.68	16.33	13.73	12.97	11.21	9.41	8.48	13.40	11.36	10.26	8.50	6.69	15.17	12.52
112	5.15	1.72	7.11	4.22	9.78	11.32	12.04	10.41	10.63	9.74	9.74	9.29	7.99	6.32	8.92
113	19.15	10.81	12.05	13.36	10.53	9.68	8.72	10.10	13.69	8.67	9.65	8.65	11.35	4.86	12.50
114*	7.02	4.60	12.44	12.44	10.75	9.20	7.46	12.21	16.17	13.13	10.32	7.52	6.26	5.89	7.10
206	9.43	10.69	14.86	15.95	14.89	13.60	13.27	13.91	16.13	14.52	13.37	12.23	11.62	10.60	11.98
213*	9.50	8.95	18.75	16.91	15.91	16.17	16.85	13.93	17.42	21.84	15.99	13.97	12.85	13.05	20.75
Mean	12.17	10.55	15.24	15.08	13.61	12.75	11.85	12.56	14.60	15.78	13.95	12.04	9.50	9.83	12.92
St. Dev.	4.74	4.68	3.58	4.09	2.97	3.08	3.36	3.45	2.88	4.06	3.56	3.34	2.72	3.39	3.73

*Minority Subjects; (-) Concentration not obtained

Table H14. DHEA concentrations (ng/ml) for young men during Alprazolam/DHEA Treatment

Subject	Time (h)														
	0	1	2	3	3.5	4.5	5.5	7	8.5	10	11.5	12.5	16	20	23
33	12.55	6.02	9.93	18.42	18.09	18.55	14.88	12.09	15.67	17.55	14.35	12.05	7.65	5.97	11.82
34	7.40	12.76	11.91	11.13	10.80	8.97	8.19	9.99	10.95	14.27	10.39	8.73	6.60	6.46	9.41
35	8.09	15.10	13.74	11.53	10.54	8.13	7.23	7.53	8.61	8.90	11.03	8.77	7.76	6.59	7.42
36	7.44	22.49	20.21	19.61	16.62	15.49	14.35	12.64	16.44	13.93	18.12	15.87	10.72	9.57	11.07
37	11.43	8.44	19.73	14.95	12.68	10.25	8.28	10.50	9.63	12.96	11.94	9.90	6.09	7.33	10.79
38	15.22	20.88	18.94	14.75	14.12	11.92	9.30	11.61	15.76	14.88	13.51	11.08	8.09	13.66	13.97
39	18.77	17.47	15.71	11.97	12.19	9.96	7.90	9.33	11.11	13.76	10.33	8.87	6.91	10.72	18.81
41	15.97	18.62	18.62	18.28	15.65	12.79	11.22	10.50	14.76	20.09	15.13	10.03	10.97	7.96	15.88
42	16.10	14.89	16.92	19.95	16.59	14.38	12.72	10.10	11.01	10.66	19.81	18.34	5.93	8.77	7.55
43	13.95	8.80	16.58	17.17	17.78	11.82	10.87	10.02	12.99	16.88	14.58	9.42	10.96	11.89	13.28
44	10.63	15.46	13.71	15.41	14.04	12.15	11.74	15.89	15.55	16.96	15.21	12.29	14.80	9.39	8.13
45	22.36	17.26	20.63	15.44	13.93	11.71	12.14	13.52	12.09	15.34	13.14	11.74	10.24	16.58	15.35
46	22.66	10.18	20.16	13.07	12.78	12.66	12.23	19.52	16.07	18.54	15.49	12.69	11.31	16.12	19.71
47*	11.89	19.33	16.85	11.09	10.29	8.94	7.84	7.42	11.71	11.16	12.10	10.16	7.72	9.38	10.72
48*	13.81	18.85	18.57	15.44	13.21	12.36	12.45	12.06	18.02	17.06	14.61	13.07	8.90	8.01	15.76
140	12.04	6.18	14.45	16.12	14.50	11.55	9.79	11.63	15.46	11.75	12.76	9.87	8.33	6.01	13.51
145	17.42	18.77	20.04	17.13	17.28	16.57	26.47	15.45	21.79	18.31	17.75	22.14	14.69	13.40	15.55
146*	15.61	12.08	15.41	15.32	13.83	12.47	11.57	12.25	18.24	16.89	14.95	12.48	11.42	11.48	19.50
245*	8.06	10.59	16.15	16.20	15.54	14.75	15.63	18.31	22.54	19.08	16.12	13.10	10.38	8.47	12.07
Mean	13.76	14.43	16.75	15.42	14.23	12.39	11.83	12.12	14.65	15.21	14.28	12.14	9.45	9.88	13.17
St. Dev.	4.57	5.02	3.04	2.72	2.39	2.67	4.32	3.25	3.84	3.12	2.58	3.46	2.60	3.23	3.82

*Minority Subjects

Table H15. DHEA concentrations (ng/ml) for older women during Alprazolam/DHEA Treatment

Subject	Time (h)														
	0	1	2	3	3.5	4.5	5.5	7	8.5	10	11.5	12.5	16	20	23
17	3.18	13.90	13.31	9.04	8.79	7.90	6.70	12.30	17.35	16.69	16.27	11.78	8.57	9.74	9.84
18	4.22	16.20	16.87	13.73	12.65	11.07	10.24	12.96	16.59	16.75	14.95	12.59	8.21	8.79	8.41
19	4.20	7.88	15.29	12.51	11.32	10.25	9.82	9.15	14.18	17.22	11.81	11.19	8.66	9.98	8.69
20*	8.43	3.16	11.22	14.14	15.08	12.99	12.60	10.69	15.71	15.64	14.13	12.61	10.05	9.17	7.16
21	8.04	9.16	15.58	14.91	12.87	11.83	10.52	9.53	9.84	9.92	16.08	14.19	9.74	13.50	8.63
22	5.06	8.80	12.39	9.74	10.03	10.54	9.29	9.69	8.51	10.79	14.59	13.78	10.37	9.65	13.23
23	3.82	14.19	18.02	13.56	12.26	10.77	10.77	9.12	10.45	17.95	15.92	14.37	10.37	9.25	12.47
24	5.62	17.77	15.27	16.95	11.33	9.87	7.99	9.78	12.51	15.44	13.81	10.92	7.40	7.60	9.03
25	5.70	7.63	13.07	12.79	13.24	12.69	8.59	11.98	11.69	18.53	17.73	16.13	12.97	12.56	13.90
26	2.77	23.96	25.77	18.00	19.15	16.52	14.93	13.21	21.60	23.73	20.15	15.93	11.85	13.18	10.33
27	2.25	2.40	10.86	13.39	13.50	10.80	12.46	9.99	10.29	15.97	16.27	12.74	8.32	6.89	7.56
28	1.00	10.21	20.44	15.31	13.85	11.70	10.50	9.98	13.03	14.48	12.53	12.45	9.98	8.08	8.78
29*	1.03	11.44	10.95	8.86	8.06	8.52	6.35	7.57	14.14	15.35	12.52	11.53	7.92	6.80	7.64
30*	5.14	3.77	9.53	13.71	13.36	10.03	9.08	8.60	12.06	13.82	10.74	9.27	6.32	5.72	8.59
31*	1.23	6.31	11.90	11.80	10.99	9.17	8.98	7.37	8.49	11.60	11.24	8.42	5.27	3.95	4.40
120	8.72	2.98	21.57	19.58	18.90	16.47	14.06	13.52	17.22	16.30	13.26	11.52	13.65	10.26	9.83
Mean	4.40	9.99	15.13	13.63	12.84	11.32	10.18	10.34	13.35	15.64	14.50	12.46	9.35	9.07	9.28
St. Dev.	2.51	6.04	4.49	3.00	3.04	2.44	2.41	1.93	3.64	3.28	2.52	2.11	2.25	2.61	2.38

*Minority Subjects

Table H16. DHEA concentrations (ng/ml) for older men during Alprazolam/DHEA Treatment

Subject	Time (h)														
	0	1	2	3	3.5	4.5	5.5	7	8.5	10	11.5	12.5	16	20	23
50	7.58	14.79	14.09	8.78	8.78	7.28	6.70	6.93	11.53	14.14	14.36	12.47	9.66	6.14	7.54
51	3.34	16.85	14.78	4.03	9.09	7.72	7.88	6.73	16.80	18.93	15.51	13.37	9.10	8.42	10.15
52	3.38	6.34	16.12	12.46	12.94	10.40	8.61	7.39	12.65	13.21	9.21	8.42	8.54	5.31	8.43
53	7.53	4.81	14.11	12.65	12.04	9.08	8.34	7.99	14.53	17.56	17.18	13.50	12.21	9.82	8.92
54	2.74	3.00	8.33	8.66	6.46	7.23	6.63	11.21	17.72	14.01	9.71	8.87	5.63	5.17	5.08
55	3.41	2.68	4.02	4.69	4.60	3.36	3.08	10.08	13.50	9.71	12.65	10.48	6.75	6.65	10.65
56	2.73	3.04	19.76	21.55	21.38	17.08	15.60	23.29	17.68	13.61	11.11	10.72	7.79	6.92	6.71
57	3.65	4.49	13.42	12.47	10.07	8.69	7.54	7.11	8.44	7.43	7.65	6.26	5.17	4.96	6.62
58	2.54	1.18	5.76	12.16	13.10	11.25	8.86	13.66	17.30	13.26	10.26	9.15	6.37	5.70	7.07
59	11.32	5.16	15.58	13.60	10.51	11.41	9.34	8.42	8.88	17.36	12.66	10.70	6.58	9.65	12.02
60	3.73	15.64	11.72	9.17	7.63	7.04	5.65	10.51	8.94	8.47	7.76	6.46	5.68	5.03	7.94
61*	12.33	5.56	14.46	17.87	17.00	14.72	14.27	12.30	12.78	20.13	15.45	13.30	10.10	10.09	15.09
149	3.19	14.54	16.15	14.07	13.38	13.72	11.63	10.33	11.14	10.87	9.82	9.55	8.05	7.34	8.62
160	6.15	2.84	21.88	18.83	14.23	16.11	13.93	12.45	20.48	17.56	14.26	11.60	8.69	8.05	11.53
Mean	5.26	7.21	13.58	12.21	11.52	10.36	9.15	10.60	13.74	14.02	11.97	10.35	7.88	7.09	9.03
St. Dev.	3.26	5.60	4.89	5.01	4.37	3.93	3.55	4.30	3.80	3.94	3.05	2.38	2.00	1.85	2.64

*Minority Subjects

Table H17. DHEA-S concentrations (ng/ml) for young women during Placebo Treatment

Subject	Time (h)														
	0	1	2	3	3.5	4.5	5.5	7	8.5	10	11.5	12.5	16	20	23
1	1490.02	1294.47	1256.30	1457.18	1480.47	1579.86	1703.86	1726.23	1962.53	1805.42	1976.28	1863.28	1592.50	1451.36	1437.34
3	1643.99	1420.17	1574.09	1566.95	1087.29	1421.57	1509.40	1722.64	1537.48	1670.93	1466.39	1309.39	1192.99	1425.93	1561.92
4	1498.55	1492.01	1516.08	1597.33	1561.17	1398.44	1538.00	1690.92	1674.83	1465.07	1295.29	1440.25	1348.11	1366.64	1890.04
5	2597.41	2396.45	2403.66	2512.26	2535.42	2563.34	2657.12	2539.23	2256.70	2309.55	2233.59	2112.37	1749.65	1999.18	2558.32
7	1232.84	1221.63	1280.26	1244.79	1289.78	1371.94	1463.50	1470.74	1479.29	1293.99	1292.53	1069.96	914.55	870.69	1117.60
8	848.42	897.96	1086.82	1278.49	1005.90	1004.76	1204.75	980.19	1391.90	988.04	1320.89	890.26	955.24	729.09	893.57
9	746.36	722.55	732.03	782.01	942.10	881.93	856.49	799.66	877.99	999.21	981.67	934.02	704.47	633.43	863.90
10	4544.52	4076.97	4199.58	4275.67	4380.48	4420.33	4313.63	4329.37	4152.53	4124.31	3893.13	4002.93	3791.39	3886.53	4264.83
11	1774.38	1914.49	2816.64	4506.64	4627.74	4781.73	4651.11	4687.84	4566.38	4918.96	5588.25	5362.43	4771.45	3964.80	4061.31
12	2678.15	2498.54	2293.29	2385.44	2575.06	2751.88	2966.02	2761.33	2802.25	3002.67	2970.00	2760.24	2427.49	1903.80	2358.88
14*	2609.74	2303.96	2155.51	2274.50	2353.58	2564.08	2430.64	2301.09	2459.31	2482.69	2593.67	1991.12	2000.91	2027.87	2391.31
15*	134.86	102.82	89.79	92.87	91.50	96.70	94.79	94.97	91.75	101.22	100.17	102.44	87.61	92.12	95.43
16*	716.30	969.09	1007.83	1131.16	1108.87	1139.44	1004.06	1084.31	1115.30	1172.99	1110.70	1075.69	812.63	818.13	901.77
66	2590.10	2565.06	2684.68	2760.38	2682.93	3257.49	2864.35	2650.99	2595.63	3163.46	2548.38	2484.91	2088.50	2118.28	2404.55
102	1941.61	1861.06	1815.32	1836.74	1915.19	2067.94	2024.86	1999.03	1992.62	2015.52	2005.81	1905.62	1672.16	1444.85	1652.14
111	1780.87	1765.16	1618.27	1756.64	1609.17	1650.61	1498.27	1438.22	1442.82	1524.96	1449.13	1336.58	1258.27	1486.21	1497.71
112	1731.90	1894.04	2054.48	2093.98	2077.84	2194.48	2112.81	2216.88	2067.14	2340.32	2143.76	2445.41	1911.77	1520.88	1752.93
113	2519.78	2143.29	2161.51	2306.27	2415.26	2396.22	2602.77	2778.62	2667.56	2570.61	2608.17	2468.59	1946.40	1862.29	1882.83
114*	838.72	613.99	734.22	674.69	828.04	838.20	876.48	837.92	874.38	882.50	802.36	866.56	710.16	770.00	851.66
206	929.40	791.21	1059.43	1055.91	1020.71	951.87	1037.06	950.71	817.44	902.45	1024.39	981.87	770.06	784.02	743.77
213*	1178.12	1023.51	1003.20	943.37	975.60	981.35	897.32	935.91	910.34	941.21	1014.56	991.03	924.28	803.42	1066.02
Mean	1715.53	1617.54	1692.52	1834.92	1836.39	1919.72	1919.39	1904.61	1892.20	1936.96	1924.72	1828.33	1601.46	1521.88	1726.09
St. Dev.	979.23	886.43	908.64	1084.38	1124.33	1181.56	1139.47	1137.38	1084.19	1164.58	1208.74	1188.02	1073.94	967.30	1035.01

*Minority Subjects

Table H18. DHEA-S concentrations (ng/ml) for young men during Placebo Treatment

Subject	Time (h)														
	0	1	2	3	3.5	4.5	5.5	7	8.5	10	11.5	12.5	16	20	23
33	1365.47	1255.28	1400.18	1387.27	1525.45	1442.70	1362.57	1327.32	1323.46	1369.20	1635.51	1650.47	1501.86	1502.91	1834.16
34	1574.88	1468.96	1598.89	1521.64	1532.22	1601.59	1687.54	1552.21	1687.07	1711.69	1738.93	1798.36	1615.89	1381.22	1627.23
35	1352.48	1231.33	1222.44	1215.57	1422.59	1304.39	1209.96	1272.18	1284.80	1235.66	1049.81	1060.99	1031.35	1145.31	1245.95
36	2105.21	2069.29	2210.97	2157.33	2153.80	2133.99	2169.43	2208.10	2041.79	2404.92	2262.58	2236.97	1996.88	1834.13	2256.46
37	3099.37	3256.88	3069.96	3143.64	3256.88	3255.65	3341.13	3315.89	3179.08	3347.51	3184.28	3111.08	2782.35	2573.19	2992.17
38	3684.17	3602.25	3802.85	3658.48	3483.47	3745.77	3911.37	3859.96	3755.34	3809.37	3678.93	3517.66	2690.05	2946.66	3742.49
39	2438.81	2014.78	1852.42	1804.21	1873.20	1966.24	1727.58	1846.45	1727.30	1896.83	1824.06	1692.02	1507.39	1679.95	1861.75
41	2667.19	2628.67	2609.08	2702.67	2595.18	2771.35	2644.44	2720.94	2791.54	2750.55	2773.60	2676.30	2306.64	2293.96	2750.37
42	3645.66	3841.53	3761.86	3810.90	3904.59	3966.20	3916.79	4029.04	4081.52	4181.85	4157.74	4039.84	3725.98	3512.16	3877.20
43	3171.28	3758.73	3482.93	3310.66	3310.66	3400.58	3543.05	3552.99	3430.34	3825.99	3383.46	3097.91	3111.86	3107.56	3441.27
44	2655.65	2732.03	2650.11	2683.63	2677.27	2656.82	2730.15	2848.29	3001.83	3071.41	3111.38	3082.29	2998.72	2942.51	2712.97
45	4075.88	4208.89	4072.41	4071.87	4333.88	4247.67	4134.90	4449.25	4365.15	4559.98	4433.32	4066.52	3986.20	3966.86	3845.71
46	4746.73	4710.99	4823.80	4927.35	4896.57	4824.79	4960.35	4942.19	4881.17	4885.86	5069.86	4927.35	4730.17	4713.74	4994.12
47*	2507.80	2252.28	2380.34	2230.78	2256.98	2412.33	2203.19	2167.39	2314.71	2570.99	2248.43	2165.11	1931.24	1931.64	2374.31
48*	2426.03	2419.57	2740.15	2607.41	2613.32	2718.98	2691.00	2574.90	2797.99	2816.25	2811.82	2788.62	2927.16	4460.40	2549.39
140	2230.69	2196.34	2287.22	2625.72	2487.07	2797.96	2588.15	2780.94	2752.48	2857.80	2852.00	2758.45	2433.74	2046.61	2281.80
145	2793.46	2585.58	2686.84	2653.34	2718.71	2645.77	2614.92	2503.75	2384.78	2504.68	2714.53	2786.57	2602.68	2208.79	2282.37
146*	2042.50	2004.54	2083.02	2021.61	2020.15	2100.24	1999.77	2127.41	2042.28	2071.26	2088.57	1901.56	1789.99	1908.65	2404.34
245*	2736.30	2914.98	2836.43	2846.76	2731.13	2952.43	2941.01	2850.70	2898.80	2979.04	2784.13	2696.95	2579.33	2238.39	2405.22
Mean	2701.03	2692.26	2714.31	2704.25	2725.95	2786.60	2756.70	2785.78	2775.86	2886.89	2831.73	2739.74	2539.45	2547.09	2709.44
St. Dev.	894.08	988.17	949.00	963.10	951.92	954.05	1007.11	1029.95	1009.43	1027.91	1016.80	957.71	932.05	1025.20	920.47

*Minority Subjects

Table H19. DHEA-S concentrations (ng/ml) for older women during Placebo Treatment

Subject	Time (h)														
	0	1	2	3	3.5	4.5	5.5	7	8.5	10	11.5	12.5	16	20	23
17	114.69	98.72	109.63	127.08	109.94	110.94	120.30	115.95	137.02	115.05	99.07	108.14	97.93	108.13	160.14
18	264.07	266.61	269.78	266.85	279.27	315.24	282.52	292.63	288.56	267.60	275.09	280.15	205.56	209.93	273.78
19	489.63	465.43	389.03	420.39	449.19	497.86	474.22	461.70	495.20	422.34	500.74	417.11	309.43	281.33	363.57
20*	95.67	87.31	80.79	73.61	66.81	89.75	89.17	84.53	84.28	76.95	96.99	98.52	71.78	77.35	80.26
21	231.90	310.20	346.14	292.63	307.79	447.56	394.81	332.70	390.13	363.90	457.88	394.52	404.99	408.70	593.59
22	397.02	489.16	542.79	587.90	583.76	542.51	712.45	620.06	675.68	421.24	645.99	514.14	360.08	376.00	440.41
23	236.05	268.25	320.76	228.53	244.37	240.47	397.54	263.26	270.76	277.07	285.85	239.12	176.66	159.55	247.33
24	119.98	123.55	120.36	134.06	138.98	138.37	128.74	131.41	133.43	128.32	140.87	131.39	105.54	97.93	125.78
25	159.44	174.62	153.64	147.72	150.33	185.05	183.23	176.35	146.32	169.06	170.52	173.36	127.34	94.39	143.49
26	117.62	114.23	126.43	126.52	132.74	126.17	111.78	104.81	-999.00	116.54	115.24	107.11	89.09	97.60	112.43
27	83.76	86.25	75.61	72.62	70.91	66.20	78.71	70.87	71.97	66.22	-999.00	89.27	54.43	61.86	75.74
28	66.21	64.96	61.58	54.84	70.59	67.61	76.20	69.18	65.39	72.57	68.78	75.22	64.28	57.76	54.01
29*	68.17	59.51	67.99	61.10	63.45	67.22	63.89	67.71	67.09	58.61	68.19	62.23	58.66	65.18	71.70
30*	139.42	156.42	150.20	139.68	150.17	162.24	152.93	148.77	150.69	155.03	155.64	152.44	120.48	111.99	138.01
31*	74.15	79.68	85.34	86.12	89.44	80.34	93.25	87.82	91.83	79.08	74.80	77.00	69.43	58.79	63.92
120	327.09	321.84	361.49	287.19	306.79	319.07	373.59	340.42	347.09	350.04	332.39	279.95	243.78	195.89	283.49
Mean	186.55	197.92	203.85	194.18	200.91	216.04	233.33	210.51	151.03	196.23	155.57	199.98	159.97	153.90	201.73
St. Dev.	127.46	140.04	146.94	147.63	151.43	161.38	187.60	162.13	353.48	132.72	353.74	140.24	113.37	112.43	155.34

*Minority Subjects

Table H20. DHEA-S concentrations (ng/ml) for older men during Placebo Treatment

Subject	Time (h)														
	0	1	2	3	3.5	4.5	5.5	7	8.5	10	11.5	12.5	16	20	23
50	502.78	578.52	575.88	653.35	587.54	580.89	609.78	568.40	539.18	577.25	641.52	500.48	453.81	490.84	594.65
51	202.10	226.33	237.42	254.67	210.91	237.64	246.08	269.59	257.97	254.73	227.44	233.52	208.59	249.07	265.70
52	715.71	630.14	716.15	702.92	607.99	729.79	704.29	714.64	707.08	705.15	707.37	659.16	584.43	677.34	679.08
53	680.73	472.68	612.25	627.68	640.61	561.97	469.36	555.22	670.90	736.35	492.65	471.11	492.72	427.24	775.20
54	904.55	846.21	875.18	904.55	843.22	949.03	965.25	926.54	863.14	898.22	996.27	895.52	621.83	661.19	517.08
55	2214.96	2170.90	2158.52	2130.84	2139.98	2378.40	2308.55	2095.57	2172.72	2295.55	1833.33	2129.05	1303.12	2112.61	1738.89
56	91.71	95.32	95.64	98.27	98.37	112.06	96.21	111.24	105.96	124.82	111.00	104.22	85.58	92.71	106.52
57	730.05	794.43	877.78	782.09	733.13	765.27	734.65	740.02	777.80	931.78	884.55	785.31	706.55	696.98	771.24
58	69.66	68.42	72.56	69.35	75.56	83.85	75.72	67.81	72.16	80.55	78.57	71.30	64.73	58.01	72.19
59	1460.38	1430.42	1621.57	1639.52	1695.15	1784.34	1658.24	1880.21	1769.78	1765.26	1669.76	1599.23	1198.45	1047.01	1494.10
60	1523.83	1571.09	1545.73	1581.66	1559.91	1533.02	1484.41	1584.12	1745.87	1888.97	1406.90	1487.36	1301.81	1241.16	1422.28
61*	440.46	473.74	524.14	526.40	550.90	510.55	516.07	540.02	533.06	529.61	518.49	494.61	436.87	413.31	610.73
149	546.73	586.21	561.40	556.14	546.77	675.67	649.95	595.23	639.02	617.06	651.81	625.94	509.74	527.06	500.61
160	466.36	464.61	517.70	463.43	466.92	498.85	492.58	471.67	544.33	552.12	572.62	577.30	502.99	470.23	529.33
Mean	753.57	743.50	785.14	785.06	768.35	814.38	786.51	794.31	814.21	854.10	770.88	759.58	605.09	654.63	719.83
St. Dev.	604.77	597.39	603.34	603.00	612.39	657.50	631.77	626.92	637.44	670.35	542.82	594.26	405.55	529.82	503.35

*Minority Subjects

Table H21. DHEA-S concentrations (ng/ml) for young women during DHEA Treatment

Subject	Time (h)														
	0	1	2	3	3.5	4.5	5.5	7	8.5	10	11.5	12.5	16	20	23
1	1995.54	4755.38	4647.65	4552.83	4551.84	4309.04	4153.11	3926.72	4823.88	5077.60	4619.37	4257.62	3728.81	3387.23	3434.20
3	1677.29	2060.64	3986.02	4463.88	4694.60	4985.65	4876.12	4735.27	5376.41	5515.81	5421.46	5527.85	4651.25	4697.41	4528.27
4	1733.89	1631.94	2928.39	4165.03	4178.51	4463.51	4623.37	4063.83	3947.17	4044.73	4021.29	3751.94	3692.68	2227.96	3956.45
5	2494.52	3801.04	5181.27	4896.66	4493.47	3946.67	3407.94	3494.97	4503.85	4903.84	4655.81	4364.35	3240.97	3157.77	3239.19
7	1515.79	3286.02	4294.20	4327.99	4415.89	4640.76	4159.50	3745.85	4400.21	4881.18	4406.97	4020.21	3177.37	2675.97	2717.33
8	642.52	4104.42	4366.30	3930.70	3719.18	3555.82	2885.36	2333.32	4418.87	4139.64	3508.02	2892.66	1632.30	1134.01	1484.24
9	734.85	2108.15	3891.10	4054.29	4180.21	4051.88	4055.30	3848.56	3880.18	--	5116.86	5218.18	4618.73	4194.13	4096.27
10	4119.80	5257.33	5407.76	5216.59	5214.70	5446.20	5285.99	5844.76	5739.72	5431.75	5393.48	5156.89	4728.60	4732.02	4985.54
11	1944.65	2215.63	3194.49	4346.17	4464.78	4718.04	4735.89	4870.81	5797.37	5591.67	5633.11	5480.56	4929.68	4461.61	4163.38
12	2533.24	2601.76	3987.87	4086.39	4231.85	4395.06	4776.95	4663.03	4522.24	5343.03	5579.10	5340.24	4539.45	4018.83	3832.14
14*	3101.25	2704.99	4602.52	4901.16	5217.72	5106.43	5105.00	5049.23	5332.29	4865.89	4868.28	4928.97	3862.27	3626.31	3468.48
15*	107.52	129.38	3558.31	4275.50	4213.32	4186.45	4141.41	4162.61	4907.82	5330.61	5312.99	5214.74	5072.75	4355.70	4071.06
16*	930.50	4419.74	4561.42	4325.20	4127.33	3952.90	3517.41	3596.86	4680.60	4934.78	4464.60	4097.95	3378.09	2677.13	2683.87
66	2290.55	5019.73	5317.12	4927.87	4873.25	4748.01	4494.14	5051.12	5515.04	4807.01	4673.65	4288.24	4066.09	3554.94	3458.57
102	1581.50	3521.80	4877.14	4697.03	4734.03	4718.28	4375.77	4006.64	4133.66	4539.39	5473.56	5329.75	4267.19	3681.68	3558.50
111	2283.99	2292.69	3480.27	3647.82	4072.51	4164.85	3746.14	3306.67	3399.49	4564.82	4377.68	4026.10	3412.81	2982.39	2622.39
112	2042.58	3087.98	4959.43	4856.03	4639.60	4522.55	4615.94	3334.69	4831.27	5698.02	5153.42	4854.71	4181.84	3780.55	3530.94
113	2729.35	2504.68	5196.54	5326.63	5084.50	4695.06	4506.53	4330.41	5512.10	4817.24	4470.57	4267.24	3845.17	3366.72	3469.16
114*	1568.85	3275.34	4713.63	4355.74	4091.38	3567.78	3119.74	4358.75	4375.28	4066.09	3756.03	3351.55	2781.16	2241.67	1819.54
206	1181.56	2071.13	4630.84	5060.99	4955.54	5390.71	5336.65	5294.83	5676.97	5838.95	5984.60	5874.18	5323.22	4682.00	3647.27
213*	1169.85	2318.07	4191.16	4021.94	4363.63	4226.07	4126.70	4103.57	3857.18	4872.53	5084.50	4743.33	3796.69	3510.26	3458.34
Mean	1827.60	3007.99	4379.69	4496.97	4500.85	4466.27	4287.86	4196.31	4744.36	4963.23	4855.97	4618.44	3948.91	3483.16	3439.29
St. Dev.	911.35	1250.87	697.96	452.67	407.07	518.88	670.72	797.04	698.62	526.09	647.82	777.43	859.57	934.15	826.65

*Minority Subjects; (--) Concentration not obtained

Table H22. DHEA-S concentrations (ng/ml) for young men during DHEA Treatment

Subject	Time (h)														
	0	1	2	3	3.5	4.5	5.5	7	8.5	10	11.5	12.5	16	20	23
33	1722.76	2168.21	4262.94	4750.70	4778.48	4496.02	4258.79	4114.99	4993.65	4966.87	4578.61	4080.87	3762.59	3378.96	3363.24
34	1825.37	2484.42	4377.42	4639.74	4531.68	4450.25	4197.25	4672.89	5484.09	5283.25	5186.68	5221.15	5019.19	4429.54	4329.29
35	1128.46	1980.45	4406.92	4827.07	4667.66	4927.35	4445.53	4461.02	5376.58	5405.53	5058.62	5144.56	4547.18	4129.49	4235.50
36	1760.77	2146.59	4076.10	4933.50	4778.48	4808.37	4415.13	4244.25	4694.76	5329.84	5034.01	4832.84	4083.04	3875.24	3579.87
37	2864.15	5162.16	5227.79	4964.76	5001.09	4971.21	4648.25	4667.09	5553.77	5477.73	5321.40	5205.06	4504.53	4158.84	4144.84
38	3381.27	4719.78	5480.26	5612.65	5431.54	5473.27	5263.56	4956.72	5572.91	5659.90	5617.97	5286.43	3816.46	3859.96	4622.75
39	1801.91	1722.96	3512.77	4093.43	3796.80	3327.08	2949.75	2919.52	4146.28	3711.09	3655.92	3611.47	3082.98	2758.80	2746.51
41	2002.99	2824.91	5079.71	4957.77	4652.08	4421.23	4414.25	4441.60	4991.54	4729.31	4489.00	4481.38	3982.44	3696.32	3514.18
42	3996.19	3920.89	5322.73	5647.14	5772.23	5929.21	5834.98	5854.90	5898.94	5938.59	6378.09	6237.26	5761.24	5287.61	5431.77
43	3361.53	3470.18	5905.56	6087.81	6096.44	5979.95	5704.27	5726.20	6377.39	6430.98	6056.73	6069.31	5383.28	5081.24	5115.08
44	2793.43	3265.67	4075.12	4631.29	4553.52	4773.39	4855.45	4500.81	5502.82	5331.78	5332.81	5179.48	5062.84	4578.43	4262.94
45	4339.05	5819.04	5964.15	5721.49	5947.06	6048.46	5565.20	5759.47	6041.77	5925.47	5611.21	5497.78	5360.30	5015.87	5086.90
46	4575.69	4545.89	5847.97	5954.06	5915.38	5887.14	5892.70	5722.64	6019.10	6369.10	6258.56	6138.53	5603.71	5553.64	5530.96
47*	1571.67	3300.52	4383.35	4426.06	4331.83	4533.75	4319.51	4061.66	4609.11	5116.98	5108.44	4851.21	4284.27	3818.97	3773.30
48*	2588.04	2788.91	5361.35	5873.36	5555.29	5575.98	5536.70	5291.73	5267.20	6248.91	6243.35	5696.21	5614.53	5276.04	5149.05
140	2780.49	2540.38	3573.15	4329.30	4549.55	4783.19	4707.24	4637.28	4376.84	5040.10	5630.73	5388.79	4207.53	3348.26	3472.90
145	2825.51	3093.88	4509.63	4899.86	4728.79	4771.30	4812.22	4532.53	5212.76	5278.65	5107.97	4957.18	4377.65	3951.25	3831.28
146*	1951.49	4236.30	4758.55	4341.87	4378.39	4335.60	3949.48	3890.45	4119.76	4596.09	4666.24	4363.06	3517.33	3472.96	3690.13
245*	2426.61	3717.40	4599.18	4661.56	4682.52	4515.95	4142.62	4196.52	4788.93	4814.82	4788.23	4434.04	4254.96	3618.20	3417.64
Mean	2615.65	3363.61	4774.98	5018.60	4955.20	4947.83	4732.26	4665.91	5212.01	5350.26	5269.71	5088.24	4538.21	4173.14	4173.59
St. Dev.	958.25	913.91	763.29	679.23	691.47	688.81	699.25	735.52	720.01	665.35	659.77	674.26	760.37	818.62	837.37

*Minority Subjects

Table H23. DHEA-S concentrations (ng/ml) for older women during DHEA Treatment

Subject	Time (h)														
	0	1	2	3	3.5	4.5	5.5	7	8.5	10	11.5	12.5	16	20	23
17	121.84	5792.48	6445.03	6166.27	5778.57	5715.85	5629.33	5271.49	5751.46	5644.49	5240.00	5018.57	4536.98	4033.42	3720.38
18	180.37	3043.01	4026.06	4298.86	4320.04	4286.80	4208.89	4697.58	5315.24	5292.53	5059.99	4949.81	4322.56	3824.71	4081.88
19	361.37	497.75	4574.12	5214.80	5140.44	4925.67	4657.31	4584.49	5699.35	5377.44	5042.21	4715.78	4240.10	3692.41	3614.26
20*	99.53	97.44	184.30	1863.00	2336.10	3659.94	3825.92	3067.18	3955.03	3966.02	3751.85	3643.15	2399.28	1951.82	1803.52
21	260.44	3223.54	4194.94	4059.93	3422.10	3307.58	3019.30	2654.22	2740.75	4234.94	3649.26	4000.12	2824.95	2240.26	2260.19
22	264.45	298.48	2327.44	4609.69	4832.20	4799.79	4606.77	4276.73	5580.10	5583.18	5268.23	4964.88	4104.40	3229.59	3135.66
23	343.43	4603.42	5609.99	5460.35	5480.19	5248.80	4968.73	5003.72	5527.68	6307.66	5932.45	5788.61	4946.71	4269.96	4439.95
24	112.28	2935.13	4309.74	3582.01	3483.33	3131.58	2961.77	3891.18	4512.49	4002.16	3770.29	3592.47	2818.21	2222.09	1922.62
25	140.81	260.76	4166.62	4387.47	4338.85	4471.34	4211.07	4687.98	5868.33	5909.52	5864.12	5815.66	5183.90	4672.92	4455.67
26	111.79	1954.40	4326.42	4251.75	4494.48	4186.94	3941.35	4149.64	4779.57	4642.48	3961.29	3497.52	3222.42	2637.76	2352.57
27	76.92	105.26	2384.53	3313.02	3145.41	3210.05	2956.66	2666.13	2719.65	4031.23	4258.12	3925.78	3284.62	2997.72	2638.98
28	65.11	145.14	3383.52	3719.99	3518.97	3297.81	2918.29	2666.44	3658.99	4684.30	4252.82	4019.79	3124.83	2686.68	2457.31
29*	58.13	2823.51	6571.84	6335.96	6247.64	5709.68	5622.24	5227.83	5235.92	6158.01	5450.42	5103.53	4037.47	3586.03	3391.04
30*	170.10	1012.90	4615.60	4078.22	4016.39	3872.49	3772.68	3372.82	4361.77	4995.75	4674.37	4611.32	3779.62	3072.95	3070.47
31*	66.87	1340.11	3175.10	5051.77	3447.75	3310.82	3102.13	3041.45	4186.57	5162.93	4980.18	4565.25	3420.87	2923.71	2509.30
120	271.88	349.90	3023.80	3430.33	3558.06	3844.00	3515.19	3260.65	4534.18	4688.42	4370.71	4224.41	3614.95	2984.55	2730.11
Mean	169.08	1780.20	3957.44	4363.96	4222.53	4186.20	3994.85	3907.47	4651.69	5042.57	4720.39	4527.29	3741.37	3189.16	3036.49
St. Dev.	100.65	1779.27	1594.02	1126.80	1061.46	882.79	914.25	948.85	1013.36	764.74	743.31	727.70	793.48	773.93	845.04

*Minority Subjects

Table H24. DHEA-S concentrations (ng/ml) for older men during DHEA Treatment

Subject	Time (h)														
	0	1	2	3	3.5	4.5	5.5	7	8.5	10	11.5	12.5	16	20	23
49	2011.37	2542.59	5681.88	5420.19	5418.96	5550.57	5243.27	5420.19	5336.52	5343.81	5423.28	5349.77	4728.20	4423.36	4237.24
50	480.16	4091.71	5812.83	5522.32	5290.99	4837.72	4713.69	4221.58	4499.53	4996.13	4645.99	4460.10	3625.65	3321.06	3071.82
51	274.16	3375.11	5167.89	5600.90	5460.99	5737.79	5676.99	5443.59	5133.49	5408.01	5287.63	4802.98	3948.40	3806.60	3905.13
52	652.00	693.80	2486.11	4587.60	4684.31	4261.42	4128.08	3887.39	4952.43	5349.83	5238.75	5009.05	4465.20	3982.26	4143.46
53	395.63	2766.99	4649.39	4938.00	4826.86	4339.43	4357.24	3820.34	5297.28	5214.97	4889.50	4517.82	4074.02	3561.17	3077.79
54	605.31	2028.68	4731.77	4691.29	4641.05	4126.89	4004.42	3084.44	3656.85	5447.80	4244.02	4609.26	3845.05	2757.20	2345.10
55	2896.76	1304.77	2423.53	4148.95	5386.44	5542.81	5552.54	5643.44	5831.56	6257.69	6396.14	6311.46	5663.26	4821.22	4190.19
56	79.55	84.00	2155.24	3810.92	3716.97	3577.63	3231.72	3453.85	4529.75	4191.25	3822.84	3482.40	2952.37	2249.37	1746.59
57	789.59	923.07	1291.20	2742.64	2928.54	3205.76	3238.72	3213.85	4175.34	4800.21	4527.95	4219.95	3825.99	3291.99	2766.10
58	38.42	55.08	455.14	2319.86	2905.20	2932.30	2523.18	2678.72	3911.44	3593.39	3104.44	2786.93	2066.65	1310.76	1488.69
59	1555.76	3199.95	4455.97	4510.03	4417.36	4429.31	4031.70	4189.93	4779.56	4810.34	4677.61	4620.79	3601.28	2835.51	2921.58
60	1546.76	3086.77	4742.69	4623.06	4770.82	4649.23	4417.02	4474.12	5298.64	5219.07	5148.68	5104.32	4368.90	4193.32	3999.71
61*	376.40	688.41	2121.32	3458.30	3393.55	3181.05	2950.24	2893.79	3509.85	4117.44	4414.19	4138.61	3807.03	3461.84	3230.89
149	528.98	518.40	3952.07	4177.07	4242.80	4190.30	3992.87	3802.71	5022.39	5000.67	5065.28	4878.98	4009.79	3688.92	3593.81
160	465.26	403.48	3668.11	4668.20	4893.71	4748.37	4782.47	5067.67	6355.67	6177.27	5924.54	5915.32	5508.65	4868.62	4972.39
Mean	846.41	1717.52	3586.34	4347.96	4465.24	4354.04	4189.61	4086.37	4819.35	5061.86	4854.06	4680.52	4032.70	3504.88	3312.70
St. Dev.	802.97	1358.60	1655.18	951.15	864.94	872.09	930.53	961.68	791.07	712.12	810.10	869.53	892.17	954.11	973.18

*Minority Subjects

Table H25. DHEA-S concentrations (ng/ml) for young women during Alprazolam/Placebo Treatment

Subject	Time (h)														
	0	1	2	3	3.5	4.5	5.5	7	8.5	10	11.5	12.5	16	20	23
1	2061.79	1995.15	2097.42	2246.69	2211.64	2252.65	2289.14	2288.40	2242.68	2241.68	2248.64	2228.25	1887.62	2007.39	1982.23
3	1714.60	1698.40	1677.88	1641.12	1643.03	1498.23	1404.60	1371.52	1527.86	1594.04	1529.16	1320.97	1069.87	1251.88	1497.81
4	1735.08	1802.31	1909.50	1833.37	1738.87	1634.57	1744.26	1692.47	1527.96	1629.14	1636.10	1468.93	1280.36	2336.05	1461.19
5	2459.01	2173.15	2133.87	2204.98	2025.91	1863.12	1679.36	1753.53	1692.02	1476.49	1834.57	1636.85	1643.61	1716.92	2300.18
7	1196.47	1130.03	1214.14	1254.50	1265.97	1076.50	990.87	944.37	924.08	1280.04	959.84	843.38	930.04	642.41	783.90
8	1159.47	1500.69	1122.34	1435.99	1224.71	1089.26	995.85	884.28	956.21	967.88	1216.37	1053.19	907.04	972.26	1049.40
9	1003.83	862.76	945.98	831.94	900.66	970.07	752.57	767.87	787.98	802.91	863.65	846.36	659.40	592.60	805.63
10	4277.36	4029.21	4149.68	4160.18	3993.99	3817.92	3765.67	3493.60	3462.40	3395.77	3701.24	3642.78	3294.25	3875.84	4035.03
11	1880.31	1993.89	2000.90	2182.16	2042.47	1976.43	1881.35	1859.98	1845.94	1949.76	2194.47	2172.47	1603.49	1659.64	1740.10
12	2337.87	2367.92	2483.60	2663.26	2678.41	2392.99	2067.44	2308.39	2253.34	2059.28	2182.87	2014.55	2049.45	1421.54	1555.03
14*	2376.78	2152.20	2005.96	2217.04	2212.34	2035.98	1921.01	1742.47	1727.90	1651.68	1934.58	1821.84	1560.61	1693.08	2268.42
15*	153.78	113.91	111.19	134.61	114.90	106.42	116.61	101.37	99.42	118.77	127.55	119.92	94.55	97.85	117.94
16*	725.89	872.50	893.03	885.76	836.52	828.96	731.65	793.86	783.57	779.54	853.64	831.33	582.60	557.72	565.21
66	2852.12	3158.47	3332.17	2836.84	2818.89	2698.87	2660.50	2516.73	2422.23	2594.06	2606.33	2479.57	2486.52	2261.29	2708.20
102	1426.02	1430.33	1542.02	1609.33	1680.79	1539.73	1500.34	1339.28	1380.28	1491.11	1669.06	1426.00	1420.35	1120.78	1333.98
111	2448.88	1940.51	1988.31	1906.03	1853.74	1797.95	1717.10	1577.43	1545.87	1472.83	1483.91	1366.92	1171.31	1468.64	1707.86
112	1875.48	1939.43	1972.56	1853.47	1849.51	1962.16	1629.23	1738.47	1287.77	1767.40	2253.65	1849.12	1603.75	1480.82	1700.13
113	2530.87	2347.99	1902.02	2022.59	2074.37	1916.20	1858.13	1867.60	1887.75	1824.05	1893.42	1934.04	1609.09	2180.01	2089.67
114*	729.63	730.01	727.71	635.55	648.49	596.43	612.03	603.21	667.93	593.99	644.45	518.60	553.49	451.92	614.41
206	1297.02	1329.54	1457.22	1420.80	1566.83	1416.95	1421.24	1239.43	1243.47	1213.34	1238.94	1194.21	1080.53	911.45	971.83
213*	1195.68	1112.82	1008.32	1070.96	1030.33	937.51	920.41	976.61	962.80	962.69	1104.27	1164.34	981.96	937.26	1260.86
Mean	1782.76	1746.72	1746.47	1764.15	1733.92	1638.52	1555.21	1517.18	1487.12	1517.45	1627.46	1520.65	1355.71	1411.30	1549.95
St. Dev.	908.78	862.02	889.61	871.25	844.68	808.50	796.34	762.62	738.07	724.99	785.63	769.98	712.49	844.19	863.72

*Minority Subjects

Table H26. DHEA-S concentrations (ng/ml) for young men during Alprazolam/Placebo Treatment

Subject	Time (h)														
	0	1	2	3	3.5	4.5	5.5	7	8.5	10	11.5	12.5	16	20	23
33	2418.52	2473.20	2680.57	2543.04	2560.54	2372.71	2288.74	2376.40	2327.23	2211.43	2359.67	2231.67	2166.72	2039.57	2274.81
34	1712.63	1701.09	1689.41	1631.01	1812.77	1634.61	1611.46	1583.63	1836.75	1614.12	1757.32	1874.42	1673.61	1467.13	1504.63
35	1008.89	958.90	926.08	1003.32	1074.02	908.38	902.11	783.30	769.12	815.90	877.03	851.98	956.37	743.04	829.25
36	1683.73	1684.28	1729.62	1809.43	1960.40	1642.18	1573.74	1538.54	1632.91	1589.51	1676.24	1659.78	1428.41	1415.78	1553.24
37	2905.07	3105.22	3166.98	3184.95	3163.66	2997.25	2913.66	2892.56	2834.24	2857.44	2912.20	2645.68	2492.74	2277.12	2812.71
38	4152.13	4233.57	4381.92	4313.47	4354.70	4105.48	4047.54	3916.93	3776.75	3832.21	4536.96	4128.74	3269.78	3123.25	3918.93
39	2179.60	2025.17	2040.69	1996.74	1957.29	1829.35	1934.48	1880.25	1781.89	1917.29	1988.04	1897.74	1697.12	1723.45	1842.73
41	1823.36	1831.00	1997.09	1981.50	1957.84	1802.58	1704.52	1690.68	1783.43	1809.09	1954.93	1832.22	1693.78	1703.43	1993.49
42	3629.84	3443.68	3634.16	3604.67	3656.67	3480.39	3249.80	3289.94	3306.30	3253.62	3554.38	3393.03	3313.34	3463.48	3414.36
43	2887.92	2811.66	2998.42	2982.81	2992.21	2714.60	2673.61	2638.71	2697.75	2960.72	3087.00	2786.20	2594.20	2345.56	2505.86
44	2670.21	2881.77	2681.67	2860.75	2633.58	2513.38	2619.58	2648.61	2614.41	2617.73	2868.11	2729.73	2620.27	2754.65	2640.50
45	3351.60	3339.31	3268.22	3271.80	3139.29	3282.84	3103.45	3742.80	3259.77	3237.64	3271.44	3237.05	3376.85	3005.05	2973.09
46	4553.63	4235.50	4430.57	4325.81	4386.16	4181.96	4263.53	4245.05	4191.39	4213.75	4194.03	4197.40	4045.83	4166.13	4406.23
47*	2188.92	2296.25	2086.18	1989.48	1971.91	1853.55	1763.56	1813.71	1879.16	1842.64	1919.60	1898.49	1811.06	1768.84	1904.45
48*	2992.93	3080.66	3026.37	3172.87	2911.82	2821.78	2828.17	2835.78	2835.78	2786.43	3100.01	2835.83	2506.13	1583.22	2694.04
140	3037.02	2715.61	2782.87	2958.38	2693.29	2755.40	2477.34	2708.90	2558.15	2726.92	2715.41	2746.72	2365.73	2148.58	2284.29
145	2914.49	2910.15	3229.85	2963.30	2999.75	2880.11	2850.94	3169.36	2775.52	2728.72	3059.51	3084.06	2923.26	2742.13	2934.38
146*	2123.10	1994.98	2116.37	2041.96	1994.98	1927.28	1735.02	1879.95	1809.12	1968.39	1972.14	1856.14	1796.54	2022.36	2478.20
245*	2603.68	2792.89	3015.54	2913.19	2872.91	2789.70	2677.63	2527.66	2565.29	2752.44	2916.03	2797.84	2567.61	2417.71	2261.13
Mean	2675.65	2658.68	2730.66	2713.08	2689.15	2552.29	2485.20	2534.88	2486.05	2512.42	2669.48	2562.35	2384.18	2258.45	2485.60
St. Dev.	873.55	850.80	899.35	879.48	859.06	860.73	857.36	901.23	822.74	832.97	906.19	850.83	780.74	814.74	847.33

*Minority Subjects

Table H27. DHEA-S concentrations (ng/ml) for older women during Alprazolam/Placebo Treatment

Subject	Time (h)														
	0	1	2	3	3.5	4.5	5.5	7	8.5	10	11.5	12.5	16	20	23
17	288.43	301.13	320.98	278.06	365.78	281.23	279.16	199.21	254.76	239.27	217.44	238.33	202.55	223.29	267.24
18	244.79	209.65	243.57	220.27	203.66	217.92	212.53	183.82	177.82	177.97	225.21	177.18	183.92	146.14	187.12
19	377.72	374.61	316.02	277.96	279.14	263.00	299.03	226.30	301.44	223.14	234.55	216.91	168.72	202.89	153.19
20*	90.55	102.33	128.99	90.13	82.26	70.48	72.96	70.38	70.45	76.28	88.28	74.33	64.18	64.30	71.91
21	573.04	558.60	565.30	597.22	540.31	459.15	335.26	463.73	407.35	398.02	489.43	470.61	406.76	459.59	549.42
22	307.62	408.47	1146.66	293.93	255.57	240.87	245.81	231.54	334.55	216.39	286.34	226.33	170.62	233.71	283.63
23	340.50	325.71	325.05	321.54	325.71	315.57	394.29	295.41	295.77	291.19	353.57	299.51	233.96	244.66	239.15
24	107.98	114.03	121.54	110.08	128.81	104.15	98.71	96.33	100.73	98.11	110.23	108.58	87.10	88.58	102.55
25	334.27	348.42	316.94	377.23	355.29	353.02	301.99	302.39	266.01	292.74	302.41	251.98	228.42	189.76	225.46
26	123.38	106.96	139.86	123.40	112.43	118.27	106.58	108.50	103.01	134.25	119.35	107.07	91.04	95.83	89.01
27	75.65	79.85	81.80	60.07	67.22	67.74	61.57	61.94	55.51	58.52	62.69	67.55	52.09	71.75	83.74
28	84.20	66.85	68.45	67.21	67.59	57.74	57.92	60.44	53.03	56.95	61.60	54.59	52.28	54.45	64.57
29*	62.92	60.57	70.18	71.25	74.70	67.13	69.22	56.34	55.24	60.32	63.29	64.75	58.54	63.88	57.23
30*	259.37	204.26	228.24	234.87	215.55	196.18	203.27	202.78	180.53	183.80	192.11	159.10	144.22	148.93	165.87
31*	66.46	67.35	75.09	69.02	70.50	67.17	67.71	62.31	65.97	69.52	73.11	68.63	65.46	66.94	72.20
120	362.05	419.14	407.05	345.20	342.89	315.53	312.30	326.41	299.16	279.80	279.74	255.17	226.18	224.57	288.18
Mean	231.18	234.25	284.73	221.09	217.96	199.70	194.89	184.24	188.83	178.52	197.46	177.54	152.25	161.20	181.28
St. Dev.	149.66	158.06	270.34	150.01	141.96	125.31	117.21	120.32	119.46	104.95	124.79	113.28	96.27	106.07	128.65

*Minority Subjects

Table H28. DHEA-S concentrations (ng/ml) for older men during Alprazolam/Placebo Treatment

Subject	Time (h)														
	0	1	2	3	3.5	4.5	5.5	7	8.5	10	11.5	12.5	16	20	23
50	596.40	522.39	529.86	473.23	538.89	513.81	559.40	510.91	447.91	475.14	425.37	529.10	442.52	426.19	457.59
51	193.30	213.38	207.04	204.04	191.40	201.10	214.93	191.65	176.72	221.90	170.03	181.19	161.62	186.11	213.29
52	1138.96	843.95	1016.54	906.74	880.38	936.19	716.41	762.80	823.31	759.92	777.02	874.81	678.42	761.79	844.65
53	441.57	417.48	430.70	410.37	438.29	428.56	343.74	308.52	328.40	326.67	398.47	410.35	331.69	333.48	288.17
54	753.07	762.90	925.86	544.06	749.64	689.44	805.52	567.06	594.12	668.98	620.00	671.99	510.86	437.83	649.27
55	2065.51	2113.87	2031.03	1981.77	1844.30	2140.81	1914.21	1844.10	1952.32	1522.79	1904.24	1585.79	1438.94	1433.35	452.52
56	86.49	73.91	76.91	71.89	76.16	66.47	67.45	61.50	66.50	73.69	72.55	67.64	67.96	67.10	71.85
57	695.56	619.29	658.64	605.48	631.74	636.98	639.78	601.08	603.53	593.61	548.64	574.23	473.38	571.16	569.29
58	51.91	62.32	57.48	50.73	53.20	52.19	52.24	53.08	58.94	52.17	60.27	55.44	52.67	52.69	59.11
59	1513.46	1519.51	1559.71	1480.08	1107.75	1611.84	1422.77	1381.70	1348.29	1432.84	1404.69	1383.99	1062.81	1223.99	985.30
60	1765.57	1775.37	1880.96	1777.38	1687.65	1652.76	1499.59	-	1551.04	1656.03	1589.07	1496.27	1297.25	1418.27	1663.45
61*	552.54	720.99	598.47	492.06	443.37	479.27	472.32	460.27	489.52	498.12	475.59	500.07	344.77	397.17	439.43
149	658.79	612.54	559.65	584.49	571.56	588.17	540.28	572.81	575.88	529.33	523.78	561.23	447.40	462.31	495.42
160	824.33	852.00	884.97	861.60	807.13	852.70	783.72	771.88	797.36	813.38	861.64	845.23	630.53	652.69	703.34
Mean	809.82	793.56	815.56	745.99	715.82	775.02	716.60	622.10	700.99	687.47	702.24	695.52	567.20	601.72	563.76
St. Dev.	611.31	614.80	625.19	603.75	536.50	623.82	550.05	506.51	561.97	515.52	563.65	497.02	427.89	457.89	414.35

*Minority Subjects

-Concentration not obtained

Table H29. DHEA-S concentrations (ng/ml) for young women during Alprazolam/DHEA Treatment

Subject	Time (h)														
	0	1	2	3	3.5	4.5	5.5	7	8.5	10	11.5	12.5	16	20	23
1	1849.11	4508.51	4698.79	4494.31	4412.69	4142.40	3906.38	4185.75	4917.63	4939.01	4155.00	4180.90	3522.72	2806.55	2872.66
3	1767.33	2454.02	4274.01	5082.14	4762.40	4833.27	4587.02	4456.75	5142.16	5392.11	5546.11	5436.74	4588.70	4274.94	4139.58
4	1561.92	1473.73	2860.81	4104.10	4007.51	3998.25	4550.58	3827.10	3492.08	4227.93	4849.88	4501.96	3738.84	3481.74	2954.55
5	1711.65	4722.80	5093.87	4696.06	4121.97	3517.12	2994.00	2679.89	3068.38	4002.21	4266.44	3831.93	2733.98	2307.86	2286.57
7	1075.78	3340.35	4094.40	4258.60	3547.50	3446.84	2916.16	2757.93	4092.67	3845.90	3159.21	2895.40	2374.10	2075.20	2000.74
8	769.23	2526.09	4350.14	4362.63	3855.63	3393.41	3011.97	2410.38	2874.05	4147.04	3393.63	3033.11	1903.06	1434.61	1839.89
9	904.95	1027.18	4617.97	4977.52	4945.36	4749.60	4893.07	4728.45	4660.92	4565.59	5246.38	5698.49	5255.32	4841.65	4533.55
10	4008.76	3958.65	5311.60	5462.73	5306.43	5273.54	5089.13	4989.74	5672.88	5525.43	5786.43	5227.01	4854.09	4533.93	4392.35
11	2001.55	2184.68	4567.64	4732.02	4730.31	4734.41	4698.51	4489.55	5567.99	5508.71	5391.40	5450.72	4879.08	4385.02	3773.06
12	2571.61	3006.10	4458.17	5098.63	5155.81	5242.25	4752.94	5036.12	5370.93	6206.49	5953.11	5371.69	4867.89	4101.59	4144.60
14*	2810.67	2706.64	2821.90	3547.93	3899.51	5339.71	5249.21	4471.52	5562.17	4978.86	4980.12	4749.49	4424.02	4104.11	3896.04
15*	180.46	1610.95	4510.45	4728.54	4850.32	4528.78	4129.81	4388.97	4264.04	5504.86	5275.39	5386.40	4795.91	4103.56	3893.10
16*	645.06	4106.54	4093.57	3720.96	3509.24	3143.18	2868.17	3021.78	4160.24	3982.83	3598.89	3290.70	2285.29	1849.01	1962.45
66	2250.83	2536.42	4975.98	4877.61	4766.36	4665.22	4384.77	4054.00	4245.06	5030.28	5229.43	5163.72	4438.25	4015.27	4114.68
102	1653.13	1899.55	3406.84	4091.10	4531.64	4442.24	4431.83	4015.63	4042.48	4492.10	5856.18	5743.49	4626.42	3982.84	3594.13
111	2123.64	2106.77	3758.91	4199.77	4046.28	3924.71	3488.79	3236.54	4138.35	3996.87	3731.02	3492.14	2701.17	2327.90	2198.87
112	1650.43	1830.28	4311.88	4721.53	4551.18	4650.94	5112.03	4523.66	4401.44	4293.32	4988.54	4803.28	4443.16	3982.33	3475.07
113	2543.77	2591.22	2664.21	2686.49	2507.97	2468.04	2249.88	1992.92	2151.41	1913.35	2306.94	2151.47	2357.32	1497.46	2129.09
114*	714.54	1341.41	4507.49	4462.97	4234.96	4051.93	3392.56	3647.56	5066.06	4671.20	4294.42	3821.06	3032.97	2419.61	1792.59
206	1796.83	2777.41	5130.89	5107.78	5288.11	5190.88	5036.27	5287.30	5742.59	5544.76	5228.66	5221.05	4696.64	4365.40	3923.89
213*	1273.51	995.73	4302.21	4456.20	4516.65	4286.45	4265.84	4037.13	4048.91	5359.09	4990.14	4875.90	4316.99	4049.22	4062.73
Mean	1707.85	2557.38	4229.13	4469.98	4359.42	4286.82	4095.66	3916.13	4413.45	4672.76	4677.49	4491.75	3849.33	3378.09	3237.15
St. Dev.	869.80	1081.43	750.00	625.92	674.77	770.92	892.56	915.50	972.19	918.01	983.28	1044.56	1074.27	1102.02	962.46

*Minority Subjects

Table H30. DHEA-S concentrations (ng/ml) for young men during Alprazolam/DHEA Treatment

Subject	Time (h)														
	0	1	2	3	3.5	4.5	5.5	7	8.5	10	11.5	12.5	16	20	23
33	2363.78	2345.92	3035.41	5976.87	5916.99	5985.98	5572.36	5083.77	5547.19	5677.28	5488.53	5176.80	4409.48	3842.71	3790.25
34	1418.08	4057.43	4545.44	4482.29	4414.56	4286.92	4163.08	4192.94	5098.23	5527.90	5422.83	5468.92	4988.38	4533.11	4376.16
35	1022.55	3938.98	4607.71	4189.08	4312.21	4211.70	3963.06	3646.65	3867.27	4224.58	5235.42	4855.65	4216.14	4456.32	3575.64
36	2231.81	3910.91	4708.02	4866.70	4936.17	4612.36	4498.26	4198.48	4530.07	4711.95	5308.62	5088.51	4499.28	4123.35	3932.68
37	3334.14	3346.81	4987.07	5036.73	4954.57	4657.61	4398.68	4248.32	4081.67	5123.48	4919.30	4844.02	4023.00	3666.63	3660.34
38	4334.59	5633.15	6023.85	5774.49	5639.31	5425.41	5331.32	4717.89	5142.02	5517.13	5353.52	5224.95	4467.39	4548.88	4560.50
39	2587.39	4534.00	4272.02	3593.60	3372.55	3190.79	2907.48	2616.47	3168.18	4097.69	3856.90	3689.13	2972.96	2732.29	2947.75
41	1921.08	4137.05	4684.20	4585.02	4466.72	4160.50	3921.55	3542.75	4417.48	4547.40	4215.57	4318.64	3565.76	3084.55	3021.37
42	3698.25	4498.39	5458.07	5734.97	5763.50	5906.96	5434.11	5221.47	5379.26	5247.99	6378.17	6390.84	5515.96	5527.57	5284.23
43	3474.75	3682.57	5135.82	6029.57	5405.48	5638.38	5682.41	5364.14	6146.18	6603.58	6319.66	6166.83	5740.28	5837.35	5696.18
44	2934.23	4213.53	5102.37	5298.89	5260.74	5137.73	4963.34	4973.64	5316.04	5454.39	5548.16	5561.51	5316.48	4763.98	4579.95
45	3783.99	5121.92	5537.92	5628.92	5431.84	5300.85	5359.85	5176.47	5075.71	5743.59	5745.34	5515.40	4875.30	4611.07	4769.72
46	4772.28	4869.20	5647.01	5958.38	5758.98	5903.47	5751.18	5640.88	6034.09	6386.97	6313.49	6332.80	5840.33	5682.69	5577.57
47*	1949.34	3969.28	4995.24	4605.97	4528.32	4195.39	4102.09	3959.06	4599.80	4749.29	5204.51	5110.97	4628.55	4138.90	4091.19
48*	2853.42	5630.77	5898.57	5705.66	5269.54	5270.50	5196.71	4859.99	5623.15	5775.59	5669.35	5566.64	4872.08	4594.29	4665.75
140	2756.01	2559.13	3876.56	4781.08	4855.35	4777.48	4695.12	4790.17	5255.46	5016.32	5259.18	5027.49	4736.26	3879.70	3813.04
145	3198.21	3556.30	4159.40	4630.28	4357.05	4718.00	4818.44	4754.10	5176.65	5974.87	5522.63	5303.87	4453.06	4921.56	4795.35
146*	2572.82	3123.64	4763.67	4926.06	4807.81	4506.93	4093.26	4130.24	4997.53	5250.46	4991.72	5074.34	4384.11	4066.65	4209.13
245*	2864.20	3044.26	3249.88	4061.65	4224.88	4341.30	4527.14	4584.21	5209.11	5009.58	4990.35	4707.77	4468.23	4077.36	3837.22
Mean	2845.84	4009.12	4773.06	5045.59	4930.35	4854.12	4704.18	4510.61	4982.37	5296.84	5354.91	5232.90	4630.16	4373.10	4272.84
St. Dev.	945.20	918.06	811.26	720.22	660.70	738.11	748.01	737.58	733.59	668.46	636.00	653.09	700.81	798.94	766.79

*Minority Subjects

Table H31. DHEA-S concentrations (ng/ml) for older women during Alprazolam/DHEA Treatment

Subject	Time (h)														
	0	1	2	3	3.5	4.5	5.5	7	8.5	10	11.5	12.5	16	20	23
17	126.08	4001.71	4269.73	3847.82	3553.04	3331.16	3094.83	3129.08	5272.24	5303.00	5209.36	5114.00	4031.84	3329.80	3330.90
18	164.10	3256.60	4154.01	3706.55	3526.67	3371.84	3225.81	3602.45	4880.76	5241.22	5069.73	4746.28	4119.74	3383.34	3101.57
19	485.52	1998.09	5191.76	5043.49	4822.85	4833.08	4533.61	3905.58	4382.54	5184.07	4655.14	4838.09	4053.58	3365.55	2937.60
20*	118.88	104.32	1382.54	2988.24	2814.38	2566.29	3009.07	2442.66	4087.98	3169.61	3019.54	2743.87	1876.11	1336.33	1027.06
21	375.72	997.83	3084.20	3820.35	3785.73	3755.88	3820.03	3301.74	3411.54	3729.55	5119.39	4949.43	4319.65	3612.41	3320.56
22	213.81	1573.75	4130.98	4220.13	4256.60	4206.41	3788.87	3412.77	3172.20	3714.36	5544.36	5553.85	4589.77	3690.77	3675.22
23	307.48	3278.51	5589.77	5370.30	5107.75	4903.21	4769.59	4448.61	4747.81	5969.67	5743.74	5556.71	4947.55	4275.10	4331.78
24	144.98	4450.12	4150.64	3828.89	3493.98	3340.16	2991.54	2839.50	3857.56	4909.95	4469.25	4441.00	3282.74	2707.01	2428.25
25	284.38	1425.43	4023.74	4158.65	4327.90	4512.08	3932.13	4278.01	4050.48	5238.50	5761.93	5561.09	5088.83	4561.18	4619.17
26	110.27	3924.43	4683.17	4133.05	4090.94	3879.83	3642.89	3142.42	4325.52	5447.59	5008.39	4681.78	3808.81	3174.43	2825.04
27	69.53	85.85	1144.55	2552.75	2576.75	2384.89	2581.29	2267.10	2479.13	3921.22	4040.95	3622.09	2466.31	1591.83	1387.41
28	61.34	1574.65	5006.92	5188.36	5059.03	4914.92	4534.18	4194.21	4699.11	5147.99	5080.85	4887.88	4265.20	3664.77	3479.14
29*	64.29	3994.32	4850.49	4414.23	4193.54	4023.07	4054.76	3571.68	6001.51	6004.13	5652.72	5474.23	4508.45	3795.87	3551.96
30*	218.24	654.43	2849.39	4318.94	4301.55	4089.09	3711.97	3572.27	4633.71	5218.42	4821.43	4640.91	3852.07	3176.42	3635.17
31*	81.59	627.98	3273.55	3531.38	3233.76	2784.05	2937.28	2710.72	3397.29	3932.16	4427.73	3928.86	3254.90	2203.91	2177.69
120	407.34	566.29	5581.93	5469.96	5226.17	4957.35	4763.21	4418.69	5369.80	5035.29	4958.39	4626.10	4370.40	3711.05	3244.06
Mean	202.10	2032.14	3960.46	4162.07	4023.17	3865.83	3711.94	3452.34	4298.07	4822.92	4911.43	4710.39	3927.25	3223.74	3067.04
St. Dev.	133.57	1540.37	1328.18	816.19	798.95	847.85	696.28	682.63	905.37	851.98	702.56	763.84	853.39	880.02	949.73

*Minority Subjects

Table H32. DHEA-S concentrations (ng/ml) for older men during Alprazolam/DHEA Treatment

Subject	Time (h)														
	0	1	2	3	3.5	4.5	5.5	7	8.5	10	11.5	12.5	16	20	23
50	600.26	4061.12	4153.25	3600.69	3468.52	3321.51	3211.98	2794.80	4082.65	4589.17	4971.06	4735.60	3996.25	3410.76	3278.10
51	280.86	3207.69	3813.86	3670.39	3470.44	3318.37	3342.24	3033.03	4497.65	5394.65	5385.25	5089.26	4260.98	4092.43	3790.16
52	687.66	1592.45	5710.69	6274.65	6068.48	5816.81	5388.38	5195.45	5585.10	5653.74	5564.20	5280.81	4932.78	4439.62	4721.78
53	674.58	958.97	4413.86	4619.33	4357.51	4208.54	3951.38	3699.62	5507.96	5768.47	5905.14	5546.40	5016.40	4640.19	4149.60
54	667.93	7939.09	2583.90	3988.58	3493.26	3532.31	3684.14	4016.10	6278.35	5495.00	5269.10	5463.49	4813.95	3729.25	3049.80
55	3068.34	1929.34	2049.34	2235.07	2130.79	2147.84	2294.64	3896.15	5351.07	5159.54	5716.57	5582.09	5131.98	4700.21	4646.31
56	76.78	93.76	2432.50	5685.07	5177.27	5022.18	4506.73	4265.28	4354.13	4029.34	3932.69	3628.64	3465.27	2518.65	1917.27
57	706.03	907.66	4192.73	5478.72	5192.48	5110.34	4847.70	4528.61	5231.50	4877.08	5178.19	4978.46	4177.62	3673.21	3509.27
58	70.67	57.82	166.44	2679.40	3389.83	3335.02	3026.30	3134.76	4785.63	4259.72	3758.26	3551.22	2763.83	2371.93	2227.32
59	1330.87	1339.15	3886.55	3929.28	3453.99	3689.39	3414.51	3082.57	3459.38	4619.62	4535.13	4320.94	3099.55	2603.82	2630.01
60	1577.76	4345.71	4828.27	4660.86	4545.86	4543.04	4283.90	5218.11	5181.34	5046.30	4937.16	4695.26	4306.81	4067.80	3880.64
61*	492.88	473.83	1566.61	2788.59	2967.69	3045.88	3151.99	2920.25	3058.73	4333.29	4247.73	4307.81	3784.99	3338.14	3321.30
149	455.68	3488.71	5392.25	5377.87	5353.98	5124.63	5567.08	5563.70	5509.06	5320.94	4923.93	4786.89	4616.17	4173.98	3963.35
160	437.50	499.80	6474.90	6732.84	6535.70	6442.93	6155.17	6031.27	6443.78	6699.77	6441.00	6361.08	5716.30	5320.63	5296.84
Mean	794.84	2206.79	3690.37	4408.67	4257.56	4189.91	4059.01	4098.55	4951.88	5089.05	5054.67	4880.57	4291.63	3791.47	3598.70
St. Dev.	774.35	2200.87	1743.08	1376.98	1267.84	1198.33	1113.18	1072.13	978.80	712.03	755.08	770.63	824.93	878.45	957.98

*Minority Subjects

Table H33. Cortisol concentrations (ng/ml) for young women during Placebo Treatment

Subject	Time (h)														
	0	1	2	3	3.5	4.5	5.5	7	8.5	10	11.5	12.5	16	20	23
1	12.27	3.03	1.86	13.22	16.86	12.52	10.54	5.98	9.37	8.50	6.98	8.73	1.14	4.37	2.60
3	22.29	10.70	7.44	7.72	4.95	4.72	6.68	9.83	4.38	2.16	2.57	1.51	1.87	16.10	17.37
4	21.84	9.93	10.17	9.91	5.47	4.66	10.93	10.35	5.30	1.71	2.91	2.68	6.49	8.74	20.63
5	22.97	10.13	5.84	3.78	5.20	5.81	8.25	4.36	2.70	6.77	2.94	1.96	1.88	15.12	23.64
7	39.24	27.03	18.87	23.21	20.88	25.24	18.36	19.50	24.00	12.06	14.23	7.19	4.40	22.08	23.63
8	20.63	10.63	19.22	13.31	8.16	5.11	8.74	5.85	8.63	2.20	12.08	4.09	3.44	1.40	10.51
9	31.54	20.51	12.56	11.62	8.76	11.56	10.17	5.49	7.52	14.47	5.48	3.24	0.94	2.80	30.35
10	21.15	4.43	4.56	7.37	5.24	9.62	5.33	3.93	5.01	1.69	2.70	1.18	3.14	6.27	22.79
11	20.94	16.75	22.56	22.11	17.63	16.33	19.00	18.82	12.90	12.13	15.15	9.37	3.80	1.66	22.97
12	18.40	4.81	2.94	4.24	8.94	17.64	18.34	4.92	14.14	12.97	13.60	5.49	1.99	0.80	3.44
14*	24.51	9.97	6.46	7.92	9.65	10.86	6.17	5.18	3.99	2.39	15.17	6.36	4.28	8.32	14.95
15*	20.36	12.86	8.08	6.82	4.51	3.82	5.86	12.18	6.27	3.02	2.89	4.68	2.62	8.69	15.23
16*	1.50	8.87	10.09	10.54	6.25	7.13	4.26	4.00	5.53	9.15	10.12	3.95	0.97	2.89	12.06
66	32.67	17.73	14.30	16.62	16.40	13.10	14.95	9.57	7.75	15.21	6.32	6.25	7.96	9.69	27.40
102	22.44	7.52	4.76	8.62	10.54	6.61	8.45	4.26	7.82	3.95	2.38	1.18	4.30	1.40	14.75
111	19.44	7.94	10.19	26.17	25.97	19.95	4.40	4.07	3.96	10.07	3.81	1.79	3.03	15.66	17.33
112	12.30	23.85	27.76	21.61	21.92	20.16	16.20	16.81	18.24	22.49	13.41	14.09	3.27	1.62	21.27
113	24.55	12.62	5.22	6.85	9.30	13.40	15.36	7.36	6.21	5.80	18.75	9.13	1.43	13.77	20.05
114*	11.12	5.81	4.73	2.76	6.26	4.17	6.62	5.30	6.77	3.53	3.15	3.05	3.25	8.26	12.62
206	32.31	32.77	37.89	39.61	42.91	36.96	37.12	33.13	28.97	35.85	35.34	35.96	17.78	16.91	25.09
213*	20.86	8.01	4.67	3.40	3.59	4.97	3.67	2.23	5.55	4.75	7.79	3.03	4.41	7.10	26.25
Mean	21.59	12.66	11.44	12.73	12.35	12.11	11.40	9.20	9.29	9.09	9.42	6.42	3.92	8.27	18.33
St. Dev.	8.29	7.82	9.19	9.25	9.56	8.40	7.73	7.44	6.85	8.29	7.94	7.54	3.63	6.24	7.37

*Minority Subjects

Table H34. Cortisol concentrations (ng/ml) for young men during Placebo Treatment

Subject	Time (h)														
	0	1	2	3	3.5	4.5	5.5	7	8.5	10	11.5	12.5	16	20	23
33	15.41	8.03	9.14	6.95	10.24	6.14	6.07	3.04	2.42	3.77	5.28	2.66	1.56	2.36	18.39
34	27.02	11.17	17.17	16.72	11.76	11.65	11.40	10.44	7.51	9.99	10.48	8.39	2.44	4.25	19.00
35	14.48	5.78	3.46	4.77	7.35	5.56	2.77	3.51	7.24	2.97	3.21	1.68	1.48	4.20	10.14
36	26.75	21.62	17.57	16.25	18.17	11.63	11.88	15.57	12.20	10.71	13.35	8.97	2.41	9.81	21.71
37	16.69	15.04	19.36	14.75	18.39	14.53	14.32	11.15	12.05	13.49	14.96	9.30	1.81	1.48	32.13
38	29.59	19.70	23.04	19.68	16.84	23.01	19.46	13.01	19.48	14.14	8.23	5.74	4.07	18.39	32.05
39	43.80	22.35	11.75	6.71	9.49	10.62	12.28	10.40	9.51	10.13	7.81	3.68	2.84	6.47	15.08
41	30.77	11.66	8.86	17.16	10.34	12.09	12.21	11.13	18.04	14.92	12.84	6.29	14.20	8.35	31.86
42	3.87	21.04	10.63	17.77	11.70	17.61	11.48	6.15	8.33	6.50	22.17	13.14	3.03	1.93	22.13
43	24.56	12.64	15.18	11.02	6.97	9.90	12.79	13.50	5.70	3.02	2.77	1.24	1.39	15.67	16.23
44	9.69	4.32	1.88	13.19	12.55	8.32	14.32	8.18	12.28	9.64	5.53	3.65	2.48	0.78	6.56
45	24.10	18.99	20.27	11.66	12.07	13.77	16.94	14.01	10.51	5.45	4.08	3.04	1.06	5.34	20.50
46	24.76	10.64	9.66	11.36	8.12	11.08	18.67	14.21	8.57	11.76	14.82	9.11	2.57	15.02	24.72
47*	28.74	5.81	4.12	6.31	14.20	10.04	10.79	4.88	22.94	8.31	2.71	2.03	0.98	12.85	25.16
48*	23.46	10.07	16.73	11.94	9.95	15.30	11.68	4.97	12.61	8.44	6.57	4.85	1.89	10.81	17.94
140	3.82	7.34	13.73	19.76	13.37	13.61	7.67	15.81	9.16	4.96	16.42	7.54	1.50	0.64	6.14
145	26.17	10.39	9.81	8.14	7.03	6.88	5.00	4.18	4.76	8.22	10.86	22.80	8.00	7.43	16.15
146*	21.61	7.54	5.82	4.05	7.78	6.42	4.05	3.45	2.78	1.63	2.67	1.46	0.69	7.56	42.91
245*	31.07	16.20	9.74	8.96	5.73	16.17	10.31	7.17	4.06	4.07	5.92	3.37	6.62	0.80	14.51
Mean	22.44	12.65	12.00	11.96	11.16	11.81	11.27	9.20	10.01	8.01	8.98	6.26	3.21	7.06	20.70
St. Dev.	9.88	5.83	6.00	5.03	3.77	4.41	4.61	4.44	5.55	4.02	5.56	5.20	3.25	5.49	9.33

*Minority Subjects

Table H35. Cortisol concentrations (ng/ml) for older women during Placebo Treatment

Subject	Time (h)														
	0	1	2	3	3.5	4.5	5.5	7	8.5	10	11.5	12.5	16	20	23
17	24.03	8.92	8.23	12.84	9.03	4.91	9.55	6.92	19.57	4.85	2.75	2.07	1.60	11.94	34.42
18	19.67	9.27	10.56	8.26	9.50	15.13	7.01	13.52	10.16	5.95	5.08	4.62	2.44	14.28	11.20
19	27.77	18.71	12.91	15.87	18.55	19.33	11.20	15.66	12.92	6.85	15.33	7.93	3.13	6.52	26.39
20*	21.18	10.59	6.44	6.14	5.20	5.30	9.07	3.66	3.45	2.80	14.35	7.50	2.73	6.86	16.21
21	19.35	16.40	8.68	9.50	18.16	31.60	15.61	8.90	11.59	4.24	19.82	10.64	4.77	5.67	12.64
22	22.12	9.45	10.74	6.62	6.63	7.99	9.16	6.13	7.92	3.98	6.31	10.97	1.07	10.72	21.65
23	24.61	13.06	9.64	8.99	7.68	9.41	12.77	6.43	6.12	7.08	5.34	3.15	2.01	16.96	28.59
24	25.19	10.47	7.41	7.83	7.34	7.15	11.21	7.06	7.80	7.61	10.05	4.31	2.03	8.37	22.12
25	17.90	11.20	13.97	4.97	7.72	10.77	8.24	7.88	6.15	6.38	12.33	6.38	1.52	8.42	28.84
26	23.46	18.28	15.28	11.86	14.35	9.30	13.14	15.78	--	10.15	9.84	8.49	2.28	13.63	14.38
27	27.13	21.89	17.71	13.04	9.95	9.16	13.66	8.86	22.86	14.82	--	13.24	3.79	9.05	27.31
28	19.94	14.13	12.04	14.11	11.02	8.86	15.90	10.98	13.64	14.13	17.96	7.54	9.96	30.07	15.02
29*	16.78	12.27	8.68	9.41	15.28	14.50	13.91	9.19	9.66	6.31	7.67	5.14	8.03	28.80	27.02
30*	13.33	13.33	12.47	13.86	10.93	5.50	6.12	6.13	5.66	5.25	4.07	3.01	1.44	6.89	24.51
31*	7.10	25.30	28.94	19.69	18.57	8.52	29.58	12.09	9.14	7.16	6.23	5.20	16.88	3.42	15.82
120	31.82	22.51	16.15	11.51	11.27	10.03	26.15	12.15	11.38	11.28	9.14	3.83	3.55	3.73	26.80
Mean	21.34	14.74	12.49	10.91	11.32	11.09	13.27	9.46	10.53	7.43	9.75	6.50	4.20	11.58	22.06
St. Dev.	5.95	5.20	5.45	3.92	4.39	6.67	6.42	3.58	5.21	3.48	5.21	3.19	4.17	7.91	6.97

*Minority Subjects

--Concentrations not obtained

Table H36. Cortisol concentrations (ng/ml) for older men during Placebo Treatment

Subject	Time (h)														
	0	1	2	3	3.5	4.5	5.5	7	8.5	10	11.5	12.5	16	20	23
50	12.85	8.91	11.63	10.20	9.31	6.91	10.72	4.29	4.21	10.05	3.69	2.45	3.22	11.30	19.35
51	26.86	8.90	9.08	12.82	7.35	12.40	11.33	9.79	10.88	3.96	2.76	2.87	21.82	22.93	16.89
52	20.04	4.82	10.33	5.64	4.30	4.23	3.72	2.73	3.39	1.42	1.10	0.83	2.12	19.05	23.52
53	16.67	3.98	24.17	20.08	13.13	7.27	7.72	8.77	13.71	8.90	10.76	6.27	1.90	14.18	27.40
54	30.23	12.57	23.44	13.75	10.53	16.34	9.58	20.27	18.35	11.41	7.81	4.12	1.11	12.03	24.56
55	16.20	10.73	11.21	8.59	7.10	12.15	11.34	7.38	3.70	4.96	3.90	6.53	1.03	20.25	14.41
56	21.73	13.69	13.65	12.04	8.63	9.14	8.79	14.44	8.54	7.64	4.27	2.59	1.08	7.16	18.96
57	20.83	13.28	12.61	12.79	10.55	12.57	7.58	9.00	15.24	15.17	12.62	5.10	2.38	16.05	22.13
58	14.16	11.47	8.84	11.38	9.84	14.53	10.47	4.62	7.29	5.84	5.51	3.13	2.38	1.29	27.35
59	21.88	20.20	17.61	17.72	13.41	18.80	12.20	13.91	10.59	14.39	9.85	5.34	1.89	5.13	29.10
60	24.27	19.00	15.10	10.65	9.45	9.14	8.46	15.86	13.86	4.93	2.78	3.80	3.85	6.05	20.65
61*	25.16	19.93	13.24	9.70	10.33	12.62	7.60	6.65	7.95	5.63	10.08	6.49	3.04	17.21	27.68
149	21.04	16.91	10.32	7.49	6.50	6.57	8.08	7.37	8.96	5.42	14.66	7.77	4.52	16.36	27.14
160	19.95	7.50	8.13	6.31	7.74	7.30	10.99	3.69	3.12	5.17	8.83	5.59	4.09	9.77	10.98
Mean	20.85	12.28	13.53	11.37	9.16	10.71	9.18	9.20	9.27	7.49	7.04	4.49	3.89	12.77	22.15
St. Dev.	4.85	5.29	5.05	4.04	2.48	4.17	2.23	5.17	4.79	4.01	4.18	1.97	5.28	6.34	5.54

*Minority Subjects

Table H37. Cortisol concentrations (ng/ml) for young women during DHEA Treatment

Subject	Time (h)														
	0	1	2	3	3.5	4.5	5.5	7	8.5	10	11.5	12.5	16	20	23
1	16.50	4.19	1.76	1.85	13.79	16.07	7.36	3.47	4.25	5.39	10.13	3.80	0.77	1.38	13.09
3	23.45	7.51	4.35	5.00	5.67	8.60	8.24	3.57	4.53	3.99	2.15	1.31	0.73	9.02	20.82
4	15.02	6.57	5.32	8.01	4.79	3.07	5.73	5.29	9.34	2.48	3.46	2.42	1.16	5.82	17.11
5	20.72	11.45	6.79	5.95	3.82	2.51	5.26	7.06	6.16	1.98	2.86	1.97	1.74	4.85	20.22
7	29.50	13.97	9.28	22.10	17.08	10.04	21.42	8.78	10.26	6.16	10.13	8.52	1.93	17.41	23.02
8	18.99	12.29	7.32	10.37	8.31	13.11	7.39	5.70	6.38	6.39	9.13	4.06	2.95	0.68	16.92
9	26.18	12.63	6.98	12.99	14.00	8.74	8.15	4.22	12.47		21.94	10.53	1.17	0.87	19.08
10	27.58	4.21	3.27	3.27	2.10	3.18	7.80	17.53	16.72	5.62	2.67	1.88	1.72	8.65	25.91
11	14.22	15.29	11.75	14.68	17.66	20.96	18.70	17.73	24.54	7.66	6.10	4.25	2.93	1.05	7.51
12	13.14	5.63	4.49	11.22	10.41	11.98	23.60	11.72	13.97	18.09	15.48	6.86	4.04	1.03	0.70
14*	24.72	10.07	13.27	18.41	14.03	6.94	7.27	6.48	6.18	3.61	18.80	11.74	2.38	13.49	21.75
15*	18.70	10.05	7.54	7.82	6.55	6.07	3.27	14.21	5.53	5.17	4.30	3.46	3.31	11.01	20.27
16*	14.04	6.27	6.67	7.51	11.36	12.67	11.51	6.13	7.10	6.47	5.34	2.71	2.04	3.92	18.11
66	30.03	15.79	18.77	12.43	13.44	15.03	14.58	11.06	20.35	30.39	15.13	6.56	6.71	19.90	22.63
102	24.05	12.30	9.51	4.27	11.39	18.11	10.45	3.78	4.15	5.35	8.51	2.03	1.48	0.55	13.78
111	18.21	5.07	4.73	6.04	8.23	3.68	2.39	4.21	6.16	10.06	18.22	13.26	1.47	13.82	18.30
112	31.44	17.81	30.80	24.90	22.12	13.29	16.57	15.48	15.78	15.79	8.20	6.93	5.08	10.29	9.76
113	31.18	12.84	8.94	11.77	12.93	10.97	13.35	5.49	12.64	5.45	3.92	2.41	6.03	2.24	14.48
114*	12.78	7.88	5.66	4.48	3.56	2.66	5.70	4.51	2.78	5.75	6.26	3.15	1.76	16.48	18.06
206	21.44	34.63	32.93	38.92	24.94	24.21	23.84	17.00	23.99	36.20	22.68	11.22	11.27	16.37	24.70
213*	25.10	7.18	5.64	2.38	4.63	4.48	3.10	4.58	6.02	8.39	5.99	5.37	3.64	7.95	22.78
Mean	21.76	11.13	9.80	11.16	10.99	10.30	10.75	8.48	10.44	9.52	9.59	5.45	3.06	7.94	17.57
St. Dev.	6.19	6.71	8.24	8.93	6.18	6.26	6.68	5.08	6.59	9.08	6.53	3.67	2.51	6.39	6.08

*Minority Subjects

Table H38. Cortisol concentrations (ng/ml) for young men during DHEA Treatment

Subject	Time (h)														
	0	1	2	3	3.5	4.5	5.5	7	8.5	10	11.5	12.5	16	20	23
33	24.27	12.17	11.03	13.06	10.14	9.33	7.56	5.38	8.63	6.29	6.63	2.91	1.06	1.57	18.98
34	23.94	19.73	16.94	17.64	13.39	7.42	7.33	5.87	7.45	11.82	22.21	11.10	4.44	4.38	20.57
35	21.48	5.28	4.82	22.94	22.39	22.36	12.94	5.41	3.60	4.79	4.63	2.96	2.36	5.70	18.28
36	24.75	16.00	12.59	16.03	15.37	14.12	13.92	7.45	7.82	10.32	6.25	3.65	1.59	3.05	14.56
37	26.88	12.29	14.74	10.14	8.87	9.03	8.49	7.21	8.20	6.38	11.43	6.47	1.30	8.56	24.35
38	31.05	20.51	23.16	14.96	13.96	17.31	18.99	9.42	18.49	15.85	8.16	6.05	2.02	11.92	30.75
39	41.83	27.30	17.23	12.02	7.75	7.83	11.16	20.35	10.88	5.29	8.80	4.30	2.55	15.27	24.52
41	28.08	12.05	12.17	13.90	9.71	17.35	19.70	11.22	10.49	9.86	3.34	2.27	7.52	17.79	22.14
42	33.75	47.13	11.17	5.88	5.21	3.98	6.64	4.31	9.73	4.70	7.72	3.85	2.06	23.73	10.57
43	20.28	12.68	15.37	7.96	7.72	11.82	7.88	10.39	7.52	4.25	5.05	2.83	1.13	9.42	20.14
44	2.22	4.82	2.45	12.06	8.46	13.53	24.05	8.99	6.77	9.67	12.28	8.03	12.69	7.03	1.06
45	20.80	7.65	13.11	10.18	7.01	5.86	5.68	18.18	8.63	2.92	1.72	2.40	0.70	0.85	20.37
46	23.08	27.63	7.58	9.13	7.46	9.67	17.45	16.48	11.36	7.94	8.67	5.77	2.30	16.54	29.91
47*	26.48	10.03	6.34	4.18	5.20	15.21	9.09	7.87	13.62	3.72	7.40	3.23	0.98	9.42	16.42
48*	27.25	9.19	17.56	12.95	9.10	5.88	10.52	9.71	9.07	10.09	5.23	2.46	4.66	1.70	26.38
140	23.59	6.36	19.13	22.27	16.06	7.83	11.58	12.49	10.16	19.42	13.14	5.46	0.79	0.93	11.26
145	10.51	12.36	14.44	14.31	8.06	3.61	3.70	4.19	4.94	13.39	15.70	18.50	8.69	11.30	10.61
146*	21.50	10.57	6.66	4.76	3.16	6.12	8.04	4.89	2.93	1.78	2.94	1.97	1.42	15.41	22.05
245*	25.09	20.85	17.24	15.46	15.16	11.96	11.42	11.08	6.13	3.23	17.31	6.87	10.17	2.43	18.43
Mean	24.04	15.51	12.83	12.62	10.22	10.54	11.38	9.52	8.76	7.98	8.87	5.32	3.60	8.79	19.02
St. Dev.	8.17	10.19	5.39	5.16	4.71	5.07	5.35	4.67	3.54	4.75	5.33	3.97	3.56	6.67	7.25

*Minority Subjects

Table H39. Cortisol concentrations (ng/ml) for older women during DHEA Treatment

Subject	Time (h)														
	0	1	2	3	3.5	4.5	5.5	7	8.5	10	11.5	12.5	16	20	23
17	20.20	10.16	6.12	6.01	6.38	6.28	5.87	6.14	11.39	3.38	2.19	2.80	2.30	19.11	19.07
18	25.52	12.98	8.57	9.60	11.47	11.40	8.84	8.93	8.42	4.40	2.88	2.16	2.60	15.52	24.63
19	26.25	16.99	15.19	15.87	18.71	16.42	18.46	12.73	11.28	9.84	12.82	7.04	10.17	3.73	29.58
20*	21.04	10.97	7.10	6.02	4.36	4.80	6.44	4.75	2.76	2.51	4.78	5.46	3.30	8.59	21.13
21	26.42	7.14	6.77	14.77	13.75	25.98	10.55	3.96	2.54	6.33	3.97	7.09	3.07	16.94	20.57
22	22.89	12.26	10.39	9.36	6.53	7.58	9.30	7.47	11.42	6.15	8.54	3.87	1.50	7.15	22.70
23	33.85	19.17	10.30	7.76	8.76	5.46	8.25	15.90	11.71	11.06	6.52	4.49	0.96	2.79	26.19
24	9.36	12.80	10.12	8.80	5.54	6.34	6.78	8.96	9.05	6.24	8.77	3.34	1.96	11.18	14.38
25	11.52	9.98	6.54	5.31	8.32	11.73	7.26	4.91	4.74	9.25	21.94	10.06	2.27	4.46	13.60
26	25.73	16.04	12.07	11.97	14.63	11.17	10.45	11.03	17.15	8.25	5.46	12.78	3.72	16.73	28.89
27	40.18	21.66	16.38	14.78	11.85	9.53	10.16	10.43	11.72	5.80	12.73	35.41	30.18	19.49	29.78
28	25.17	13.15	11.72	9.81	9.84	8.72	8.32	12.92	9.60	10.22	13.05	9.14	2.91	18.06	32.04
29*	16.98	9.76	8.27	6.48	10.62	13.64	10.29	8.88	8.74	8.54	10.21	6.43	4.75	6.81	18.99
30*	16.51	9.13	9.05	5.77	6.00	5.02	8.22	9.08	5.77	5.45	8.12	3.61	3.96	7.46	24.37
31*	11.80	17.22	46.60	26.29	20.49	13.79	9.81	17.18	12.16	8.74	4.87	3.03	1.33	8.79	23.84
120	34.17	24.71	16.60	10.50	7.67	6.81	17.75	10.47	7.70	5.27	10.12	5.65	6.43	33.65	31.94
Mean	22.97	14.01	12.61	10.57	10.31	10.29	9.80	9.61	9.13	6.96	8.56	7.65	5.09	12.53	23.86
St. Dev.	8.61	4.89	9.66	5.39	4.68	5.46	3.56	3.80	3.82	2.52	5.00	7.96	7.06	8.04	5.73

*Minority Subjects

Table H40. Cortisol concentrations (ng/ml) for older men during DHEA Treatment

Subject	Time (h)														
	0	1	2	3	3.5	4.5	5.5	7	8.5	10	11.5	12.5	16	20	23
50	16.32	8.54	12.60	7.21	5.69	9.90	12.22	4.27	4.74	3.21	2.00	3.15	8.45	19.27	15.82
51	16.53	11.43	8.82	8.17	10.02	15.77	7.83	7.98	6.99	4.82	5.34	3.13	13.88	16.47	26.95
52	20.04	4.86	3.09	2.47	3.01	2.92	2.12	2.72	1.96	7.39	1.59	1.07	2.32	9.18	20.49
53	8.49	9.80	24.00	22.97	15.34	8.95	14.63	12.51	6.31	8.75	11.13	6.24	1.15	21.59	21.55
54	24.60	22.11	15.31	13.73	11.21	15.06	13.42	6.11	10.69	6.92	1.88	3.88	1.12	6.40	14.01
55	23.25	15.47	11.90	13.79	14.10	13.61	11.98	7.40	9.99	3.05	2.14	1.54	4.46	6.70	8.63
56	16.96	12.52	16.25	11.83	11.05	11.02	8.39	16.65	12.10	5.49	5.28	2.99	1.63	7.98	22.82
57	32.69	12.38	18.94	17.86	12.39	17.39	11.22	17.03	16.90	16.26	10.36	4.57	3.47	4.91	31.73
58	25.24	11.63	16.47	10.70	11.15	12.01	11.96	9.75	10.59	8.60	19.12	9.24	1.76	10.39	32.29
59	25.30	18.80	13.76	11.59	15.76	15.25	9.04	14.22	13.10	12.05	10.86	6.41	5.12	13.99	18.36
60	28.22	13.98	16.93	12.16	12.81	19.86	11.29	12.61	11.85	11.15	5.43	4.59	3.22	13.05	22.22
61*	23.54	23.75	16.46	13.45	12.58	12.71	11.56	14.17	7.51	3.18	7.40	3.38	2.92	11.99	18.34
149	23.94	17.26	13.72	6.98	9.67	8.47	11.16	9.92	5.66	13.01	14.55	7.82	5.93	10.34	25.32
160	16.11	6.04	7.32	8.30	6.44	5.03	4.69	3.52	8.40	2.86	3.68	4.10	5.09	1.79	19.25
Mean	21.52	13.47	13.97	11.52	10.80	12.00	10.11	9.92	9.06	7.62	7.20	4.44	4.32	11.00	21.27
St. Dev.	6.17	5.58	5.18	5.03	3.66	4.69	3.41	4.77	3.88	4.24	5.34	2.29	3.44	5.54	6.49

*Minority Subjects

Table H41. Cortisol concentrations (ng/ml) for young women during Alprazolam/Placebo Treatment

Subject	Time (h)														
	0	1	2	3	3.5	4.5	5.5	7	8.5	10	11.5	12.5	16	20	23
1	9.35	6.28	9.85	14.05	9.81	3.77	6.07	7.03	8.16	2.39	4.05	2.61	0.77	12.48	1.66
3	21.12	8.40	6.92	5.20	3.61	1.40	0.92	4.01	4.12	2.53	4.04	1.18	0.56	9.29	18.16
4	21.63	7.33	6.33	4.91	2.63	1.13	5.37	4.80	2.81	1.42	7.98	3.35	0.94	2.98	4.51
5	20.84	6.83	5.76	10.48	7.61	4.01	2.81	7.58	5.02	2.69	7.42	3.59	1.29	4.00	10.12
7	30.52	15.02	11.32	18.89	11.76	6.03	3.69	3.03	5.62	19.97	4.91	2.68	5.60	5.00	19.13
8	23.85	11.23	5.57	18.88	12.56	7.83	5.25	2.53	3.26	1.81	11.55	5.05	3.17	0.57	17.27
9	25.14	11.27	17.80	12.77	11.62	4.54	2.10	2.02	9.55	3.63	5.52	2.83	0.94	5.21	17.59
10	30.68	4.04	9.81	3.64	2.99	1.21	1.51	2.03	2.08	1.02	4.36	1.79	1.33	18.79	28.47
11	7.05	13.68	21.41	25.53	20.72	14.32	9.71	5.60	9.32	6.54	16.32	11.99	2.21	1.07	9.94
12	2.29	6.10	8.69	14.71	9.94	4.75	3.93	11.66	11.79	5.05	10.24	4.93	3.41	0.74	1.85
14*	26.81	12.37	6.64	8.96	9.57	3.95	2.42	1.61	1.42	1.14	14.53	7.24	3.01	9.33	22.90
15*	25.47	12.06	8.23	5.51	4.24	2.74	2.35	3.31	2.46	3.75	4.02	2.00	1.05	6.99	15.28
16*	1.77	6.60	6.47	6.00	3.71	1.64	1.16	7.18	4.10	3.90	5.70	2.12	0.68	2.65	5.11
66	28.52	28.33	26.83	11.44	8.76	4.28	3.96	1.96	3.89	11.87	14.91	8.20	3.13	9.84	16.71
102	19.14	8.57	12.18	9.14	6.34	2.53	1.99	1.22	3.83	2.76	11.37	13.14	2.03	1.12	8.07
111	16.60	7.93	5.18	10.58	7.24	4.41	2.28	3.12	5.86	3.29	5.71	1.77	2.15	9.26	16.06
112	18.47	16.91	17.92	13.27	9.52	4.77	3.76	4.35	5.45	3.54	15.71	6.35	1.02	2.78	6.90
113	22.19	7.24	3.95	7.44	4.57	2.39	1.75	7.60	4.35	2.40	3.50	2.46	0.68	16.21	9.13
114*	20.21	10.88	6.98	5.29	4.37	2.62	2.86	2.64	5.58	1.69	3.86	1.56	4.02	2.38	15.01
206	26.85	27.78	26.67	36.16	34.46	25.40	22.72	11.96	11.19	5.76	14.35	8.69	4.45	2.37	13.01
213*	20.26	7.38	3.74	7.73	6.11	2.80	2.14	5.16	8.58	2.41	6.45	3.77	6.42	7.86	29.19
Mean	19.94	11.25	10.87	11.93	9.15	5.07	4.23	4.78	5.64	4.26	8.40	4.63	2.33	6.23	13.62
St. Dev.	8.41	6.47	7.08	7.83	7.18	5.47	4.69	3.09	3.00	4.32	4.54	3.43	1.71	5.14	7.77

*Minority Subjects

Table H42. Cortisol concentrations (ng/ml) for young men during Alprazolam/Placebo Treatment

Subject	Time (h)														
	0	1	2	3	3.5	4.5	5.5	7	8.5	10	11.5	12.5	16	20	23
33	6.84	10.84	12.54	9.78	7.55	3.36	3.57	5.06	2.21	2.54	3.20	1.21	0.72	6.02	13.86
34	18.86	16.24	20.96	11.34	9.80	5.23	4.14	8.21	2.04	4.29	6.61	2.95	3.08	0.83	8.06
35	19.68	5.40	17.56	12.94	7.04	3.58	2.02	1.50	2.31	1.24	2.29	1.38	5.84	1.40	10.48
36	21.50	17.38	19.37	16.79	15.53	7.32	4.17	2.87	4.16	5.71	5.29	3.55	1.05	6.02	19.77
37	21.27	19.05	15.10	15.64	12.58	6.76	6.93	3.26	5.90	7.10	5.57	1.97	1.08	1.38	27.02
38	38.05	27.46	30.61	23.43	20.06	14.79	10.84	6.37	6.53	7.88	15.87	8.98	7.16	15.76	37.29
39	43.97	19.28	14.18	10.50	7.43	3.92	7.44	13.06	10.81	4.86	13.82	6.96	1.62	18.75	14.10
41	30.60	15.21	15.51	19.15	13.07	9.44	4.50	4.27	13.05	5.19	11.00	4.98	5.69	9.38	28.45
42	22.77	9.77	12.11	25.98	14.83	12.41	5.85	2.04	2.01	4.13	15.43	7.70	2.82	3.64	3.16
43	20.06	13.68	16.00	14.48	5.67	4.23	2.71	3.14	2.82	15.10	9.09	3.53	7.57	17.12	19.16
44	7.97	3.67	2.46	2.07	1.60	0.80	2.05	13.01	10.38	12.50	15.98	8.37	1.21	15.40	2.32
45	26.51	9.21	4.51	6.98	3.85	3.68	2.21	3.37	2.51	0.97	0.84	1.24	5.26	2.41	3.24
46	29.14	7.83	13.76	8.27	6.07	4.51	7.32	6.45	5.68	3.18	4.37	2.70	1.96	19.24	26.47
47*	18.46	9.10	9.16	7.16	3.78	2.08	1.95	2.38	9.57	1.61	4.43	1.86	0.98	9.99	23.32
48*	24.68	12.13	10.71	18.39	10.46	4.92	3.28	2.80	5.09	8.21	9.75	4.61	1.01	21.10	16.86
140	19.87	6.84	21.73	22.70	14.10	7.00	3.84	3.63	3.21	9.65	8.67	3.97	1.62	1.31	15.00
145	10.98	10.88	13.07	8.01	5.36	3.30	6.20	3.96	2.08	4.41	5.77	16.48	3.76	2.25	9.25
146*	24.12	4.10	7.21	3.87	2.96	1.40	1.50	2.04	3.38	8.11	4.75	2.44	1.40	14.16	20.51
245*	15.73	12.86	16.20	23.99	11.96	7.15	4.19	1.93	2.43	8.36	15.03	8.55	3.33	2.32	2.51
Mean	22.16	12.15	14.36	13.76	9.14	5.57	4.46	4.70	5.06	6.05	8.30	4.92	3.01	8.87	15.83
St. Dev.	9.19	5.99	6.44	7.12	5.01	3.59	2.43	3.41	3.47	3.77	4.94	3.84	2.24	7.26	9.95

*Minority Subjects

Table H43. Cortisol concentrations (ng/ml) for older women during Alprazolam/Placebo Treatment

Subject	Time (h)														
	0	1	2	3	3.5	4.5	5.5	7	8.5	10	11.5	12.5	16	20	23
17	18.89	7.72	13.33	6.26	5.16	3.61	2.16	3.31	5.86	3.97	2.82	6.39	18.50	24.64	26.78
18	28.26	19.60	11.37	8.28	4.90	4.54	7.55	9.37	4.20	4.84	4.62	4.05	14.79	2.70	20.09
19	34.80	21.23	17.01	10.16	8.19	4.40	3.20	1.91	13.77	4.91	4.98	3.07	1.22	7.83	18.14
20*	7.59	21.40	11.15	5.20	5.93	2.80	2.20	2.66	2.45	2.32	8.53	3.29	2.74	7.83	10.45
21	28.63	3.54	9.83	8.77	4.89	1.61	0.90	8.38	2.60	1.78	3.92	5.17	3.12	22.24	9.53
22	22.83	10.42	5.23	3.41	2.95	2.11	3.90	3.68	9.95	3.67	2.86	1.71	0.88	11.71	21.94
23	17.54	19.04	13.78	6.60	5.60	2.80	3.95	2.82	5.24	3.03	11.82	5.39	2.52	16.44	19.50
24	16.97	9.71	6.32	3.61	2.25	1.39	1.41	1.98	2.17	2.48	8.88	3.81	2.71	5.96	7.10
25	17.82	9.81	8.10	13.79	9.49	6.60	4.01	4.84	2.13	2.29	12.98	6.76	3.45	8.94	10.44
26	17.80	16.09	18.50	23.45	20.05	12.95	17.44	14.45	8.43	27.82	19.34	14.79	5.37	31.41	10.89
27	23.17	18.90	18.70	9.81	10.11	6.35	6.53	3.72	2.80	2.13	11.16	11.65	6.34	12.24	20.18
28	18.47	7.43	17.89	14.60	11.72	7.50	6.51	5.96	3.55	6.41	7.54	4.27	24.01	13.72	23.19
29*	29.52	5.51	14.68	18.84	13.12	5.55	3.99	5.03	10.09	4.23	13.84	9.29	7.64	13.01	9.70
30*	19.36	8.76	11.86	6.77	9.07	6.85	6.00	8.62	10.79	3.72	5.57	2.37	3.67	13.46	23.74
31*	19.04	23.73	31.47	22.84	18.81	12.87	7.95	9.07	10.10	6.39	3.75	3.43	3.92	11.35	12.77
120	24.08	17.38	11.55	7.46	5.40	3.46	3.91	7.38	3.30	1.97	3.25	2.39	1.79	8.91	29.71
Mean	21.55	13.77	13.80	10.62	8.60	5.34	5.10	5.82	6.09	5.12	7.87	5.49	6.42	13.27	17.13
St. Dev.	6.49	6.52	6.25	6.36	5.21	3.51	3.91	3.47	3.82	6.23	4.83	3.62	6.75	7.39	7.03

*Minority Subjects

Table H44. Cortisol concentrations (ng/ml) for older men during Alprazolam/Placebo Treatment

Subject	Time (h)														
	0	1	2	3	3.5	4.5	5.5	7	8.5	10	11.5	12.5	16	20	23
50	18.76	8.80	11.95	5.73	3.71	2.41	11.80	4.66	2.36	2.13	2.35	2.11	12.84	16.41	4.87
51	19.44	11.05	14.65	12.56	8.73	7.30	12.49	6.29	9.75	4.61	2.41	2.04	22.70	18.51	20.78
52	5.65	3.65	3.54	3.58	2.28	3.10	1.56	0.94	1.28	1.36	1.16	0.93	1.77	14.03	8.50
53	16.22	11.49	25.43	17.50	12.07	6.30	4.90	4.27	2.31	2.38	7.76	3.64	1.17	4.73	10.31
54	23.53	23.28	12.66	4.81	5.00	3.36	3.10	7.12	5.22	3.34	1.76	1.27	0.70	9.57	38.44
55	16.34	15.58	11.12	9.24	7.51	4.89	4.87	8.64	3.39	1.57	2.34	1.36	1.20	4.21	12.21
56	24.47	16.06	17.29	12.26	11.65	4.62	4.56	3.00	3.89	4.12	7.82	2.55	1.68	16.01	17.01
57	31.15	9.30	22.59	10.16	7.99	4.77	3.14	6.99	3.07	1.69	5.24	2.93	1.64	20.49	20.93
58	17.85	13.87	16.75	11.77	8.06	4.45	3.97	2.84	2.51	5.47	5.77	3.14	1.35	17.54	17.31
59	20.14	16.29	15.73	7.04	7.29	5.17	6.31	6.93	5.06	4.83	4.97	3.79	1.55	21.25	16.74
60	25.93	13.37	14.66	8.24	5.97	3.41	2.63	0.39	4.49	2.61	2.18	2.63	2.11	16.51	20.51
61*	25.81	21.66	17.87	8.77	5.57	4.27	4.25	3.91	5.55	3.04	4.05	2.63	1.54	4.41	14.21
149	30.60	18.16	11.26	9.10	9.39	6.20	6.23	9.24	12.13	6.37	12.52	8.50	7.39	14.95	26.36
160	25.19	12.37	7.22	8.74	5.63	2.56	8.05	6.32	3.33	4.34	10.05	6.48	0.83	6.03	15.35
Mean	21.51	13.92	14.48	9.25	7.20	4.49	5.56	5.11	4.60	3.42	5.03	3.14	4.18	13.19	17.40
St. Dev.	6.64	5.18	5.65	3.57	2.77	1.45	3.24	2.70	2.99	1.57	3.43	2.06	6.29	6.15	8.25

*Minority Subjects

Table H45. Cortisol concentrations (ng/ml) for young women during Alprazolam/DHEA Treatment

Subject	Time (h)														
	0	1	2	3	3.5	4.5	5.5	7	8.5	10	11.5	12.5	16	20	23
1	8.06	4.60	2.61	8.79	5.32	3.87	4.69	10.78	4.45	2.64	8.47	3.26	3.37	1.02	1.03
3	22.48	10.98	7.91	5.81	4.04	2.26	1.06	5.91	4.09	3.56	5.99	2.69	0.76	2.69	18.15
4	20.15	4.89	5.80	3.76	2.99	1.60	1.62	4.69	1.54	1.46	4.67	1.89	0.55	10.90	7.65
5	22.27	8.53	7.81	6.09	4.65	2.81	1.99	3.34	4.76	7.84	9.12	4.82	1.76	7.97	12.17
7	23.88	15.68	9.14	11.57	7.06	3.17	1.77	3.22	6.54	6.68	6.49	2.51	1.42	8.79	22.55
8	13.48	9.53	6.75	14.43	9.34	4.59	2.19	4.22	3.01	2.45	5.27	3.36	1.11	0.59	20.15
9	26.94	9.91	12.92	15.35	9.63	4.28	3.27	1.41	1.90	4.60	9.95	4.41	0.84	6.19	18.69
10	16.24	5.01	2.77	3.03	2.64	0.99	0.72	1.97	1.81	2.31	7.25	3.42	0.58	5.97	17.10
11	15.34	17.62	16.73	14.69	11.32	8.15	5.23	3.74	7.55	4.79	13.90	8.95	2.16	2.11	12.73
12	0.19	5.39	7.00	17.27	11.52	6.16	4.10	12.41	13.39	5.16	12.04	6.42	1.18	1.33	1.39
14*	23.28	13.46	9.54	6.76	4.83	14.14	15.83	5.70	3.22	4.16	10.07	5.15	3.17	13.41	16.58
15*	20.51	14.80	7.96	6.97	5.59	2.79	2.16	1.68	2.35	3.74	7.52	3.74	1.31	15.23	18.96
16*	4.76	5.45	6.53	4.99	2.93	1.40	1.74	7.97	2.09	10.26	9.38	3.49	1.22	2.26	13.87
66	22.38	12.25	10.53	10.48	6.72	3.89	3.09	2.11	2.28	6.24	8.11	5.20	1.67	9.11	17.96
102	21.13	14.20	10.04	8.36	6.43	2.75	3.22	3.27	5.05	2.36	10.20	3.23	0.98	4.92	18.58
111	19.57	6.57	6.69	11.11	5.83	2.33	1.63	0.85	1.57	2.58	4.80	1.31	2.00	17.84	6.32
112	29.29	25.30	24.93	24.85	21.44	14.67	9.42	5.42	5.19	6.81	11.36	7.48	2.47	0.96	9.52
113	22.22	17.70	6.48	7.65	4.10	2.93	2.34	1.88	4.62	1.03	6.52	3.46	5.54	1.20	17.72
114*	15.00	10.20	4.67	3.68	2.82	2.58	1.54	1.98	1.27	1.29	4.38	1.77	0.71	2.71	4.11
206	38.65	37.61	36.50	40.46	32.78	28.05	24.42	22.61	12.16	7.82	6.19	8.99	7.08	5.55	12.22
213*	21.00	5.13	4.80	4.60	4.03	1.84	5.14	2.17	3.99	5.50	7.25	3.60	1.39	8.09	21.31
Mean	19.37	12.13	9.91	10.99	7.91	5.49	4.63	5.11	4.42	4.44	8.04	4.25	1.97	6.14	13.75
St. Dev.	8.35	7.97	7.84	8.66	7.14	6.37	5.67	5.03	3.27	2.49	2.59	2.16	1.66	5.03	6.50

*Minority Subjects

Table H46. Cortisol concentrations (ng/ml) for young men during Alprazolam/DHEA Treatment

Subject	Time (h)														
	0	1	2	3	3.5	4.5	5.5	7	8.5	10	11.5	12.5	16	20	23
33	24.21	9.44	11.69	9.49	7.92	3.98	3.44	3.31	1.83	9.85	3.91	2.82	1.58	1.06	17.30
34	14.19	17.32	12.46	12.59	9.34	5.31	3.77	9.62	6.77	7.84	9.38	7.30	2.67	2.70	14.89
35	13.36	10.01	8.43	8.33	5.89	3.10	1.98	1.99	3.19	1.46	5.77	2.92	2.58	3.58	10.43
36	16.95	16.54	16.97	19.12	15.17	9.70	7.12	3.26	5.57	3.33	6.96	4.43	0.90	1.47	15.80
37	33.80	14.11	23.70	16.98	15.54	9.39	4.22	5.81	5.95	4.44	11.57	4.96	1.26	9.81	23.72
38	39.13	27.82	26.74	23.12	20.74	12.53	7.79	12.96	10.12	7.92	16.54	12.11	11.86	22.48	32.15
39	40.88	14.56	10.40	14.23	10.63	6.35	5.40	13.55	10.57	6.87	11.90	5.67	3.10	10.64	27.88
41	23.59	14.43	13.62	14.40	9.74	5.49	4.58	2.59	4.10	12.78	12.54	6.24	8.19	3.62	20.88
42	35.06	17.94	11.08	30.29	20.17	10.17	6.98	2.51	1.55	2.12	16.48	4.65	1.11	9.93	4.55
43	19.79	12.74	13.83	12.09	6.02	3.88	2.97	2.93	3.21	13.46	6.87	2.61	7.57	18.82	18.97
44	11.12	6.78	3.48	13.67	8.36	3.96	4.16	5.34	4.29	7.47	9.95	4.05	10.61	1.35	0.70
45	27.44	8.23	8.85	5.85	3.67	1.91	1.76	3.57	3.46	1.18	0.69	0.66	1.69	15.30	13.46
46	26.26	9.87	15.61	7.74	6.62	4.10	4.41	9.75	5.75	5.53	7.36	3.94	1.52	7.60	14.32
47*	28.41	10.08	14.86	6.34	3.96	2.13	2.53	3.39	4.98	2.90	3.96	2.13	1.31	7.86	10.79
48*	21.62	10.77	12.31	15.00	7.66	5.10	4.16	3.56	7.87	5.06	9.75	5.24	0.81	2.23	19.42
140	15.50	5.87	16.00	22.42	10.81	8.20	5.12	4.91	10.84	3.48	13.86	5.52	3.51	1.02	17.44
145	23.21	22.32	14.26	6.21	3.82	4.42	30.14	6.36	15.48	4.51	10.39	24.87	4.93	4.94	9.19
146*	22.35	9.70	5.88	6.45	3.36	2.17	2.94	2.76	1.69	1.39	8.13	2.51	0.82	1.43	20.98
245*	18.13	15.30	30.15	14.01	12.57	9.09	7.78	2.69	2.88	3.51	15.63	10.09	4.53	1.45	4.31
Mean	23.95	13.36	14.23	13.60	9.58	5.84	5.86	5.31	5.79	5.53	9.56	5.93	3.71	6.70	15.64
St. Dev.	8.59	5.47	6.66	6.64	5.25	3.11	6.16	3.57	3.73	3.63	4.40	5.34	3.42	6.42	7.99

*Minority Subjects

Table H47. Cortisol concentrations (ng/ml) for older women during Alprazolam/DHEA Treatment

Subject	Time (h)														
	0	1	2	3	3.5	4.5	5.5	7	8.5	10	11.5	12.5	16	20	23
17	22.00	11.23	14.01	8.68	6.77	3.74	5.14	4.80	6.01	7.13	4.72	3.48	3.75	19.47	29.03
18	21.85	15.24	9.05	6.16	3.76	3.92	3.47	6.41	5.76	5.29	5.55	2.50	1.23	14.20	7.84
19	21.31	15.94	17.71	12.45	7.87	5.73	2.87	2.82	1.70	5.16	8.55	7.08	1.75	11.82	16.81
20*	24.13	10.10	7.08	4.38	3.39	2.33	2.67	1.48	2.06	1.62	11.09	13.45	11.74	10.63	7.96
21	20.57	5.09	4.99	7.65	4.87	1.94	1.78	5.79	5.82	2.05	1.88	1.14	3.45	20.95	11.80
22	14.95	9.50	5.63	6.15	4.45	3.38	7.36	4.56	6.80	4.72	4.17	3.75	1.57	7.98	23.06
23	31.86	15.38	11.07	8.23	4.95	2.97	3.51	1.50	3.20	3.24	8.73	4.11	1.00	3.80	32.15
24	28.89	8.68	4.77	2.90	2.56	1.34	1.43	2.00	4.43	1.86	5.78	3.12	1.43	11.36	12.85
25	21.49	12.33	7.40	4.69	3.79	2.57	11.50	6.04	6.23	6.91	12.89	11.39	2.22	5.92	9.99
26	27.10	16.33	17.64	14.95	12.45	9.73	22.46	12.57	10.79	6.04	5.27	4.45	3.89	24.80	10.78
27	31.16	25.83	22.13	14.46	11.03	7.98	6.88	4.74	3.97	2.81	12.47	9.09	5.40	14.62	32.09
28	15.10	11.45	18.34	15.84	14.05	9.34	5.94	6.94	5.02	4.45	10.65	5.67	13.87	20.29	13.17
29*	20.95	13.12	13.90	9.61	6.30	5.74	5.40	10.17	15.09	13.20	18.76	11.15	13.01	15.78	16.67
30*	25.18	13.43	8.99	8.10	6.86	5.61	3.43	3.87	4.25	5.18	4.40	2.80	0.80	6.06	21.61
31*	25.09	13.98	26.95	18.55	13.41	8.50	8.68	2.87	5.54	10.76	8.38	3.49	2.23	6.88	4.61
120	41.05	21.90	16.94	10.58	8.60	4.69	3.57	7.05	4.45	3.09	10.64	4.46	20.51	13.04	21.67
Mean	24.54	13.72	12.91	9.59	7.19	4.97	6.01	5.23	5.70	5.22	8.37	5.70	5.49	12.98	17.01
St. Dev.	6.53	5.00	6.61	4.54	3.73	2.70	5.14	3.05	3.27	3.17	4.29	3.66	5.94	6.13	8.75

*Minority Subjects

Table H48. Cortisol concentrations (ng/ml) for older men during Alprazolam/DHEA Treatment

Subject	Time (h)														
	0	1	2	3	3.5	4.5	5.5	7	8.5	10	11.5	12.5	16	20	23
50	27.67	7.97	10.05	4.27	3.49	1.90	5.69	4.92	3.33	1.78	2.23	5.20	17.45	7.66	14.09
51	26.62	18.53	12.30	11.66	8.73	8.39	9.75	6.21	3.87	5.79	4.80	4.02	15.22	15.44	17.08
52	9.36	3.62	5.98	3.18	2.33	1.72	2.32	1.66	1.61	1.28	0.67	0.56	12.29	0.90	17.79
53	25.70	11.02	19.94	15.01	10.36	5.00	4.00	3.59	3.53	4.08	9.81	4.25	20.41	13.86	15.89
54	20.50	8.22	14.72	6.79	3.17	2.23	2.14	17.18	7.33	4.34	2.92	2.16	1.37	11.71	19.25
55	8.83	10.24	11.97	8.89	8.43	3.24	1.72	5.45	3.04	2.10	3.42	1.50	2.33	7.20	18.93
56	24.16	18.28	17.56	11.79	9.60	7.32	3.97	3.31	2.19	2.20	5.11	1.79	1.48	8.31	26.38
57	25.54	19.83	21.77	15.71	11.13	6.48	3.31	4.00	2.27	4.84	9.40	4.14	8.46	14.19	22.95
58	34.79	12.05	10.29	11.82	8.67	4.13	3.19	7.49	8.83	3.46	10.43	4.76	1.31	5.36	29.91
59	27.76	15.25	13.49	12.65	7.30	7.74	5.18	5.05	2.91	9.46	5.99	3.33	0.98	18.12	23.03
60	23.02	16.40	16.62	10.68	7.68	5.13	3.24	3.95	14.59	4.56	3.43	2.64	4.07	8.81	24.75
61*	31.42	14.72	12.59	11.30	8.70	5.24	4.10	3.11	4.18	5.58	4.33	2.34	1.26	11.60	28.67
149	16.73	19.85	19.10	15.37	10.82	6.95	7.16	4.05	7.06	7.97	5.34	4.62	7.83	13.84	25.29
160	22.45	8.52	6.76	3.64	3.41	2.22	9.21	2.46	1.50	2.09	8.21	4.24	1.47	4.48	18.28
Mean	23.18	13.18	13.80	10.20	7.42	4.84	4.64	5.17	4.73	4.25	5.44	3.25	6.85	10.11	21.59
St. Dev.	7.42	5.11	4.78	4.26	3.04	2.32	2.51	3.77	3.61	2.40	3.00	1.42	6.86	4.81	4.94

*Minority Subjects

APPENDIX I

Figures for Chapter 7

Latency, Duration, Accuracy, DSST and CS versus time

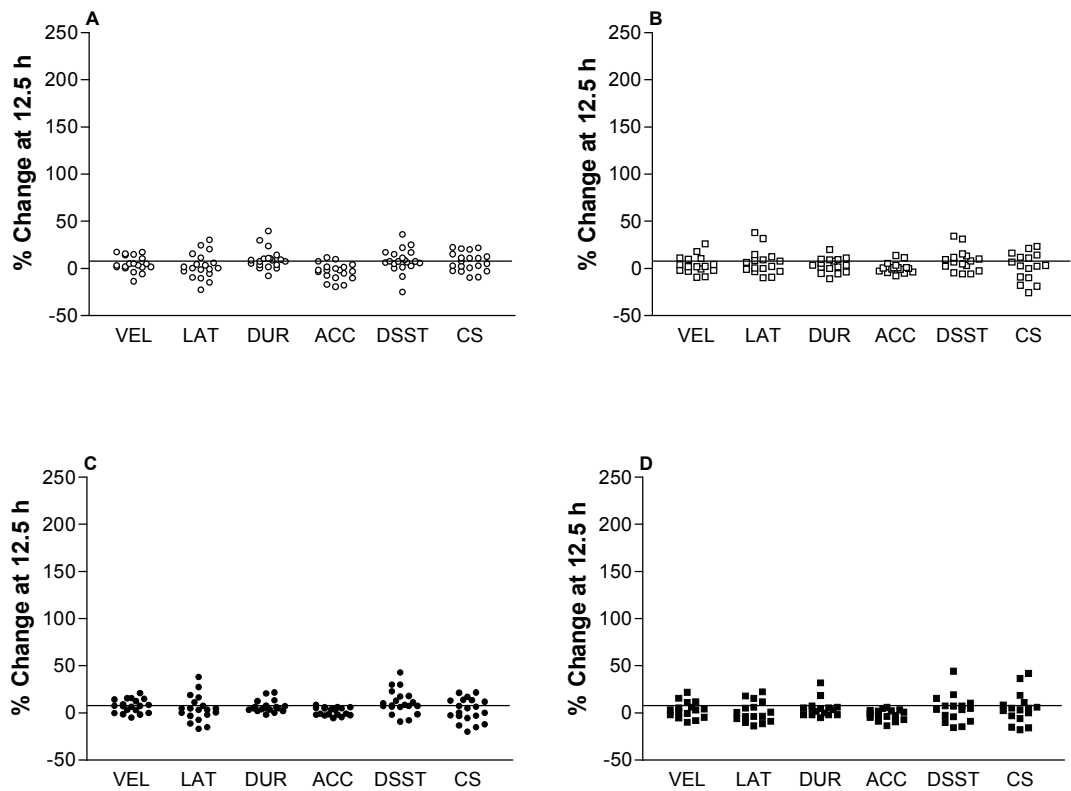


Figure I.1. Scatter plots of percent change in performance from baseline at the 12.5 h time point for the young women (panels A and B), and young men (panels C and D). The SEM variables, VEL (velocity), LAT (latency), DUR (duration), and ACC (accuracy) are from saccades to the 8 degree target. DSST= digit symbol substitution test and CS = card sorting. The horizontal line indicates the 10% threshold. Values are considered to be equivalent to baseline if they are $\leq 10\%$ of baseline values. Hollow symbols indicate PL/ALP treatment, filled symbols indicate DH/ALP treatment.

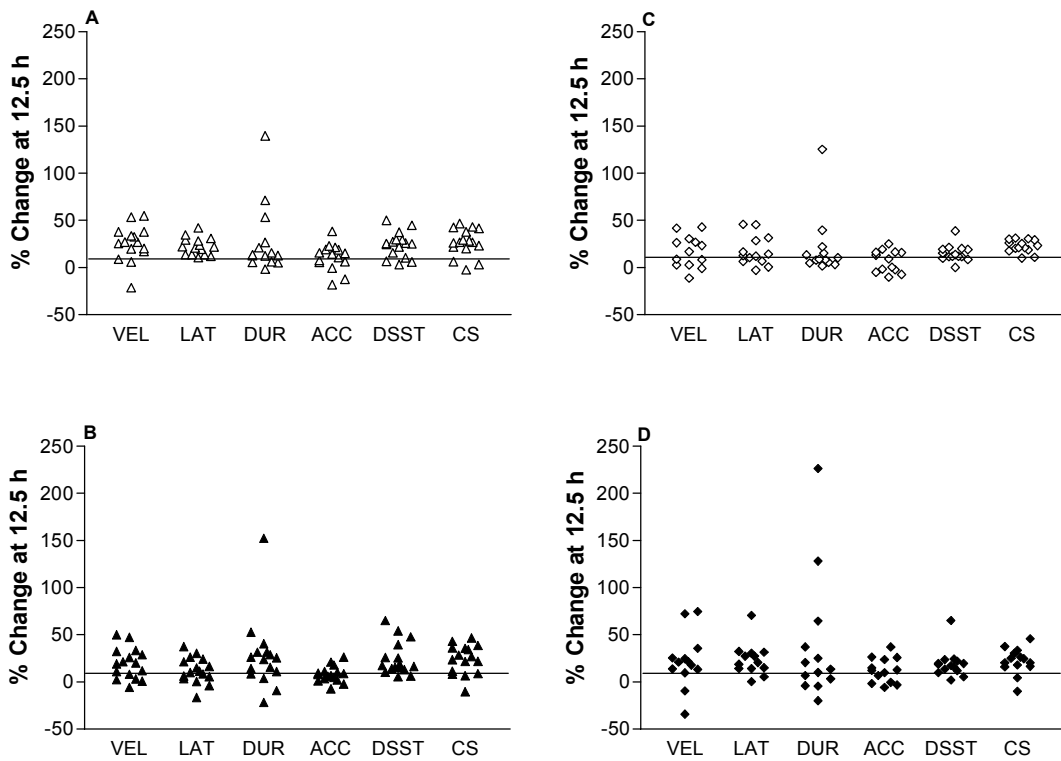


Figure I.2. Scatter plots of percent change in performance from baseline at the 12.5 h time point for the young women (panels A and B), and young men (panels C and D). The SEM variables, VEL (velocity), LAT (latency), DUR (duration), and ACC (accuracy) are from saccades to the 8 degree target. DSST= digit symbol substitution test and CS = card sorting. The horizontal line indicates the 10% threshold. Values are considered to be equivalent to baseline if they are $\leq 10\%$ of baseline values. Hollow symbols indicate PL/ALP treatment, filled symbols indicate DH/ALP treatment.

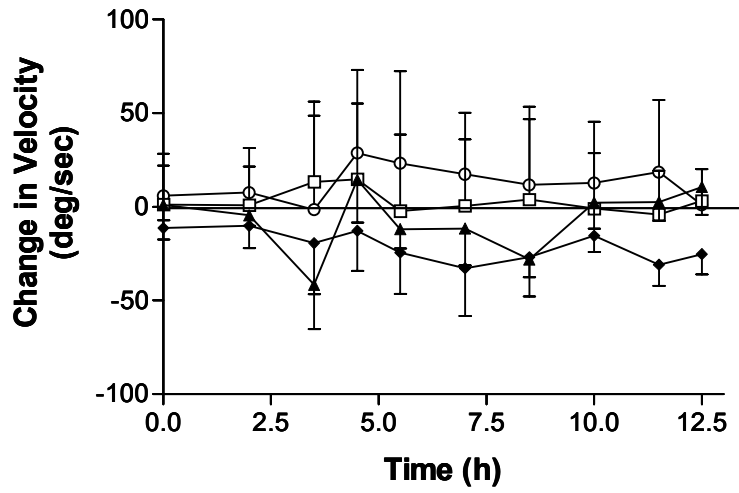


Figure I.3. Line plots of change in velocity between the two treatments (DHEA/Alp - PL/Alp) for the 8 degree saccades for young women (O), young men (□) older women (▲), older men. Points above the horizontal line less impairment during the DHEA/Alp treatment. Points below the horizontal line indicate more impairment during the the DHEA/Alp treatment.

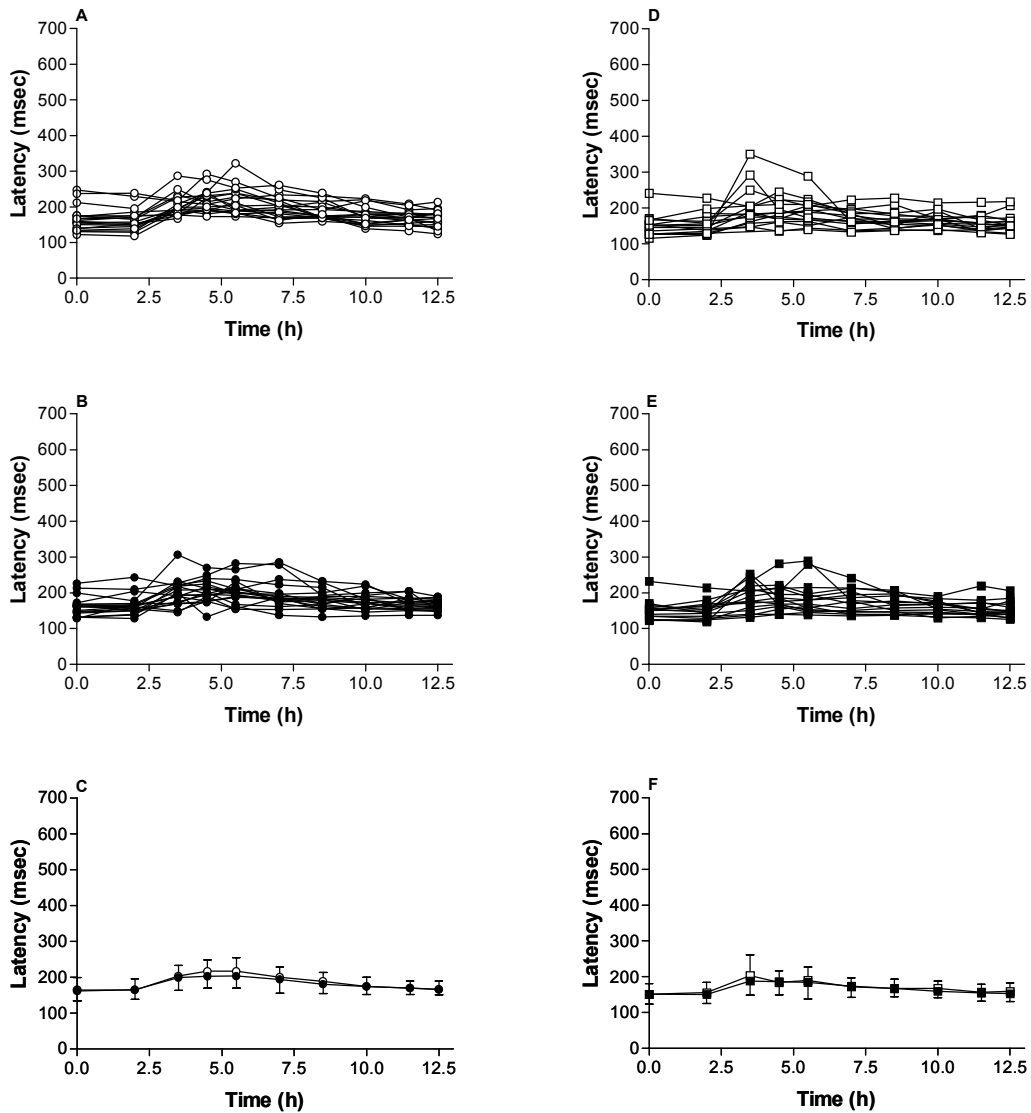


Figure I.4. Line plots of latency vs. time for the 8-degree saccades for the young subjects. Individual latency data from the PL/ALP treatment are in panels A, young women (○), and B, young men (□). Individual latency data from the DH/ALP treatment are in panels C, young women (●), and D, young men (■). The mean data with standard deviations are in panels E (young women) and F (young men).

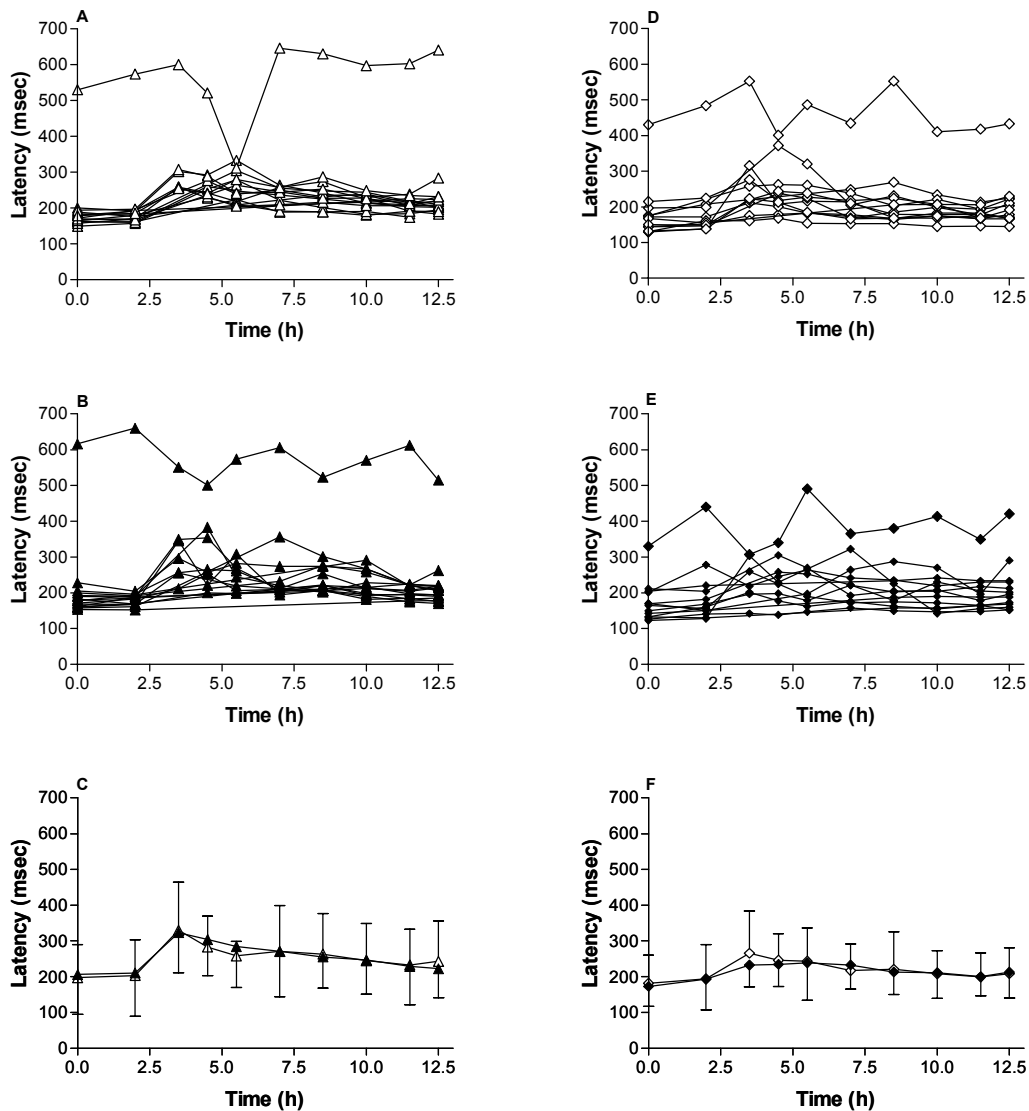


Figure I.5. Line plots of latency vs. time for the 8-degree saccades for the older subjects. Individual latency data from the PL/Alp treatment are in panels A, older women (\triangle), and B, older men (\diamond). Individual latency data from the DHEA/Alp treatment are in panels C, older women (\blacktriangle), and D, older men (\blacklozenge). The mean data with standard deviations are in panels E (older women) and F (older men).

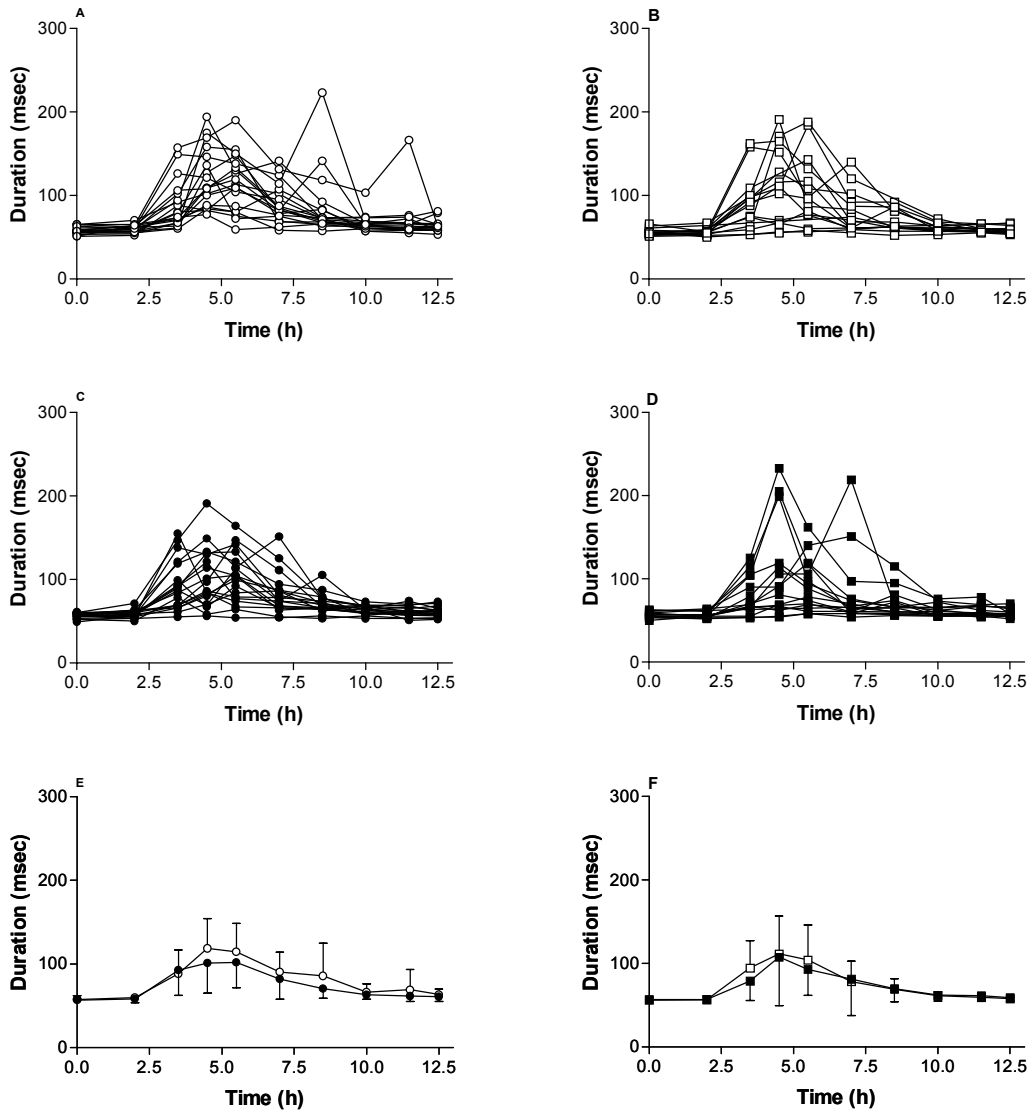


Figure I.6. Line plots of duration vs. time for the 8-degree saccades for the young subjects. Individual duration data from the PL/ALP treatment are in panels A, young women (○), and B, young men (□). Individual duration data from the DH/ALP treatment are in panels C, young women (●), and D, young men (■). The mean data with standard deviations are in panels E (young women) and F (young men).

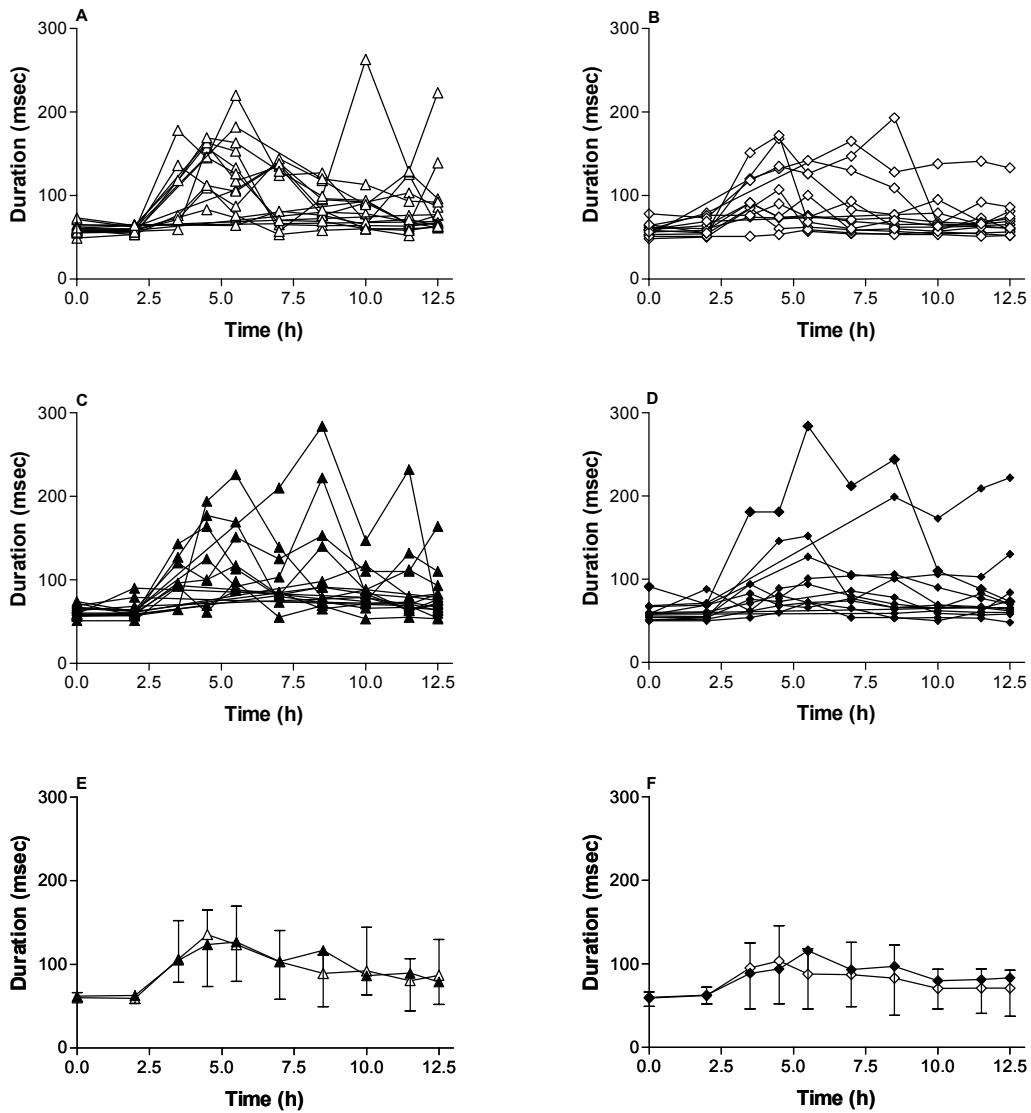


Figure I.7. Line plots of duration vs. time for the 8-degree saccades for the older subjects. Individual duration data from the PL/Alp treatment are in panels A, older women (\triangle), and B, older men (\diamond). Individual duration data from the DHEA/Alp treatment are in panels C, older women (\blacktriangle), and D, older men (\blacklozenge). The mean data with standard deviations are in panels E (older women) and F (older men).

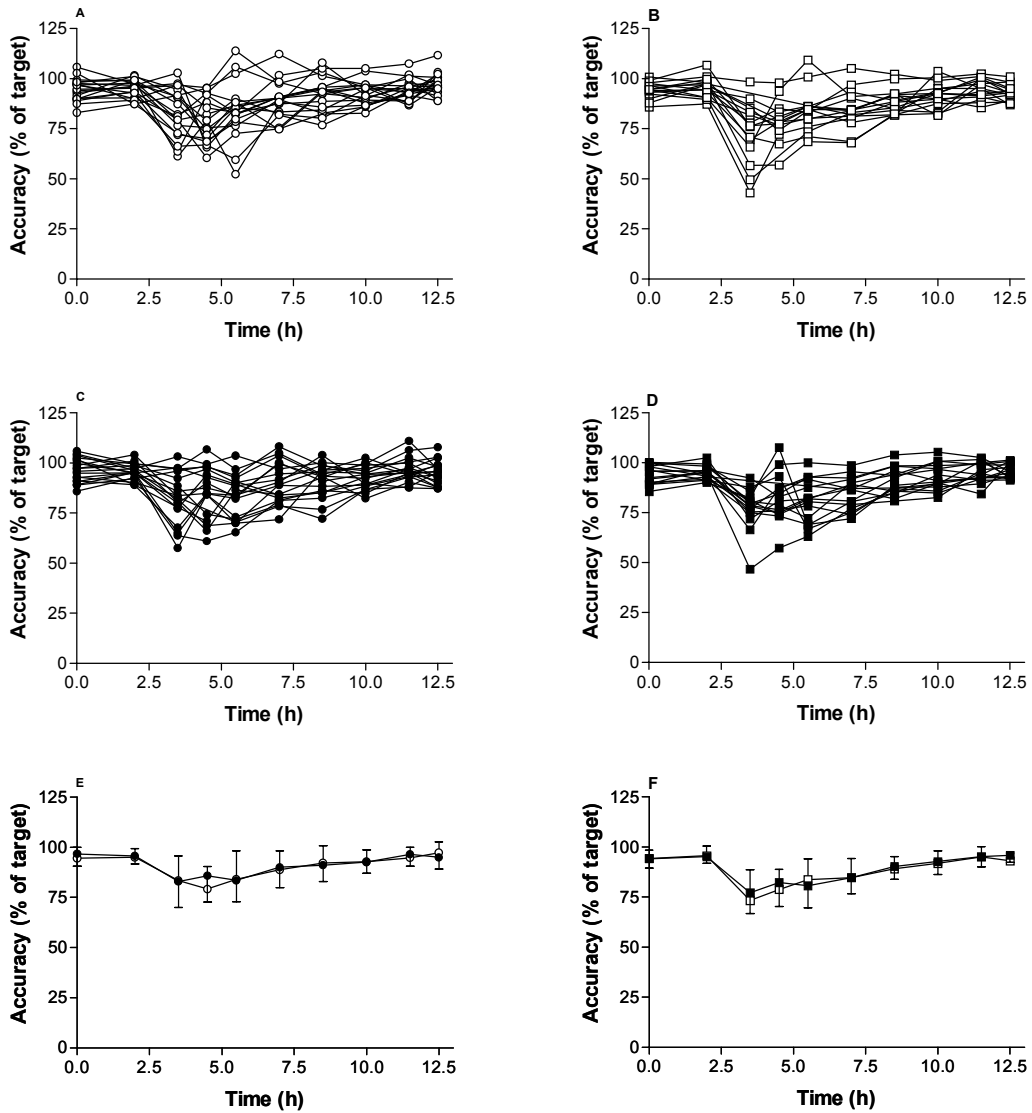


Figure I.8. Line plots of accuracy vs. time for the 8-degree saccades for the young subjects. Individual accuracy data from the PL/ALP treatment are in panels A, young women (○), and B, young men (□). Individual accuracy data from the DH/ALP treatment are in panels C, young women (●), and D, young men (■). The mean data with standard deviations are in panels E (young women) and F (young men).

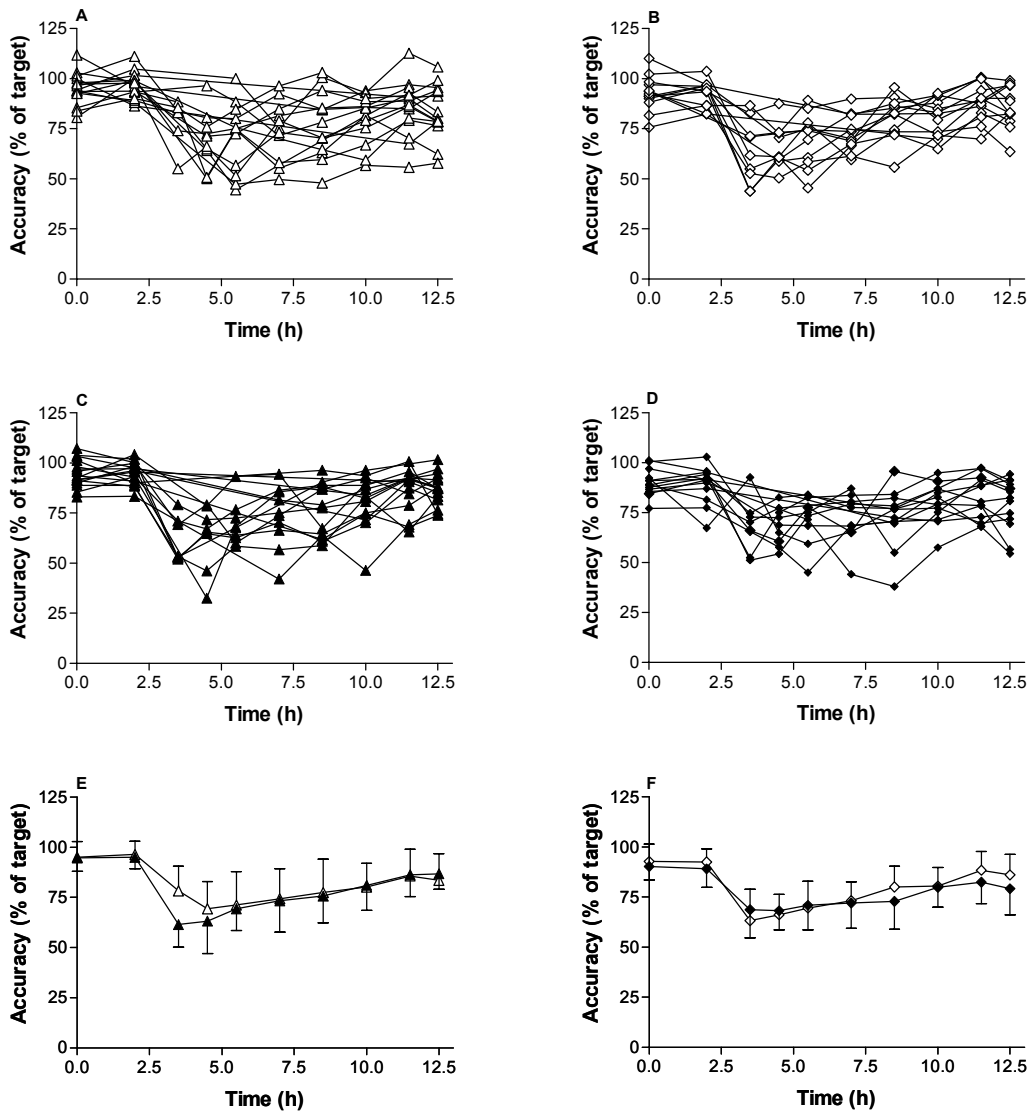


Figure I.9. Line plots of accuracy vs. time for the 8-degree saccades for the older subjects. Individual accuracy data from the PL/Alp treatment are in panels A, older women (\triangle), and B, older men (\diamond). Individual accuracy data from the DHEA/Alp treatment are in panels C, older women (\blacktriangle), and D, older men (\blacklozenge). The mean data with standard deviations are in panels E (older women) and F (older men).

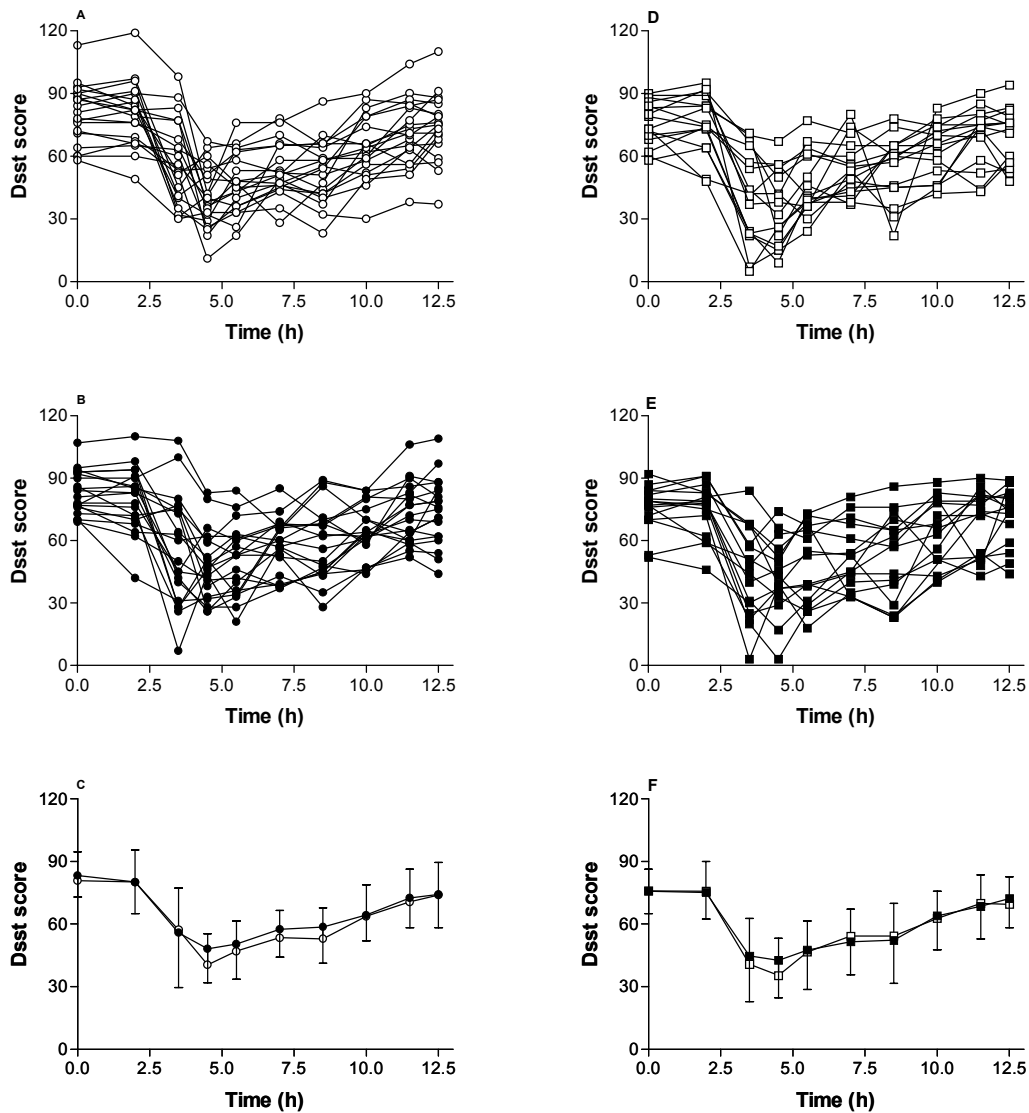


Figure I.10. Line plots of DSST score vs. time for the young subjects. Individual DSST scores from the PL/ALP treatment are in panels A, young women (○), and B, young men (□). Individual DSST scores from the DH/ALP treatment are in panels C, young women (●), and D, young men (■). The mean data with standard deviations are in panels E (young women) and F (young men).

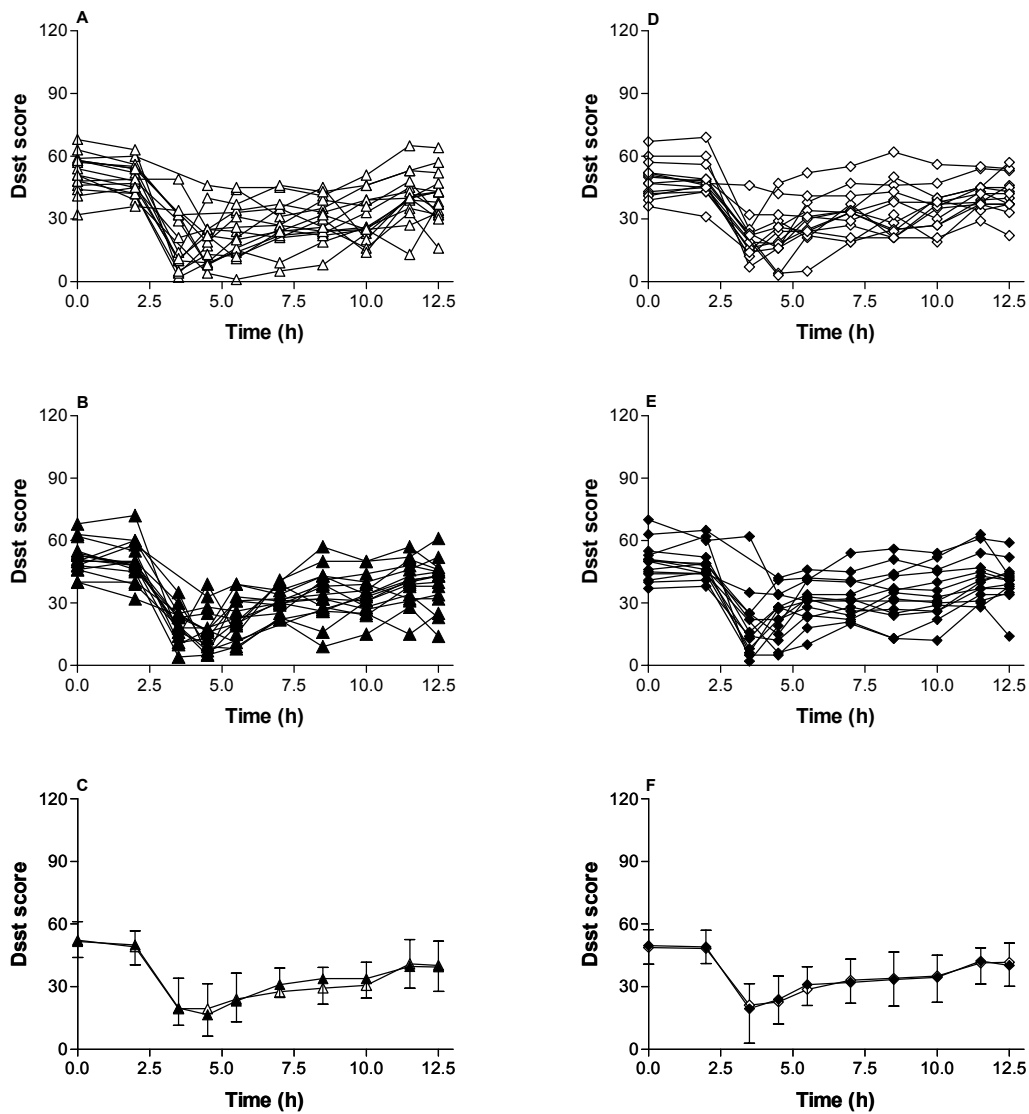


Figure I.11. Line plots of DSST score vs. time for the older subjects. Individual DSST scores from the PL/Alp treatment are in panels A, older women (\triangle), and B, older men (\diamond). Individual DSST scores from the DHEA/Alp treatment are in panels C, older women (\blacktriangle), and D, older men (\blacklozenge). The mean data with standard deviations are in panels E (older women) and F (older men).

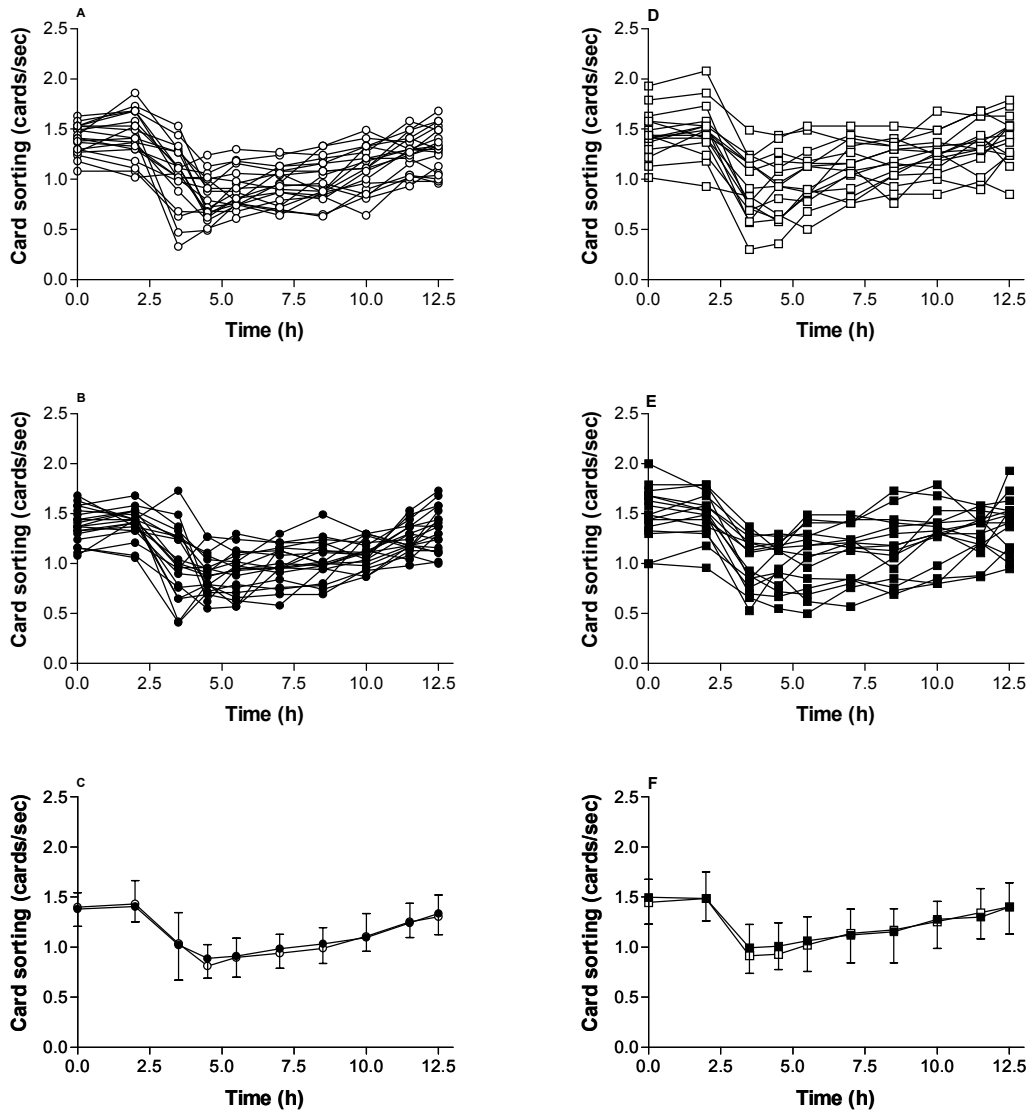


Figure I.12. Line plots of Card Sorting vs. time for the young subjects. Individual Card Sorting data from the PL/ALP treatment are in panels A, young women (○), and B, young men (□). Individual Card Sorting data from the DH/ALP treatment are in panels C, young women (●), and D, young men (■). The mean data with standard deviations are in panels E (young women) and F (young men).

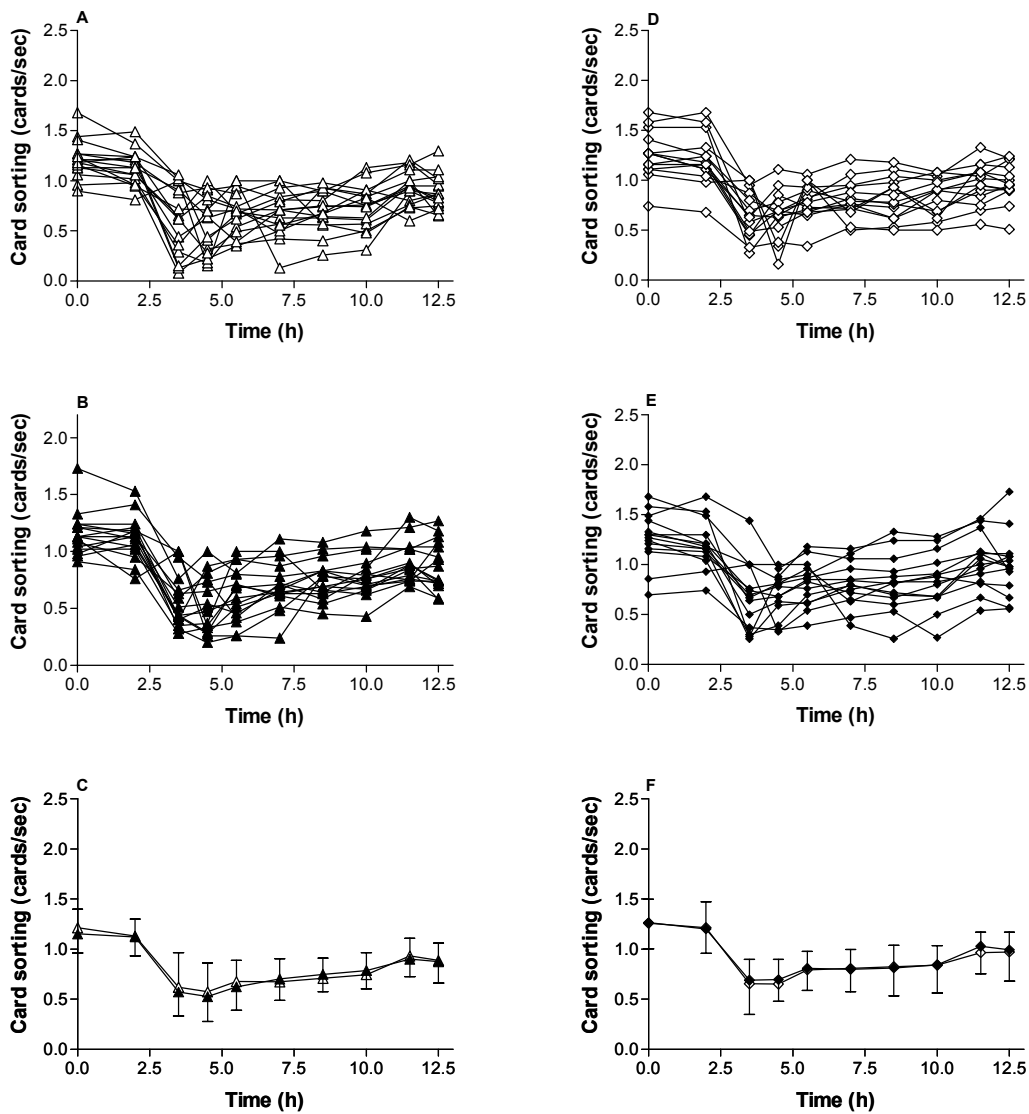


Figure I.13. Line plots of Card Sorting data vs. time for the older subjects. Individual Card Sorting data from the PL/Alp treatment are in panels A, older women (\triangle), and B, older men (\diamond). Individual Card Sorting data from the DHEA/Alp treatment are in panels C, older women (\blacktriangle), and D, older men (\blacklozenge). The mean data with standard deviations are in panels E (older women) and F (older men).