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Functional Connectivity of EEG LORETA in Cortical Core Components of the Self and the Default Network (DNt) of the Brain

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To the Graduate Council:

I am submitting herewith a dissertation written by Rex Lee Cannon entitled "Functional Connectivity of EEG LORETA in Cortical Core Components of the Self and the Default Network (DNt) of the Brain." I have examined the final electronic copy of this dissertation for form and content and recommend that it be accepted in partial fulfillment of the requirements for the degree of Doctor of Philosophy, with a major in Psychology.

Debora R. Baldwin, Major Professor

We have read this dissertation and recommend its acceptance:

Gregory L. Stuart, Jacob J. Levy, John H. Dougherty

Accepted for the Council:
Carolyn R. Hodges

Vice Provost and Dean of the Graduate School

(Original signatures are on file with official student records.)

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A Dissertation Presented for The Doctor of Philosophy Degree
The University of Tennessee, Knoxville

Rex Lee Cannon
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ABSTRACT

INTRODUCTION: Recent research exploring cortical functional connectivity defines a default network (DNt) of brain function and activation of a core midline network (CMS) in the processing of self. The electroencephalographic (EEG) activity in these components of the human DNt and CMS is not well understood. **METHODS:** This study was conducted with 63 participants. Individuals were recorded during eyes-closed (ECB) and eyes-opened (EOB) baselines and active task (AT) conditions (e.g., self-referential, self-image, self-concept, recent symptomology, other face and object processing). We estimated EEG source localization with standardized low resolution electromagnetic tomography (sLORETA). Subjective experience was obtained for baselines and photographic conditions. **RESULTS:** The ECB resting condition shows higher activity in all frequencies as compared to all other conditions. Likewise, the active tasks show differential effects for increased activity as compared to EOB for each region of interest (ROI) in each frequency domain. **CONCLUSION:** The data are in agreement with other neuroimaging techniques (fMRI/PET) investigating the DNt of brain function and further shows that the 3-dimensional localization accuracy of LORETA EEG is sufficient for the study of the DNt. In examining both within and between functional core regions there was a higher degree of activity in lower frequency bands during eyes closed; however, this pattern does not extend to all ROIs for all frequency domains. The differences may represent functional connectivity relating to endogenous/exogenous attention states as opposed to the simple concept of “resting” or “non-activity”. Further study of the functional relationships between EEG frequencies within and between regions in the default network and during self-specific processing may prove important to understanding the complex nature of neocortical functional integration.

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CHAPTER I: INTRODUCTION

Despite the enormity of research on the self, self consciousness and self-awareness, the self as a construct proves to be an enigma that continues to be a topic of concentrated research and debate among numerous disciplines. The self in psychology is embraced as an important area of study by certain divisions and less important to others. Yet, in the most basic sense the self is, in all probability at the core of normal, adaptive functioning. Moreover, disruptions in the self are implicated in abnormal and maladaptive functioning. The use of self in psychology typically represents a reflexive term (e.g., self-acceptance, self-actualization); however, there are six broad, unsystematic concepts of the self that are frequently used. According to the psychological dictionary, 1) the self is considered a hypothetical entity representing an inner agent or force with controlling and directing functions, 2) the self is considered an inner witness to events, or 3) the totality of personal experience and expression, 4) the self is also considered a synthesis, 5) an organized, personalized whole, or as conscious awareness or personal conception and, 6) as an abstract goal or end point (Reber, 1995). In one of the more profound descriptions of existence (or the self as being) Soren Kierkegaard proposed:

> *The way of objective reflection makes the subject accidental, and thereby changes existence into something different, something vanishing. The objective way of reflection leads away from the subject to the objective truth, and all the while the subject and his subjectivity become indifferent, and this indifference is precisely its objective validity; for all interest, like all decisiveness, is grounded in subjectivity. The way of objective reflection leads to abstract thought, to mathematics, to historical knowledge of different kinds; and it always leads away from the subject, whose existence or non-existence, and from the objective point of view entirely correctly, becomes infinitely indifferent. Entirely correctly, since as Hamlet says existence and non-existence have only subjective significance. . .*

This description has important implications for the development of an operational construct of self, such that our internal biases, attitudes, perceptions and judgments of self can, and in fact do influence or distort our view of self (self perception) and the world (self-in-experience). This distortion often impairs or hinders our flight to objectivity. In a few sub-disciplines of psychology, the notion of self is evident. From the implicit measures of racism and prejudice in social psychology to the biological drives of Freud, the self is explored. This manuscript will provide potential mechanisms for investigating the phenomenon of self from a neuroscientific perspective.

In exploring the neural basis of self, several authors agree (this one included) that the self is simply a collection of memories and mnemonic-functions that are intrinsically linked through neural pathways (nodes or hubs) and are a result of experiential learning, operant and classical conditioning, habituation, sensitization and perceptual processing (Squire, 1999). The neuroscientific method offers the potential to elucidate on the self-concept as being a set of organizational networks containing memories, mnemonic-functions and concepts (or more simply knowledge) for direction and implementation of plans, actions, decisions and perceptions (Churchland, 1988) as well as overall adaptive functioning.

In working with clinical populations (e.g. chemical dependency, depression, PTSD and schizophrenia) one finds idiosyncratic attitudes and beliefs that are common among groups. I will discuss substance abusers as an example. Regardless of socioeconomic status and upbringing, there is a pattern of negativism in this population that is not often evident unless one is exposed to hearing the life narratives of these individuals. It is rare, if ever that a life narrative mentions any experience in early life that instilled happiness or joy. In fact, most of these patients will begin the story with the most tragic and self-defaming items one can imagine and

this becomes the theme for the narrative. This gradually changes over the course of years and over the course of telling the story. In the earliest versions of the narrative, there is no cohesion and most are quite difficult to follow – except of course where there is negative content. For example, when the story is directly discussant of the self – it is almost always negative in context. This led me to the hypothesis that perception of self and self-in-experience must involve hubs or nodes in the brain that form neural assemblies directly responsible for the organization and maintenance of content for the self – be it positive or negative. Therefore, this should be a focus of concentrated effort to determine if activity patterns in the brain involved in self could be changed or in fact are being changed or influenced by psychotherapeutic techniques or medications.

This work will deal with the self as a primary agent, director, witness and narrator of experience in both intrapersonal and interpersonal contexts, as well as the summation of perceptions of social, familial, interpersonal, intrapersonal and educational experiences over the lifespan. I define this function of the self as being developed and maintained through self-perception (*SP*) and experiential schemata (*ES*), which is a neurologic progression in human development involving a fundamental self organization process. This process is based in the formulation of concepts of self originating in the perceptions of self (endogenous) formed through interactions with others and the environment (exogenous). These encoded schemata become the foundation for prevailing emotions, motivations, attitudes, and attributions relating to self and self-in-the-world that are maintained, reinforced and entrenched in neural coding mechanisms (neural hubs) formed through dendritic arborization over the lifespan. Numerous studies cited throughout this manuscript demonstrate that development of neural mechanisms are influenced by experience, in the neocortex, basal ganglia and brain stem regions. SP and ES are

the primary content of this research manuscript and are assumed to provide a primary function in both normal and maladaptive processes in the human condition. Self perception is the individual's ability to respond differentially to his or her own behavior and its controlling variables. More specifically, it is considered a product of social interactions (Mead, 1934; Ryle, 1949; Skinner, 1957). Self perception is often contrasted with the dissonance theory of cognitive psychology, which proposes that if a person holds two cognitions that are inconsistent with one another, this disagreement will produce internal pressure and anxiety, or an aversive motivational state (dissonance) (Festinger, 1957). Rather than hold these two concepts as separate, integrating them may provide a more useful platform for examining dysfunctional self processing and the neural mechanisms utilized to reconcile this lack of functional integration.

Relevant to this manuscript is an important element of perception. It pertains to SP and ES described by William James (James, 1952) as a stream of thought that involves choice, such that of all present sensations very few are picked out as salient to objective reality at a given moment. Thus the brain (he uses the term mind) decides what sensation will be held more real and valid than all the rest. He proposed that this is a superb illustration of selective industry. This industry is then posited to deal with things given in perception and that empirical thought is dependent on experience and the conceptualization of these percepts are dependent to a large degree on attentional habits. Further, he suggests that a stimulus may be presented to an individual thousands of times. However, if the stimulus is persistently not noticed, then it cannot enter into experience (James, p.185). The concept of selective industry is an important consideration in the organization of self. The degree to which the individual attends to positive or negative perceptions of self, in addition to positive or negative perceptions of self-in-experience

may be considered a foundational selective industry process through which the concept of (beliefs and attitudes) self is defined.

In exploring self in the brain, several lines of neuroscience research will be reviewed in the following sections. First, I discuss neuro-affective development and self organization. This is an important area of neuroscientific study, such that the earliest life experiences can influence functional connectivity patterns in the brain. Second, I will briefly review neuroimaging data exploring the default mode network in the brain, reward and self processing. If the self is as James posits "*So our self feeling in this world depends entirely on what we back ourselves to do,*" then it stands to reason that the processing of self (image and experiential/perceptual) would activate regions similar to reward mechanisms in both positive and negative contexts. Third, I will briefly cover known neuroimaging data and functional neuroanatomy as a function of EEG. Fourth, I will review neuroimaging data from studies of self awareness, autobiographical memory, object processing, and self perception and experiential schemata. Fifth, I will discuss experiential schemata, as it relates to emotion and the stress hormone cortisol. Sixth, I will briefly cover cognitive theory and depression. Finally, I will discuss psychological theories of self, followed by the rationale and specific aims and hypotheses for this study.

CHAPTER II: LITERATURE REVIEW

Neuro-Affective-Development and the Organization of the Self

Self-organization is a fundamental process in the developing human being. This process is formulated through interactions with the environment, including social relationships, functional relationships with objects and an intimate relationship with self. In many situations individuals formulate interactions with the environment based on reference to the self and its influence on internal states. It is posited that a default core of self in the brain involves cortical midline and brain stem centers active in affective (emotional) processes and self-affect-regulation (Panksepp, 2003, 2005). Supporting evidence indicates a core self to be an adaptation that is species specific, and maintains equilibrium in the overall functioning of the species within the context of its social, cultural and behavioral environments (Call & Tomasello, 2008; Rilling, et al., 2007). It is known that critical periods in neural development exist and disruptions or delay in these specific periods can produce severe effects in maturation and specificity of human functioning. Case studies of feral children (e.g., Genie, Kamala & Amala) demonstrate that the absence of certain experiences early in life cannot be compensated for by later exposure. More simply, the individual cannot make up for earlier lack of experiential learning and exposure (McCrone, 2002).

A more recent notion posits the concepts of experience-expectant and experience-dependent sensitive periods can be viewed as organizing constructs for highlighting the role that caregiving and other environmental factors may play in the ontogenesis of neuro-regulatory and self-regulatory processes across the lifespan (Cicchetti & Rogosch, 1997). These concepts represent fundamental processes in the neuro-affective-developmental regulation of emotion that is of considerable interest concerning the effects of negative life experiences or negative percepts

of self and self-in-experience on the developing human being (R. Cannon, Lubar, & Baldwin, 2008; Izard, Libero, Putnam, & Haynes, 1993).

Studies have shown differences in the frontal EEG patterns of infants of depressed mothers as compared to controls. More specifically, there was increased frontal activity during sad expressions in frontal but not parietal regions. The authors concluded that infants of depressed mothers show greater amplitude of EEG power in right frontal cortex during the expression of negative emotions (Dawson, Panagiotides, Klinger, & Spieker, 1997). Research with 3-month old infants of depressed mothers demonstrated the infants could discriminate sad from happy expressions but they did not perceive sad expressions as novel (Hernandez-Reif, Field, Diego, Vera, & Pickens, 2006). This is in line with adult data of depressed individuals, such that adults tend to exhibit asymmetries in frontal lobes specific to excess alpha frequency increased in the left prefrontal cortex. These frontal asymmetries are likely to involve brain regions associated with affect including the anterior cingulate cortex (Devinsky, Morrell, & Vogt, 1995).

There is a growing body of literature demonstrating that prenatal exposure to substances of abuse may adversely impact normal development including cognitive and affective processing (Singer, et al., 2005). The likelihood of developing attentional disorders may be increased in children exposed to substances in utero (Mayes, 1999). Exposure to toxins is thought to inhibit reuptake of dopamine, norepinephrine, and serotonin in cortical regions involved in both attention and arousal. Animal studies have shown that prenatal exposure to cocaine does impair selective attention processes (Stanwood & Levitt, 2001; Stanwood, Washington, & Levitt, 2001).

Neural pathways (schemata) are formed in early development in order to organize our social, familial and self concepts. Within this context, the encoding of experiential information

through learning and perception are on a developmental continuum. A combination of both internal and external worlds can produce negative effects on the developing self-concept. This self concept, which may begin as early as 10-months of age, if influenced by negative experiences and a prevalent pattern of negative self-reference (perception), may increase an individual's likelihood to develop psychological distress (Gendolla, Abele, Andrei, Spurk, & Richter, 2005; Parker, 1994; Schafer, 1973). In essence, self-organization, self-perception, social and familial identity and self-definition may begin to form very early in the developmental process. Additionally, early childhood activates brain regions involved in imitation, affect interpretation and responsiveness and in the broadest sense perceptual processing of facial expressions and the environment by means of mirror neuron pathways in the brain. These mirror neurons are involved in processing external gestures, prosody and posture. These neural pathways are also suggested to play a key role in the infant's interactions with primary caregiver and vice versa. Moreover, the child is able to interact, sense, imitate and respond to the caregiver, which in turn may influence the development of a theory of mind (Jones, 2009; Learmonth, Lamberth, & Rovee-Collier, 2005; Meltzoff, 1990).

An operationalized definition for experiential schemata (self-in-experience), as used in this work, posits it as a neurologic progression in human development involving a fundamental self-organization process. This process is based in the formulation of concepts of self originating in perceptions of self (endogenous) formed through interactions with others and the environment (exogenous). These encoded schemata become the foundation for prevailing emotions, motivations, attitudes, and attributions relating to self and self-in-the-world that are maintained, reinforced and entrenched in neural coding mechanisms formed through dendritic arborization over the lifespan (R. Cannon, et al., 2008). These perceptual processes can lead to the

development of a self-perpetuating, negative-reinforcement circuit. This circuit or network is specific to negative affective processes, which in turn, lead to the misinterpretation and personalization of interactions and events through an unregulated, dysfunctional dendritic pruning process. In other words, synapses are errantly pruned, i.e. disallowing the adaptation and dispensation of new information relating to self and self-in-experience. More simply, the self in essence can become a negative-conditioned-stimulus involving core self and default mode brain regions. Research has shown that negative self-esteem and negative self-image can have deleterious effects on social and interpersonal relationships and is suspected to play a role in numerous psychological disorders, including, anorexia/bulimia, social phobia, depression, anxiety, schizophrenia and substance related disorders (Fries, Frey, & Pongratz, 1977; Gneo, Natoli, Menghini, & Galanti, 1986; Gordon, Lee, Dulcan, & Finegold, 1986).

It is also necessary to provide an operational definition that has to some extent been evasive since William James posited “everyone knows what attention is.” Attention in the context of this work is a specific, sequential cerebral directive for reduction of sensory responses to or from competing streams of exogenous and endogenous stimuli in order to facilitate the encoding and subsequent storage of a stream or streams of interest for a selective potential or immediate best response. This operational definition includes those variants of attention discussed by other authors and researchers (e.g., focused, selective, visual, auditory and tactile variants). Attention is inherently important and necessary to the overall executive functioning of the individual and disruptions to attentive processes do influence other cognitive processes and vice versa.

Default Network in Early Development

This section emphasizes the importance of early experiences on the default mode of brain function (Corbetta, et al., 1998; Gusnard, Akbudak, Shulman, & Raichle, 2001; M. E. Raichle, et al., 2001; Raichle & Snyder, 2007; Shulman, et al., 1997). The Default mode network (DNt) consists of twelve functionally related regions (Table 1 in the appendices, hereafter all tables and figures are in the appendices) that are consistently shown increased in activity as compared to functionally specific cognitive tasks or eyes-opened resting conditions (Shulman, et al., 1997; Shulman, et al., 1999; Shulman, Schwarz, Miezin, & Petersen, 1998). The DNt is synonymous with resting state network (RSN); however, the RSN has been suggested to include numerous networks of functionally connected neuronal assemblies (Damoiseaux, et al., 2008; Damoiseaux, et al., 2006; Fransson, et al., 2007). Recent work by Fair and colleagues (2008) have demonstrated that the brain's default mode network (DNt) exhibits less functional connectivity in children than in adults. The DNt is proposed to support such core functions as theory of mind, self-related activities such as autobiographical self, stimulus independent thought, self-projection, self-reference and introspective processes (Fair, et al., 2008).

Another, less accepted idea is that the DNt is directly involved in self-internally directed mental activity (Gusnard, et al., 2001). The reduced functional integration or synchronous activity within this default mode network in children as compared to adults stresses the importance of experience and the formation of neural pathways on the developing human being. Moreover, if this network does perform a critical role in the organization and conceptualization of self, then the effects of self-perception in relation to experiential schemata undoubtedly provide important foci for normal and abnormal development with regard to the self organization process. A recent study demonstrated similarities in DNt structures between humans and

chimpanzees, such that both species exhibited high levels of activity in rostral lateral and dorsolateral PFC. Humans showed the highest level of activity in more dorsal areas of medial prefrontal cortex (PFC) in Brodmann area (BA) 9 and BA 32, whereas chimpanzees showed more widespread activity, including activity in more ventral areas of (BA 10). Similar to human studies, higher resting state activity was shown in the posterior cingulate in chimpanzees. The left-lateralized activity related to language and concept processing or mentalizing in humans was not observed in chimpanzees (Rilling, et al., 2007). Similarly, research exploring resting state networks (RSN) in the infant brain, concluded that long-range functional connectivity is evident during the earliest phases of human brain development (Fransson, et al., 2007). The adult brain may include up to 10 of these RSN networks; however, five RSN were identified in the infant brain, including the medial aspects of the occipital cortex (posterior cingulate) differing from RSN attributed to predominantly cortical regions residing along the somatosensory and motor cortex in the adult brain (De Luca, Beckmann, De Stefano, Matthews, & Smith, 2006). RSN activity in infants specific to the temporal lobe and the inferior parietal cortex that largely included the primary auditory cortex in the superior temporal gyrus has also been described in the adult brain (Damoiseaux, et al., 2006; De Luca, et al., 2006; Greicius, Krasnow, Reiss, & Menon, 2003; White, et al., 2009). Thus, we can surmise that a pattern of functional connectivity between regions in the cortex is differentially active during baseline and decreased in activity during specific tasks, given this pattern of resting activity or DNt has been shown to be similar in chimpanzees, infants, children, and adults.

A stable, consistent pattern of neural activity and functional connectivity between neuronal assemblies within these cortical regions may provide important diagnostic considerations with respect to many developmental disorders as well as psychological syndromes

in the adult population. Discovery of idiosyncratic biological markers for such disorders can only benefit our holistic understanding of psychological syndromes and enhance development of more disorder specific treatment planning and implementation of evidence based neurophysiological outcome measures.

Neuroanatomy of default mode network, Reward and Core Self

In this section each of the regions of the brain shown to be active during tasks related to self processing and the DNt are briefly reviewed. In neuroimaging studies, there is a very high degree of overlap in regional activation patterns during tasks. Thus, the human brain is perhaps best described as a complex system of complex systems. In essence, a reductionist approach to neural functions may hinder the discovery of complex functional systems. Indeed the mechanisms and specificity of its functions are the greatest of enigmas.

Figure 1 in the appendices is an illustration of similar regions in the brain shown to be activated during reward, self-referential tasks and DNt studies. Evaluation of stimuli and decision making processes (i.e., executive functions) involve numerous brain regions, including those implicated in the much debated brain reward system (BRS) (Woodward, Chang, Janak, Azarov, & Anstrom, 1999). The brain reward system (BRS) is proposed to involve mesolimbic, prefrontal and basal ganglia structures, including the insular, somatosensory, orbitofrontal (OFC), anterior cingulate (AC) and dorsolateral prefrontal cortices (DLPFC), as well as the amygdala, hippocampus, midline thalamic nuclei, ventral pallidus, pedunculopontine nucleus, hypothalamus, substantia nigra and ventral tegmental area (VTA). Additionally, these regions are implicated in a specific reward network, involving the nucleus accumbens (NaC) that is affected by drug and alcohol abuse, gambling and most appetitive behaviors. The NaC is a primary source of inhibitory GABAergic neurotransmitters (Bechara, 2005; Everitt and Robbins, 2005).

This reward system is shown to be active during the comprehension of humor, which is also suggested to involve equivalent faculties as social communication and social processing (Brown, Paul, Symington, & Dietrich, 2005).

Reward is important when considering the self for two explicit reasons. First, in many situations in the human condition rules describing interdependencies between different actions do exist and exploitation of these rules can lead to one type of reward being more salient than another. Secondly, abstract concepts involve rules governing rewarding behaviors and in the most basic sense appreciation of the abstraction invariably depends on a congruency effect of both language and cognition for reward learning and decision making. These types of reward processes are shown to involve dorsal and ventral striatum, and ventromedial prefrontal cortex (O'Doherty, Hampton, & Kim, 2007; Schonberg, Daw, Joel, & O'Doherty, 2007).

Functional magnetic resonance imaging (fMRI) investigations of brain regions implicated in humor have increased in the past few years, and many of these studies utilize methods in which the participants rated cartoons, television clips or written words, jokes, and humorous stories. Much of the research reported similar results, with increased activation of the left temporo-occipital junction, left inferior frontal gyrus, supplementary motor area (BA 6), and a subcortical network involving the ventral striatum, NaC, and other hypothalamic and amygdaloid regions (Mobbs, Greicius, Abdel-Azim, Menon, & Reiss, 2003; Moran, Wig, Adams, Janata, & Kelley, 2004). Damage to the right frontal cortex (aphasics) negatively influences performance on nonverbal cartoon completion tasks as compared to left frontal damage with diminished capacity to establish clarity without impairment to the sensitivity and appreciation of the surprise element (Bihrle, Brownell, Powelson, & Gardner, 1986). Social comprehension involves interconnected, bilateral networks, and persons with agenesis in the corpus callosum performed

less efficiently than controls in evaluation of narrative joke forms, narrative memory, set-switching, and use of literal language (Brown, Paul, Symington, & Dietrich, 2005). It is maintained that humor contains both cognitive and affective elements and that these processes elicit activity in the left hemisphere relating to clarity and integration of information, whereas the right hemisphere is reportedly active in the emotional aspects associated with the surprise element of humor (Moran, et al., 2004). Research has demonstrated that activation of reward system structures also occurs during tasks associated with self-reference and self-relatedness, including the NaC, VTA and ventromedial prefrontal, left inferior frontal and anterior cingulate cortices (de Greck, et al., 2008; Kelley, et al., 2002).

Anterior Cingulate Gyrus

One of the primary brain regions involved in consciousness, self-awareness, learning, reward and decision making processes and the DNt is the anterior cingulate gyrus (AC) (Devinsky, Morrell & Vogt, 1995). Of particular importance to this study is its involvement in neuro-developmental, self-regulatory and affective processes. In animal studies the AC is shown to be intricately involved in the encoding and schemata formation (neural pathways) of the external and internal worlds. Helmeke and colleagues studied social and environmental influence on infant rats with: (i) undisturbed control animals, (ii) handled animals, (iii) animals which were repeatedly parentally deprived during the first 3 postnatal weeks, and (iv) animals which were treated similar to group (iii) and thereafter kept in chronic social isolation. The results of this and a parallel study revealed the sensitivity of the dorsal AC to environmental changes and emotional challenges during early periods of postnatal brain development. Experience-induced synaptic alterations were observed several weeks after the animals were returned to undisturbed social conditions. Thereby indicating that these environmentally induced arborization processes can be

enduring and perhaps even permanent. The observed elevated, presumably excitatory synaptic input into a cortical part of the limbic system may reflect developmental adaptations of the maturing brain towards repeated emotional challenges (Helmeke et al. 2001).

The AC has one of the highest densities of opioid receptors in the central nervous system and plays an intricate role in nociception and monitoring the affective component in pain processing. Studies have demonstrated that lesions or removal of specific portions of the AC produced effects in the experience of pain, specifically, reducing the affective component and the experience of painful stimuli. Injections of morphine are shown to elevate cerebral blood flow to rostral and ventral portions of AC. Additionally, the AC projects extensive afferent thalamocortical connections shown to be involved with Enkephalin-immunoreactive neurons and noradrenergic neurons in addition to opioid neurons in locus cereleus. These projections and functions implicate the AC in numerous clinical syndromes (Nimchinsky, Vogt, Morrison, & Hof, 1995; Oya, et al., 2005; Vogt, Wiley, & Jensen, 1995; Woodward, et al., 1999).

Research indicates that persons with attention deficit/hyperactivity disorder (ADHD) fail to activate the cognitive division of the AC during Stroop interference tasks. Similarly, it is shown that persons with ADHD produce slower reaction times to stimuli and this involves response selection processes in the AC (Colla, et al., 2008). Studies suggest the cognitive division of the AC is activated during divided attention tasks, and the affective division is decreased in activation during cognitive tasks and vice versa (Bush, Luu, & Posner, 2000; Devinsky, et al., 1995). PET and fMRI neuroimaging experiments have reported activation of the AC in memory (Dudukovic & Wagner, 2007; Kaneda & Osaka, 2008; Nyberg, et al., 2003), cognition (Allman, Hakeem, Erwin, Nimchinsky, & Hof, 2001), emotion (Allman, et al., 2001; Beauregard, Levesque, & Bourgouin, 2001; Bush, et al., 2000; Phan, Liberzon, Welsh, Britton,

& Taylor, 2003; Phan, Wager, Taylor, & Liberzon, 2002) as well as decision making and reward processes (Bush, et al., 2002; Kennerley, Walton, Behrens, Buckley, & Rushworth, 2006; Walton, Croxson, Behrens, Kennerley, & Rushworth, 2007).

Functions of the AC have been evaluated in both animal and human studies. These functions include motor control and response selection, avoidance and approach response monitoring, conditioned emotional learning, motivational processes, reward, decision making, and all inclusive components of executive functioning. Similar epilepsy and lesion studies indicate the AC to play a direct role in visceromotor functions, control of vocalization and communication of internal states, skeletomotor control, nociception and memory processes, as well as language and working memory/attentive processes. It also is implicated in social interactions, affect-regulation and psychopathology (Bush, et al., 2000; Devinsky, et al., 1995). Several theories relating to the role of the AC in attentional and executive processes have been suggested without clarity of the interactions between the AC and the left and right dorsolateral prefrontal cortices (LPFC and RPFC), despite the probability that attentional processes are the most investigated function of the AC (Bench, et al., 1993; Posner & Rothbart, 1998).

It has been proposed that the AC detects the need for executive control and signals the prefrontal cortex (PFC) to execute the control (Cohen, Botvinik, & Carter, 2000; Markela-Lerenc et al., 2004). Similarly, research proposes that the AC is in effect a gating mechanism between the cortex and subcortical regions (D. A. Pizzagalli, Oakes, & Davidson, 2003). These two ideas are supported given that the AC along with other subcortical nuclei receives inputs from regions involved in memory, emotion, reward, nociception, and autonomic functioning. The AC is thought to be more involved in decision making processes whereas the posterior cingulate is

proposed to perform integrative and evaluative processes (Bush, et al., 2000; Devinsky, et al., 1995).

Orbital Frontal Cortex

The orbitofrontal cortex (OFC) is instrumental to emotional regulation, encoding and retrieval, self-regulation and most cognitive processes in normal populations. It is also implicated in numerous psychological disorders, including schizophrenia (Lacerda, et al., 2007; C. T. Toro, Hallak, Dunham, & Deakin, 2006), depression, obsessive-compulsive and anxiety disorders (Drevets, 2007; C. Toro & Deakin, 2005), personality disorders (New, et al., 2007; Resnick, Driscoll, & Lamar, 2007) and substance use disorders (R. Z. Goldstein, et al., 2007). It is also shown to be involved in tasks regarding social cognition, interpreting the mental states of others (theory of mind), self reference, encoding, reality monitoring, suicidal ideation, and empathic processes along with other regions included in this review (Berthoz, Armony, Blair, & Dolan, 2002; Critchley, 2005; du Boisgueheneuc, et al., 2006; Fleck, Daselaar, Dobbins, & Cabeza, 2006; Goel, Grafman, Sadato, & Hallett, 1995; Kensinger & Schacter, 2005; Kim & Hamann, 2007; Walton, et al., 2007).

The OFC is shown as one of the more metabolically active regions in the DNt. It is shown increased in activity during the processing of self and self-relatedness and theory of mind tasks (assigning mental states to others). It has been shown to play a particular role in negative self perception and is suspected to play an important role in the development of addictive disorders. Its location in the brain and connections to neocortex, thalamus, limbic structures and brain stem nuclei implicate it in a wide range of human behaviors and psychological dysfunction (Gusnard, 2005; Gusnard, et al., 2001; Nelson, et al., 2009).

Posterior Cingulate and Precuneus

The posterior cingulate (PC) and precuneus module is the only node in the DNt to interact with all other nodes (Fransson & Marrelec, 2008); however, the EEG activity involved in these intrinsic interactions is not known. Moreover, strong associations between the precuneus and PC are shown to be involved in cognitive and self-referential tasks. Similarly, research has demonstrated there is decreased coherency between DNt regions in Alzheimer's disease, especially concerning the role of the PC and left hippocampus (Greicius, Srivastava, Reiss, & Menon, 2004). The PC is suggested to among the most metabolically active regions in the RSN in healthy individuals (M. E. Raichle, et al., 2001). Moreover, diffusion tensor imaging research suggests that disruptions in functional connectivity between the PC and hippocampus produces effects in connections to the medial temporal and frontal cortices (Y. Zhou, et al., 2008). Thus implicating it to play an important role in memory as well as verbal and integrative functionality (Lustig, et al., 2003). The PC (BA 31) is a vaulted structure located bilaterally along the mid-line. It is dorsal to the corpus callosum, inferior to the cingulate sulcus and superior to the callosal sulcus (Vogt, Nimchinsky, Vogt, & Hof, 1995). The PC is adjacent the AC, such that the AC and PC inclusively with central cingulate (CG) form the cingulate gyrus. Functionally, the PC is considered an evaluative region, involved with assessing environmental stimuli and in memory functions (Vogt, Finch, & Olson, 1992) and pain (Vogt, Derbyshire, & Jones, 1996). It is also considered important to verbal production and comprehension in addition to attentional processes and higher order visual processing (R. Cannon, Congedo, Lubar, & Hutchens, 2009; Choo, et al., 2008).

Amygdala

The amygdala, like the hippocampus shares extensive connections to brain stem, autonomic and higher executive regions of the brain and is important to numerous behavioral functions, including appetite, sexual behaviors, aggressivity, reward, decision making, aversion, emotion, memory, social functioning, fear responses, alerting, orienting and learning (Alonso-Deflorida & Delgado, 1958; Chen, Tenney, Kulkarni, & King, 2007; Dardou, Datiche, & Cattarelli, 2007; Egger & Flynn, 1962; Evans, et al., 2007). It is also suspected to play a role in numerous psychiatric syndromes (e.g., Alzheimer's disease, depression, anxiety and schizophrenia) (Blair, 2007; Bremner, 2007; Caetano, et al., 2007; Grillon, 2007) and addictive disorders (Adinoff, 2004; Di Chiara, et al., 1999). The amygdala is shown to project and receive connections from orbitofrontal, temporal and hypothalamic regions. There has been some disagreement about many of these connections in humans, since they are not shown in rats or hamsters. Researchers suggest this can be attributed to species-specific connections developed over time and to the complexity of the external world since the amygdala does share extensive projections with regions involved with all sensory modalities (de Olmos, 1972).

It is also known that stimulation effects are habituated to very rapidly in the amygdala. This region when stimulated in humans produces similar effects as animal studies, with primarily feelings of fear or rage (Delgado, et al. 1968; Stevens, et al. 1969). Alternatively, stimulation of regions in the temporal lobe produced feelings of fear but not rage (Jasper, 1954). Removal of the bilateral temporal lobes, including the amygdala produced behavioral changes such as a decrease in belligerence and reductions in fear to normally fear inducing objects, tendencies to investigate orally and contact inedible objects, and increases in inappropriate sexual behaviors. These symptoms collectively were referred to as Kluever – Bucy Syndrome (1939). The

amygdala, like the hippocampus and other limbic regions plays an important role in many adaptive human behaviors in addition to dysfunctional contexts.

Hippocampus

The hippocampus has extensive afferent and efferent connections throughout the cortex and is thought to be instrumental to a variety of human behaviors, including, memory, language, emotion, executive functions, learning, reward, decision making, mating behavior and long term potentiation of stress (Awad, Warren, Scott, Turkheimer, & Wise, 2007; Bast, 2007; Boutros, et al., 2007). Dysfunctions in the hippocampal formation are implicated in numerous psychiatric disorders including, depression (Gass & Riva, 2007; Maletic, et al., 2007; Sahay & Hen, 2007), schizophrenia (Barch, 2005; Woodruff-Pak & Gould, 2002), bipolar disorder (Frey, et al., 2007; Itokawa & Yoshikawa, 2007) and addictive disorders (del Olmo, et al., 2006; Nestler, 2001; Robbins & Everitt, 2002). The hippocampus is involved in memory and the processing of emotion, stress and long term potentiation processes of learning (Diamond, Campbell, Park, Halonen, & Zoladz, 2007; Joels, Krugers, & Karst, 2007).

Ventral Tegmental Area (VTA)

The ventral tegmental area (VTA) is implicated in numerous appetitive, sexual and reward behaviors. fMRI research of brain regions activated during orgasm in females with spinal cord injuries included the hypothalamic paraventricular nucleus, amygdala, accumbens-bed nucleus of the stria terminalis-preoptic area, hippocampus, basal ganglia (especially putamen), cerebellum, and anterior cingulate, insular, parietal and frontal cortices, and lower brainstem (central gray, mesencephalic reticular formation, and the nucleus of the solitary tract in the medulla oblongata). The authors concluded that the vagus nerve provides a spinal cord-bypass pathway for vaginal cervical sensibility and that activation of this pathway can produce analgesia

and orgasm. Another study of sexual stimulation of the clitoris (compared to rest) showed significant increase in regional cerebral blood flow (rCBF) in the left secondary and right dorsal primary somatosensory cortex. This demonstrated the first account of neocortical processing of sexual clitoral information. Contrarily, orgasm was associated with profound rCBF decreases in the neocortex when compared with the controls, namely in the left lateral orbitofrontal cortex, inferior temporal gyrus and anterior temporal pole. The authors posited that decreased blood flow in the left lateral orbitofrontal cortex was indicative of behavioral disinhibition during orgasm in women, and that the decrease in activity in the temporal lobe was related to high sexual arousal. Additionally, cerebellar nuclei were posited to be involved in orgasm-specific muscle contractions, and activation of the ventral midbrain and right caudate nucleus indicates a role for dopaminergic pathways in female sexual arousal and orgasm (Komisaruk & Whipple, 2005).

Brain regions involved in male ejaculation show primary activation in the mesodiencephalic transition zone, including the VTA, which is shown active in rewarding behaviors. Other regions of increased activity included the central tegmental field, zona incerta, subparafascicular nucleus, and the ventroposterior, midline, and intralaminar thalamic nuclei. There was also increased activity in the lateral putamen and adjoining parts of the claustrum. Salient activity increase in the cortex was restricted to Brodmann areas 7/40, 18, 21, 23, and 47 in the right hemisphere. These findings are different from rodent studies and conversely, the amygdala and adjacent entorhinal cortex did not show increased activation. Thus, the authors concluded the cerebellum plays an important role in ejaculatory processes in conjunction with the other regions. The VTA plays an important role in sexual behavior, maternal behavior and reward and addictive disorders. It is also shown to be important to the processing of self and

social mechanisms (Kenny, Chartoff, Roberto, Carlezon, & Markou, 2009; Laviolette & van der Kooy, 2004; Nikulina, Miczek, & Hammer, 2005; Schumann, Michaeli, & Yaka, 2009).

Insular Cortices

The insular cortex has been demonstrated to play an active role in choices made from an affective perspective as compared to those made from a cognitive perspective. The insular cortex is a region of convergance of multisensory inputs and is implicated in numerous human functions (Craig, 2009). Recent data demonstrated the insula plays an important role in conjunction with the thalamus in activation or suspension of the default mode state, as well as playing a role in epeliptiform activity (Gotman, et al., 2005). It is thought to play an important role in emotion, especially the affective component of pain processing (Sawamoto, et al., 2000). It is also demonstrated to play an important role in depression relative to the DNt. Connectivity and regional activity in the DNt in depressed patients was shown to differ from controls in an emotional performance task. Importantly, DNt regions have been significantly correlated with both depression severity and feelings of hopelessness (Sheline, et al., 2009). Similar research implicates the right fronto-insular cortex in switching between central executive and default mode regions (Sridharan, Levitin, & Menon, 2008). Research has demonstrated increased levels of activity during emotion-related tasks in the amygdala, insula, and anterior cingulate cortices with these regions being significant predictors in heart rate responses in the presentation of emotional facial expressions (Yang, et al., 2007).

Dorsolateral Prefrontal Cortices

The dorsolateral prefrontal cortices (DLPFC) have been shown active in a high degree of cognitive, attention and memory related experiments (Barde & Thompson-Schill, 2002; Dehaene & Changeux, 2000; Fuster, 2000a, 2000b). Regions in the left prefrontal cortex (LPFC) have

been shown to be involved in working memory, disinhibition and cognitive processes. The LPFC is considered to be involved in attention and conceptualization processes, in addition to theory of mind tasks, interpreting the mental states of others and self and other facial recognition tasks (Brady, Campbell, & Flaherty, 2004; R. Cannon, Congedo, M., Lubar, J., Hutchens, T. , 2009; R. Cannon, et al., 2007; R. Cannon, Lubar, J, 2008; R. Cannon, Lubar, J., Gerke, A., Thornton, K., Hutchens, T., McCammon, V, 2006; DeBruine, 2004; Gara, et al., 1993).

Studies have shown that mental state considerations explicitly reflecting on aspects of one's own mental state or attributions made about the mental states of others employ these dorsal anterior cingulate and dorsal medial prefrontal regions (Frith & Frith, 2006; Gusnard, Akbudak, Shulman, & Raichle, 2001; Gusnard, 2005). Similarly, imaging studies targeting retrieval of personal or episodic memories involving verbal and nonverbal material (Cabeza & Nyberg, 2000; Cabeza et al., 2003) have implicated this same prefrontal region. Deficits in left prefrontal and occipital regions have been shown to lead to disruptions to self-monitoring, and self-evaluation processes that also involve limbic and brainstem fear centers (Lidell, Brown et al 2005). Studies have demonstrated that depressed individuals had left anterior decreased activation characterized by increased alpha activity compared with individuals not experiencing depression. Lesions to the left hemisphere have been shown to produce increased depression, dysthymia and negative emotions associated with dysphoric mood. Contrarily, lesions to the right hemisphere have been associated with dysfunction in interpreting the emotional states of others as well as social appropriateness and intrapersonal monitoring (Lubar, Congedo, & Askew, 2003).

The Default Network, Self and Reward

In the past decade, neuroimaging research has demonstrated that during specific cognitive tasks the human brain exhibits increased spatial organization in neuronal activation (Steyn-Ross, Steyn-Ross, Wilson, & Sleigh, 2009). The default mode network (DNt) was derived from this body of neuroimaging results utilizing PET and fMRI techniques. Consistent decrease in neural activity as measured by local decrease in cerebral blood flow and blood-oxygenated level-dependent (BOLD) is shown in these studies. PET is a direct measure of local neuronal activity (Raichle, 1998), such that neural activity shows increases in regional cerebral glucose metabolism (rCGM) to brain regions involved in changing mental activities or cognitively demanding tasks (Shulman, et al., 1997; Shulman, et al., 1999; Shulman, Ollinger, Linenweber, Petersen, & Corbetta, 2001). The fMRI BOLD response is an indirect measure of neural activity. Despite the advantages of increased spatial resolution, there remain limitations to the temporal resolution and ambiguity associated with the interpretation and reporting of results (Logothetis, Pauls, Augath, Trinath, & Oeltermann, 2001; Logothetis & Wandell, 2004). There is often a high degree of overlap in activation of brain regions during cognitive, memory, attentional and affective tasks which adds to the difficulty in interpreting fMRI results (Cabeza & Nyberg, 2000). Despite these challenges this DNt effect has been replicated in numerous studies (Fransson, 2005; Gusnard, et al., 2001; M. E. Raichle, et al., 2001). The regions associated with the DNt and *a priori* regions of interest (ROI) for this study are shown in table 1 in the appendices. In the table from left to right is the orientation within the brain, (i.e., right, left, medial) and Brodmann area (BA), the x, y, and z coordinates and the neuroanatomical label.

The DNt is typically associated with a ‘resting state’ which is described as an ‘idling, non-cognitive brain.’ This state is typically observed with the individual relaxing with the eyes-

closed (or eyes-closed baseline). The ROI in table 1 are typically shown increased in activity during baseline as compared to cognitive or working memory tasks (Greicius, et al., 2003; Gusnard & Raichle, 2001). The description of 'resting state' in published studies is given as 'subjects were instructed to relax with their eyes closed' with the subjects' confirmed report of this condition after the scans (De Luca, et al., 2006; Gusnard, 2005; Gusnard, et al., 2001; Hagmann, et al., 2008). Recent data examining self-relatedness demonstrated that the same regions often recruited during reward including the bilateral nucleus accumbens (NaC), ventral tegmental area (VTA) and ventromedial prefrontal cortex (VMPFC) were also active during self-relatedness. Furthermore, the fMRI signal time courses showed no difference between early BOLD signals between reward and self-relatedness. Additionally, both conditions differed in late BOLD signals with self-relatedness showing higher signal intensity. The conclusion was that sustained recruitment of the reward system is also demonstrated during self-relatedness, suggesting an important relationship between reward and self (de Greck, et al., 2008).

Increasing knowledge of the functional relationships between DNt may be aided by studying the Electroencephalogram (EEG) activity in the DNt since it provides very good temporal resolution in milliseconds (Steyn-Ross, et al., 2009) and with the advent of EEG source localization techniques (Pascual-Marqui, 2002; Pascual-Marqui, et al., 1999) it is possible to explore EEG activity in neocortical and limbic regions associated with DNt. Low-resolution electromagnetic tomography (LORETA) and the standardized version (sLORETA) are inverse solutions that have been validated as accurate for estimating the potential sources of the scalp EEG (Bai, Towle, He, & He, 2007; Thatcher, North, & Biver, 2005b). However, to date the EEG activity in the DNt regions has not been investigated.

Brief Review of Electroencephalogram

EEG rhythms are proposed to correspond to the synchronized synaptic activity of large numbers of neurons across neural pathways (or networks). The specific functions of EEG oscillatory activity still involves much uncertainty; however, the suggestion that synchronization of distributed neural networks functionally integrates differential brain structures (Bushara, et al., 2003) is an important direction for further study. In the following sections I will briefly cover known associations of activations with EEG frequency bands.

In normal populations, the delta frequency is most notably associated with the onset of sleep (Lubin, Nute, Naitoh, & Martin, 1973). However, it is also suggested to play a particular role in encoding and retrieval as well as having a primary role in overall intelligence measures (Knyazev, Savostyanov, & Levin, 2005; Kurova & Cheremushkin, 2007). The theta frequency is notably associated with memory processes. It also plays a role in encoding and retrieval as well as executive attention (R. Cannon, Congedo, M., Lubar, J., Hutchens, T. , 2009; R. Cannon, et al., 2007). Moreover, in combination with the gamma frequency, it is involved in reward, motivation and cognitive processing (Klimesch, 1999; Klimesch, et al., 2006; Klimesch, Schack, & Sauseng, 2005; Knyazev, et al., 2005; Lehmann, Henggeler, Koukkou, & Michel, 1993) the possible governing of cognitive processes (Basar, Basar-Eroglu, Karakas, & Schurmann, 1999, 2001) and visual encoding and retrieval processes (Fink & Neubauer, 2006; Schmid, Tirsch, & Scherb, 2002; Thatcher, North, & Biver, 2008). Alpha activity is thought to be involved in all variants of attention, including alerting, orienting and sustained attention, as well as visual processing and cognitive preparedness (Angelakis, Lubar, & Stathopoulou, 2004; Angelakis, Lubar, Stathopoulou, & Kounios, 2004; R. Cannon, et al., 2009; R. Cannon, et al., 2007). Additionally, alpha is shown to play a role in evaluation of self and mental state decoding (R.

Cannon, et al., 2008; Sabbagh & Flynn, 2006). Beta activity is proposed to be involved in affective and cognitive processes, attention as well as executive functions and psychopathology (Clarke, et al., 2007; Ray & Cole, 1985; Spironelli, Penolazzi, & Angrilli, 2008).

The EEG activity in these DNt and CMS structures to date has not been investigated. However, recent studies have examined correlations between EEG alpha activity (Goldman, Stern, Engel, & Cohen, 2002; Laufs, et al., 2003) and ultra-slow EEG frequencies (<0.01 – 0.05 Hz) with the fMRI BOLD signal (De Luca, et al., 2006). Coherency between ultra-slow EEG and BOLD led to the identification of five distinct resting state networks (RSN)(De Luca, et al., 2006), and there were varying results for the alpha correlates of BOLD (Danos, Guich, Abel, & Buchsbaum, 2001; Goldman, et al., 2002). If the DNt is a stable and persistent component of the human brain, then it is important to improving our understanding of how the healthy brain functionally communicates behavioral directions in a minimally stimulated state as opposed to specific activated tasks. Such study may prove pivotal for increasing our knowledge of functional connectivity among neural mechanisms as well as discovery of biological markers for disruptions in these mechanisms in psychopathology.

DNt and Self

The DNt is a very important consideration in the experimental observation of the self, which has in recent years become a priority topic in neuroscience research. The tasks utilized are often self-recognition or self-referential. The self-referent tasks utilize stimuli that are self-relevant or self-related (Craik, 1999; Kelley, et al., 2002). In the Craik study, PET was utilized to examine cortical regions that may be involved in the representation of self based on prior studies demonstrating activation patterns during episodic memory retrieval (Nyberg, 1998; Nyberg, McIntosh, & Tulving, 1998). Participants carried out self-related processing in the context of

memory encoding. The results demonstrated notable decreases in DNt regions during all phases of the experiment, specifically, to right BA 6, BA 7, and 40 and left BA 37, 7, 34, 40 in addition to the right anterior cingulate. This data was unclear as to the direct involvement of the self in the right frontal regions as hypothesized. However, the authors concluded that the left prefrontal cortex was active during the self encoding condition. More importantly, that part of the self concept exists in the form of context-free schematic knowledge (Craik, 1999). A similar fMRI study investigated self-referential processing. The results showed increases in similar regions as the aforementioned study, with occipital and hippocampal additions as well as the caudate and thalamus (Kelley, et al., 2002). The authors also concluded that self-referential information is better remembered than adjectives judged relevant to other persons, demonstrating the self-reference superiority effect.

Several cortical midline structures (CMS) are posited to be involved in a 'core self.' The concept of a core self is a topic of heated discussion and exploration (R. Cannon, et al., 2008; Grimm, et al., 2008; Gusnard, et al., 2001; Northoff & Bermpohl, 2004; Northoff, et al., 2006; Northoff & Panksepp, 2008; Schneider, et al., 2008). The brain regions identified as being intricately involved in the core self consist of the orbital frontal, anterior cingulate, dorsomedial prefrontal and posterior cingulate cortices (Panksepp & Northoff, 2009). These regions are proposed to form a functional unit, and also show similar connections with brain regions outside of this cortical midline unit. These connective regions include the ventro and dorsolateral prefrontal cortex, the amygdala, insular cortex, limbic system, hippocampus, mid-brain and brain stem regions (Northoff & Bermpohl, 2004). This functional unit and its associated connections are posited to maintain cognitive and affective domains relative to the self. The domains of the self are shown to be specifically related to regions in the right prefrontal cortex and right parietal

lobes; however, these regions in right prefrontal cortex (RPFC) may be more appropriately involved in attentional and saliency processes. The proposed domains of self are representation, monitoring, evaluation, integration, self-awareness, unity, agency, spatial perspective, ownership, mind reading, emotion and autobiographical memory (Northoff & Bermpohl, 2004). The authors relate these concepts to Damasio's notion of 'core self' (A. Damasio, 2003a, 2003b; A. R. Damasio, et al., 2000) and suggest that a combination of exogenous and endogenous stimuli contributes to the experience of the self as a unit.

Interestingly, in cognitive tasks the regions elucidated on in the proposed midline network show deactivation similar to the DNt during cognitive tasks, while showing similar patterns of increased activation during 'resting state' conditions. Given this activation pattern, there are four primary regions proposed to be functionally involved in the core self based on imaging experiments using self-reflective tasks. These regions and hypothesized functions are the orbitomedial prefrontal cortex or orbitofrontal cortex (representation), anterior cingulate gyrus (monitoring), dorsomedial prefrontal cortex (evaluation) and posterior cingulate gyrus (integration) (Northoff & Bermpohl, 2004). Many of these brain regions show considerable overlap in activity between tasks. For example, during tasks of executive functions or executive attention activation of the anterior cingulate, dorsolateral prefrontal cortex and right prefrontal and parietal regions is shown (Cabeza, Dolcos, Graham, & Nyberg, 2002; Cabeza, et al., 2003; R. Cannon, et al., 2009; R. Cannon, et al., 2007). Similar fMRI research evaluating the cortical regions involved with reflective self-awareness show metabolic increases in the anterior cingulate, precuneus, middle frontal, temporal and parietal regions (Kjaer, Nowak, & Lou, 2002). Figure 2 in the appendices illustrates the DNt regions with numerical identification relative to table 1. The red in the image indicates right hemisphere, the blue is midline or middle

and the green is left hemisphere.

Damasio (1994) discusses the continuous monitoring of the body by the brain as specific content and images are processed, exacting not only changes in brain electrical activity but also chemical reactions. Thus, as the brain communicates and orchestrates the affective state of the individual in response to these contents and images relating to self and self-in-experience, it is plausible that a large scale feedback loop or network is formed involving not only perceptual processes but autonomic functioning as well. Thereby, offering the possibility that some individuals may be susceptible to habituate to, not only emotional and personality aspects of self, but also may become habituated to an aroused state. Interestingly, learning and other inherent drives are suggested to have origins in the amygdala, hippocampal and brain stem mechanisms (Smythies, 1966). It may also be that the orbital frontal, anterior cingulate and structures and neuronal populations in the mesolimbic reward centers and DNt mechanisms, including the amygdaloid complex share an attribute of synaptic permanency. Therefore, many of these regions may be less susceptible to plasticity effects and novel learning relative to self and self-in-experience.

Self awareness and Experiential Schemata

There is a growing body of literature exploring brain activation patterns during autobiographical memory, self-reference, self-image and self-face processing (Elfgren, et al., 2006; Fossati, et al., 2003; Fox, Iaria, & Barton, 2008; Kaplan, Aziz-Zadeh, Uddin, & Iacoboni, 2008; Kesler-West, et al., 2001; Uddin, et al., 2008; Uddin, Kaplan, Molnar-Szakacs, Zaidel, & Iacoboni, 2005; Vuilleumier, Armony, Driver, & Dolan, 2001). Cognitive processing of the self, specifically the face, as well as other and object processing continues to be a topic of considerable interest to researchers. The processing of other, objects and possibly the self

extends to the earliest periods of development (Bahrick & Pickens, 1995; Farroni, et al., 2005; Valenza, Simion, Cassia, & Umilta, 1996). Although, research suggests that mirror recognition of self does not occur in humans before 18-months of age, we are unsure at what point the developing self concept begins to take form. Facial images have been utilized to investigate social and emotional processing in individuals with psychiatric disorders and normal controls (Senra, Sanchez-Cao, Seoane, & Leung, 2007). These types of studies typically utilize self-recognition as the functional imaging task (Kircher, et al., 2001; Uddin, et al., 2008). To date, the proposed study will be the first of its kind to explore EEG source localization during an extended period of evaluation of an image of self, other and an object in a normal population.

Self-recognition versus novel face task participants showed increased activation in the right hippocampal formation, including the insula, anterior cingulate, left prefrontal and superior temporal cortex. Whereas, when viewing another familiar face (partner) only the right insula showed differences (Kircher, et al., 2001). fMRI experiments using morphed images of self as opposed to other found increased activation in the inferior parietal lobule, inferior prefrontal and occipital regions and the comparison image of other increased activity in medial prefrontal cortex and precuneus (Uddin, et al., 2005). The differences between these two studies may be related to the functional demands of the experiment and the methods to which the self was presented to participants.

Several researchers propose a right hemispheric dominant role in the processing and recognition of self involving the right prefrontal cortex (Keenan, Freund, Hamilton, Ganis, & Pascual-Leone, 2000; Keenan, Ganis, Freund, & Pascual-Leone, 2000). Devinsky (2000) suggested the right hemisphere is intricately involved in the generation of self-concept in relation to the environment and the emotional, physical and social selves. Lesions in the right fronto-

temporal regions produce poor insight into one's own condition. In addition to deficits in self-monitoring and self-regulation, the right hemisphere is posited to provide more efficient use of feedback to self monitor (Kaplan & Zaidel, 2001; Reis & Zaidel, 2001; Zaidel & Kosta, 2001). There is however, debate about the functional specificity of the right prefrontal region in face processing and self-recognition.

Self-Perception and Experiential Schemata: Emotion and Stress Hormones

The use of physiological indices as a measure of emotion is based on the assumption that different emotions are associated with distinctive patterns of physiological responses. There is considerable evidence for physiological response patterns indicating that autonomic activity is differentiated along multiple evaluative dimensions of emotion (Averill, 1983; Dienstbier, Hillman, Lehnhoff, Hillman, & Valkenaar, 1975; M. L. Goldstein, 1968; Lang, 1979; Lang, Kozak, Miller, Levin, & McLean, 1980; Rosenblatt & Thickstun, 1977), although the neural patterns of autonomic activity associated with different emotions are not well understood.

The hypothalamic-pituitary-adrenal axis (HPA) and the neurochemical consequences of stress are well studied. Acute stress is shown to activate the sympathetic nervous system, in part through the release of adrenalin and noradrenalin. Increased levels of the adrenergic neurotransmitters manifest in behavioral reactions in the form of irritability, arousal and the startle response. These adrenergic increases play a role in post traumatic stress disorder in children and adults (Schwarz & Perry, 1994). Chronic or long term exposure to stressful stimuli activates the HPA axis which causes a release of cortisol. It is thought that stress is a subjective experience, viz., that what is stressful to one individual may not be stressful to another. Similarly, an event that induces stress at one instant in time may not produce the same effect in the next instant (Thornton & Andersen, 2006).

The HPA axis is involved with the long term adaptation to stress, and the stress hormone linked to this pathway is cortisol (Sapolsky, 2004). In general, cortisol is a favorable hormone that is important in the regulation of physiological systems. Cortisol performs a role in the regulation of metabolism by mobilizing energy resources to provide energy for the body. However, elevated levels of cortisol are connected with depression (Holsboer, 2001), diminished immunity (Dickerson & Kemeny, 2004), hypertension and diabetes (McEwen, 1998). Cortisol secretion operates in conjunction with circadian rhythms, with peaking levels in the morning and lower levels at night.

Numerous regions in the cortex are associated with this stress-induction and stress-reduction process, including the hypothalamus, hippocampus, pituitary gland, brain-stem, prefrontal and limbic regions. Neurons in the hippocampus are shown to be particularly susceptible to prolonged exposure to increased cortisol, and deleterious effects are shown in memory functions. Similar effects are also shown in the prefrontal cortices and this combination of effects is associated with the manifestation of depressive symptoms (J. LeDoux, 1998; J. E. LeDoux & Gorman, 2001). Stress leads to subjective anxiety, endocrine activation of HPA axis and cardiovascular changes (Sinha, Catapano, & O'Malley, 1999).

Research has shown that the effects of early experiences can negatively impact cortisol levels permanently. For example, animals that display a heightened stress response throughout the lifespan do so as a result of possible negative effects on the hippocampal formation and the ability of the hippocampus to perform efficiently when special effort is necessary (J. E. LeDoux & Gorman, 2001). Cortisol levels have also been shown to be elevated in children raised in orphanages or with insecure attachment to caregivers (Gunnar, 1998).

With respect to neurophysiology, EEG studies with nonhuman primates have reported that right PFC activity was associated with higher cortisol levels (Kalin, Larson, Shelton, & Davidson, 1998; Kalin, Shelton, & Davidson, 2000). Similarly, 6-month old infants with extreme right frontal EEG at rest had higher cortisol levels overall, as compared to infants with extreme right frontal EEG during a withdrawal task. Thus, it was concluded that the right prefrontal cortex plays an important role in withdrawal-related emotional behavior and fearful temperament (Buss, et al., 2003; Kalin, Shelton, & Barksdale, 1987).

Associations between cortisol patterns and personality have been observed in early childhood, specifically, among preschool boys. Flatter daily cortisol slopes were associated with negative affect, sadness, and shyness (Dettling, Gunnar, & Donzella, 1999). Similarly, increased social fear was shown to predict flatter diurnal cortisol slopes among preschool boys and girls (Watamura, Donzella, Alwin, & Gunnar, 2003). Other research has shown no differences between cortisol levels during a social stress test among adolescent participants (Bouma, Riese, Ormel, Verhulst, & Oldehinkel, 2009). In addition, research in young participants has shown that levels of self-esteem and locus of control predicted the cortisol stress response and only participants with low self-esteem showed a significant cortisol release in response to the task (Pruessner, Hellhammer, & Kirschbaum, 1999).

Experiential Schemata and Depression

Major Depressive Disorder (MDD) is one area of focus in glucocorticoids research. Studies suggest the etiology of depression is more biologically based; however, there are implications that it also relates to psychoimmunological, neurophysiological and internal (real or imagined) stress response processes. Depression is associated with negative cognitive processes, hopelessness and a dysfunctional view of the world and the individual's place in it (Hammen,

2003). Females are two-times more likely to suffer from depression than males; however, it is suggested that males are less likely to seek psychiatric help than are females. Additionally, males suffering from depression are often diagnosed with comorbid substance abuse disorders (Marcus, et al., 2005). The characteristics of depression are reported as hopelessness, loss of enjoyable activity interests (Anhedonia), worthlessness, low-self esteem, negative self-image, negative self-efficacy and external locus of control or a negative view of internal locus of control, i.e., responsible for everything bad that happens, and a negative view of the world (R. J. Davidson, Jackson, & Kalin, 2000; R. J. Davidson, Putnam, & Larson, 2000). This begs the question as to what degree negative self perception and negative view of self in experience influence the neural mechanisms involved in MDD.

Neurophysiological data provides information regarding the cortical regions involved in depression. Lubar et al (2004) report increased alpha activity in the left frontal and prefrontal regions in chronic depressives. This data coincides with other imaging techniques that have identified similar metabolic changes in the same region, as well as asymmetries between left and right hemispheres. Research has demonstrated the right prefrontal cortex and right limbic regions show an increase in alpha and beta activity during anger memory reclamation and during the evaluation of self and self-in-experience when the experience is negative. Interestingly, overlap in regional activity occurs during the evaluation of practical joking and humor (R. Cannon, et al., 2008; R. Cannon, Lubar, J., Clements, J.G., Harvey, E., Baldwin, D., 2008; R. Cannon, Lubar, J., Thornton, K., Wilson, S., Congedo, M, 2004).

Studies report that the stress response initiates increased glucocorticoid levels in the brain, and metatoxic levels of cortisol can cause neuronal damage to specific structures involved in the interpretation of stress, especially the hippocampus (Sala, et al., 2004). Of particular note,

is the finding that hippocampal lesions are shown to ablate the cortisol stress response in humans. This suggests that the hippocampus and its role in memory and learning are vital to both reactive and autonomic adaptive functions. Neuroimaging studies have shown that there is decreased hippocampal volume in patients suffering from MDD as compared to normal controls (Frodl, et al., 2006; Neumeister, et al., 2005; Rosso, 2005).

The cognitive model of emotional disorders infers that the interpretation of events influences both the emotional and behavioral responses to said events. Moreover, it is suggested that beliefs and experiential information determine perception and interpretation of events (Beck, 2008; Beck & Rush, 1985). Beck and associates describe a model of emotional disorders in which schemata are formed, and these sets of beliefs and assumptions relating to self are suggested to be encoded with emotional material (Beck, 1964; Beck, Hollon, Young, Bedrosian, & Budenz, 1985). Cognitive theory suggests that there are programs that are genetically determined which result in observable behavior patterns. These patterns are also proposed to be influenced by cognitive processing, emotive valence, self-regulation and motivation (R. J. Davidson, 2000; R. J. Davidson, Jackson, et al., 2000; R. J. Davidson, Putnam, et al., 2000; R. J. Davidson & Slagter, 2000). These schemata (programs) are reported to influence automatic processes, including affective, perceptive and behavioral responses that result from evolutionary patterns in animals and humans (R. J. Davidson, 2004). Young (1990) proposes that early life experiences and relationships with others influence the development of early maladaptive schemas (EMS). These EMS are suggested to influence self-identity and are maintained, develop and elaborated on throughout the lifespan (Young, 1990). Moreover, these schemata are suggested to influence the development of common themes, such as, security, autonomy, gratification, self-control and self-expression—these are reported to be vital to the development

of self. EMS can cause distress in the individual and more interestingly, changing or confronting these core beliefs can result in marked distress (Young, 1990). It is proposed that activation of these maladaptive schemata evokes intense negative emotions. Another description of schemata report them as synapses that form in the brain through which information is filtered and this filter defines the information as positive, negative, fear evoking or initiating aggressive action (Smythies & Sykes, 1966). Thus the stress response plays an important role in understanding the neural and hormonal responses to self.

Psychology and the self

A unitary view of the self in western thought is an evasive concept. However, numerous theorists propose different perspectives on the construct of self and its functional properties. The self has been proposed as a soul, activity, awareness, consciousness or cognitive structure to name but a few (Parker, 1994). The self is a diverse enigma and considering even singular components of this phenomenon proves ambiguous and often creates more questions than answers. These questions create heated debate in the philosophical sense, yet several psychological theorists have attempted to describe the self in terms of development and personality with specific concentration on integrative functioning of sensory processes, including, perception, somasthesis, kinesthesis, visual, auditory and other sensory processing (Parker, 1994).

Many, if not all of these theories, have origins in the conceptualizations of William James (1952). He defines perception as a stream of thought that involves choice. He further contends that of all present sensations (kinesthetic, somatosensory, auditory, visual and proprioceptive) very few are picked out as salient to objective reality at a given moment. Thus the brain (he uses the term mind) decides what sensation will be held more real and valid than all the rest. He

proposed that this is a superb illustration of selective industry. This industry is then posited to deal with things given in perception and that empirical thought is dependent on experience and the conceptualization of these percepts are dependent to a large degree on attentional habits. Further, he suggests that a thing may be presented to an individual thousands of times; however, if the thing is persistently not noticed, then it cannot enter into experience (James, p.185). The constituent parts of the self (or multiplicities) of the self are proposed to be 1) material, 2) social, 3) spiritual and 4) pure Ego. These modules of self can be surmised as performing an integrated and differential function that influences cognitive and affective processes as well as behaviors.

Maslow (1970) developed the concept of a self-actualizing person based on his studies with healthy, creative people as opposed to Freudian work with clinical populations. This concept focused on successful people that exhibited a drive for self-determinism and self-realization. The basic principles of Maslow's work proposed that human beings have a hierarchy of needs that must be met in order to facilitate self-awareness and self-acceptance. The hierarchy of needs are 1) physiological needs (food and water) 2) a sense of security, 3) to love and be loved, 4) self-esteem and 5) self-actualization (Maslow, 1970).

Carl Rogers (1980) developed the person-centered approach which proposed that human beings are basically good and are endowed with self-actualizing tendencies. The likelihood of reaching this self-actualized state was inherently dependent on a growth enhancing environment generally consisting of genuineness, acceptance and empathy. He defined genuineness as being open with feelings, transparent and self-disclosing. Acceptance consists of unconditional positive regard, or an attitude of grace that encourages and values despite shortcomings. Empathy is the ability to share and mirror feelings and reflect meanings. Both Maslow and Rogers viewed the self-concept as a central feature of personality. The self-concept is proposed to be all the

thoughts and feelings evoked by the "who am I" question (Rogers, 1980). The self in many ways has been assimilated into the study of personality and social psychology.

Gordon Allport proposed that opportunistic functioning was relatively unimportant for understanding most human behavior (Allport, 1968). He posited that human behavior is motivated by a different construct of the expressive self, which he deemed propriate (proactive and future directed) functioning. He suggested that phenomenology of the self is experienced (or subjective) and is composed of the aspects of experiencing salient sensory stimuli as most essential. His functional definition of the self is for all intensive purposes a developmental theory. He proposed that the self has seven functions, which are integrated on a developmental continuum: 1) the sense of body 2) self-identity 3) self-esteem 4) self-extension 5) self-image 6) rational coping and 7) propriate striving. These integrative functions of self are also proposed to be a primary force in personality traits and personal dispositions.

Although there are varying degrees or multiplicities of self, in research with humans and primates there are clear patterns of identifying self as different from the other (Parker, 1994). The self as considered on a developmental continuum is influenced, positively or negatively by environment and experience. The self (James, 1952) is a composite of memories, learning and knowledge and as James suggested the present I and me are directly related to prior experiences of the I and me and this integration facilitates consciousness of the self (James, p.185). Further, he suggests the "I" and "me" are best used for the *empirical person* and the *judging thought* (James, p.239). This is an important consideration for these early studies of the self. The neural processes engaged during the recognition and evaluation of the "*me"* may prove to be important to understanding the neural processing of the judging thought (or cognitive patterns) associated with perception of self and self-in-experience. Personality theorists pose many interesting

concepts that are potential topics for neuroscientific investigation. Inevitably, a modest understanding of the neural patterns of self is just a prelude of things to come. These are exciting times for both psychology and neuroscience.

Evolution and the self

It is often the case that when speaking of evolutionary or adaptive constructs there is an automatic reaction to engage in a polemic discourse for which no resolution exists. Agreement is not often obtainable or foreseeable. If anything, history has taught us this lesson in a most egregious fashion. Therefore, this lesson in futility will remain at the forefront of this brief section.

When we think of the self there are several core aspects that are prominent, self-awareness, differentiation of self from the world and self from other (individuation) and consideration of the most vital human functions contributing to the organization, maintenance and definition of self. Research has demonstrated that self recognition is observable in humans, apes, elephants, magpie, dolphins and other species (Plotnik, de Waal, & Reiss, 2006; Prior, Schwarz, & Gunturkun, 2008). In fact, single celled organisms, cells and bacteria are proposed to have a mechanism for quorum sensing or the phenomenon whereby the accumulation of signaling molecules enable a single cell to sense the number of bacteria (cell density) or more simply to differentiate its own boundaries from other cells and to efficiently monitor environmental conditions to potentiate increased survival (Bodini, Manfredini, Epp, Valentini, & Santori, 2009; Ishikawa, Rompikuntal, Lindmark, Milton, & Wai, 2009). This line of research is beyond the scope of this manuscript; however, it does offer very intriguing contradictions to the notion of hominodea superiority in the area of self-awareness.

Additionally, in considering consciousness (although this is not done by very many authors) the self must be at the center of the discussion. There are typically four responses associated with mirror self recognition in studies with both animals and humans, the social response, physical inspection of the mirror, repetitive mirror testing behaviors and self-directed behavior (Parker, 1994). It is unclear as to the point in human history at which the self immerged; however, it might be proposed that the origins of the self began with the origin of language (e.g., gestures, verbal, chemical, etc. . .). Authors have proposed several conceptual notions of the self including the sensory-motor self, a minimal self or 'core/mental self' (A. R. Damasio, 1999). These two concepts are suggested to relate to William James' notion of the physical and mental selves. There have been other suggestions such as the autobiographical self, the facial self, social self and emotional self (Frith & Frith, 2005; Gallagher & Frith, 2003; Gusnard, 2005; Turk, Heatherton, Macrae, Kelley, & Gazzaniga, 2003; K. Vogeley, et al., 2001; K. Vogeley, Kurthen, Falkai, & Maier, 1999; K. Vogeley, et al., 2004). Yet another proposed form for the self is the experiential self, which is suggested to be a process manifested in subjective experience—the self as considered an experiential self that mediates ownership of experience (Legrand, 2003; Northoff, et al., 2006) and can be examined using self referential tasks. The operational definition of experiential schemata and self perception in this manuscript may describe this process with a more appropriate, disambiguous approach.

In discussions with colleagues about the evolutionary/genetic potential for developing a self, several intriguing ideas were suggested. One suggestion proposed that a self is necessary for survival, such that interactions with the world would be dangerous and perhaps even superfluous if there was not a self to determine a starting point. This would apply to predator prey models and also intrinsic hazards in the environment that self-other-world distinction is necessary for

potentiated survival, additionally the world would not make sense to a non-self (Dirk De Ridder, MD, PhD, personal communication). Another discussion broached the field of quantum physics, such that the self and world (or universe) functions like two protons. Even if these two protons are accelerated, to say, the speed of light, there will remain a relationship between them. Regardless of distance, when one stream (or waveform) is interrupted it produces an effect on the other stream (or waveform). The self provides a function of objective interaction with the universe and only when the observer effect (slit theory) is produced by the self is the congruency between self and world or other interrupted (Donald Barrs, PhD, personal communication).

Thus in the most reasonable sense, the self may be developed to provide a self-other, self-world distinction that provides a reference point, at any given moment, in order to make sense of the world. As to whether the development of self is under genetic control, this is unknown; however, given that language is equipotent, the self possibly has this same quality. The important considerations of the self are the specific components of human existence that are most likely contribute to the development, organization, maintenance and functional integration of the self. The self and its development are most likely dependent on neuronal assemblies associated with language, reward and emotion.

The review in this manuscript covers numerous emotional, cognitive, motivation and appetitive processes. An overlap in activation exists between these processes and self in the brain reward system, limbic regions, brain stem regions, basal ganglia and neocortical regions, including the default network. These relationships and the overlapping activity between the functional tasks ought to be an area of focused study. In touching upon this daunting topic, one concept stands out, in order to consider what consciousness might be – we must first understand what the self might be and what direct or indirect role it plays in consciousness. Or more simply,

can there be consciousness without a self? Human cognition is inherently dependent on language and of course cognition plays an intricate role in reward, emotional regulation and maintaining the safety of the physical body. Reward is based on external and internal states, and therefore it has intrinsic properties of the physical and emotional components of self. Emotion is interdependent with these two other components, yet also plays an important role in self-regulation and maintaining the safety of the physical body (i.e., fight or flight). Numerous psychopathologies may have origins in disruptions in one or more of these self-component processes. This will be a concentrated effort of future study.

Rationale, Specific Aims and Hypotheses

The DNt like other novel concepts is not without controversy (Buckner & Vincent, 2007; Mason, et al., 2007; Morcom & Fletcher, 2007). There is debate about what constitutes a 'resting state' with suggestions that it reflects internally directed mental activity (Gilbert, Dumontheil, Simons, Frith, & Burgess, 2007) whereas others posit it as mind wandering (Mason, et al., 2007). This study aimed to address four problems associated with the DNt. First, the EEG activity associated with the DNt has not been investigated and 3-dimensional source localization techniques (LORETA) may be appropriate for study of the DNt. Secondly, differentiating functional self-specific tasks in regions of the DNt has not been investigated. Third, specific EEG frequency changes in functional connectivity in the DNt during resting or active tasks are not well understood and finally, the phenomenology of the resting state has not been obtained and clarified.

This study proposes that many of the differences in activation patterns between self-recognition and self-viewing are founded in the underlying processes involved during the task or the subjective experience of the participants when viewing an image of self (Kircher, Seiferth,

Plewnia, Baar, & Schwabe, 2007; Kircher, et al., 2001; Turk, et al., 2003). The phenomenology of the cognitive, emotional and perceptual experiences of participants during tasks involving self processing and studies describing the default mode of brain processing is not typically utilized in neuroimaging experiments (Gusnard, et al., 2001; Gusnard & Raichle, 2001; K. A. Raichle, et al., 2001; M. E. Raichle, et al., 2001; Simpson, Drevets, Snyder, Gusnard, & Raichle, 2001; Zacks, et al., 2001) and remains a topic of both confound and continued interest (Kai Vogeley & Fink, 2003). A recent theoretical investigation and critical review of neuroimaging results for studies investigating the self proposes the interesting question as to whether the results from these types of experiments are enough to say that the proposed cerebral network (core midline self) is functionally and specifically devoted to the self (Legrand & Ruby, 2009).

There are four primary aims for this research study with several secondary aims within each component. First, although PET and fMRI studies provide invaluable information about regional specific activity in the brain, there is relatively little information about the functional integration of EEG frequencies between the neural assemblies during resting state evaluations and functionally specific tasks. Thus, this study seeks to determine if EEG source localization using sLORETA can be utilized to study the DNt. As the number of functional processes associated with EEG frequencies increases during functional tasks the data can be integrated with results from other imaging techniques to form a more coherent picture of functional processes. Secondly, this study aims to examine the EEG activity in the most likely cortical regions associated with a hypothesized core midline self as related to the DNt. Third, this study aims to examine levels of stress related hormones (cortisol) during the processing of an image of self and during the completion of self specific assessment instruments. Therefore, the current study will attempt to identify functionally specific neural mechanisms involved in self-image

processing, self-perception, and perception of self in experience. It is predicted that during this type of self processing, increased activity within and between regions associated with emotion, memory and self-regulation will play a key role. The cortical mechanisms active during this process will be directly associated with cortisol increase. Finally, differences between genders in all tasks and conditions will be evaluated. In the following sections I present each primary component part of the study with specific and secondary hypotheses to be tested.

1: The Default Mode Network (DNt): EEG LORETA can be utilized to study the DNt. The hypotheses to be tested in this component are:

nH1: There will be no differences in current source density between all conditions in the DNt regions and over the entire neocortex.
nH2: ROI are not differentially active for both condition and frequency
nH3: No ROI in DNt are significantly related to SELF tasks
nH4: Hammer and object ROI = Self Specific ROI
nH5: males equal females for all conditions in DNt regions
nH6: ratings of subjective reports will not equate to attention

2: Cortisol Response: There will be cortisol differences as a function of condition.

nH1: There will be an increase in cortisol as a function of self evaluation
nH2: The cortisol difference will not be correlated with emotion/self-regulation regions
nH3: The cortisol difference will not be significantly correlated with hemisphere
nH4: The cortisol difference will not be associated with any specific EEG frequency domain

3: Gender Differences across all measures: There will be gender differences as a function of conditions.

nH1: Males and females will not differ in all task conditions
nH2: Males and females will not differ on all behavioral measures
nH3: Males and females will not differ on cortisol levels (pre, post and difference)

CHAPTER III: METHODS

Participants

This study was conducted with 63 non-clinical participants, 34 female and 29 males with a mean age of 19.28, SD = 2.0. Data inclusion was based on the length of usable EEG for each file to be analyzed ≥ 60 seconds. All participants were recruited via the University of Tennessee Human Research Participation pool and all received extra course credit for their participation. Exclusion criteria was assessed by a standard questionnaire previously used by our laboratory and consisted of previous head trauma, neurological or neurovascular disease, psychiatric diagnosis or recent drug or alcohol use (within the prior 14 days). All participants read, signed and agreed to protocol approved by the university institutional review board. Our sample was restricted to participants with English as first language due to the emotionally and introspectively latent content in the specific behavioral measures.

Apparatus and EEG Collection

Electroencephalogram (EEG) was collected and stored using Deymed Diagnostics Truscan EEG Acquisition system with a band pass set at 0.5–64.0 Hz at a rate of 256 samples per second. During the recordings real-time impedance for electrodes and reference leads was available on screen and was adjusted during recording if they exceed the protocol limits. Truscan utilizes fiber optics for the EEG recordings. These were monitored in real time by the research assistant (RA) and if any evidence of drowsiness (excessive slow wave activity) or excess muscle contamination or eye-movement artifacts occurred, the RA was instructed to stop the EEG recording, allow the participant to readjust or refocus and then continue. To minimize artifacts during all EEG procedures, a 15.4 inch monitor was utilized and placed in position such

that the participant was looking in a downward direction at the monitor. This tended to help minimize eye-movement artifacts and reduce reading-scanning effects.

Electrocaps:

Electro-Caps are an EEG electrode application technique. They are made of an elastic spandex-type fabric with recessed, pure tin electrodes attached to the fabric. The electrodes on the standard caps are positioned to the International 10-20 method of electrode placement (Jasper, 1958).

Instruments:

Self Perception and Experiential Schemata Assessment (SPESA)

The SPESA is designed for sensitivity to negative, average or positive perceptions of self, and perception of self-in-experience (ES) in three life domains; childhood, adolescence and adulthood (R. Cannon, et al., 2008). There are a total of 45 items, 15 items in each domain with four possible responses. The items are scored (2, 1, -1, -2). The items are similar in content in dissimilar order for each domain of development. The SPESA takes less than ~6 minutes to administer and 10 minutes to score. The SPESA was first employed in a chemical dependency treatment program and later used in a recent study by our laboratory with recovering substance abusers and normal controls (R. Cannon, et al., 2008). The reliability analysis a group of 56 shows significant inter-item correlations (ICC) between domains tested (child/adol = .798), (child/adult = .516), (adol/adult = .590). The results of the two-way random effects model with an internal consistency definition provide an intra-class correlation coefficient of .81 for average measures with $F(2, 55) = 5.72$, $p = .000$. Similar internal validity analysis was conducted on a group of 136. The results show Chronbach's alpha of .81, with ICC of .52 for single measures and .77 for average measures with $F(1, 135) = 5.27$, $p = .000$. The inter item correlations show

.763 between childhood and adolescence, .492 between childhood and adulthood and .547 between adolescence and adulthood. A group of 50 individuals were retested at an eight week interval. These were compared using a two-way random effects model with an absolute agreement definition. The results show Chronbach's alpha of .95 for single and.97 for average measures with F (1, 2139) = 35.92, p = .000. The SPESA is reliable and internally consistent. Table 2 in the appendices shows example items from the SPESA.

Brief Symptom Inventory 18 (BSI 18)

The BSI 18 (Derogatis, 2001) is a brief, highly sensitive self-report system inventory designed to serve as a screen for psychological distress and psychiatric disorders in medical and community populations. The BSI 18 is an 18-item survey in which respondents are asked to indicate on a 5-point scale (0 = not at all to 4 = extremely) to what degree they have been troubled by symptoms during the past week. The BSI-18 includes three subscales – anxiety, depression and somatization. Scores for each subscale are summed and a Global Symptom Index is derived by summing across scales. Higher scores indicate higher levels of symptom severity. The BSI-18 is appropriate for populations 18 or older. Table 3 in the appendices contains example items from each scale. The test-retest and internal consistency estimates for the BSI 18 are .74 to .89 respectively.

The Tennessee Self Concept Scale (TSCS)

The Tennessee Self Concept Scale (Fritts, 1964) at one time was one of the more widely used self-regard instruments; however, without much published research. There were no definitions published for the constructs which guided inclusion of items. There are 90 items in the scale. The participants are asked to answer items on a 5-point scale from 0 – completely false to 5 – completely true. The favorability of each item is either positive or negative. 8 of the items

in the abbreviated scale are positive and 12 are negative. There were three rows that were agreed upon by seven clinical psychologists that include identity or what I am, self-satisfaction or how I accept myself and my behavior or how I act and also five self columns including physical, moral-ethical, personal, family and social. The author of the scale reported high reliability amongst college students; however, issues regarding education level influencing responses and random answers from participants were also proposed as confounding issues. The TSCS did not show positive associations with CPI self acceptance scale and Maslow's security S-II scores or the 16 PF confident adequacy scores. Rather than utilize the entire scale. Twenty items were extrapolated for the physical, disgust and introspective items that best reflected (face validity) concept of self and self in experience. A total self-regard score is derived from the 90 items, with higher scores indicating higher self regard. This abbreviated version utilized the same procedures with the total score equaling the sum of the subscales utilized. Table 4 in the appendices shows example items from the TSCS.

Saliva Sampling.

Participants were seated comfortably and while relaxing in the sitting position, participants expectorated into a sanitized 50 mL collection tube once per minute over a three minute period (Navazesh, 1993). Once collected, saliva samples were centrifuged for ten minutes and then alloquated in microtubes (two per sample) and stored at -70 degrees Celsius for subsequent analysis. The total time between pre and post salivary cortisol samples was ~40 minutes. We also obtained data relative to menstrual cycle for female participants, medications, time of day and other variables as indicated by (Kudielka, Hellhammer, & Wust, 2009).

Salivary Analysis.

Supernatants were analyzed for total cortisol concentration using the High Sensitivity Salivary Cortisol Enzyme Immunoassay Kit (Salimetrics Inc., PA). The assay can detect cortisol levels from 0.003 to 3.0 μg/dL. The samples were run in duplicate and Chronbach's alpha revealed a reliability of .99 for this study.

EEG data collection

After collection of saliva, participants were escorted to the EEG collection laboratory where a digital photograph was taken and transferred to the computer image interface. Participants were advised of all procedures and equipment. The ears and forehead were then cleaned for recording with a mild abrasive gel (NuPrep) to remove any oil and dirt from the skin. The head was measured and marked prior to EEG recording using a measure of head circumference and the distance between the nasion and inion to determine the appropriate cap size for recording and placement of frontal electrodes (Electrocap, Inc; Blom, & Anneveldt, 1982). After fitting the caps, each electrode site was injected with electrogel and prepared so that impedances between individual electrodes and each ear were < 10 KΩ. The EEG cap is referenced with linked ears and ground with 9mm tin cups. The Electrocap is also referenced at FPz.

Participants were introduced to the EEG screen and artifact production, then instructed to attempt to control eye, tongue, neck and jaw movements and encouraged to relax as much as possible during the recordings. The participants were recorded in eight conditions. First, four-minute eyes-closed (ECB) and eyes-opened baselines (EOB) were obtained. The participants then completed 3 assessment instruments (see behavioral measures). The times for each of the assessments are: SPESA (~6 minutes), the BSI (~3 minutes) and the TSCS (~3 minutes). Each of

the assessment instruments were presented in Microsoft Power Point, with slide exposure for each item within the SPESA, BSI and TSCS being computer generated for 8 seconds. The participants were reminded to attempt to control blinks when responding to the assessment items, and to avoid scanning the screen when reading the items. They were asked to read the entire question and each response and then respond verbally with the choice that best reflects their respective answer. Participant responses were marked within the EEG record by the RA using the F1, F2, F3, F4 and F5 keys. The participants were then recorded for four minutes while viewing an image of a hammer, an image of a novel female face with a neutral expression (the same for all) and the picture of self taken prior to capping. The background for all the images is a pale blue with no distracting marks or other noticeable images. The expression of the other is neutral. She is of normal features and is not wearing clothing or other items that might be considered distracting. The age of the novel female is 35. There was a ~1.5 minute interval between stimulus presentations during which the research assistant was advised to encourage the participant to stretch and move around to avoid discomfort. Upon completion of all EEG measures, the participants cleaned the electrogel from hair and returned to cortisol sampling area and provided the post salivary sample. The participants then completed the subjective reports for baselines and the image conditions. They also completed each of the assessment instruments in written form. This is a standardized protocol that has been employed with 160 participants in both clinical and normative samples.

Procedures

As the participants entered the laboratory at the time of their scheduled session, they were greeted by a research assistant (RA) then read and signed the informed consent for the research protocol. Any questions the participants had were answered by the RA. The data were collected

during the spring 2009 semester and all measures were collected between the hours of 10:00 am and 3:00 pm Monday through Friday.

EEG Data Pre-Processing

The EEG data was evaluated for gross artifacts using Truscan Explorer and then transferred to a specified computer folder for fine artifact detection and rejection. The EEG stream was edited using Eureka 3 software (Novatecheeg). EEG resampling was obtained by means of natural cubic spline interpolation, since the EEG is a continuous signal constituted by oscillation of potential differences over time (M. Congedo, Ozen, C., Sherlin, L. , 2002). All active task conditions and baseline data were processed with particular attention given to the frontal and temporal leads. All episodic eye blinks, eye movements, teeth clenching, jaw tension, body or neck movements and possible EKG (Electrocardiogram) were removed from the EEG stream. Data were excluded if there was not 60 seconds of usable EEG data for all study conditions. 4 to 6 seconds of EEG prior to the participant response for the SPESA, BSI and TSCS conditions was extrapolated. Fourier cross-spectral matrices were then computed and averaged over 75% overlapping four-second artifact-free epochs, which resulted in one cross-spectral matrix for each subject for each discrete frequency. The EEG data were analyzed utilizing the following frequency domains: Delta (0.5 – 3.5 Hz); Theta (3.5 – 7.5 Hz); Alpha 1 (7.5 – 10.0 Hz); Alpha 2 (10.0 – 12.0 Hz) and Beta (12 .0 – 32.0 Hz).

Standardized Low-resolution electromagnetic tomography (sLORETA)

Standardized low-resolution electromagnetic tomography (sLORETA) is an inverse solution for estimating cortical electrical current density originating from scalp electrodes utilizing optimal smoothing in order to estimate a direct 3D solution for the electrical activity distribution. This method computes distributed electrical activity within the cerebral volume,

which is discretized and mapped onto a dense grid array containing sources of electrical activity at each point in the 3D grid. This methodology produces a low error solution for source generators and provides statistical maps modeling distribution currents of brain activity utilizing realistic electrode coordinates (Towle et al., 1993) for a three-concentric-shell spherical head model co-registered on a standardized MRI atlas (Talairach, & Tournoux, 1988). This allows adequate approximation of anatomical labeling within the neocortical volume, including the anterior cingulate (AC) and hippocampus. LORETA and the standardized version are accessible as freeware for research purposes, and LORETA is the only inverse solution developed for real-time neurofeedback use. It is also demonstrated to estimate current density sources efficiently with 19 electrodes (M. Congedo, 2006; Herrmann, Rommler, Ehlis, Heidrich, & Fallgatter, 2004; Holmes, Brown, & Tucker, 2004; Isotani, et al., 2001; Lehmann, et al., 2001; Lehmann, et al., 2005; Lehmann, Faber, Gianotti, Kochi, & Pascual-Marqui, 2006; Liu, Gao, Schimpf, Yang, & Gao, 2004; Liu, et al., 2005; Pae, et al., 2003; Pascual-Marqui, 2002; Pascual-Marqui, Esslen, Kochi, & Lehmann, 2002; Pascual-Marqui, et al., 1999; Pascual-Marqui, Michel, & Lehmann, 1994; Thatcher, Biver, & North, 2007; Thatcher, North, & Biver, 2005a; Thatcher, et al., 2005b).

Data Analysis

In order to assess the electrophysiological differences within subjects in the experimental conditions, sLORETA was employed to localize the generators of the scalp EEG power spectra. The sLORETA solution space is restricted to the cortical gray matter in the digitized Montreal Neurological Institute (MNI) atlas with a total of 6239 voxels at 5 mm spatial resolution (Pascual-Marqui, 2002; Pascual-Marqui, et al., 2002). The average common reference was computed prior to the sLORETA estimations. The calculated tomographic sLORETA images correspond to the estimated neuronal generators of brain activity within each frequency domain

(Frei, et al., 2001). This procedure resulted in one 3D sLORETA image for each subject for each frequency range. To test the specific hypotheses in this study a linear mixed model with repeated measures was utilized to assess the differences between current source density levels in DNt between experimental conditions. In order to evaluate the DNt regions between conditions and interregional functional connectivity a region of interest (ROI) file with the MNI coordinates for the 12 seed points for the DNt regions was constructed. Each of the ROI values consisted of the current source density levels from each ROI seed in table 1 and one single voxel (its nearest neighbor). The resulting file produced log transformed average current source density across multiple EEG segments for all subjects for each seed (ROI). These data were organized into Microsoft Excel spreadsheets and then entered into SAS 9.13 and SPSS 16 for analysis.

The null model hypothesis and the type III test of fixed effects were tested with alpha set at .05 using the Tukey adjustment for alternative hypothesis testing. The mixed model employed compound symmetry for the covariance structure, such that observations obtained closer together in time exhibit higher covariance as compared to observations taken farther apart in time. The mixed model utilized residual maximum likelihood estimation method. Residual variance was calculated via the model profile and the model fixed effects were calculated via the Prasad-Rao-Jeske-Kackard-Harville (Prasad, 1990; Rao, 1972; Shaalje, 2002) fixed effects method with the Kenward-Roger (Kenward, 1997) degrees of freedom method. Least square means (LSM) are in effect, within group means adjusted for the other effects in the model. LSM estimate the marginal means for balanced populations and are also referred to as estimated population marginal means (Searle, 1980). The type III test of fixed effects utilized in this model assesses the degree of difference between the LSM of conditions. Bivariate correlation analyses were employed to assess functional connectivity between DNt regions and CMS.

The obtained subjective reports for baseline and image conditions were rated by 3 independent raters. The baselines were rated for content specific to attentional focus or other functions (e.g., mind wandering, non-attention). The image conditions were rated for positive or negative content. Agreement between raters was assessed using a two-way random effects model with an absolute agreement definition.

In order to assess the electrophysiological differences between genders in the experimental conditions over the entire neo-cortex, multiple voxel-by-voxel comparisons were conducted in a nonparametric test for functional brain imaging (Nichols and Holmes, 2002) with spatial – smoothing, signal-to-noise at 1 and linear scaling. sLORETA was employed to localize the generators of the scalp EEG power spectra. Tomographic sLORETA images corresponding to the estimated neuronal generators of brain activity within each given frequency range were calculated (Frei, et al., 2001). This procedure resulted in one 3D sLORETA image for each subject for each frequency range. The significance threshold was based on a randomization test utilizing 5000 data randomizations. The mean current density for all frequencies within conditions and between genders was compared and t-values plotted onto a MRI template. A similar randomization procedure was utilized to evaluate the correlations between the difference between pre and post cortisol and the estimated neural generators of EEG. The cortisol difference scores were entered into a text file. This file was entered into analytic procedures in which it was regressed onto the difference between the activation task and eyes-opened baseline. This procedure results in tomographic maps of the significant correlations between neural regions and EEG frequencies with the cortisol difference. Randomization and Permutation tests are demonstrated to produce significant control of the family wise error rate (Type I error) in multiple hypothesis testing (Edgington, 1987; Good, 1994, 2005) and are frequently utilized in

neuroimaging studies (Blair & Karniski, 1994; Holmes, Blair, Nichols & Holmes, 1996; Westfall & Young, 1993). This method of analysis has been utilized in studies by our lab and others (Cannon, Lubar, Thornton, Wilson & Congedo, 2004; Cannon, et al. 2007; Cannon, Lubar, Clements, Harvey & Baldwin, 2008; Congedo, Lubar & Joffe, 2004; Papageorgiou, et al 2007; Sherlin, et al 2006; Zumsteg, Andrade & Wennberg, 2006). The means for the behavioral measures were compared using independent t-tests with gender coded 1 = male and 0 = female. The assessment instruments were counter-balanced in the post session paper completion. This was done to assess the self-reported emotional disposition of participants. The SPESA was administered last as it has one item that requests the emotional state as a result of completing the instrument. The frequency of positive or negative responses were assessed and compared with a chi-square test.

CHAPTER IV: RESULTS

In the following sections the results are presented according to the hypotheses set to be tested. Section A reports the results for the overall hypothesis that activity in the DNt can be evaluated using EEG LORETA. This section also includes the secondary hypotheses to be tested. nH1) that there are no differences in CSD between conditions, nH2) that the DNt ROI are not differentially activated by condition or frequency, nH3) that no ROI in the DNt appear to be self-specific, nH4) that the self-specific tasks are not different from the other and hammer image conditions, nH5) there are no differences between genders in the DNt and nH6) the subjective reports do not equal attention.

Section B reports the results for the cortisol analyses. The overall hypothesis proposes there will be cortisol differences as a function of condition. The secondary hypotheses to be tested are nH1) pre EEG cortisol does not differ from post EEG, nH2) difference between pre and post cortisol does not correlate with cortical regions involved in emotion and self-regulation, nH3) cortisol differences will show a lateralized effect and nH4) cortisol difference will not be correlated with any specific EEG frequency domain.

Section C reports the results for gender differences. The overall hypothesis proposes there will be gender differences as a function of condition. The secondary hypotheses to be tested are: nH1) mean CSD for males is equal to mean CSD for females for all experimental conditions, nH2) genders are equal on all behavioral measures and nH3) genders will not differ on pre, post or the difference in cortisol levels.

A: Hypotheses Set I EEG LORETA can be used to study the DNt.

According to the overall hypothesis of set 1, the results for the grand means of current source density levels in the DNt are shown in Figure 3 in the appendices. In the figure are the

mean current source density levels for each condition (the average of all roi). The ECB CSD levels are significantly higher than all other conditions, whereas the EOB CSD levels are significantly lower than ECB for all conditions and for all active tasks. This differential effect for EOB and AT however, does not apply to all ROI in all frequencies. The type 3 tests of fixed effects show these differences are significant for ROI, condition and ROI by condition. The ROI by condition effect shows significance only in the beta frequency with $F(77, 6240) = 1.31$, $p = .038$. Significant fixed effects occur in beta for ROI $F(11, 6240) = 35.89$, $p < .000$ and condition $F(7, 6240) = 25.85$, $p < .000$. Delta shows significant effects for ROI $F(11, 6240) = 40.79$, $p < .000$ and condition $F(7, 6240) = 33.09$, $p < .000$. Theta shows an overall effect for ROI $F(11, 6240) = 14.31$, $p < .000$ and condition $F(7, 6240) = 32.87$. Alpha-1 shows a significant effect for ROI $F(11, 6240) = 21.72$, $P < .000$ and condition $F(7, 6240) = 33.26$, $p < .000$. Alpha-2 shows significant effects for ROI $F(11, 6240) = 25.21$, $p < .000$ and condition with $F(7, 6240) = 29.73$, $p < .000$.

Figure 4 in the appendices illustrates the differences for the mean (log) current source density (CSD) for delta, theta, alpha-1, alpha-2 and beta for ROI by condition. The DNt ROIs are plotted on the x axis and the conditions are plotted within the figure. These graphs provide a visualization of the differences in CSD for each frequency domain in each DNt ROI between conditions.

Tables 5 (delta), 6 (theta), 7 (alpha-1), 8 (alpha-2), and 9 (beta) in the appendices show the mixed model results corresponding to figure 4, in the tables from left to right are the comparison (ROI by condition) the ROI/cond compared to ROI/cond, the estimate, t value for the comparison and the probability. From top to bottom is each ROI by condition compared to the same ROI by each condition: Legend 0 = EOB, 1 = ECB, 2 = SI, 3 = ES, 4 = BSI, 5 = TSCS,

6 = Other (O), 7 = Hammer (H). As the results are discussed to clarify and simplify, when the terms more activity or less activity are used, this means significantly higher or lower levels of current source density. The results for the mixed model will be presented in the order of tables 5 through 9. The results for ROI comparisons and other measures are reported by number prescribed by table 1 (e.g., R1, R2). For simplification, the presentation of results will be presented with the ROI number and contrasts that were significant.

According to hypotheses nH1) and nH2), table 5 in the appendices shows the results of the mixed model comparisons for the beta frequency. R1) ES, BSI and TSCS conditions show higher degrees of CSD as compared to the image conditions. R3) BSI and ES conditions show more activity than O and H. R6) ES condition shows more activity than BSI, O and H. R7) ES shows more activity than TSCS, O and H. R8) SI shows more activity than ES, while ES shows more activity than O or H. BSI also shows more activity than O and H. TSCS shows more activity than H. R11) SI and TSCS show more activity than H. R12) The SI condition shows more activity than ES, BSI, O and H. R1 shows no effect for ECB compared to all tasks, while R2, R4, R5, R9, R10 show effects for only baseline conditions (e.g., EOB < ECB).

Table 6 in the appendices shows the results of the mixed model comparisons for the delta frequency. R1) SI shows less activity than ES, BSI and TSCS. ES, BSI and TSCS show more activity than O or H. R6) SI condition shows less activity than ES. R7) ES condition shows more activity than O and H. R2, R3, R4, R8, R9, R10, R11, and R12 show only baseline effects.

Table 7 in the appendices shows the results of the mixed model comparisons for the theta frequency. R1) BSI shows less activity than SI and ES. The BSI shows more activity than TSCS, O and H. R3) SI shows less activity than BSI. R4) SI shows less activity than ES. R6) ES shows more activity than H. R7) ES shows more activity than O and H. R8) SI shows more activity than

H. ES shows more activity than O and H, as does BSI and TSCS. R11) SI shows more activity than O and H, additionally, ES, BSI and TSCS show more activity than O. R12) SI shows more activity than H. R2, R5, R9, and R10 show only baseline effects.

Table 8 in the appendices shows the mixed model results for the alpha-1 frequency. R1) BSI shows more activity than O and H. TSCS shows more activity than H. R2) SI shows more activity than H as does BSI. TSCS shows more activity than O and H. R6) SI shows less activity than ES, whereas ES shows more activity than BSI, O and H. R7) ES shows more activity than TSCS, O and H. R8) SI shows less activity than BSI and TSCS. BSI shows more activity than O and H. R11) SI shows more activity than ES, O and H. TSCS shows more activity than H. R3, R4, R5, R9, R10, and R12 show only baseline effects.

Table 9 in the appendices show the mixed model results for the alpha-2 frequency. R1) BSI and TSCS show more activity than H. R3) SI shows less activity than BSI. ES and BSI show more activity than O and H. TSCS shows more activity than O. R6) ES and TSCS show more activity than H. R7) ES shows more activity than O and H. R8) SI shows less activity than TSCS, and TSCS shows more activity than O and H. R10) SI shows more activity than O and H. BSI shows more activity than H and TSCS shows more activity than O and H. R12) SI shows more activity than H. R2, R4, R5, R9, and R11 show only baseline effects.

The differences for the hammer and other conditions are found in table 8 in the appendices for the theta frequency. The H condition shows increase in R9 (medial BA10). The O shows increase in R9 (medial BA 10) and R5 (left lateral BA8). These two conditions show increase relative to EOB only.

The results for interregional functional temporal correlations in figure 5 of the appendices (and supplemental data) demonstrate differential patterns of association for each condition. The

functional connectivity (FC) maps first and foremost are descriptive in nature and address the hypothesis of differences in functional connectivity as a function of task condition. Only those correlations that met the statistical threshold of significance ($\leq .05$) are plotted in the maps. The ECB and EOB conditions appear similar in FC. In all frequency domains differential patterns of FC involve posterior cingulate and left parietal regions. Left BA 39 shows more FC with bilateral frontal areas during ECB. Left BA 40 shows a similar pattern in EOB. The left prefrontal cortex shows a larger degree of FC in ECB between left temporal and medial anterior regions. The right prefrontal and parietal BA 40 show a high degree of FC with left prefrontal, medial anterior regions and left parietal regions in all frequency domains with specific patterns observable in posterior cingulate and precuneus.

The image conditions show patterns of FC that involve a lesser degree of DNt regions than both baseline and assessment conditions. However, FC appears to exhibit specificity to each of the image conditions. More regions appear associated during the hammer and other conditions as compared to the self image. In the SI condition, the right prefrontal region is highly interactive with left prefrontal regions including medial BA32 and BA10 in the delta frequency. The hammer and other conditions do not show this bilateral frontal FC. In the hammer and other conditions the right frontal shows FC with left lateral and left temporal ROI. There is a pattern of FC between bilateral parietal regions in the hammer and other conditions that is not present in the self image. Right BA40 shows specific FC per image condition. The posterior cingulate shows FC with left BA10/47 and left BA 8 and 9 during the self and other conditions. Only BA 8 and 10 produce the same pattern of FC with posterior cingulate in the hammer condition.

The assessment conditions show differential patterns of FC compared to the images, in addition to between each other. There are patterns of FC between left BA39 and 40 with frontal

and temporal regions in the left hemisphere for all assessments. Bilateral parietal FC with posterior cingulate is shown in all conditions; however, specificity appears to be relative to frequency. Medial prefrontal and posterior regional FC appears in all assessment conditions, again with apparent specificity to frequency within task. The right prefrontal ROI shows bilateral FC with medial and lateral left prefrontal and temporal regions in the assessment conditions, however, not in all frequencies. Left temporal BA20 and left superior frontal BA10 show specific FC in the ES and TSCS that is not shown in the BSI condition. Medial regions BA9 and 11 show FC with left lateral and temporal regions in all of the assessment conditions in all frequencies except for delta in the TSCS. Overall the ES and BSI conditions show greater recruitment of resources in regional interconnectivity patterns than the TSCS condition.

According to hypotheses nH1 and nH2, which state the ROI are not differentially active and the conditions do not differ (in DNt and throughout the cortex), as well as nH4) hammer and other are not different from self-specific conditions. The results for the voxel by voxel sLORETA comparisons are shown in table 10 in the appendices. In the table from top to bottom are the results for each of the task conditions compared to eyes-opened baseline, followed by the results for the comparisons between image specific tasks and finally the differences between assessment instrument tasks. From left to right are the frequency, the maximum and minimum estimates by sLORETA, x, y, z coordinates, Brodmann Area/anatomical label, hemisphere, t-value and the probability of t. The shaded areas in the table highlight the regional maximal increased current source density between conditions. The data do not support any of the hypotheses that the ROI in the DNt and activity in cortex do not differ by condition.

The SPESA (ES) condition shows increased current source density in the delta frequency at right BA 6 middle frontal gyrus, alpha-1 at left BA 13 insular cortex, and alpha-2 in right BA

8 superior frontal gyrus. The maximum decrease between conditions is shown in alpha-1 at right precuneus and in beta at left BA 46 middle frontal gyrus.

The BSI shows maximal increased CSD in the delta frequency at BA32 right anterior cingulate, theta at right BA10 middle frontal gyrus and alpha-2 at right BA40 inferior parietal lobule. The maximum decreases occur in alpha-1 in right BA19 cuneus, alpha-2 in right BA11 superior frontal gyrus and in beta at right BA9 middle frontal gyrus.

The TSCS shows maximum increased CSD in delta at right BA11 middle frontal gyrus, theta at left BA 10 middle frontal gyrus, alpha-1 at left BA45 inferior frontal gyrus, alpha-2 at right BA7 superior parietal lobule and beta at left precuneus. Maximum decrease occurs in theta at left BA10 middle frontal gyrus, alpha-1 in left BA7 precuneus, alpha-2 in right BA11 superior frontal gyrus and in beta at left BA10 superior frontal gyrus.

The SI condition shows maximum increased CSD in delta at right BA39 superior temporal gyrus, theta at left BA11 middle frontal gyrus, alpha-1 at right BA9 middle frontal gyrus, and beta at medial BA30 posterior cingulate. The maximum decreases occur in delta at right BA20 uncus, theta at left BA6 middle frontal gyrus, alpha-1 at medial BA23 precuneus, alpha-2 at left BA19 fusiform gyrus and beta at left BA11 superior frontal gyrus.

The other (O) condition maximum increased CSD occurs in delta at right BA40 supramarginal gyrus, alpha-1 at left BA6 superior frontal gyrus, and alpha-2 at BA8 right superior frontal gyrus. Maximum decreased CSD occurs in theta at left BA24 anterior cingulate, alpha-1 at left BA7 precuneus, alpha-2 at left BA40 inferior parietal lobule and beta at right BA39 middle temporal gyrus.

The hammer (H) condition shows maximum increased CSD at right BA8 medial frontal gyrus. The maximum decreases in CSD occur in alpha-1 at right BA20 inferior temporal gyrus, alpha-2 at left BA11 left superior frontal gyrus and beta at left BA11 superior frontal gyrus.

The maximum increased CSD between SI and O occurs in delta at left BA11 superior frontal gyrus (although this is just above the significance threshold), and beta at right BA7 superior parietal lobule. The maximum decreases in CSD occur in delta at left BA24 anterior cingulate, theta at BA10 left medial frontal gyrus, alpha-1 at right BA6 superior frontal gyrus, alpha-2 at right BA20 uncus and beta at left BA19 cuneus.

The maximum increased CSD between SI and H occurs in delta at left BA10 superior frontal gyrus, theta at left BA47 inferior frontal gyrus and beta at left BA6 precentral gyrus. The maximum decreased CSD occurs in delta at right BA20 inferior temporal gyrus, theta at medial BA23 cingulate gyrus, alpha-1 at left BA17 cuneus, and alpha-2 at left BA21 middle temporal gyrus.

The maximum increased CSD between O and H occurs in delta at right BA18 middle occipital gyrus, alpha-1 at right BA9 inferior frontal gyrus, alpha-2 at right BA35 parahippocampal gyrus and beta at left BA7 precuneus. The maximum decrease in CSD occurs in theta at left BA4 precentral gyrus, alpha-1 at left BA18 lingual gyrus, and beta at right BA37 fusiform gyrus.

The ES condition compared to BSI shows increased CSD in delta theta at right BA6 paracentral lobule, alpha-1 at right BA39 supramarginal gyrus, alpha-2 at right BA11 rectal gyrus and beta at right BA18 cuneus. The maximum decreases in CSD occur in delta at right BA25 medial frontal gyrus, theta at left BA13 insular cortex, alpha-1 at right BA6 superior frontal gyrus and beta at BA46 middle frontal gyrus.

The ES compared to TSCS shows increased CSD in delta at left BA6 medial frontal gyrus, theta at right BA18 middle occipital gyrus, alpha-1 at right BA11 medial frontal gyrus, alpha-2 at right BA11 middle frontal gyrus and beta at right BA19 cuneus. The maximum decrease in CSD between conditions occurs in delta at right BA47 inferior frontal gyrus, theta at left BA13 insular cortex, alpha-1 at right BA6 medial frontal gyrus, and beta at left BA20 uncus.

The BSI compared to TSCS shows increased CSD in delta at left BA21 middle temporal gyrus, theta at right BA18 middle occipital gyrus and beta at left BA20 inferior temporal gyrus. The maximum decrease is shown in delta at right BA40 inferior parietal lobule.

According to nH5) there will be no differences between genders in the DNt. Figure 6 in the appendices shows the results for the comparisons between the CSD means in DNt regions for gender in each task condition. The ECB condition showed no differences. From left to right are the conditions. The images are a horizontal view of the brain. The ROIs showing difference are plotted in the map with color representing frequency. Delta = green, Theta = red, Alpha-1 = blue, Alpha-2 = purple and Beta = yellow.

The EOB differences occur in left BA 10 in the theta, alpha-1 and alpha-2 frequencies and in medial BA32 in the theta frequency. The ES condition shows significantly lower CSD for the alpha-2 frequency in left BA20. The TSCS condition shows more beta activity at left BA20. The BSI condition shows higher levels of CSD for the delta frequency at left BA39, beta frequency at right BA8/9, delta frequency at medial BA32 and beta activity at left BA10/47. The SI condition shows increases in the delta frequency at medial BA31/7 and beta activity at left lateral BA8. The other condition shows increases in the delta frequency at right BA40 and decreased alpha-2 and beta activity at medial BA32. The hammer condition shows the largest number of differences between genders. Importantly, the comparisons show less activity in

females as compared to males. There is decreased delta, theta, alpha-1 and alpha-2 activity at left BA40. Decreased CSD occurs in the delta at left BA39, theta and beta at right BA40. There is less CSD in the delta, theta and alpha-1 at left BA8 and finally less CSD in alpha-1 at left BA20. Thus there appear to be a large number of differences between genders in the hammer condition; however, the differences are limited to 5 regions with frequency specificity.

According to hypothesis nH3) no ROI in the DNt would be related to self-specific processing. Figure 7 in the appendices shows those regions significantly different in activity, as compared to baseline and the other and hammer conditions during self-specific tasks in each frequency domain. The images are a horizontal slice through the brain at z=15. Regions are approximated for 2-D rendering. The blue regions in the image are those showing increased CSD during the SI condition. The yellow regions in the image are those showing increased CSD during the ES condition. The red regions in the image are those showing increased CSD during the BSI condition. The pink regions are those showing increased CSD during the TSCS condition. Midline activity is shown in all frequencies except alpha-2 in anterior medial regions. The posterior cingulate/precuneus does not show significant increase during the SI task. It is shown active in the anterior midline in theta, alpha-1 and beta frequency domains. The anterior medial regions shown increased during these tasks are BA11 rectal and orbital gyrus, anterior cingulate (BA24 and 32), BA9 and BA10/47. The posterior cingulate is also active during many of the tasks; however, it appears to be preferential to concept oriented language, whereas experiential information appears more involved with midline occipital BA17/18 and 19, in addition to left/right temporal and parietal regions in the both the DNt and right hemisphere. The regions of self specific activity in the named DNt regions and regions throughout the cortex were

significantly different from the control images and baseline, thus we reject the null hypothesis that these are not self-specific regional activations.

According to hypothesis nH6) that the subjective reports would not equate to attentional processes, the interrater agreement for ECB shows a Chronbach's Alpha (CA) of .95 with the intraclass correlation coefficient (ICC) of .86 for single measures and .95 for average measures with $F(62) = 19.26$, $p = .000$. The EOB shows (CA) .96 with an ICC .90 for single measures and .96 for average measures with $F(62) = 29.23$ $p = .000$. In both the baseline conditions ~89 percent of the reports were rated as attentional processing and ~11 percent reported attempts to not become bored. The attention to internal state (boredom) could be included in the attention category; however, given the possibility of error it remained coded separately. Thus the data do not support the hypothesis that the subjective experience of the participants in this study during baselines does not equal attention.

B: Hypotheses Set II Cortisol differences exist as a function of condition.

The first overall hypothesis for this section proposed that there would be a positive increase in salivary cortisol due to self evaluation. This was not supported by the data, such that a significant post – pre EEG condition decrease in cortisol occurred for the total group with $t(61) = 3.94$, $p = .000$. The second, third and fourth hypotheses were not supported such that emotion and self-regulation regions did show significant correlations with the difference between pre and post session cortisol levels. Hemisphere and specific EEG frequencies also show associative properties with the cortisol decrease. These differences will be examined more closely in the following section. The dispositional emotional state response in the SPESA for post session revealed a significant pattern of positive affect. 90 percent of the participants

endorsed positive items, while 10 percent endorsed negative items (57+, 6-). The comparison yielded a chi-square of 41.49, $p < .000$.

Neural correlates for the difference (significant decrease) between pre and post cortisol levels are plotted in table 11 of the appendices. From left to right and top to bottom are the results for the cortisol difference regressed on each task condition MNI map after paired comparisons between the task and baseline. In the graphs within each section, the ordinate shows the value of rho for the correlation and the specific cortical regions are on the abscissa. Frequency specific correlations are plotted within the graph.

Left BA10 in alpha 2 is shown to be consistent in H, BSI and TSCS with the ES showing a similar effect in the right hemisphere. Left BA20, while shown to have positive associations in SI with alpha-2 and beta in TSCS, also shows negative associations with the CD in theta for BSI and alpha-1 in H and O. Left BA7 shows positive associations with CD in delta for BSI, TSCS, ES and SI and a positive association with alpha-1 in right BA7 for the O condition. Left BA9 shows a positive association to CD in theta for the ES condition, but a negative association with CD in both BSI and TSCS in alpha-1. Left BA8 shows positive associations with CD in the theta frequency in BSI and TSCS conditions. The ES condition shows a similar result in right BA8. BA13 in BSI shows a positive association between CD and alpha-1 in the right hemisphere. A negative association with CD in theta is shown for the O condition. This region also shows a negative association with CD in alpha-1 for TSCS in the left hemisphere. Left BA37 shows positive associations between CD and beta in BSI and TSCS, while ES shows a negative association in beta and a positive association in alpha-1. The SI condition shows a negative association in theta for left BA37 and the O condition shows a negative association in delta and a positive association in alpha-2. Right BA30 shows a negative association with CD in alpha-2 in

the H condition and a positive association with CD in alpha-1 for the BSI condition. Left BA6 shows a positive association in alpha-2 for the BSI and delta for ES, while right BA6 shows a negative association for the H condition in theta. Left BA21 shows negative associations with CD in both the ES and TSCS conditions in the theta frequency. Left BA32 shows a positive association with CD in BSI in delta, while in the ES condition a negative association is shown in alpha-1 in the left and delta in right BA32. Left BA19 shows a positive association with CD in the alpha-2 frequency and a negative association in delta for the BSI condition.

The regions shown to have task specific associations are the ES, TSCS, SI, O and H. The BSI shows a similar task-region effect with at least one region in other conditions. The ES task-specific positive associations with CD occur in alpha-1 at right BA28 and BA3. The TSCS specific positive associations with CD occur in the delta frequency at left BA23, alpha-1 at right BA38, alpha-2 at left BA31 and beta at left BA 18. The SI condition specific positive associations with CD occur in theta at left BA4 (a negative association also occurs for alpha-2), and beta at right BA40. A negative association is shown in alpha-1 at left BA40. The H condition specific positive association with CD occurs in theta at left BA30. The O condition specific positive association with CD occurs in theta at left BA41, while a negative association occurs in alpha-2 at left BA34.

C: Hypotheses Set III Gender differences as a function of condition

The data do not support the first hypothesis in this section that the sLORETA comparisons by task condition would not differ between genders. There are significant differences between genders in all task conditions. Similarly, the data did not support that there would be no differences between genders in the behavioral measures; however, the differences shown only applied the SPESA adulthood scale and the TSCS disgust scale. The hypothesis that

cortisol did not differ as a function of gender was supported. There were no significant differences shown between genders in pre, post or the difference between pre and post cortisol data. The results between genders will be covered in more detail in the following sections.

The results for the voxel by voxel sLORETA comparisons for each of the experimental conditions between genders are shown in table 12 of the appendices. In the table from left to right are the frequency, sLORETA max and min, Brodmann area/anatomical label, x, y, z coordinates, hemisphere and p-value for the comparison. From top to bottom are the results for each of the conditions (female > male). The differences between genders will be presented by condition in the following section.

The BSI shows maximal increase as compared to males in delta at right BA11 middle frontal gyrus, alpha-1 at right BA9 middle frontal gyrus, alpha-2 at right BA7 superior parietal lobule and beta at BA22 superior temporal gyrus. Maximum decreases occur in delta at left BA22 superior temporal gyrus, theta at left BA27 parahippocampal gyrus, alpha-1 at left BA4 precentral gyrus, alpha-2 at left parahippocampal gyrus and beta at right BA7 postcentral gyrus.

The SI maximum increase in CSD between genders occurs in delta at right BA18 middle occipital gyrus, alpha-1 at left BA9 precentral gyrus, alpha-2 at right BA20 fusiform gyrus and beta at right BA9 middle frontal gyrus. Maximum decreases in CSD between genders occur in delta at right BA40 inferior parietal lobule, theta at right BA19 cuneus, alpha-1 at left BA37 middle occipital gyrus, alpha-2 at medial BA9 middle frontal gyrus and beta at left BA20 fusiform gyrus.

The ES condition maximum increase in CSD between genders occurs in delta at left BA31 paracentral lobule, theta at BA19 cuneus, alpha-1 at right BA8 superior frontal gyrus, and

beta at left BA20 fusiform gyrus. Maximum decreases occur in delta at left BA18 middle occipital gyrus, and theta at right BA6 superior frontal gyrus.

The TSCS maximum increase between genders occurs in delta at left BA 11 orbital gyrus, alpha-1 at left BA11 superior frontal gyrus and beta at left BA20 sub-gyral. Maximum decreases occur in delta at BA19 left fusiform gyrus, theta at left BA34 parahippocampal gyrus, alpha-1 at right BA40 inferior parietal lobule and beta at right BA6 middle frontal gyrus.

The O condition maximum increase in current CSD between genders occurs in delta at right BA2 postcentral gyrus, theta at right BA9 superior frontal gyrus, alpha-1 at left BA6 medial frontal gyrus and beta at left BA23 cingulate gyrus. Maximum decreases occur in delta at left BA31 precuneus, alpha-1 at left BA10 superior frontal gyrus, and alpha-2 at BA13 right inferior frontal gyrus.

The H maximum increase in CSD in delta occurs at left BA23 cingulate gyrus, theta at left BA19 cuneus and alpha-1 at right BA39 middle temporal gyrus. Maximum decreases occur in delta at right BA10 medial frontal gyrus, theta at left BA24 anterior cingulate and beta at left BA11 superior frontal gyrus.

The subjective ratings for each of the image conditions showed excellent agreement. The O condition showed Chronbach's alpha (CA) of .95 and average measure of .95 with $F(62) = 28.19$, $p < .001$, as did the rating for the hammer with CA of .96 and average measures of .96 with $F(62) = 20.12$, $p < .001$. The self image ratings showed CA of .98, with average measures .98, $F(62) = 45.49$, $p < .000$. There were no significant differences between genders for the subjective reports for the other $t(61) = -1.89$, $p = .066$ and hammer $t(61) = .113$, $p = .911$. There was a significant difference between genders for the image of self, with females rating the image significantly more negative than males $t(61) = 2.21$, $p = .031$. Although the differences for other

and hammer did not reach significance, the tendency for the other condition was that males rated the novel female face more critically than females. In the hammer condition, females tended to associate the hammer with a song or visualized a family member (namely the father) using the hammer to build something, whereas males tended to view their own experience with the tool.

Table 13 in the appendices shows the results for the comparisons between genders for all behavioral measures. In the table from top to bottom is the measure and from left to right are gender, sample size, mean, standard deviation and standard error for the mean. The only differences between genders occur in the adulthood scale of the SPESA with males rating present adulthood more negatively than females $t(61) = 2.03$, $p = .046$ and the disgust scale of the TSCS with females showing a significantly lower score than males $t(61) = 2.17$, $p = .034$. Internal consistency analysis for each of the behavioral measures in this study population show the scales in the TSCS with a CA of .56, $F(62) = 2.62$, $p = .000$. The BSI scales show CA of .74, $F(62) = 3.85$, $p = .000$, and SPESA scales show CA of .72, $F(62) = 3.60$, $p = .000$.

CHAPTER V: DISCUSSION

This study set out with three primary goals. First, to determine the plausibility of using an EEG 3-D source localization technique (sLORETA) to examine the default network of the brain, and to further examine functional differences within this network during self-specific processing. Second, to examine affect related neural processing possibly associated with self-specific tasks and the subsequent associations between salivary cortisol levels, EEG frequencies and cortical regions. Finally, to determine qualitative and quantitative differences between genders in all study measures. The findings in this study indicate further study of the DNt using EEG source localization (sLORETA) methods is warranted. Further, the data demonstrate that both regional increases and changes in interregional functional connectivity occur in DNt regions between the study conditions. Contrary to the hypothesis that self-specific processing would elicit a negative affective response resulting in increased salivary cortisol levels, the opposite effect occurred. Each condition in this study showed specific neural associations with the decreased cortisol levels, which may reflect a positive affective state associated with positive self percepts and experience. More importantly, regions in the left prefrontal cortex appear to play an important role in self-related-affect and self-regulatory processes. Gender differences proved variable by conditions, such that no differences were found in the DNt during eyes-closed baseline and minimal differences within the DNt regions in all conditions. There were, however, considerable differences over the entire neocortex during each of the experimental conditions. Minimal differences were found in the behavioral measures and cortisol did not differ between genders in baseline, post stimulus and the difference levels. Finally, the data propose, at least in this study population, that the ‘resting state’ may be better described as a functional state of attention and self-regulation. The obtained data support the notion that regions within the default network are

involved in self-specific processing. Cortisol may be regulated to some degree by top-down processing involving prefrontal regions predominantly in the left hemisphere, with more specific regional associations in the right hemisphere. Additionally, the lack of substantial gender differences in our data suggests that males and females in this population exhibit tendencies toward positive self perception. The overall gender differences in the neocortex in each of the experimental tasks may reflect the processes of associative learning and recall, and salience effects in females, viz. that category or concept specific (i.e., does depression carry the same salience between genders?) knowledge may directly influence the cortical processing of specific concepts and the affective components engaged by these processes.

In discussing the results, it is important to reiterate the proportions for the regions of interest in the DNt section of this study. The data for the DNt regions was obtained by extrapolating the current source density in one (center of Brodmann Area) $5mm^3$ voxel and its nearest neighbor, one, $5mm^3$ voxel. Therefore, the regions discussed here are no more than $10mm^3$ of the total volume in the respective center of the Brodmann Area. It is also necessary to keep in mind that with sLORETA the solution space is restricted to the gray matter in the cortex and limbic regions.

The human brain is perhaps best described as a complex system of complex systems. In essence a reductionist approach to neural functions may hinder the discovery of complex functional systems. Indeed the mechanisms and specificity of its functions are the greatest of enigmas. The DNt continues to be a topic of focused interest and offers promise in increasing our understanding of how the brain orchestrates complex functional processes, including cognition, affect, self-regulation and memory to name but a few. Raichle (2000) proposed that a baseline or

control state is fundamental to the understanding of most complex systems. Moreover, that defining a baseline state in the human brain, the most complex system, introduces difficult and specific challenges to researcher. He also proposes that left unconstrained, its activity will vary unpredictably. It may very well be that this lack of stability will continue to confound the interpretation of neuroimaging results (Raichle, et al 2000).

EEG LORETA in DNt

This is the first study of its kind to examine the EEG activity in the DNt in extensive detail. According to the global hypothesis that EEG LORETA can be used to study the DNt, the results clearly show similar effects for the overall current density levels as PET and fMRI studies in baselines and active tasks (Gusnard & Raichle, 2001; M. E. Raichle, et al., 2001; Shulman, et al., 1997; Shulman, et al., 2001; Shulman, et al., 1998). Figure 3 and the fixed effects of the mixed model analysis demonstrate that similar CSD level increases or decreases occur as a result of eyes-closed baseline as compared to eyes-opened baseline. Similar effects are shown for active tasks as compared to eyes-opened baseline and between active task conditions.

The experimental conditions for this study consisted of eyes-opened baseline, eyes-closed baseline, viewing a picture of a hammer, a picture of a novel female face and a picture of self and evaluating perception of self, self-in-experience, self-concept and a recent symptom inventory. According to the first hypothesis (n1) under this section the mean current source density in DNt regions would not differ as a function of condition. This hypothesis was not supported by the data. The mixed model results show that significant regional increases do occur according to condition in many of the ROI. This effect however, does not apply to all ROI in all

frequency domains. These regional increases will be discussed briefly by frequency domain in the following sections.

Delta shows no regional increases for active task conditions in left BA40 or right BA40, left lateral B8, left or medial BA10, left BA10/47 or left BA20. Increases do occur in medial regions and in the posterior cingulate and precuneus during language/concept based conditions compared to the image conditions. The left parietal lobe (BA39) regional decrease indicates that processes involving self image or self perception may be less relative to this region than recent symptoms and abstract concepts. The right prefrontal (BA 8/9) region is typically active in tasks of self recognition; however, in the delta frequency there is less activity during the self image than the self perception task. Left BA9 shows a possible focus toward experiential information as opposed to object processing and the anterior cingulate shows similar specificity for self conceptual information.

Theta shows no regional increases or decreases for active task conditions in left BA 40, left lateral BA8, medial BA10 and left BA10/47. Posterior cingulate/precuneus again shows a possible selective increase relative to the BSI, such that it shows higher activity levels than self image, self perception, and self concept measures as well as the control image conditions. Left BA39/19 shows the same pattern with BSI showing more activity than the self image. The right parietal region (BA40) shows increase relative to self-perception and experiential schemata as compared to self image. A similar effect is noted in right prefrontal BA8/9 as compared to the hammer. Regions in the left hemisphere in theta appear to have a selective industry toward self specific information as opposed to objects and other persons. These regions include medial

anterior cingulate (BA32), left lateral prefrontal cortices, including BA9, BA10 and temporal BA20.

Alpha-1 shows no regional increases or decreases for active task conditions in left BA39/19 or right BA40, left lateral BA8, medial BA10, left BA10/47 and left temporal BA20. Increases in posterior cingulate/precuneus BA31 continue to favor the assessment conditions over image processing. Self-image and abstract, self-conceptual information appears to show specificity to the angular gyrus and BA19 in left parietal regions as opposed to image processing. The right prefrontal region continues to show preferential activity increases relative to self-perception and self-in-experience as contrasted with self-image, abstract concepts or object and other face processing. A similar effect is shown in left BA9, such that the ES condition is more active than self-concept, other and image processing. Left BA10 increases in the BSI condition more than self-image, self-concept and the other control images. The anterior cingulate increases relative to self image and self-concept more than experiential schemata, and the other image conditions.

Alpha-2 shows no regional increases or decreases for active task conditions in left and right BA40, left lateral BA8, medial BA10 and 32. Similar to other frequency bands the posterior cingulate shows increase specific to the BSI and TSCS as compared to the image conditions. Left parietal BA39/19 shows a similar increase with the assessments producing more activity than images, including self. Right frontal BA8/9 continues to show increase in self perception and self concept tasks as compared to objects. Left BA9 increases specific to self-perception as compared to object or other face. Left BA10 shows an increase specific to self concept (TSCS) as contrasted with all image conditions. Left BA10/47 shows increases specific to self image,

symptomology and self concept as compared to the other image conditions. Left BA20 continues to show increase for self image as opposed to an object.

Beta shows no regional increases or decreases for active task conditions in left and right parietal regions (BA40), left lateral BA8, medial BA10 and left BA10/47. As in the other frequency domains posterior cingulate shows increases relative to the assessment conditions as opposed to the images. A similar effect is shown in left BA39/19 for BSI and ES only. Right frontal BA8/9 continues to show increase relative to self-perception rather than BSI or image conditions and left BA9 in the same fashion contrasted with self concept and images. Left BA10 increases relative to the assessment conditions as opposed to all image conditions. Medial BA32 continues to show increase specific to self-image and self concept. Left lateral BA20 shows increase specific to self image as contrasted with BSI, self perception, and the other image conditions.

Thus, according to hypotheses (nH2) that suggests the ROI would not show differential activity patterns for both condition and frequency, this is not supported by the data. Additional hypotheses propose that (nH3) no ROI in the DNT are significantly related to self tasks and that the (nH4) control images (other and hammer) will not differ from self-specific ROI. The data do not offer support to these hypotheses and provide evidence suggesting that self-specific regional activation and functional connectivity do differ from both the hammer and other conditions. Similarly, a self-specific midline pattern of activity during the processing of self does appear to reside partly within the DNt, in addition to other neocortical and possible subcortical regions. Figure 7 shows the regions of self-specific increases in activity for each frequency domain. Increased activity is shown in all frequencies except alpha-2 in anterior medial regions.

Of particular interest is the lack of activity in the posterior cingulate/precuneus during the SI and control image task conditions. This may offer evidence of its importance in language and construct processing as well as evaluative and integrative functions specific to verbal and written information (Bush, et al., 2000; Z. Zhou, et al., 2008). The anterior medial regions shown active during these tasks are BA11 rectal and orbital gyrus, anterior cingulate (BA24 and 32), BA9 and BA10/47. Experiential information appears more involved with midline occipital BA17/18 and 19, in addition to left/right temporal and parietal regions in the both the DNt and right hemisphere. fMRI and PET data in self related and self recognition tasks show increased activity in similar regions as this study, including orbital prefrontal, ventromedial prefrontal, anterior and posterior cingulate cortices in addition to ventral and dorsolateral prefrontal cortex, bilateral parietal cortex, insular cortices, basal ganglia and other limbic and subcortical/brainstem regions (R. Cannon, et al., 2008; A. Damasio, 2003a, 2003b; A. R. Damasio, et al., 2000; de Greck, et al., 2008; Gusnard, et al., 2001; Kircher, et al., 2007; Kjaer, et al., 2002; J. LeDoux, 2003; Northoff, et al., 2006). Yet, controversy exists as to whether the stimuli used in many of these experiments are specifically self-related or rather embedded within other cognitive, emotional and autobiographical processes (Legrand & Ruby, 2009; Northoff & Bermpohl, 2004).

The anterior cingulate appears to show a selective activation for both self image and self concept in most frequencies except alpha-2. These functional increases offer support to the notion presented by Damasio (1994) that the AC in combination with other regions are involved in a network of core self. The AC is proposed to be in a perfect position in the cortex to facilitate and integrate such a core self network, given its connections with affective, cognitive, somatosensory, visceral and motor systems. The AC as shown by the obtained data is directly involved in the functions of self-image, self-concept in nearly all frequencies, in addition to

possibly monitoring recent internal states and self perception and experiential schemata in the theta frequency only. PET and fMRI experiments have shown similar results as this study, with the exception of the lack of involvement of the right prefrontal region in self image evaluation and its concentration to left temporal BA20 in all frequencies except for delta. This difference may solely be represented by the difference between self-recognition and longer evaluation of self image, which does involve focal feature detection and evaluation (Devue, et al., 2007; Gusnard, et al., 2001; Kircher, et al., 2002; Kircher, et al., 2000; Platek, et al., 2006; Sugiura, et al., 2000; Sugiura, et al., 2005).

According to hypotheses set 1 (n5) there would be no differences between genders in DNt regions. The obtained data do not support this hypothesis and offers evidence to the contrary except for the eyes-closed baseline (otherwise known as resting state). Figure 6 in the appendices shows the differences between genders in DNt regions for each condition. Differences are shown in the EOB in two regions, left BA10 in theta, alpha-1 and alpha-2 and theta in medial BA32. The reasons for these specific differences are unknown. However, changes in BA10 can be shown in any cognitive paradigm (Burgess, Dumontheil, & Gilbert, 2007; Burgess, Gilbert, & Dumontheil, 2007; Gilbert, Williamson, et al., 2007; Okuda, et al., 2007) and have also been shown in studies with affect regulation components (R. J. Davidson, 2004; Levesque, et al., 2003, 2004). Lesions to this region in humans do not impair performance on tests of intellectual performance, memory, language, motor skills, visual perception, and problem-solving abilities. Rather, specific impairments occur in self-organized behavior or open-ended procedures that require the individual to monitor and regulate self in an organized manner and in tasks that require self-maintenance of attentional processes, which may also be placed under the category of self-regulation (Burgess, Dumontheil, et al., 2007). Therefore, it is possible that the

differences in these two regions presents a self-regulatory function in females as compared to males, since BA32 in the anterior cingulate is also shown to involved in self-regulation, emotional processing and numerous other variants of attention (R. Cannon, et al., 2009; R. Cannon, et al., 2007; Devinsky, et al., 1995).

The ES and TSCS conditions show one region of difference between genders in the DNt. The ES shows less activity in left BA20 in females as compared to males, while the TSCS shows significantly more activity in the same region in females. BA20 is part of the inferolateral temporal lobe and is suggested to play a role in higher order visual processing, recognition memory and semantic memory in association with BA37, 38, ventromedial prefrontal cortex and limbic regions (Mummery, et al., 2000; Staiman, 1998). Females show increased CSD during the BSI condition in delta at left BA39 and BA32, and beta at right BA8/9 and left BA10/47. BA39 is thought to be involved in the integration of visual and tactile stimuli in addition to speech and lesions to this area results in dyslexia or alexia plus agraphia (A. R. Damasio & Geschwind, 1984). Thus this increase may be associated with the extent to which females engaged in more integrative processes during the evaluation of recent symptoms, as well as the cognitive and affective components of each item. BA8 is shown to be active during tasks of decision making and uncertainty (Volz, Schubotz, & von Cramon, 2005) and is shown to play an important role in executive attention and self-regulation (R. Cannon, Congedo, M., Lubar, J., Hutchens, T. , 2009; R. Cannon, et al., 2007; R. Cannon, Sokhadze, E., Lubar, J., Baldwin, D., 2008), emotion (A. R. Damasio, et al., 2000) and self image processing (Butcher, 2001). This increased activity may reflect the emotional salience deriving from the evaluation of the constructs of depression, anxiety and somatic symptoms. BA10/47 is also shown active in emotion and physiological response to external stimuli (Critchley, Daly, et al., 2000; Critchley, Elliott, Mathias, & Dolan,

2000). BA32 is also involved in executive functions, decision making and numerous self regulatory functions and may play an important role in the evaluation of the items and recruitment of neural regions involved in conceptual and emotional elements of the items (Bush, et al., 1999; Bush, et al., 2000; Bush, et al., 2002; Davis, et al., 2000; D. Pizzagalli, et al., 2001; D. A. Pizzagalli, et al., 2003).

Females show increased CSD in delta at posterior cingulate and beta at left BA8 during the SI condition. The subjective reports for the females for the SI condition show significantly more negative valence toward the image of self than males. The reports are critical of the picture and their appearance; however, it must be noted that these reports did not contain negative reference to life history, character or other negative referential themes as shown in clinical samples (R. Cannon, et al., 2008). These two regions are important to decision making, uncertainty, evaluative and integrative functions and self-regulation. Females show increased CSD in delta at right BA40 and decreased alpha-2 and beta at medial BA32. In reference to the subjective reports females rated the other female face in a more positive fashion than males (although these did not reach significance). The decrease in BA32 may reflect this positive valence in regards to making decisions about another face. A large number of female participants associated the face with their mother or someone they knew, in addition to the colors of the clothing worn by the woman in the image. BA40 is involved in the integration of visual and tactile information, in addition to attentional processes. The AC and BA40 have been shown to have an intricate relationship in sustained attention tasks in addition to cognitive and affective processing (Cabeza & Nyberg, 2000; R. Cannon, et al., 2009; R. Cannon, et al., 2007; De Ridder, Van Laere, Dupont, Menovsky, & Van de Heyning, 2007).

The hammer condition presents the greatest number of differences between genders. Importantly, the comparisons show less activity in females as compared to males. There is decreased delta, theta, alpha-1 and alpha-2 activity at left BA40. Females show less CSD in the delta frequency at left BA39 and in the theta and beta at right BA40. There is less CSD in the delta, theta and alpha-1 frequencies at left BA8 and finally less CSD in the alpha-1 frequency at left BA20. Thus there appear to be large differences between genders; however, the differences are limited to 5 regions with frequency specific differences. The subjective reports indicate that females tend to associate the use of a hammer with the father or other significant male person, or with a song, whereas males tended to examine the details of the hammer and associate its use as a tool with their own experience. Thus the differences between genders may be directly related to associations and representations in the cortex.

Finally, hypothesis (n6) suggests the subjective reports obtained from the participants regarding the mental activities employed during baseline recordings would not equate to attentional processing. The data do not support this hypothesis. The independent ratings indicate the major thought processes during these recordings (eyes-opened and eyes-closed) involve attentional processes. Whether it be attention to the physical body (e.g., eye and muscle movements) or the internal state (avoiding boredom, planning or paranoia), all subjects were engaged in some form of attentional and self-regulatory/monitoring behaviors. Thus attention and self regulation constitute the phenomenology of the resting state in this study.

Cortisol Correlates

According to hypotheses set 2 (n1) there would be a significant increase in salivary cortisol as a function of self evaluation. The data do not support this hypothesis and in fact show the opposite, a decrease in salivary cortisol as a function of self evaluation. The current study is

the first to investigate the combination of neocortical and EEG frequency associations with cortisol levels as a function of self-perception, experiential schemata, self-concept and self-image, other face and object evaluations. The results in table 11 may offer insight into how the brain perceives and processes stimuli in addition to cortical regions and frequencies involved in positive/negative emotional states and their effects. The decreased cortisol is assumed to be relative to having a non-clinical sample with self-reported positive life experiences (R. J. Davidson, 2004). In effect the results may represent the cortical regions directly involved with positive affect associated with the task conditions. The significant positive emotional disposition responses add further evidence of this positive affective state. The assessments and subjective reports associated with the images were collected with the consideration that an intricate relationship exists between cortical regions involved in emotion and cognition.

According to hypothesis n2, the cortisol decrease would not be associated with cortical regions shown to be involved in emotion and self-regulation. The data do not support this hypothesis and show that associations exist between cortisol levels and regions known to be involved in emotion and self-regulation. Hypothesis n3 proposes there would be a laterality effect related to cortisol increase or decrease. This hypothesis was affirmed to some degree; however, there are bilateral interactions associated with the cortisol decrease shown in this study, thus we reject this hypothesis and conclude there is a bilateral cortical effort involved in the decreased cortisol shown in this study. Hypothesis n4 proposes there will be no specific EEG frequency association with the decrease in cortisol. The obtained data do not support this hypothesis, rather it is demonstrated that specific EEG frequencies are associated with cortisol levels in specific cortical regions. Finally, hypothesis n5 proposes that the cortisol decrease will not be associated with DNt regions. The data do not support this hypothesis and demonstrate that

specific regions within the DNt are associated with the cortisol decrease in this study. Moreover, regional associations appear specific to the task condition and frequency domain.

The cortical regions associated with the cortisol decrease across more than one condition in the left hemisphere are: *BA10 medial frontal gyrus, *BA20 inferior temporal gyrus (all conditions), *BA7 superior parietal lobule, *BA8 superior frontal gyrus, *BA9 middle frontal gyrus, BA37 fusiform gyrus, BA6 superior frontal gyrus, BA21 inferior temporal gyrus, *BA32 anterior cingulate and BA19 lingual-fusiform gyrus. The regions shown to have associations with cortisol decrease in the right hemisphere are: BA30 posterior cingulate, BA13 insular cortex, *BA8 superior frontal gyrus, and BA10 medial frontal gyrus. Those regions with an asterisk are specific to the DNT, thus refuting hypothesis n5. Recent PET data investigated psychosocial stress and the results showed that increased cortisol was significantly correlated with increased BGM in medial prefrontal cortices BA9 and BA10 (Kern, et al., 2008); however, more salient findings were associated with increased BGM in lateral aspects of the prefrontal cortex, which is consistent with findings showing that unpleasant emotions, including anxiety tend to show patterns of increased right prefrontal activity (R. J. Davidson, 2002; R. J. Davidson, Coe, Dolski, & Donzella, 1999). Similar data propose the prefrontal cortex provides a top-down mechanism for regulation of the HPA response with consideration of the region and nature of the stressor. Moreover, regions in left prefrontal (BA6, BA9) have been shown to be inversely correlated with increased amygdala activity (Dedovic, Duchesne, Andrews, Engert, & Pruessner, 2009).

The differences between the patterns associated with CD may delineate between conceptual and perceptual, and experiential self processing, as well as elucidating on language processing in the human brain. Research has proposed that while right posterior regions of the

brain specialize in the perception of affective stimuli of both positive and negative valence, both left and right anterior regions of the cortex may be involved in the experience of emotion (R. J. Davidson, Kalin, & Shelton, 1993; Wheeler, Davidson, & Tomarken, 1993). This idea is in agreement with the current data. More specifically, the left prefrontal regions shown by the data are also proposed to be more active during the experience of positive emotions and reward that mediate approach related and appetitive goals (R.J. Davidson, 1994) and hypoactivity in these regions is associated with depression (R. J. Davidson, 2003). Similarly, a recent LORETA study found that higher task-independent alpha-2 activity within left dorsolateral prefrontal and medial orbitofrontal regions was associated with stronger bias to respond to reward-related cues (D. A. Pizzagalli, Sherwood, Henriques, & Davidson, 2005). This is best reflected by the regions shown to be functionally associated with the decrease in cortisol, such that a concept (i.e. depression or anxiety) must be encoded by the individual as salient (defective or a situation to address) in the cortex for it to be salient enough in the individual's experience to produce an affective response.

Debate continues as to the specific role of the prefrontal cortices in affectual processes and their relationship in emotion with subcortical regions (R. J. Davidson, 2004). The results of this section are in agreement with studies showing a lateralized effect in functional tasks in affect processing. A concept must have meaning to be considered salient, meaningful or stressful. As mentioned earlier in the introduction, human beings tend to attend to salient stimuli and ignore others. It is clear that frontal lobe monitoring plays an important role in response mechanisms (Slachevsky, et al., 2003) and self-affect-regulation (Adolphs, Tranel, & Damasio, 2003; A. R. Damasio, et al., 2000; Gianotti, et al., 2008; Smith, et al., 2006). Perfusion fMRI data showed increased activity in right hemisphere regions as a result of psychological stress and cortisol showed positive associations with increased activity in the anterior cingulate, putamen, posterior

cingulate, precuneus and insular cortex (Wang, et al., 2005). Thus, recent research using PET and fMRI techniques to study the effects of psychosocial stress and the neural correlates of cortisol increases are in agreement with the current data.

Gender Differences

According to hypotheses set 3 there would be no differences between genders in (nh1) all task conditions, (nH2) in all behavioral measures and (nH3) in pre, post and difference in cortisol levels. The first hypothesis was not supported by the data, such that there are differences between genders in the sLORETA maps for each condition. The second hypothesis was supported to a degree, such that only two subsets of the behavioral measures showed significant difference. Finally, the data supported the third hypothesis, such that there are no differences between genders in the salivary cortisol levels.

Table 12 shows the differences between genders in the sLORETA comparisons for all conditions. Females tend toward a more bilateral processing in all assessment and photograph conditions except for the self image. Similar findings discussing a tendency toward bilateral processing in healthy females have been reported (Kemp, Silberstein, Armstrong, & Nathan, 2004). This however, may be attributed to the content in the subjective reports, such that females were more critical of the self-image picture than their male counterparts. This criticality of self and appearance may involve predominantly the right hemisphere with the exception of BA9 in the left hemisphere. Table 13 shows the differences between genders for all behavioral measures. From top to bottom are the measures and from left to right is sex, sample size, the mean, standard deviation and standard error for the mean. Only two differences are shown between genders in all behavioral measures, including pre, post and the difference between pre and post salivary cortisol measures.

Conclusions and Limitations:

This study sought to demonstrate that it is possible to examine the default network of the brain using 3-D source localization techniques. This goal was supported by the obtained data. The results determined there were significant differences in the DNt that can be differentiated and visualized during several self-specific and non-self tasks. Subsequently, further study of the EEG in DNt is warranted. The data also support the concept that DNt regions in the midline do perform a role in self concept and self image in conjunction with other cortical regions. Thus it might be concluded that a core self network exists in the brain; however, involving numerous regions rather than specific midline structures. Additionally, specific components of the self do appear to elicit differential activity patterns. The cortisol results indicate that positive affect relating to self consists of bilateral interactions with a predominant effect in the left hemisphere.

The cortico-cortical interactions might reflect that the left hemisphere operates in the capacity of language (i.e., concepts and knowledge components) while the right may specifically involve attentional processes for determining the salience of the knowledge from the left vPFC or more simply, a top-down bilateral process of inhibitory regulation of emotion which influences activation of the HPA axis. This is an important area for future research.

There are limitations to the current findings. The functional connectivity and cortisol analyses are descriptive in nature and as such no inference of causality or directionality can be made. EEG source localization techniques have less spatial resolution than fMRI/PET techniques, yet EEG techniques do provide very good temporal resolution which is very important to the tasks within this study. This study utilized convenient samples obtained from the university setting, which may not adequately represent the general population. Therefore larger,

diverse sampling should be the topic of future studies. It would also be of great benefit to cross-validate the measures in this study using two or more imaging techniques.

Overall the data provide preliminary evidence for the use of sLORETA in examining the default network. More importantly, the process of construct neurophysiology appears to be a valid approach, such that examining psychological assessment instruments and the constructs projected to be measured may in fact produce differential regional and functional connectivity patterns in the brain that can be visualized and evaluated in both normative and clinical samples.

Future Directions:

This study is the first in a stepwise pattern of research exploring the self and construct neurophysiology. One of the primary goals of future studies is to obtain large samples for construction of a database for task conditions. It is a goal for future studies to implement the procedures from this study in clinical samples (e.g., depression, addiction, and obesity). It is also desireable to implement personality and attachment scales into this protocol in order to evaluate the regional activity and functional connectivity patterns associated with these constructs. Another important direction is to construct a complex linear model with repeated measures that will be able to operate on the correlation structure. Finally and most importantly, it is desired to develop disorder specific protocols in LORETA neurofeedback training utilizing specific regions and frequencies defined in this study in order to enhance self-affect-regulation in clinical syndromes. This process offers the potential to influence neural regions shown in this study and others to be directly involved in affect regulation. In combination with other therapeutic methods, training the EEG in specific neuronal populations shown to be involved in the processing of self and affect may afford a more rapid and longer lasting (potentiated) treatment response. Additionally, if the data continues to develop in the desired direction, this type of

neurophysiological measure can be implemented to evaluate both treatment outcomes and efficacy. Thus, the potential functions derived from the data in this study are nothing short of intriguing.

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APPENDICES

APPENDIX I: FIGURES

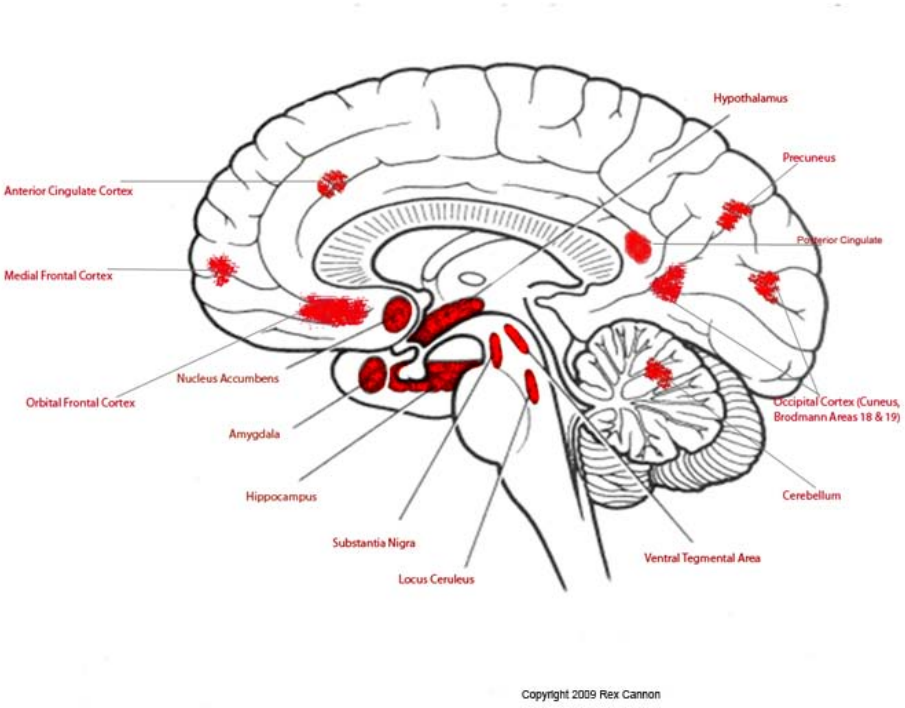


Figure 1: Neuroanatomical regions shown active during reward, self and DNt

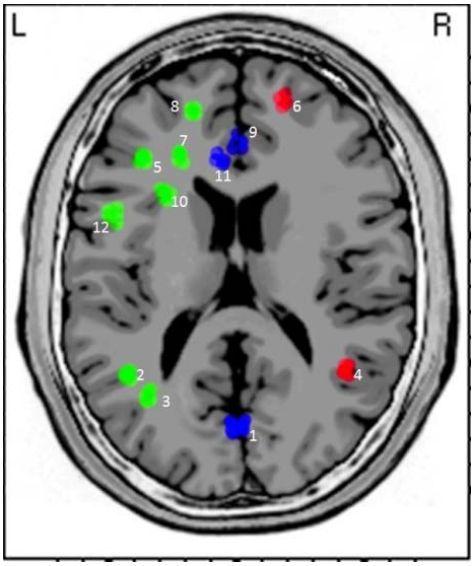


Figure 2: DNt Regions, colors represent hemisphere, green is left, blue is midline and red is right.

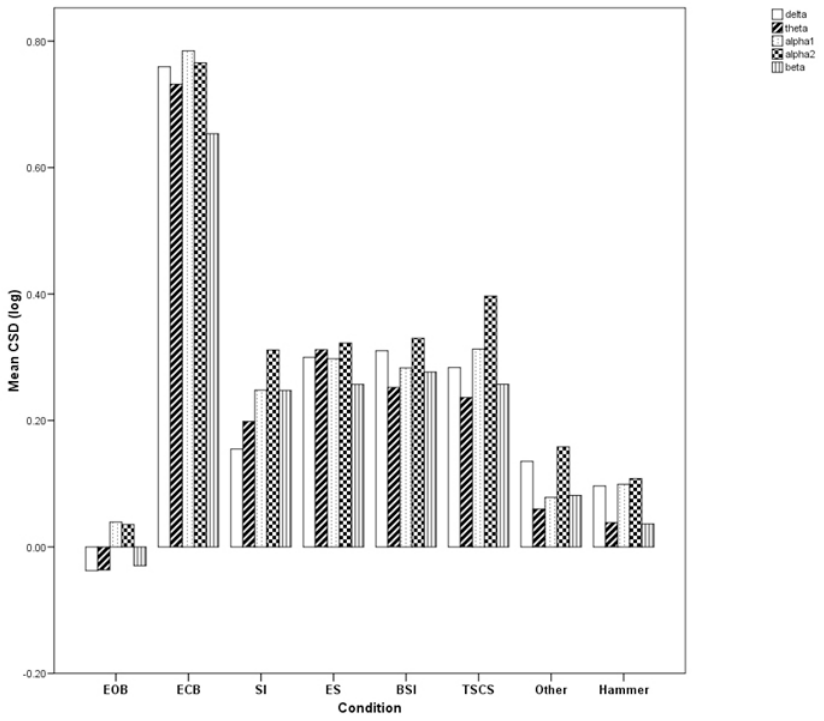


Figure 3: Grand mean for current source density (log) by condition for each frequency domain. On the ordinate is the mean CSD, on the abscissa is the conditions and the frequency domains are plotted within the graph.

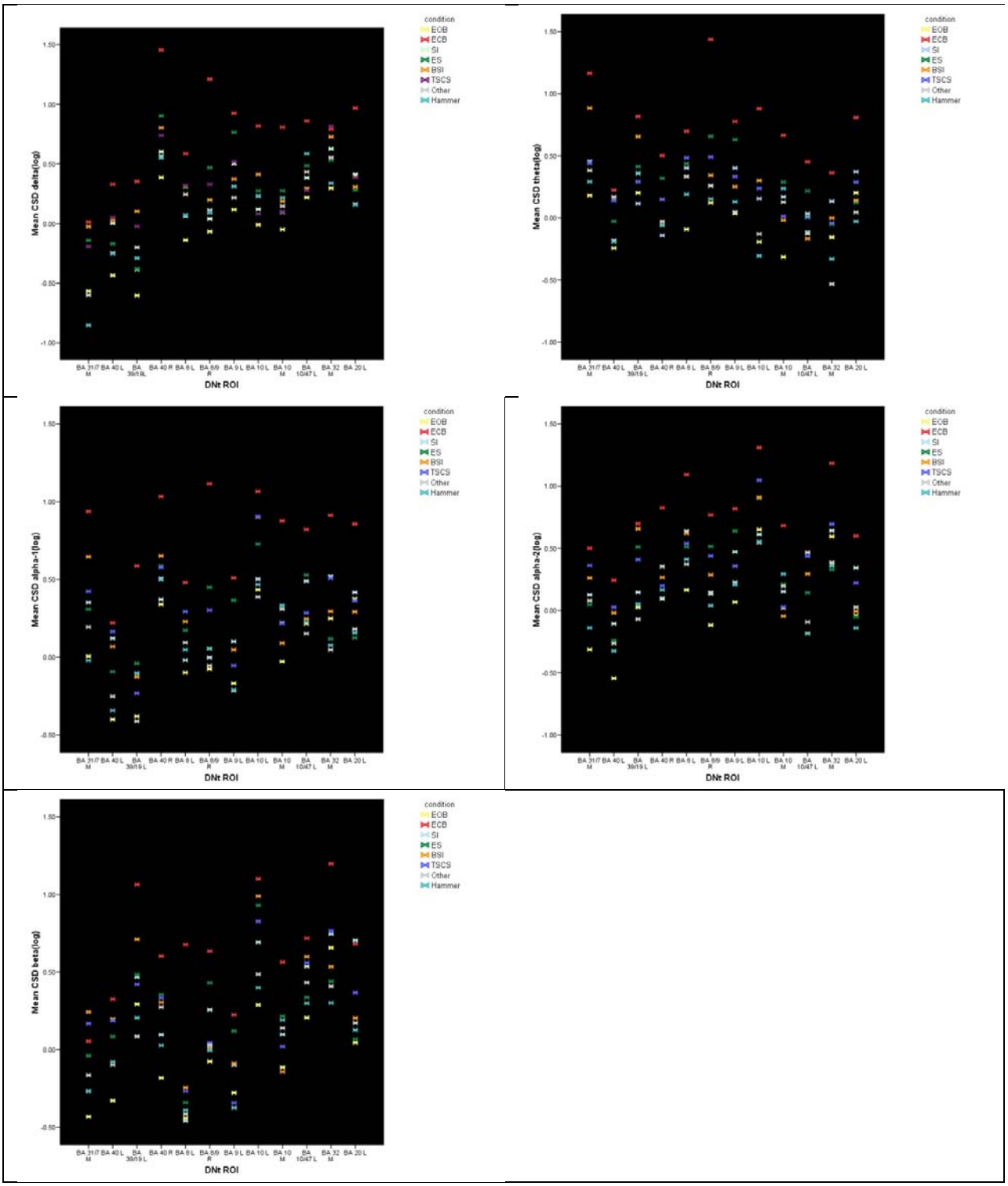


Figure 4: Plots of mean current source density for each frequency domain. From left to right and top to bottom are delta, theta, alpha-1, alpha-2 and beta. Within the figures, the ordinate shows the mean CSD for frequency domain and the abscissa shows each of the DNt regions. The conditions are plotted within the graph.

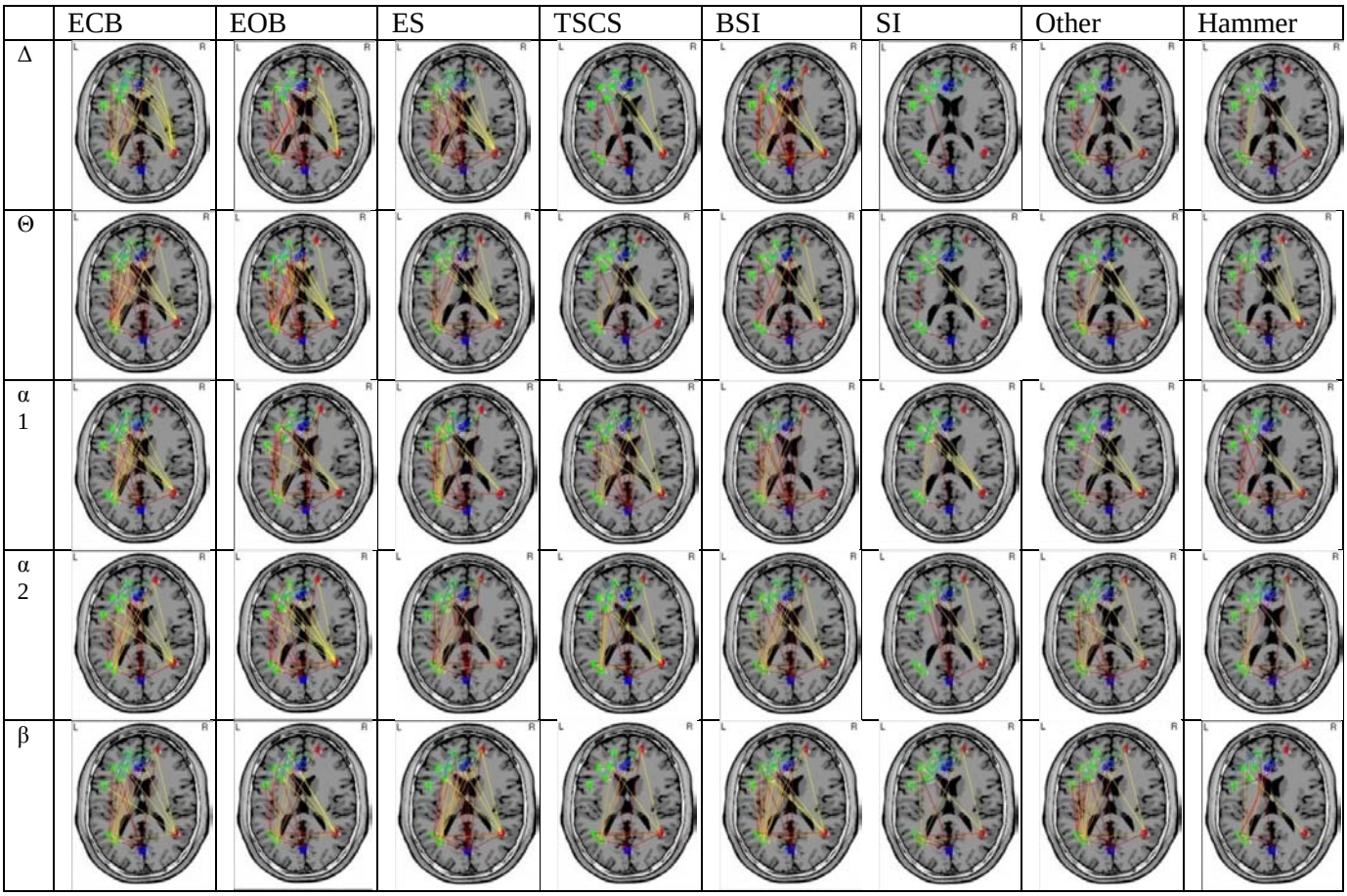


Figure 5: Interregional functional connectivity between the DNt regions for all conditions. From top to bottom are the respective EEG frequency domains Δ = Delta (0.5 – 3.5 Hz), Θ = Theta (3.5 – 7.5 Hz), α1 = Alpha-1 (7.5 – 10.0 Hz), α2 = Alpha-2 (10.0 – 12.0 Hz), β = Beta (12.0 – 32.0 Hz). From left to right is each of the conditions. Color Legend: 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11. Only correlations with significance < .05 are plotted.

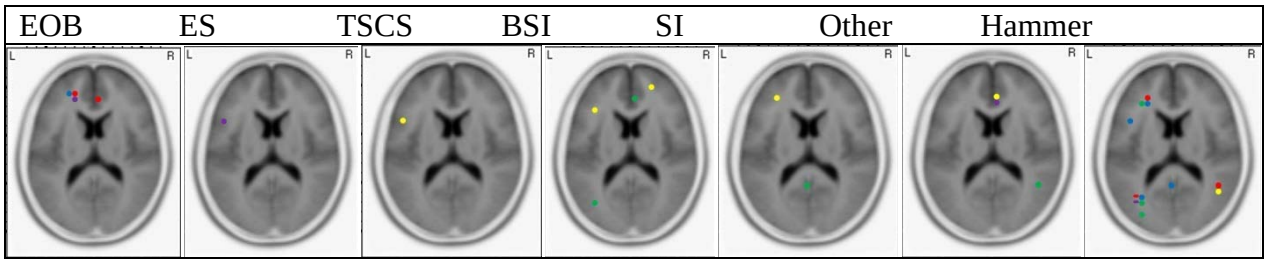


Figure 6: Gender differences in DNt regions for each task condition. The ECB condition showed no differences. From left to right are the conditions. The images are a horizontal view of the brain. The ROIs showing difference are plotted in the map with color representing frequency. Delta = green, Theta = red, Alpha-1 = blue, Alpha -2 = purple and Beta = yellow.

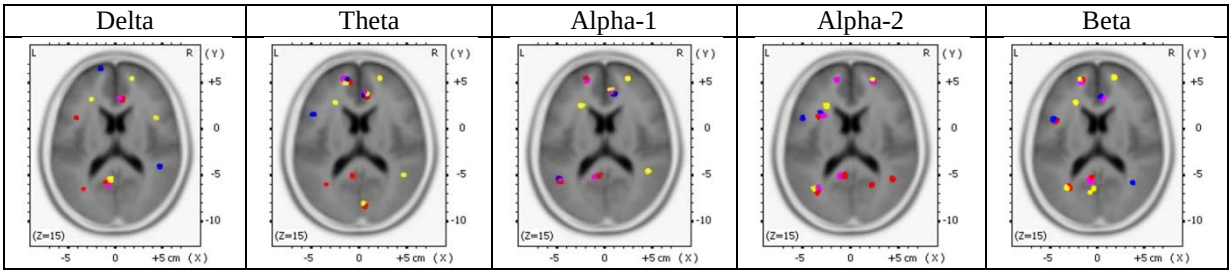


Figure 7: Regions of self-specific activation in each frequency domain. The images are a horizontal slice through the brain at z=15. Regions are approximated for 2-D rendering. The blue regions in the image are those showing increased CSD during the SI condition. The yellow regions in the image are those showing increased CSD during the ES condition. The red regions in the image are those showing increased CSD during the BSI condition. The pink regions are those showing increased CSD during the TSCS condition.

APPENDIX II: TABLES

Table 1: Regions identified in the default mode of brain.

Orientation Brodmann Area	*X*	*Y*	*Z*	*Neuroanatomical label*
1 Medial 31/7	-5	-49	40	Dorsal Posterior Cingulate/Somatosensory Association Cortex
2 Left 40	-53	-39	42	Parietal Lobe/supramarginal gyrus
3 Left 39/19	-45	-67	36	Angular Gyrus (Wernicke's area)
4 Right 40	45	-57	34	Parietal Lobe/supramarginal gyrus
5 Left lateral 8	-27	27	40	Frontal eye fields
6 Right 8/9	5	49	36	Frontal lobes
7 Left 9	-15	55	26	Dorsolateral prefrontal cortex
8 Left 10	-19	57	8	Anterior prefrontal cortex
9 Medial 10	-1	47	-4	Middle frontal lobe
10 Left 10/47	-33	45	-6	Inferior frontal lobe
11 Medial 32	3	31	-10	Anterior cingulate
12 Left 20	-49	-19	-18	Inferior temporal gyrus

Table 2: Example items from the SPESA

Childhood	***Adolescence***	***Adulthood***
1: I feel that my childhood was	**16: In my teenage years, I felt**	**32: I feel that my adult life is**
A: Happy	A: Content	A: Frustrating
B: Satisfactory	B: Frustrated	B: Enjoyable
C: Unhappy	C: Depressed	C: Happy
D: Traumatic	D: Happy	D: Depressing

Table 3: Example items from the BSI

Somatization	***Depression***	***Anxiety***
1: Faintness or dizziness	**2: Feeling no interest in things**	**3: Nervousness or shakiness inside**
A: Not at all	A: Not at all	A: Not at all
B: A Little Bit	B: A Little Bit	B: A Little Bit
C: Moderately	C: Moderately	C: Moderately
D: Quite a bit	D: Quite a bit	D: Quite a bit
E: Extremely	E: Extremely	E: Extremely

Table 4: Example items from the TSCS

Physical	***Disgust***	***Introspective***
1: I am an attractive person	**13: I despise myself**	**15: I am as smart as I want to be**
A: Completely false	A: Completely false	A: Completely false
B: Mostly false	B: Mostly false	B: Mostly false
C: Partly false and partly true	C: Partly false and partly true	C: Partly false and partly true
D: Mostly true	D: Mostly true	D: Mostly true
E: Completely true	E: Completely true	E: Completely true

Table 5: Mixed model results for beta frequency. In the table from left to right is the roi/condition < > roi/condition, beta, t-value and probability.

R/C		R/C		β	t	p
1	0	1	1	-0.4861	-2.40	0.0165
1	0	1	4	-0.6745	-3.33	0.0009
1	0	1	5	-0.5992	-2.96	0.0031
1	2	1	4	-0.5087	-2.51	0.0121
1	2	1	5	-0.4334	-2.14	0.0326
1	4	1	6	0.4073	2.01	0.0446
1	4	1	7	0.5115	2.52	0.0117
1	5	1	7	0.4362	2.15	0.0315
2	0	2	1	-0.6530	-3.22	0.0013
2	0	2	2	-0.5222	-2.58	0.0100
2	0	2	3	-0.4122	-2.03	0.0421
2	0	2	4	-0.5240	-2.58	0.0098
2	0	2	5	-0.5151	-2.54	0.0111
2	1	2	6	0.4230	2.09	0.0370
2	1	2	7	0.4046	2.00	0.0460
3	0	3	1	-0.7695	-3.80	0.0001
3	0	3	4	-0.4171	-2.06	0.0397
3	1	3	2	0.5954	2.94	0.0033
3	1	3	3	0.5796	2.86	0.0043
3	1	3	5	0.6407	3.16	0.0016
3	1	3	6	0.9775	4.82	<.0001
3	1	3	7	0.8573	4.23	<.0001
3	3	3	6	0.3979	1.96	0.0497
3	4	3	6	0.6251	3.08	0.0021
3	4	3	7	0.5049	2.49	0.0128
4	0	4	1	-0.7855	-3.87	0.0001
4	0	4	3	-0.5355	-2.64	0.0083
4	0	4	4	-0.4867	-2.40	0.0164
4	0	4	5	-0.5156	-2.54	0.0110
4	0	4	6	-0.4555	-2.25	0.0247
4	1	4	2	0.5065	2.50	0.0125
4	1	4	7	0.5762	2.84	0.0045
5	0	5	1	-1.1165	-5.51	<.0001
5	1	5	2	1.1338	5.59	<.0001
5	1	5	3	1.0167	5.01	<.0001
5	1	5	4	0.9196	4.54	<.0001
5	1	5	5	0.9417	4.65	<.0001
5	1	5	6	1.0909	5.38	<.0001
5	1	5	7	1.0662	5.26	<.0001
6	0	6	1	-0.7108	-3.51	0.0005
6	0	6	2	-0.3323	-1.64	0.1012
6	0	6	3	-0.5056	-2.49	0.0127
6	1	6	4	0.6232	3.07	0.0021
6	1	6	5	0.5921	2.92	0.0035
6	1	6	6	0.6061	2.99	0.0028
6	1	6	7	0.6383	3.15	0.0016
6	3	6	4	0.4180	2.06	0.0393
6	3	6	6	0.4009	1.98	0.0480
6	3	6	7	0.4331	2.14	0.0327
7	0	7	1	-0.5015	-2.47	0.0134
7	0	7	3	-0.3975	-1.96	0.0500
7	1	7	5	0.5668	2.80	0.0052
7	1	7	6	0.5985	2.95	0.0032
7	1	7	7	0.5984	2.95	0.0032
7	3	7	5	0.4628	2.28	0.0225
7	3	7	6	0.4945	2.44	0.0147
7	3	7	7	0.4944	2.44	0.0148
8	0	8	1	-0.8123	-4.01	<.0001
8	0	8	2	-0.4052	-2.00	0.0457
8	0	8	3	-0.6426	-3.17	0.0015
8	0	8	4	-0.7011	-3.46	0.0005
8	0	8	5	-0.5383	-2.65	0.0080

(Table 5 continued)

8	1	8	2	0.4071	2.01	0.0447
8	1	8	6	0.6134	3.03	0.0025
8	1	8	7	0.7016	3.46	0.0005
8	2	8	3	-0.2375	-1.17	0.2415
8	3	8	6	0.4438	2.19	0.0286
8	3	8	7	0.5319	2.62	0.0087
8	4	8	6	0.5022	2.48	0.0133
8	4	8	7	0.5904	2.91	0.0036
8	5	8	7	0.4275	2.11	0.0350
9	0	9	1	-0.6780	-3.34	0.0008
9	0	9	3	-0.3287	-1.62	0.1050
9	0	9	5	-0.1351	-0.67	0.5052
9	1	9	2	0.4657	2.30	0.0216
9	1	9	4	0.7064	3.48	0.0005
9	1	9	5	0.5429	2.68	0.0074
9	1	9	6	0.4253	2.10	0.0360
10	0	10	1	-.5107	-2.52	0.0118
10	1	10	7	0.4171	2.06	0.0397
11	0	11	1	-0.5398	2.66	0.0078
11	1	11	2	0.4509	2.22	0.0262
11	1	11	3	0.7563	3.73	0.0002
11	1	11	4	0.6626	3.27	0.0011
11	1	11	5	0.4319	2.13	0.0332
11	1	11	6	0.7890	3.89	0.0001
11	1	11	7	0.8943	4.41	<.0001
11	2	11	7	0.4434	2.19	0.0288
11	5	11	7	0.4625	2.28	0.0226
12	0	12	1	-0.6348	-3.13	0.0017
12	0	12	2	-0.6571	-3.24	0.0012
12	1	12	3	0.6136	3.03	0.0025
12	1	12	4	0.4761	2.35	0.0189
12	1	12	6	0.5093	2.51	0.0120
12	1	12	7	0.5540	2.73	0.0063
12	2	12	3	0.6359	3.14	0.0017
12	2	12	4	0.4984	2.46	0.0140
12	2	12	6	0.5316	2.62	0.0088
12	2	12	7	0.5763	2.84	0.0045

Table 6: Mixed model results for delta frequency In the table from left to right is the roi/condition < > roi/condition, beta, t-value and probability.

R/C		R/C		β	t	p
1	0	1	1	-0.5781	-2.86	0.0043
1	0	1	3	-0.4256	-2.10	0.0355
1	0	1	4	-0.5413	-2.67	0.0075
1	1	1	2	0.6106	3.02	0.0026
1	1	1	6	0.6101	3.01	0.0026
1	1	1	7	0.8651	4.27	<.0001
1	2	1	3	-0.4582	-2.26	0.0236
1	2	1	4	-0.5739	-2.84	0.0046
1	2	1	5	-0.4076	-2.01	0.0441
1	3	1	6	0.4577	2.26	0.0238
1	3	1	7	0.7126	3.52	0.0004
1	4	1	6	0.5734	2.83	0.0046
1	4	1	7	0.8283	4.09	<.0001
1	5	1	6	0.4071	2.01	0.0444
1	5	1	7	0.6620	3.27	0.0011
2	0	2	1	-0.7633	-3.77	0.0002
2	0	2	2	-0.4368	-2.16	0.0310
2	0	2	4	-0.4633	-2.29	0.0221
2	0	2	5	-0.4863	-2.40	0.0163
2	1	2	3	0.4995	2.47	0.0136
2	1	2	6	0.5754	2.84	0.0045
2	1	2	7	0.5827	2.88	0.0040

(Table 6 continued)

3	0	3	1	-0.9563	-4.72	<.0001
3	0	3	4	-0.7066	-3.49	0.0005
3	0	3	5	-0.5796	-2.86	0.0042
3	0	3	6	-0.4034	-1.99	0.0463
3	1	3	2	0.7380	3.65	0.0003
3	1	3	3	0.7297	3.61	0.0003
3	1	3	5	0.3767	1.86	0.0628
3	1	3	6	0.5529	2.73	0.0063
3	1	3	7	0.6420	3.17	0.0015
3	2	3	4	-0.4883	-2.41	0.0159
3	3	3	4	-0.4800	-2.37	0.0178
4	0	4	1	-1.0696	-5.28	<.0001
4	0	4	3	-0.5162	-2.55	0.0108
4	0	4	4	-0.4162	-2.06	0.0398
4	1	4	2	0.8534	4.22	<.0001
4	1	4	3	0.5534	2.73	0.0063
4	1	4	4	0.6534	3.23	0.0013
4	1	4	5	0.7181	3.55	0.0004
4	1	4	6	0.8910	4.40	<.0001
4	1	4	7	0.9052	4.47	<.0001
5	0	5	1	-0.7246	-3.58	0.0003
5	0	5	3	-0.4429	-2.19	0.0287
5	0	5	4	-0.4534	-2.24	0.0251
5	0	5	5	-0.4587	-2.27	0.0235
5	1	5	2	0.5243	2.59	0.0096
5	1	5	7	0.5150	2.54	0.0110
6	0	6	1	-1.2768	-6.31	<.0001
6	0	6	3	-0.5350	-2.64	0.0082
6	1	6	2	1.1717	5.79	<.0001
6	1	6	3	0.7418	3.66	0.0002
6	1	6	4	1.0123	5.00	<.0001
6	1	6	5	0.8812	4.35	<.0001
6	1	6	6	1.0972	5.42	<.0001
6	1	6	7	1.1198	5.53	<.0001
6	2	6	3	-0.4299	-2.12	0.0337
7	0	7	1	-0.8069	-3.99	<.0001
7	0	7	2	-0.3831	-1.89	0.0584
7	0	7	3	-0.6473	-3.20	0.0014
7	0	7	5	-0.4016	-1.98	0.0473
7	1	7	2	0.4237	2.09	0.0364
7	1	7	4	0.5508	2.72	0.0065
7	1	7	5	0.4052	2.00	0.0453
7	1	7	6	0.7075	3.50	0.0005
7	1	7	7	0.6129	3.03	0.0025
7	3	7	6	0.5479	2.71	0.0068
7	3	7	7	0.4533	2.24	0.0252
8	0	8	1	-0.8262	-4.08	<.0001
8	0	8	4	-0.4224	-2.09	0.0369
8	1	8	2	0.6959	3.44	0.0006
8	1	8	3	0.5430	2.68	0.0073
8	1	8	4	0.4038	2.00	0.0461
8	1	8	5	0.7337	3.62	0.0003
8	1	8	6	0.5864	2.90	0.0038
8	1	8	7	0.5840	2.89	0.0039
9	0	9	1	-0.8572	-4.23	<.0001
9	1	9	2	0.7130	3.52	0.0004
9	1	9	3	0.5332	2.63	0.0084
9	1	9	4	0.6196	3.06	0.0022
9	1	9	5	0.7074	3.50	0.0005
9	1	9	6	0.6612	3.27	0.0011
9	1	9	7	0.5919	2.92	0.0035
10	0	10	1	-.6411	-3.17	0.0015
10	1	10	2	0.4754	2.35	0.0189
10	1	10	3	0.3741	1.85	0.0646
10	1	10	4	0.5641	2.79	0.0053
10	1	10	5	0.5821	2.88	0.0040
10	1	10	6	0.4263	2.11	0.0352

(Table 6 continued)

11	0	11	1	-0.4937	-2.44	0.0148
11	0	11	4	-0.4305	-2.13	0.0335
11	0	11	5	-0.5176	-2.56	0.0106
11	1	11	7	0.4527	2.24	0.0254
11	5	11	7	0.4767	2.36	0.0186
12	0	12	1	-0.5708	-2.82	0.0048
12	1	12	2	0.5570	2.75	0.0059
12	1	12	3	0.6881	3.40	0.0007
12	1	12	4	0.6621	3.27	0.0011
12	1	12	5	0.5811	2.87	0.0041
12	1	12	6	0.8044	3.97	<.0001
12	1	12	7	0.8134	4.02	<.0001

Table 7: Mixed model results for theta frequency In the table from left to right is the roi/condition < > roi/condition, beta, t-value and probability.

R/C		R/C		β	t	p
1	0	1	1	-0.9815	-4.83	<.0001
1	0	1	4	-0.7039	-3.46	0.0005
1	1	1	2	0.7066	3.47	0.0005
1	1	1	3	0.7241	3.56	0.0004
1	1	1	5	0.7195	3.54	0.0004
1	1	1	6	0.7796	3.83	0.0001
1	1	1	7	0.8709	4.28	<.0001
1	2	1	4	-0.4290	-2.11	0.0349
1	3	1	4	-0.4465	-2.20	0.0282
1	4	1	5	0.4419	2.17	0.0298
1	4	1	6	0.5019	2.47	0.0136
1	4	1	7	0.5933	2.92	0.0035
2	0	2	1	-0.4667	-2.29	0.0218
2	0	2	2	-0.4132	-2.03	0.0422
2	1	2	6	0.4033	1.98	0.0474
2	1	2	7	0.4159	2.05	0.0409
3	0	3	1	-0.6140	-3.02	0.0025
3	0	3	4	-0.4527	-2.23	0.0260
3	1	3	2	0.7006	3.45	0.0006
3	1	3	3	0.4028	1.98	0.0477
3	1	3	5	0.5243	2.58	0.0100
3	1	3	6	0.4586	2.26	0.0242
3	1	3	7	0.4531	2.23	0.0259
3	2	3	4	-0.5393	-2.65	0.0080
4	0	4	1	-0.5580	-2.74	0.0061
4	1	4	2	0.6424	3.16	0.0016
4	1	4	6	0.5309	2.61	0.0091
4	1	4	7	0.5615	2.76	0.0058
4	2	4	3	-0.4601	-2.26	0.0237
5	0	5	1	-0.7889	-3.88	0.0001
5	0	5	2	-0.4919	-2.42	0.0156
5	0	5	3	-0.5276	-2.59	0.0095
5	0	5	4	-0.4243	-2.09	0.0370
5	0	5	5	-0.5755	-2.83	0.0047
5	0	5	6	-0.4255	-2.09	0.0365
5	1	5	7	0.5074	2.50	0.0126
6	0	6	1	-1.3161	-6.47	<.0001
6	0	6	3	-0.5344	-2.63	0.0086
6	1	6	2	1.1802	5.80	<.0001
6	1	6	3	0.7817	3.84	0.0001
6	1	6	4	1.0943	5.38	<.0001
6	1	6	5	0.9464	4.65	<.0001
6	1	6	6	1.1760	5.78	<.0001
6	1	6	7	1.2826	6.31	<.0001
6	3	6	7	0.5009	2.46	0.0138
7	0	7	1	-0.7388	-3.63	0.0003
7	0	7	2	-0.3642	-1.79	0.0734

(Table 7 continued)

7	0	7	3	-0.5928	-2.91	0.0036
7	1	7	4	0.5247	2.58	0.0099
7	1	7	5	0.4425	2.18	0.0296
7	1	7	6	0.7274	3.58	0.0004
7	1	7	7	0.6459	3.18	0.0015
7	3	7	6	0.5814	2.86	0.0043
7	3	7	7	0.4999	2.46	0.0140
8	0	8	1	-1.0720	-5.27	<.0001
8	0	8	3	-0.4934	-2.43	0.0153
8	0	8	4	-0.4930	-2.42	0.0154
8	0	8	5	-0.4297	-2.11	0.0346
8	1	8	2	0.7245	3.56	0.0004
8	1	8	3	0.5786	2.85	0.0045
8	1	8	4	0.5790	2.85	0.0044
8	1	8	5	0.6423	3.16	0.0016
8	1	8	6	1.0111	4.97	<.0001
8	1	8	7	1.1863	5.83	<.0001
8	2	8	7	0.4619	2.27	0.0232
8	3	8	6	0.4325	2.13	0.0335
8	3	8	7	0.6078	2.99	0.0028
8	4	8	6	0.4321	2.12	0.0336
8	4	8	7	0.6074	2.99	0.0028
8	5	8	6	0.3688	1.81	0.0698
8	5	8	7	0.5441	2.68	0.0075
9	0	9	1	-0.9787	-4.81	<.0001
9	0	9	2	-0.4841	-2.38	0.0173
9	0	9	3	-0.6022	-2.96	0.0031
9	0	9	6	-0.4399	-2.16	0.0306
9	0	9	7	-0.5502	-2.71	0.0068
9	1	9	2	0.4946	2.43	0.0150
9	1	9	4	0.6825	3.36	0.0008
9	1	9	5	0.6519	3.21	0.0014
9	1	9	6	0.5388	2.65	0.0081
9	1	9	7	0.4285	2.11	0.0352
10	0	10	1	-0.5787	-2.85	0.0044
10	1	10	2	0.5648	2.78	0.0055
10	1	10	4	0.6179	3.04	0.0024
10	1	10	5	0.4472	2.20	0.0279
10	1	10	6	0.4159	2.05	0.0409
10	1	10	7	0.4401	2.16	0.0305
11	0	11	1	-0.5206	-2.56	0.0105
11	1	11	3	0.4144	2.04	0.0416
11	1	11	5	0.4041	1.99	0.0469
11	1	11	6	0.8948	4.40	<.0001
11	1	11	7	0.6936	3.41	0.0007
11	2	11	6	0.6648	3.27	0.0011
11	2	11	7	0.4637	2.28	0.0226
11	3	11	6	0.4803	2.36	0.0182
11	4	11	6	0.5320	2.62	0.0089
11	5	11	6	0.4906	2.41	0.0159
12	0	12	1	-0.6057	-2.98	0.0029
12	1	12	2	0.4360	2.14	0.0321
12	1	12	3	0.6860	3.37	0.0007
12	1	12	4	0.6668	3.28	0.0010
12	1	12	5	0.5188	2.55	0.0108
12	1	12	6	0.7630	3.75	0.0002
12	1	12	7	0.8356	4.11	<.0001
12	2	12	7	0.3996	1.96	0.0495

Table 8: Mixed Model Results for alpha – 1 frequency In the table from left to right is the roi/condition < > roi/condition, beta, t-value and probability.

R/C	R/C	β	t	p
1	0	1	1	-0.9314	-4.66	<.0001
1	0	1	4	-0.6383	-3.19	0.0014
1	0	1	5	-0.4183	-2.09	0.0363

(Table 8 continued)

1	1	1	2	0.5861	2.93	0.0034
1	1	1	3	0.6293	3.15	0.0016
1	1	1	5	0.5131	2.57	0.0102
1	1	1	6	0.7443	3.73	0.0002
1	1	1	7	0.9581	4.80	<.0001
1	4	1	6	0.4511	2.26	0.0240
1	4	1	7	0.6649	3.33	0.0009
1	5	1	7	0.4450	2.23	0.0260
2	0	2	1	-0.6214	-3.11	0.0019
2	0	2	2	-0.5215	-2.61	0.0091
2	0	2	4	-0.4694	-2.35	0.0188
2	0	2	5	-0.5654	-2.83	0.0047
2	1	2	6	0.4722	2.36	0.0181
2	1	2	7	0.5636	2.82	0.0048
2	2	2	7	0.4638	2.32	0.0203
2	4	2	7	0.4117	2.06	0.0394
2	5	2	6	0.4162	2.08	0.0372
2	5	2	7	0.5076	2.54	0.0111
3	0	3	1	-0.9662	-4.84	<.0001
3	1	3	2	0.6899	3.45	0.0006
3	1	3	3	0.6279	3.14	0.0017
3	1	3	4	0.7126	3.57	0.0004
3	1	3	5	0.8192	4.10	<.0001
3	1	3	6	0.9986	5.00	<.0001
3	1	3	7	0.6910	3.46	0.0005
4	0	4	1	-0.6918	-3.46	0.0005
4	1	4	2	0.6606	3.31	0.0009
4	1	4	3	0.4441	2.22	0.0263
4	1	4	4	0.3809	1.91	0.0566
4	1	4	5	0.4531	2.27	0.0234
4	1	4	6	0.5247	2.63	0.0086
4	1	4	7	0.5333	2.67	0.0076
5	0	5	1	-0.5780	-2.89	0.0038
5	1	5	2	0.4994	2.50	0.0124
5	1	5	7	0.4309	2.16	0.0310
6	0	6	1	-1.1906	-5.96	<.0001
6	0	6	3	-0.5249	-2.63	0.0086
6	1	6	2	1.1163	5.59	<.0001
6	1	6	3	0.6657	3.33	0.0009
6	1	6	4	1.0611	5.31	<.0001
6	1	6	5	0.8127	4.07	<.0001
6	1	6	6	1.1702	5.86	<.0001
6	1	6	7	1.0611	5.31	<.0001
6	2	6	3	-0.4506	-2.26	0.0241
6	3	6	4	0.3954	1.98	0.0478
6	3	6	6	0.5046	2.53	0.0116
6	3	6	7	0.3955	1.98	0.0478
7	0	7	1	-0.6773	-3.39	0.0007
7	0	7	3	-0.5338	-2.67	0.0076
7	1	7	2	0.4081	2.04	0.0411
7	1	7	4	0.4616	2.31	0.0209
7	1	7	5	0.5635	2.82	0.0048
7	1	7	6	0.7248	3.63	0.0003
7	1	7	7	0.7176	3.59	0.0003
7	3	7	5	0.4199	2.10	0.0356
7	3	7	6	0.5812	2.91	0.0036
7	3	7	7	0.5741	2.87	0.0041
8	0	8	1	-0.6313	-3.16	0.0016
8	0	8	4	-0.4674	-2.34	0.0193
8	0	8	5	-0.4698	-2.35	0.0187
8	1	8	2	0.5628	2.82	0.0049
8	1	8	3	0.3371	1.69	0.0915
8	1	8	6	0.6785	3.40	0.0007
8	1	8	7	0.5970	2.99	0.0028
8	2	8	4	-0.3989	-2.00	0.0459
8	2	8	5	-0.4013	-2.01	0.0446
8	4	8	6	0.5146	2.58	0.0100

(Table 8 continued)

8	4	8	7	0.4331	2.17	0.0302
9	0	9	1	-0.9024	-4.52	<.0001
9	1	9	2	0.6533	3.27	0.0011
9	1	9	3	0.5557	2.78	0.0054
9	1	9	4	0.7847	3.93	<.0001
9	1	9	5	0.6596	3.30	0.0010
9	1	9	6	0.5674	2.84	0.0045
9	1	9	7	0.5431	2.72	0.0066
10	0	10	1	-0.6061	-3.03	0.0024
10	1	10	4	0.5746	2.88	0.0040
10	1	10	5	0.5359	2.68	0.0073
10	1	10	6	0.6685	3.35	0.0008
10	1	10	7	0.5945	2.98	0.0029
11	0	11	1	-0.6636	-3.32	0.0009
11	1	11	2	0.3926	1.97	0.0494
11	1	11	3	0.7943	3.98	<.0001
11	1	11	4	0.6176	3.09	0.0020
11	1	11	5	0.4055	2.03	0.0424
11	1	11	6	0.8641	4.33	<.0001
11	1	11	7	0.8360	4.18	<.0001
11	2	11	3	0.4016	2.01	0.0444
11	2	11	6	0.4714	2.36	0.0183
11	2	11	7	0.4433	2.22	0.0265
11	5	11	6	0.4586	2.30	0.0217
11	5	11	7	0.4304	2.15	0.0312
12	0	12	1	-0.4824	-2.41	0.0158
12	1	12	2	0.4399	2.20	0.0277
12	1	12	3	0.7314	3.66	0.0003
12	1	12	4	0.5647	2.83	0.0047
12	1	12	5	0.4927	2.47	0.0137
12	1	12	6	0.6768	3.39	0.0007
12	1	12	7	0.6998	3.50	0.0005

Table 9: Mixed model results for alpha-2 frequency. In the table from left to right is the roi/condition < > roi/condition, beta, t-value and probability.

R/C		R/C		β	t	p
1	0	1	1	-0.8138	-4.02	<.0001
1	0	1	2	-0.4397	-2.18	.0297
1	0	1	4	-0.5742	-2.84	.0045
1	0	1	5	-0.6761	-3.34	.0008
1	1	1	3	0.4536	2.24	.0249
1	1	1	6	0.4210	2.08	.0374
1	1	1	7	0.6389	3.16	.0016
1	4	1	7	0.3993	1.98	.0483
1	5	1	7	0.5012	2.48	.0132
2	0	2	1	-0.7867	-3.89	.0001
2	0	2	2	-0.4369	-2.16	.0308
2	0	2	4	-0.5246	-2.59	.0095
2	0	2	5	-0.5709	-2.82	.0048
2	1	2	3	0.4836	2.39	.0168
2	1	2	6	0.5060	2.50	.0123
2	1	2	7	0.5667	2.80	.0051
3	0	3	1	-0.6707	-3.32	.0009
3	0	3	3	-0.4829	-2.39	.0170
3	0	3	4	-0.6280	-3.11	.0019
3	1	3	2	0.5515	2.73	.0064
3	1	3	6	0.7673	3.79	.0001
3	1	3	7	0.6446	3.19	.0014
3	2	3	4	-0.5087	-2.52	.0119
3	3	3	6	0.5794	2.87	.0042
3	3	3	7	0.4568	2.26	.0239
3	4	3	6	0.7246	3.58	.0003

(Table 9 continued)

3	4	3	7	0.6019	2.98	.0029
3	5	3	6	0.4781	2.36	.0181
4	0	4	1	-0.7320	-3.62	.0003
4	1	4	2	0.7269	3.60	.0003
4	1	4	3	0.4770	2.36	.0183
4	1	4	4	0.5602	2.77	.0056
4	1	4	5	0.6280	3.11	.0019
4	1	4	6	0.4703	2.33	.0201
4	1	4	7	0.6596	3.26	.0011
5	0	5	1	-0.9262	-4.58	<.0001
5	0	5	2	-0.4719	-2.33	.0196
5	0	5	4	-0.4531	-2.24	.0251
5	1	5	2	0.4542	2.25	.0247
5	1	5	3	0.5808	2.87	.0041
5	1	5	4	0.4731	2.34	.0193
5	1	5	5	0.5529	2.73	.0063
5	1	5	6	0.7206	3.56	.0004
5	1	5	7	0.6811	3.37	.0008
6	0	6	1	-0.8863	-4.38	<.0001
6	0	6	3	-0.6322	-3.13	.0018
6	0	6	4	-0.4042	-2.00	.0456
6	0	6	5	-0.5561	-2.75	.0060
6	1	6	2	0.6223	3.08	.0021
6	1	6	4	0.4821	2.38	.0171
6	1	6	5	0.3302	1.63	.1025
6	1	6	6	0.6357	3.14	.0017
6	1	6	7	0.7285	3.60	.0003
6	3	6	7	0.4744	2.35	.0190
6	5	6	7	0.3983	1.97	.0489
7	0	7	1	-0.7499	-3.71	.0002
7	0	7	2	-0.4041	-2.00	.0457
7	0	7	3	-0.5720	-2.83	.0047
7	1	7	4	0.4595	2.27	.0231
7	1	7	5	0.4602	2.28	.0229
7	1	7	6	0.5898	2.92	.0035
7	1	7	7	0.6104	3.02	.0025
7	3	7	6	0.4118	2.04	.0417
7	3	7	7	0.4325	2.14	.0325
8	0	8	1	-0.6582	-3.26	.0011
8	0	8	5	-0.3971	-1.96	.0496
8	1	8	2	0.6965	3.44	.0006
8	1	8	3	0.4076	2.02	.0438
8	1	8	4	0.3984	1.97	.0488
8	1	8	6	0.7637	3.78	.0002
8	1	8	7	0.7541	3.73	.0002
8	2	8	5	-0.4354	-2.15	.0313
8	5	8	6	0.5026	2.49	.0129
8	5	8	7	0.4930	2.44	.0148
9	0	9	1	-0.6599	-3.26	.0011
9	1	9	2	0.5278	2.61	.0091
9	1	9	3	0.4695	2.32	.0203
9	1	9	4	0.7257	3.59	.0003
9	1	9	5	0.6523	3.23	.0013
9	1	9	6	0.4850	2.40	.0165
10	0	10	1	-0.6544	-3.24	.0012
10	0	10	2	-0.6480	-3.20	.0014
10	0	10	4	-0.4765	-2.36	.0185
10	0	10	5	-0.6195	-3.06	.0022
10	1	10	6	0.5642	2.79	.0053
10	1	10	7	0.6577	3.25	.0011
10	2	10	6	0.5578	2.76	.0058
10	2	10	7	0.6513	3.22	.0013
10	4	10	7	0.4799	2.37	.0176
10	5	10	6	0.5293	2.62	.0089
10	5	10	7	0.6229	3.08	.0021
11	0	11	1	-0.5878	-2.91	.0037
11	1	11	2	0.5386	2.66	.0077

(Table 9 continued)

11	1	11	3	0.8500	4.20	<.0001
11	1	11	4	0.8035	3.97	<.0001
11	1	11	5	0.4874	2.41	.0160
11	1	11	6	0.7951	3.93	<.0001
11	1	11	7	0.8225	4.07	<.0001
12	0	12	1	-0.6369	-3.15	.0016
12	1	12	3	0.6491	3.21	.0013
12	1	12	4	0.6048	2.99	.0028
12	1	12	6	0.5707	2.82	.0048
12	1	12	7	0.7374	3.65	.0003
12	2	12	7	0.4815	2.38	.0173

Table 10: Results for voxel by voxel comparisons for each task condition to eyes-opened baseline and between tasks. From top to bottom are the specific task compared to EOB followed by image comparisons and then assessment conditions comparisons. From left to right are the frequency, the maximum and minimum estimates by sLORETA, x, y, z coordinates, Brodmann Area/anatomical label, hemisphere, t-value and the probability of t. Shaded areas indicate regional maximum increase in current source density between conditions.

Frequency	***Max/min***	***x,y,z coordinates***	***Brodmann area/anatomical label***	***hemisphere***	***t-value***	***p***
			SPESA > EOB			
delta	max	(30, 5, 65)	BA 6, middle frontal gyrus	R	3.15	0.002
alpha-1	max	(-30, 20, 35)	BA 13, insular cortex	L	3.19	0.002
	min	(5, -65, 40)	BA 7, precuneus	R	2.29	0.025
alpha-2	max	(5, 45, 50)	BA 8, superior frontal gyrus	R	2.86	0.005
beta	min	(-45, 35, 20)	BA 46, middle frontal gyrus	L	4.15	0.0001
			BSI > EOB			
delta	max	(10, 25, 25)	BA 32, anterior cingulate	R	3.32	0.001
theta	max	(10, 65, 20)	BA 10, middle frontal gyrus	R	2.25	0.028
alpha-1	min	(10, -80, 35)	BA 19, cuneus	R	2.68	0.009
alpha-2	max	(40, -55, 60)	BA 40, inferior parietal lobule	R	2.77	0.007
	min	(15, 65, -15)	BA 11, superior frontal gyrus	R	3.23	0.001
beta	min	(35, 40, 40)	BA 9, middle frontal gyrus	R	3.24	0.001
			TSCS > EOB			
delta	max	(40, 55, -10)	BA 11 middle frontal gyrus	R	3.23	0.001
theta	max	(-35, 60, -5)	BA 10, middle frontal gyrus	L	2.35	0.022
	min	(-10, -30, 40)	BA 31, posterior cingulate	L	2.76	0.007
alpha-1	max	(-50, 20, 20)	BA 45, inferior frontal gyrus	L	2.33	0.023
	min	(15, -75, 50)	BA 7, precuneus	R	2.56	0.012
alpha-2	max	(30, -65, 60)	BA 7, superior parietal lobule	R	2.66	0.009
	min	(25, 60, -15)	BA 11, superior frontal gyrus	R	2.99	0.004
beta	max	(-20, -45, 30)	BA 31, precuneus	L	2.72	0.008
	min	(-10, 65, -5)	BA 10, superior frontal gyrus	L	3.23	0.001
			SELF > EOB			
delta	max	(45, -60, 20)	BA 39, superior temporal gyrus	R	2.56	0.012
	min	(30, -10, -35)	BA 20, uncus	R	2.65	0.01
theta	max	(-30, 35, -15)	BA 11 middle frontal gyrus	L	2.11	0.038
	min	(-30, 15, 60)	BA 6, middle frontal gyrus	L	3.04	0.003
alpha-1	max	(30, 30, 35)	BA 9, middle frontal gyrus	R	2.35	0.022
	min	(0, -60, 20)	BA 23, precuneus	M	2.42	0.018
alpha-2	min	(-50, -70, -20)	BA 19, fusiform gyrus	L	2.79	0.007
beta	max	(0, -50, 15)	BA 30, posterior cingulate	M	3.11	0.002
	min	(-20, 65, -10)	BA 11, superior frontal gyrus	L	3.30	0.001
			Other > EOB			
delta	max	(60, -55, 20)	BA 40, supramarginal gyrus	R	3.05	0.003
theta	min	(-15, -5, 50)	BA 24, anterior cingulate	L	2.59	0.011

(Table 10 continued)

alpha-1	max	(10, 10, 55)	BA 6, superior frontal gyrus	L	2.62	0.011
	min	(-5, -80, 50)	BA 7, precuneus	L	2.07	0.042
alpha-2	max	(15, 50, 45)	BA 8, superior frontal gyrus	R	2.59	0.011
	min	(-55, -25, 30)	BA 40, inferior parietal lobule	L	2.10	0.039
beta	min	(35, -65, 25)	BA 39, middle temporal gyrus	R	3.15	0.002
			Hammer > EOB			
alpha-1	max	(5, 45, 45)	BA 8, medial frontal gyrus	R	2.65	0.01
	min	(65, -10, -25)	BA 20, inferior temporal gyrus	R	2.23	0.029
alpha-2	min	(-25, 45, -15)	BA 11, superior frontal gyrus	L	2.95	0.004
beta	min	(-25, 45, -15)	BA11, superior frontal gyrus	L	2.95	0.004
			Self > Other			
delta	max	(-20, 65, -10)	BA 11, superior frontal gyrus	L	1.97	0.053
	min	(-15, -20, 45)	BA 24, anterior cingulate	L	3.53	0.0007
theta	min	(-20, 55, 25)	BA 10, medial frontal gyrus	L	2.32	0.023
alpha-1	min	(10, -5, 70)	BA 6, superior frontal gyrus	R	2.68	0.009
alpha-2	min	(25, 0, -45)	BA 20, uncus	R	2.05	0.044
beta	max	(20, -75, 55)	BA 7, superior parietal lobule	R	3.94	0.0002
	min	(-10, -100, 20)	BA 19, cuneus	L	2.22	0.03
			Self > Hammer			
delta	max	(-30, 60, 0)	BA 10, superior frontal gyrus	L	3.23	0.0019
	min	(50, -5, -40)	BA 20, inferior temporal gyrus	R	3.06	0.003
theta	max	(-30, 25, -20)	BA 47, inferior frontal gyrus	L	2.33	0.023
	min	(0, -65, 15)	BA 23, cingulate gyrus	M	2.61	0.011
alpha-1	min	(-10, -100, -5)	BA 17, cuneus	L	2.52	0.014
alpha-2	min	(-60, -55, 0)	BA 21, middle temporal gyrus	L	2.14	0.036
beta	max	(-15, -20, 70)	BA 6, precentral gyrus	L	2.64	0.01
			Other > Hammer			
delta	max	(20, -100, 5)	BA 18, middle occipital gyrus	R	2.42	0.018
theta	min	(-30, -20, 45)	BA 4, precentral gyrus	L	3.06	0.003
alpha-1	max	(50, 5, 35)	BA 9, inferior frontal gyrus	R	2.08	0.041
	min	(-20, -100, -10)	BA 18, lingual gyrus	L	2.09	0.041
alpha-2	max	(25, -25, -25)	BA 35, parahippocampal gyrus	R	3.17	0.002
beta	max	(-25, -75, 50)	BA 7, precuneus	L	2.18	0.033
	min	(45, -55, -30)	BA 37, fusiform gyrus	R	2.25	0.028
			SPESA > BSI			
delta	min	(5, 25, -20)	BA 25, medial frontal gyrus	R	3.45	0.001
theta	max	(-5, -35, 60)	BA 6, paracentral lobule	L	2.27	0.026
	min	(-40, 15, 0)	BA 13, insular cortex	L	2.34	0.022
alpha-1	max	(55, -65, 30)	BA 39, supramarginal gyrus	R	3.03	0.003
	min	(5, -10, 70)	BA 6, superior frontal gyrus	R	2.07	0.042
alpha-2	max	(10, 30, -25)	BA 11, rectal gyrus	R	2.74	0.008
beta	max	(-5, -95, 5)	BA 18, cuneus	L	1.97	0.053
	min	(-45, 35, 20)	BA 46, middle frontal gyrus	L	2.75	0.007
			SPESA > TSCS			
delta	max	(-5, -15, 55)	BA 6, medial frontal gyrus	L	2.93	0.004
	min	(50, 45, -10)	BA 47, inferior frontal gyrus	R	2.99	0.004
theta	max	(15, -100, 10)	BA 18, middle occipital gyrus	R	2.86	0.005
	min	(-40, 15, 0)	BA 13, insular cortex	L	2.52	0.014
alpha-1	max	(-5, 35, -15)	BA 11, medial frontal gyrus	L	3.22	0.002
	min	(5, -10, 65)	BA 6, medial frontal gyrus	R	2.77	0.007
alpha-2	max	(45, 50, -10)	BA 11, middle frontal gyrus	R	2.42	0.018
beta	max	(5, -90, 25)	BA 19, cuneus	R	2.30	0.024
	min	(-30, -15, -35)	BA 20, uncus	L	3.51	0.000
			BSI > TSCS			
delta	max	(-40, 0, -40)	BA 21, middle temporal gyrus	L	3.06	0.003
	min	(45, -40, 45)	BA 40, inferior parietal lobule	R	2.17	0.033
theta	max	(15, -100, 10)	BA 18, middle occipital gyrus	R	2.71	0.008
beta	max	(-45, 0, -40)	BA 20, inferior temporal gyrus	L	2.28	0.026

Table 11: Neural correlates for the difference (significant decrease) between pre and post cortisol levels. From left to right and top to bottom are the results for cortisol difference regressed on each task condition MNI maps after paired comparisons between the task and baseline. In the graphs within each section the ordinate shows the rho and cortical regions are on the abscissa. Frequency specific correlations are plotted in the graph.

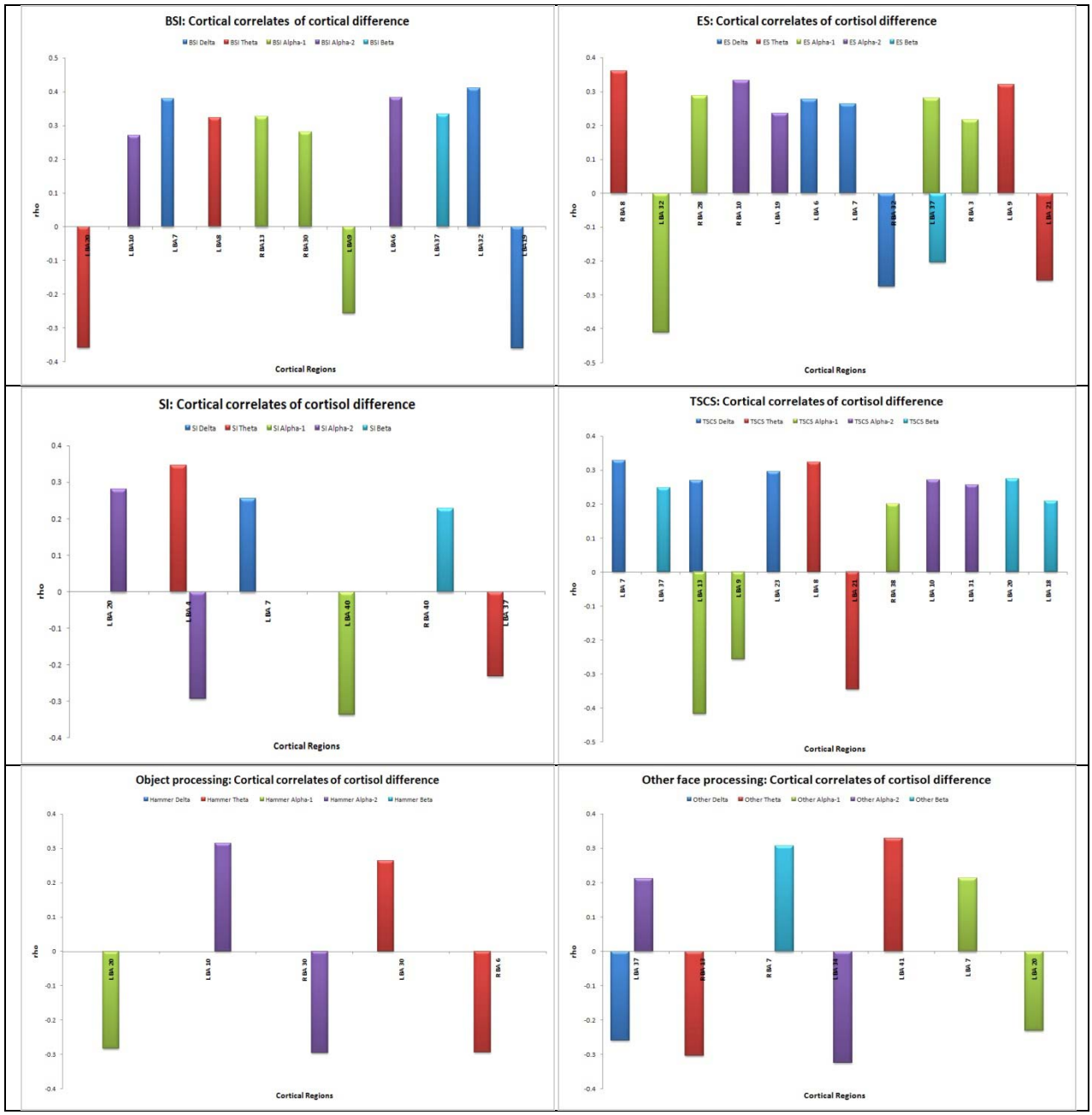


Table 12: Gender differences (female > male) for each task condition.

Frequency	*sLOR*	*Brodmann Area/Cortical region*	*x*	*y*	*z*	*hemi*	*t*	*p*
		Brief Symptom Inventory (BSI)						
Delta	Max	BA 11 Middle frontal gyrus	35	40	-20	R	2.76	0.007
	Min	BA 22 Superior temporal gyrus	-65	-25	0	L	-2.58	0.006
Theta	Min	BA 27 Parahippocampal gyrus	-20	-30	-5	L	-2.19	0.032
Alpha-1	Max	BA 9 Middle frontal gyrus	30	30	40	R	3.28	0.000
	Min	BA 4 Precentral gyrus	-50	-15	40	L	-3.26	0.001
Alpha-2	Max	BA 7 Superior parietal lobule	30	80	45	R	2.99	0.003
	Min	BA 19 Parahippocampal gyrus	-30	-50	-5	L	-3.39	0.001
Beta	Max	BA 22 Superior temporal gyrus	-65	-50	15	L	3.70	0.004
	Min	BA 7 Postcentral gyrus	10	-55	65	R	3.03	0.003
		Self Image (SI)						
Delta	Max	BA 18 Middle Occipital gyrus	15	-100	10	R	3.20	0.001
	Min	BA 40 Inferior parietal lobule	65	-40	35	R	-2.27	0.026
Theta	Min	BA 19 Cuneus	5	-95	25	R	2.11	0.038
Alpha-1	Max	BA 9 Precentral gyrus	-40	15	40	L	2.50	0.015
	Min	BA 37 Middle Occipital gyrus	-55	-75	0	L	-3.15	0.002
Alpha-2	Max	BA 20 Fusiform gyrus	55	-20	-30	R	2.05	0.044
	Min	BA 9 Middle frontal gyrus	0	35	55	M	-2.92	0.004
Beta	Max	BA 9 Middle frontal gyrus	50	25	40	R	2.39	0.019
	Min	BA 20 Fusiform gyrus	-60	-10	-30	L	-2.23	0.029
		Self Perception and Experiential Schemata (SPESA)						
Delta	Max	BA 31 Paracentral lobule	-10	-15	50	L	3.39	0.001
	Min	BA 18 Middle Occipital gyrus	-25	-95	10	L	-2.63	0.010
Theta	Max	BA19 Cuneus	25	-95	25	R	2.59	0.011
	Min	BA 6 Superior frontal gyrus	20	5	70	R	-2.59	0.011
Alpha-1	Max	BA 8 Superior frontal gyrus	10	45	50	R	3.22	0.002
	Min	BA 39 Supramarginal gyrus	-55	-65	30	L	-2.74	0.008
Alpha-2	Min	BA 21 Middle temporal gyrus	65	-50	-5	R	-2.14	0.036
Beta	Max	BA 20 Fusiform gyrus	-45	-35	-20	L	3.68	0.004
	Min	BA 11 Middle frontal gyrus	25	45	-5	R	-3.34	0.001
		Tennessee Self Concept Scale (TSCS)						
Delta	Max	BA 11 Orbital gyrus	-15	40	-25	L	2.51	0.014
	Min	BA 19 Fusiform gyrus	-45	-75	-20	L	-2.31	0.024
Theta	Min	BA 34 Parahippocampal gyrus	-15	-10	-20	L	-2.91	0.005
Alpha-1	Max	BA 11 Superior frontal gyrus	-15	65	-15	L	3.24	0.001
	Min	BA 40 Inferior parietal lobule	50	-55	45	R	-2.60	0.011
Alpha-2	Min	BA 9 Middle frontal gyrus	-30	25	40	L	-2.73	0.008
Beta	Max	BA 20 sub gyral	-45	-10	-25	L	2.92	0.004
	Min	BA 6 Middle frontal gyrus	25	20	60	R	-2.77	0.007
		Other						
Delta	Max	BA 2 postcentral gyrus	65	-25	40	R	3.86	0.000
	Min	BA 31 precuneus	-15	-60	25	L	-2.16	0.034
Theta	Max	BA 9 superior frontal gyrus	5	55	35	R	2.68	0.009
Alpha-1	Max	BA 6 medial frontal gyrus	-5	30	40	L	2.48	0.015
	Min	BA 10 superior frontal gyrus	-25	55	0	L	-1.98	0.052
Alpha-2	Min	BA 13 inferior frontal gyrus	40	25	10	R	-2.40	0.019
Beta	Max	BA 23 cingulate gyrus	-5	-20	30	L	3.59	0.006
		Hammer						
Delta	Max	BA 23 Cingulate Gyrus	-5	-25	30	L	3.62	0.006
	Min	BA 10 medial frontal gyrus	10	45	15	R	-2.69	0.009
Theta	Max	BA 19 cuneus	-5	-90	25	L	2.82	0.003
	Min	BA 24 anterior cingulate	-10	-5	45	L	-2.04	0.022
Alpha-1	Max	BA 39 middle temporal gyrus	60	-60	10	R	2.08	0.041
Beta	Min	BA 11 Superior frontal gyrus	-25	45	-15	L	-2.66	0.004

Table 13: Results for gender differences for all study behavioral measures. * = significant < .05. From left to right are the measure, gender 0=female, 1 = male, sample size, mean for the measure, standard deviation and standard error for the mean.

	sex	N	Mean	Std. Deviation	Std. Error Mean
SPESA childhood	.00	34	20.6471	11.86511	2.03485
	1.00	29	21.4138	7.68355	1.42680
SPESA adolescence	.00	34	19.0294	5.65945	.97059
	1.00	29	16.9310	5.99959	1.11410
SPESA adulthood*	.00	34	22.6471	5.52066	.94679
	1.00	29	18.8966	8.92566	1.65745
SPESA total	.00	34	62.3235	19.18288	3.28984
	1.00	29	57.2414	19.18641	3.56283
BSI somatization	.00	34	1.7059	2.06749	.35457
	1.00	29	1.6207	2.04265	.37931
BSI depression	.00	34	3.2647	3.25957	.55901
	1.00	29	3.9655	3.78420	.70271
BSI anxiety	.00	34	2.5294	2.35147	.40327
	1.00	29	3.3103	2.89215	.53706
BSI Global Severity Index	.00	34	7.5000	5.94036	1.01876
	1.00	29	8.8966	7.68740	1.42751
TSCS physical	.00	34	12.1471	2.28476	.39183
	1.00	29	12.0690	2.32887	.43246
TSCS disgust*	.00	34	7.7941	2.85805	.49015
	1.00	29	9.5517	3.56156	.66137
TSCS introspection	.00	34	8.5294	1.72741	.29625
	1.00	29	8.3793	2.02509	.37605
TSCS self regard	.00	34	28.4706	5.48958	.94145
	1.00	29	30.0000	5.66316	1.05162
cortisol difference	.00	34	.0453	.05785	.00992
	1.00	29	.0403	.10076	.01871
cortisol pre	.00	34	.1756	.08425	.01445
	1.00	29	.1924	.13796	.02562
cortisol post	.00	34	.1303	.05781	.00991
	1.00	29	.1521	.09507	.01765

APPENDIX III: FORM B

FORM B
APPLICATION

FORM B

IRB # 6291-B

Date received in ORC _____

THE UNIVERSITY OF TENNESSEE, KNOXVILLE

Application for Review of Research Involving Human Subjects

I: Identification of Project: **02/05/2008**

1: Project Directors:

Principal Investigator	Rex Cannon, BA Department of Psychology University of Tennessee, Knoxville 37996 Brain Research and Neuropsychology lab 865-300-4983 rcannon2@utk.edu
Faculty Advisors:	Debora Baldwin, PhD Department of Psychology University of Tennessee, Knoxville 37996 Brain Research and Neuropsychology lab 865-974-3222 jlubar@utk.edu dbaldwin@utk.edu

Department	Psychology Brain Research and Neuropsychology Laboratory
Starting Date	**01/20/09**
Completion Date	**12/01/09**
External Funding	N/A
Grant Submission Deadline	N/A

Title of Project: **Self Perception and Experiential Schemata: Neuromodulation of EEG as an intervention for addictive disorders**

II. Objective of Project and Brief Literature Review

In recent years neuroimaging techniques in addiction research have provided a large body of research into the mechanisms of reward and decision making processes and the associated neural activity. There have also been advances in animal models of craving and withdrawal features of addiction. Likewise, there has been extreme diligence in uncovering genetic and cognitive components and specific neural effects of specific substances. However, research into the cognitive, affective and perceptual elements of self in addicted populations has remained relatively unexplored, especially in persons recovering from substance use disorders. It may be that a common neurophysiological pattern exists in this population that may provide important information regarding possible antecedents to substance use disorders and knowledge about specific neural substrates for intervention strategies. **The primary aim of stage 1 of this study is to investigate neurophysiological activity in the default network of the brain using a 3-D source localization technique (sLORETA). The differences in source localization of the electroencephalogram (EEG) of this phase I normative data will be contrasted with data of recovering substance abusers in later studies. The primary aims of stage 2 of this study is to employ low-resolution electromagnetic tomographic neurofeedback (LORETA Neurofeedback) in the right anterior cingulate gyrus and right occipital lobe to reduce hyperactivity in limbic and orbitofrontal regions shown to be involved in addictive disorders and validation by functional magnetic resonance imaging (fMRI).**

This research study proposes to investigate neural mechanisms involved in perception of self and self-in-experience in recovering substance abusers and non-clinical controls. We propose that specific EEG frequencies in cortical and limbic regions play an intricate role in substance use disorders and recent developments in the EEG-biofeedback method offer the ability to train individuals to self-regulate specific EEG frequencies. This type of spatial-specific neuro-operant learning in limbic and cortical regions shown abnormal in substance abusing populations may prove important to the advancement of functional knowledge of addiction and the development of more efficacious, evidence based treatment models for these disorders (R. Cannon, et al., 2008; Sokhadze, Cannon, & Trudeau, 2008). We have found functional abnormalities in eyes-opened and eyes-closed resting baseline EEG involving prefrontal, occipital and limbic regions in recovering substance abusers compared to controls. Additionally, during the evaluation of self and self-in-experience (evaluating self in relation to family, peers and self in childhood, adolescence and adulthood) recovering substance abusers (abstinent > 6 months) showed significant increases in regions also activated during drug related cues; namely, orbitofrontal and insular cortices, and limbic regions in the right hemisphere specifically in the

alpha frequency domain (8 – 12 Hz). This region specific activity may reflect a neural mechanism relative to negative self reference that is responsive to EEG changes induced by drugs of abuse. More significantly, this negative self reference loop may represent an antecedent state that increases the likelihood of developing substance use disorders, such that increased higher frequencies in limbic regions possibly reflects increased dopamine levels posited to be important to SUD. The proposed study will expand on neurophysiological differences between recovering substance abusers and non-clinical controls when evaluating self and self-in-experience and employ *a priori* regions of training (ROT) for spatial-specific neuro-operant learning with LORETA neurofeedback. Specifically, we will train individuals to increase 14 – 18 Hz activity in a seven voxel cluster of neurons in the right anterior cingulate gyrus and to increase 8 – 12 Hz activity in a three voxel cluster of neurons in the right occipital cortex. This research study is a final step in the development of the SPESA Model for treatment of addictive disorders. Our research developments in the EEG-biofeedback technique afford the opportunity to train individuals to increase or decrease specific EEG frequencies in specific regions of the brain. Low-resolution electromagnetic tomographic (LORETA) neurofeedback (LNFB) is demonstrated effective in training research participants to increase low-beta activity in the dorsal left anterior cingulate gyrus and bilateral prefrontal cortices. Moreover, our recent data demonstrates that it is possible to train recovering substance abusers to increase this same frequency in the right dorsal AC. **A Secondary aim of this study is to examine cortisol effects produced by specific cortical activation patterns initiated by the specific cognitive/affective/perceptual tasks in this study. We will examine overall differences in affective, perceptual, cognitive and personality mechanisms between RSA and controls for all obtained measures and finally, examine the effects of LNFB training on these stress hormones over time.** No study to date has evaluated personality or concept of self measures utilizing neuroimaging techniques in recovering substance abusers; moreover, research on cortisol levels and concordant brain activation during these tasks is scant. Of particular interest to addiction research is the lack of published articles in using the search terms “effective treatment for substance use disorders”, or “effective treatment for addictive disorders.” It is of interest to this study to examine possible reasons for the high relapse rate in substance abusing populations and the neural components of interpersonal and decision making processes that continue to be problematic after substantial periods of continued abstinence from all mood altering chemicals. This study offers the potential for recovering substance abusers to regulate brain areas involved in both addiction and decision making processes, but more significantly the processing of self. Moreover, the information in the region of interest analysis may provide important information about how regions of the brain interact in both normal and clinical populations during each stage of this study. This research will enhance the implementation of a treatment model that covers the neural, social, cognitive/affective/perceptual and self components of addictive disorders.

To date, studies that identify schematic source generators and their relationship with alcoholism using quantitative Electroencephalography (qEEG) and low-resolution electromagnetic tomography (LORETA) are scant. We have however, conducted studies using LORETA in numerous contexts, detection of limbic activation (Cannon, et al, 2004), neurofeedback in sub-cortical regions (Cannon et al, 2006), topographical analysis of neurofeedback training (Cannon, et al 2006) and differentiation of function between the anterior cingulate gyrus and dorsolateral prefrontal cortex (Cannon, et al 2006). This study is designed to

assess the schemata relating to self in the alcoholic and identify the relative generators in the cortex. This study proposes that there is a dysfunctional connectivity between neuronal populations in the cognitive and affective regions in the dorsolateral prefrontal cortex and the anterior cingulate gyrus. Furthermore, this dysconnectivity hinders the integration of affect and intellect and adversely influences self concept and the development of positive schemata, social interactions and personality characteristics.

III: Description of Subjects and Informed Consent:

Participants will be recruited from the University of Tennessee, psychology human participation in research site. The university students will receive extra course credit for their participation. The clinical sample will be recruited from the local community of Alcoholics Anonymous. The participants will be recruited by advertisement sheets posted in local meeting facilities providing contact information for interview with the primary investigator. This will be a voluntary participation and no money will be paid. Approximately twenty-five adult participants will be recruited, between the ages of 18 and 50. The participants will be selected according to length of abstinence, e.g., 30 days, 90 days of continuous abstinence from drug or alcohol use. There will be an equal number of males and females. The criteria for exclusion will include serious head trauma, history of epilepsy or neurological and psychotic disorders. Those subjects that agree to participate will be presented with an informed consent form, which must be read and signed before their participation begins. See the attached Informed Consent Form.

IV: Methods and Procedures:

This research study will be conducted using both the within and between subjects experimental designs. We will use random assignment to the treatment condition and maintain a wait-list control group for comparison. This is the most ethically sound method for this type of research for two primary reasons. First, it is extremely difficult to conduct a sham (or placebo) neurofeedback protocol due to the nature of the operant training and subjects often becomes aware that they are earning points for doing nothing. Colleagues have suggested using an alternative region of training as a control (e.g. telling the subjects they are learning in one location while directing the training to an alternative location). This is a feasible control; however, given the limited knowledge we have about the specific functions of brain regions and frequency specific function, this would be better suited in a facility that provided constant supervision. In simplest terms we have insufficient knowledge about frequency specific function in specific neuronal populations and the behavioral effects of increasing or decreasing activity in any region of the cortex other than those previously employed by our lab and others. Thus, given this lack of knowledge it is both ethically and morally responsible to utilize baseline – neurofeedback – baseline for this methodology.

D:1 Participants

Participants will be recruited from local 12 Step programs with verifiable periods of continued abstinence > 6 months from all mood altering chemicals. We will seek a total of 100 participants

for the RSA group, 50 male and 50 female and 100 control participants from populations of both traditional and non-traditional college students, 50 male and 50 female. We will attempt to maintain an age-similar grouping. Exclusionary criteria for participation will include previous head trauma, history of seizures, recent drug or alcohol use, and *previous psychiatric diagnosis will be set for the control group; however, due to the high comorbidity rate amongst substance abusers, depression will not be considered for exclusion for the RSA group. It will be coded and entered into the analysis. The RSA group will have received a prior AXIS I diagnosis of substance use disorder as defined by the Diagnostic and Statistical Manual of Mental Disorders, Fourth Ed (DSM-IV - APA, 2000).

D:2 Psychometric and Personality Measures

We will administer three measures of self perception, self concept and recent symptomology while EEG is continuously recorded in order to evaluate source localization associated with each of the constructs proposed to be measured by these instruments. Similar to previous studies of neurofeedback for addictive disorders we will include measures of personality, optimism and self concept: (1) The Self-Perception and Experiential Schemata Assessment (SPESA) (Neuropsychservices, Inc); (2) The Brief Symptom Inventory (BSI 18); and (3) 20 items from the Tennessee Self Concept Scale (Fitts).

D:3 Apparatus and EEG collection

The participants will be prepared for EEG recording using a measure of the head circumference and the distance between the nasion and inion to determine the appropriate cap size for recording (Blom & Anneveldt, 1982) (Electrocap, Inc). The head will be measured and marked prior to each session to maintain consistency. The ears and forehead will be cleaned for recording with a mild abrasive (NuPrep) gel to remove any oil and dirt from the skin. After fitting the caps, each electrode site will be injected with electrogel and prepared so that impedances between individual electrodes and each ear are < 6 KΩ and less than 1 KΩ difference between electrodes. Impedances are monitored in real time during the recording procedures. The LNFB training will be conducted using the 19-leads of the standard international 10/20 system (Jasper, 1958) with linked ears and ground reference. The cap will be referenced at FPz. The data will be collected and stored utilizing the Deymed Truscan Acquisition system with a band-pass set at 0.5–64.0 Hz at a rate of 256 samples per second. We will utilize standard 9mm tin cup ear electrodes. Each session will require approximately sixty minutes for completion. The EEG frequencies to be analyzed are delta (0.5 – 3.5 Hz), theta (3.5 – 7.5 Hz), alpha *1 (7.5 – 10.0 Hz), alpha 2 (10.0 – 12.0 Hz), beta (12 – 32 Hz).*

D:4 EEG Assessment Recordings

Upon arrival to the laboratory the participants will complete all informed consent and inclusion criteria procedures; including self-report, substance abuse, medical and demographic questionnaire. A 640x480 photograph of the participant will be taken prior to EEG capping. The subjects will then provide a saliva sample for a pre session measure. After capping the participants will be seated in front (~55 cm) of a 20’ computer monitor. We will obtain four-minute eyes-closed and eyes-opened baseline recordings for comparison. We will also collect subjective reports from the participants for every EEG condition in this experiment including baselines. The subject will then complete four assessment instruments presented in Microsoft PowerPoint (8 seconds per item) while the EEG is continuously recorded and responses will be recorded in the EEG record: (1) The Self-Perception and Experiential Schemata Assessment

(SPESA) (Neuropsychservices, Inc); (2) The Brief Symptom Inventory (BSI 18) and (3) 20 items from the Tennessee Self Concept Scale (Fitts). We will allow for a two-minute resting period and then collect the photograph viewing conditions. The participants EEG will be recorded while viewing an image of a hammer; an image of a female face (other) in a neutral expression and the image of self taken prior to capping. The subjects will view each photograph for four minutes. The total procedure will take approximately 60 minutes. One saliva sample will be taken upon arrival to the laboratory and a post salivary cortisol sample will be collected at the end of all EEG recordings for comparison and correlation analysis. The participants will then complete all assessment instruments in written form. Table 1 contains total time for each condition.

Procedure	Length
SPESA	6 min
BSIQ	4 min
LOT	4 min
TSC	4 min
Photograph of hammer	4 min
Photograph of other	4 min
Photograph of self	4 min
Total time with rest	**42 min**

Table 4: Procedures and total time

D:5 Cortisol Measures

Subjects will be asked to rinse mouth and after 3 minutes, expectorate into a sanitized 50mL collection tube pre assessment and post assessment. Once collected the saliva samples will be centrifuged for ten-minutes and then alloquated into microtubes and stored at 20 degrees Celsius for subsequent analysis. Supernatants will be analyzed for total cortisol concentration using the High Sensitivity Salivary Cortisol Immunoassay Kit (Salimetrics, Inc). This assay can reliably detect cortisol levels from 0.003 to 3.0 mg/dL.

The samples will be run in duplicate then compared for significance and used in correlation analysis with the obtained assessment scores and LORETA source localization maps.

V: Specific Risk and Protection Measures:

EEG data acquisition will be performed in the biological psychology/neuroscience laboratory under the supervision of Rex Cannon, MA. Lab assistants will be utilized and will work under the supervision of the principal investigator. Scalp EEG presents minimal risk to human subjects. It has been used in this laboratory for over twenty-years without incident.

Subjects will be recruited via flyers advertising for volunteers in local AA meetings or by personal interview by the primary investigator.

Confidentiality will be of utmost importance. The names, personal information, and scores regarding participants will be kept in a locked file cabinet in room 308 of Walter's Life Science Building. Access will be restricted to the Principal investigator and named faculty

advisors. Data entry in the computer will not include names or other identifying information. After the data collection process, all lists of subject names will be destroyed. After each participant completes the experiment, their photo will be deleted and all traces thereof removed. The EEG data will be stored in the computer and database, as it will only involve subject numbers. All data will be available to only the principal investigator and will remain password protected throughout its use. The data will be maintained in a secure section of the lab and will be archived for future use by the principal investigator. Participants will be scheduled at intervals preventing interaction to maintain confidentiality. A 15 minute debriefing period will be offered to participants to discuss and process any negative emotional effects from this assessment procedure.

VI: Benefits vs. Risks:

The benefit for the participants in this study is an awareness and understanding of the influence of perception and negative thought patterns. The benefits to science are numerous, including a possible understanding of the neural activation relating to self-awareness, self-image, self-perception and specific cortical and schematic patterns involved in alcoholism. The risk to the physical or psychological well being of any participant in this experiment is minimal. Experiments with EEG have been conducted in this laboratory for over twenty years without incident.

The principal investigator will inquire as to the psychological state of each individual upon completing this procedure.

VII: Qualifications of the Investigators:

Rex Cannon is a graduate student in the Experimental Psychology program at the University of Tennessee. He received his Masters degree from UTK in 2007. He has worked in the Brain Research and Neuroscience laboratory for four years of experience administering qEEG. He is experienced in LORETA imaging, LORETA Neurofeedback, designing experiments, analyzing data and statistical modeling. He has over seven years working with both addictive and mental disorders.

Dr. Debora Baldwin is an Associate Professor of Psychology with considerable research experience in the area of biological psychology. She has published several studies and supplemental textbooks within this field.

VIII: Adequacy of Facilities to Support Research:

The physical requirements for carrying out this experiment are completely adequate. The Psychology Department at the University of Tennessee has the requisite space and computer equipment necessary for the implementation of this research.

Data collection will be conducted in the Brain Research and Neuropsychology Laboratory in Walter's Life Science 305-A. Dr Lubar or the University of Tennessee owns all equipment to be

used. All instrumentation and testing materials used in this study are comparable to those used in hospital and clinical settings.

IX: Responsibility of Project Director:

Compliance will be maintained according to the policies established by the University of Tennessee, Committee on Research Participation. The project director subscribes to the principles stated in "The Belmont Report" and standards of professional ethics in all research, development and related activities involving human subjects under the auspices of The University of Tennessee, Knoxville.

A: Approval will be obtained from the university committee prior to instituting any change in the research project.
B: Development of any unexpected risks will be reported to the University Committee.
C: A status report (Form D) will be submitted at 12-month intervals or as requested by the committee attesting to the current status of the project.
D: Signed consent statements will be kept for the duration of the project and for a minimum of three years thereafter.
E: The principle directors will train and supervise undergraduate students in the data collection process. Students working in the lab receive letter grades for their work (Psy 489).

Project Directors: _____
Rex Cannon
_____
Date

Faculty Advisors: _____
Debora Baldwin
_____
Date

APPENDIX IV: INFORMED CONSENT

Informed Consent Form

Title of Project: *Addiction: Self Perception and Experiential Schemata*

Principal Investigators: Rex Cannon, MA
Debora Baldwin, PhD

Objective of Project: You will participate in the evaluation of the EEG (electroencephalography or electrical activity) of your brain in three assessment conditions; first, while completing the Self Perception and Experiential Schemata Assessment, then The Brief Symptom Inventory and finally, select items from the Tennessee Self Concept Scale. Prior to beginning this procedure you will provide a saliva sample before and after the assessment procedures. We utilize saliva to measure cortisol levels (a stress hormone) as influenced by this assessment procedure. We will then record your EEG while looking at and evaluating a picture of your face, another person's face and at an object. We will take a digital photo of you prior to the recording procedure which will be destroyed at the end of your session. We will record four-minute eyes-closed and eyes-opened baselines (resting, relaxed condition EEG) prior to the experimental conditions for comparison.

In order to record the electrical activity (EEG) of your brain an electrocap with 19 sensors will be placed on your head. Electrogel will be applied to each site using a plastic syringe. This gel forms a conductive pathway between the sensor and the scalp. There is no significant discomfort with this procedure either in the preparation or the wearing of the cap during testing. Two ear clips and one ground electrode will be utilized for referential purposes. This requires the cleaning of your ear lobes and forehead prior to capping. All creams and gels used in this process are hypoallergenic with no risk of irritation. These procedures have been utilized extensively worldwide without report of incident. You will be asked to regulate eye-movements, teeth clenching, tongue movements, etc, since these movements interfere with the recording procedure.

Amount of time required:
The total time to complete this experiment is approximately 1.5 hours or 90 minutes.

Confidentiality:
Only the principal investigators will have access to information regarding your person and performance. The data gathered in this study will be shared professionally in published works; however, no identifying information will be released to any one for any reason. All data will be stored in a locked room in the Biological Psychology/Neuroscience Research Laboratory for at least five years following completion and publication of this study. The pictures will be destroyed after the recordings are collected and all subsequent data will be archived. All data associated with your participation will be kept confidential and will not be released to any person for any reason.

Debriefing:
It is possible that this assessment will evoke negative emotions. You will be given a list of resources for processing of these emotions should they be a problem.

Permission:
I hereby grant Rex Cannon permission to archive and use the data obtained from my participation in this study as necessary. I understand that no personal information will be disclosed. My signature below grants this permission.

If you have any questions or require further future information, address correspondence to any of the principle investigator or faculty advisors:

Rex Cannon rcannon2@utk.edu
Debora Baldwin dbaldwin@utk.edu

Department of Psychology
University of Tennessee
Knoxville, TN 37996-0900
865-974-3222 or 865-974-3360

Compliances Section
Office of Research
1534 White Avenue
Knoxville, TN 37996-0145
865-974-3666

Statement of Consent: I certify that I have read and fully understand the procedures contained within this form and agree to participate in the research described therein. My participation is given voluntarily and without coercion or undue influence.

_____	_____	_____
Signature of Participant	Printed Name	Date

_____	_____	_____
Signature of Witness	Printed Name	Date

APPENDIX V: SUBJECT QUESTIONAIRRE

Subject Information

All information is confidential and will not be released to any person for any reason.
Please answer as honestly as possible.

Initials: _____ File Name:_____
Age: _____
DOB:

Sex: (circle one) Male Female

Handedness: (circle one) Right Left Ambidextrious

Date/Time_____

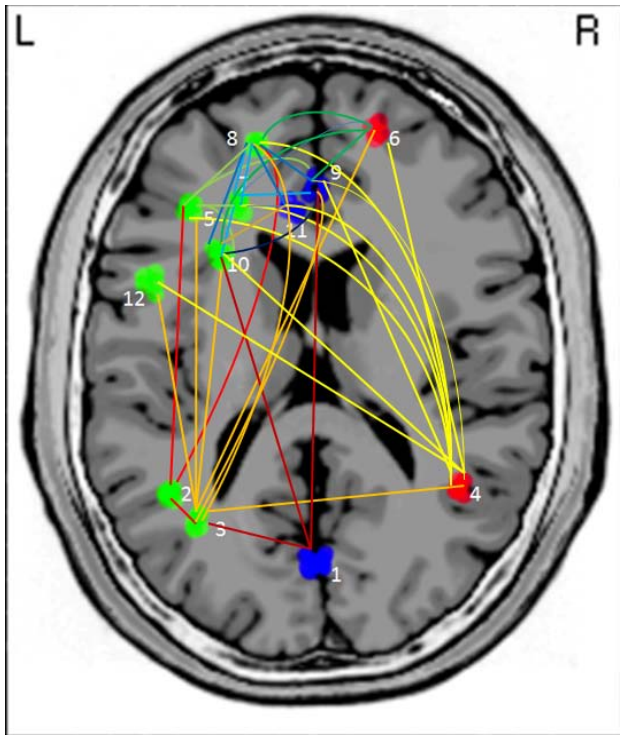
Questionnaire

1. Have you ever had an injury to your head? _____
2. Have you ever been unconscious?
3. Have you ever been diagnosed with any mental disorder (this includes Depression, Anxiety, Schizophrenic, etc.)? _____
4. Do you currently or have you ever taken any psychotropic drugs? _____
5. Do you currently take any medications? _____
6. If so what medication and for what?
7. Have you in the past two weeks used any non-prescription drugs (marijuana, etc.)?
8. Do you have a history of alcoholism?
9. Have you ever been diagnosed with cerebrovascular disease? _____
10. Do you have a history of Migraines? _____
11. Have you ever been diagnosed with epilepsy? _____
12. Have you ever been diagnosed with a learning disorder and/or ADD/ADHD?
13. Have you ever been diagnosed with any type of sleep disorder? _____

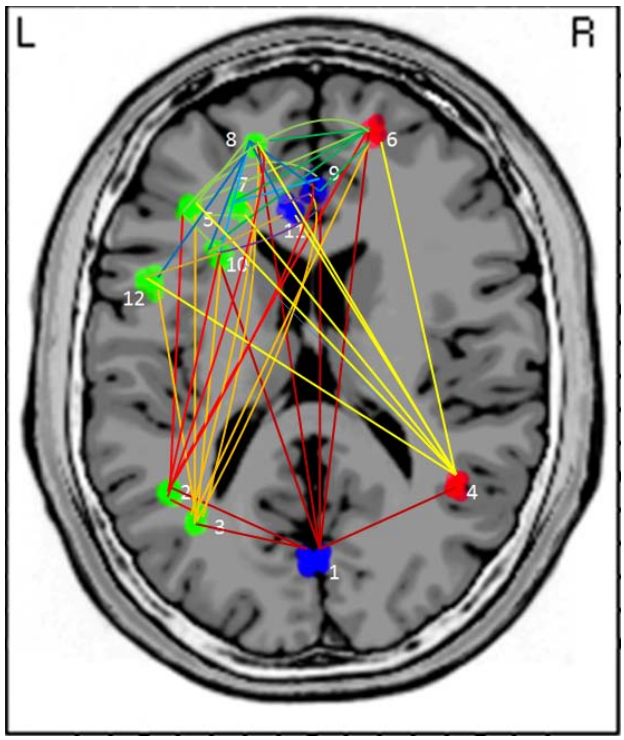
This study will investigate your ability to change your brain-wave patterns in desired directions with the aid of feedback provided by a computer. It is only you that can achieve changes. The computer will not interfere with your brain activity. Please use the space below to explain your motivation in participating to this study:

APPENDIX VI: SUPPLEMENTAL MATERIAL

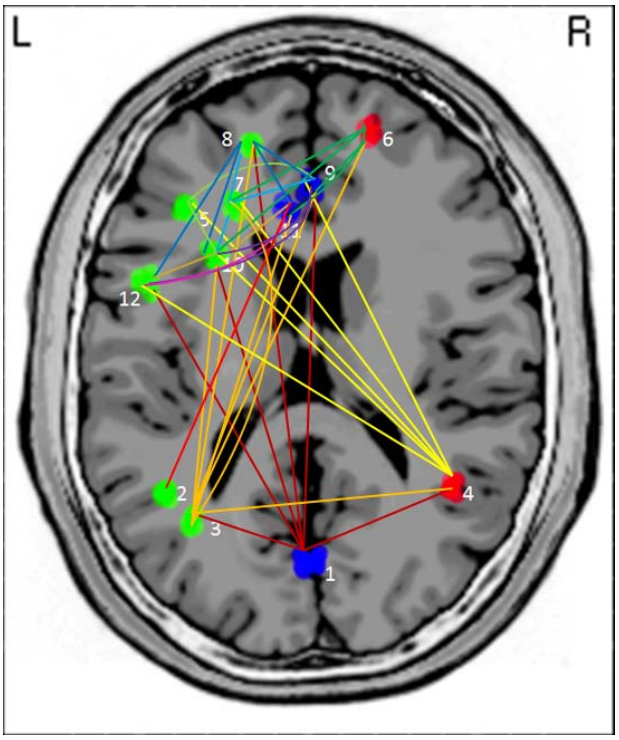
FUNCTIONAL CONNECTIVITY IMAGES



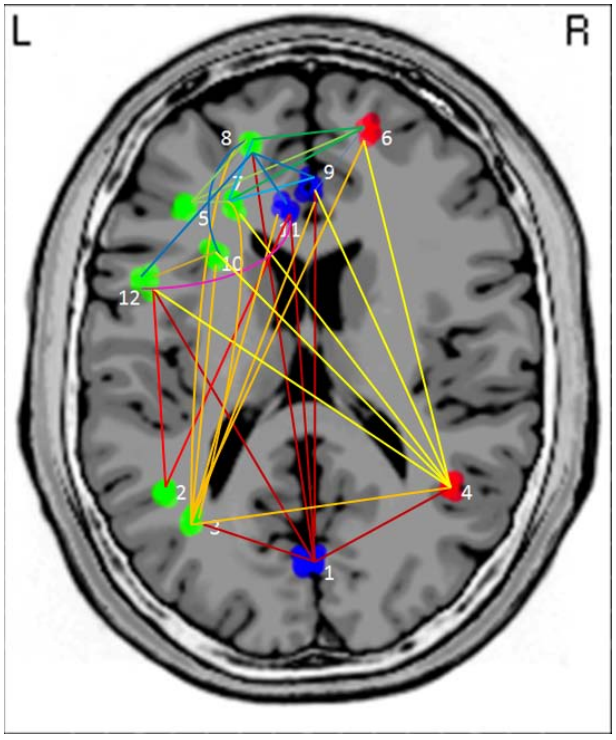
S1 1: ECB Delta



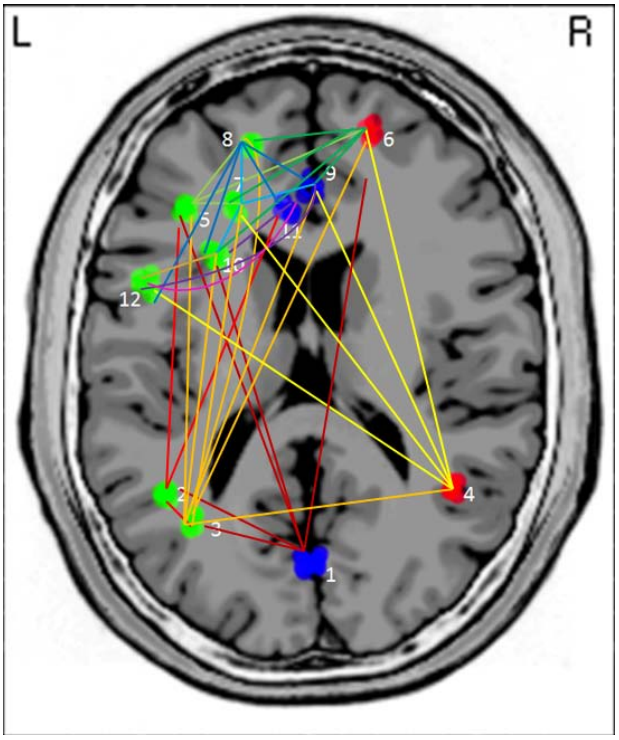
S1 2: ECB Theta



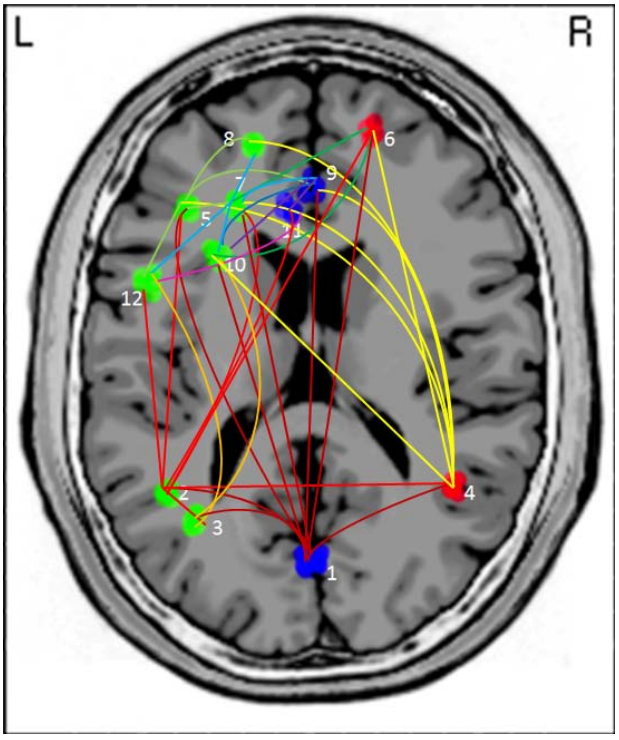
S1 3: ECB Alpha-1



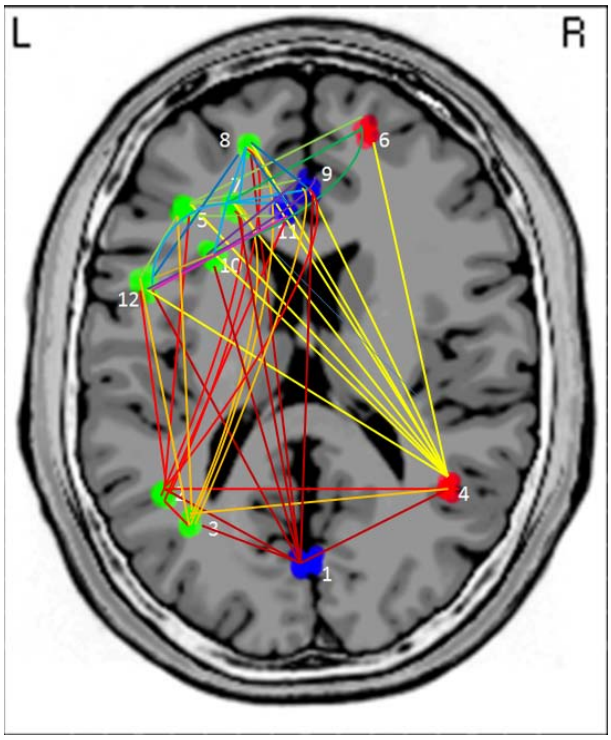
S1 4: ECB Alpha-2



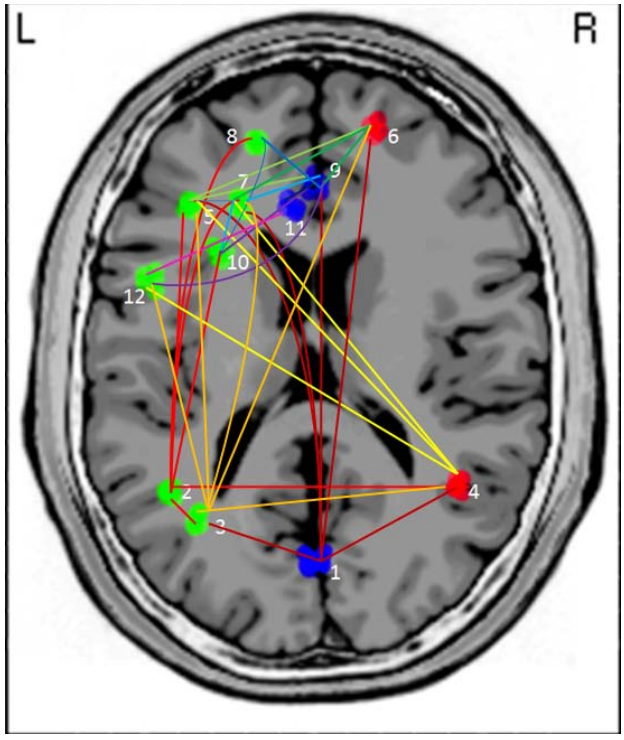
S1 5: ECB Beta



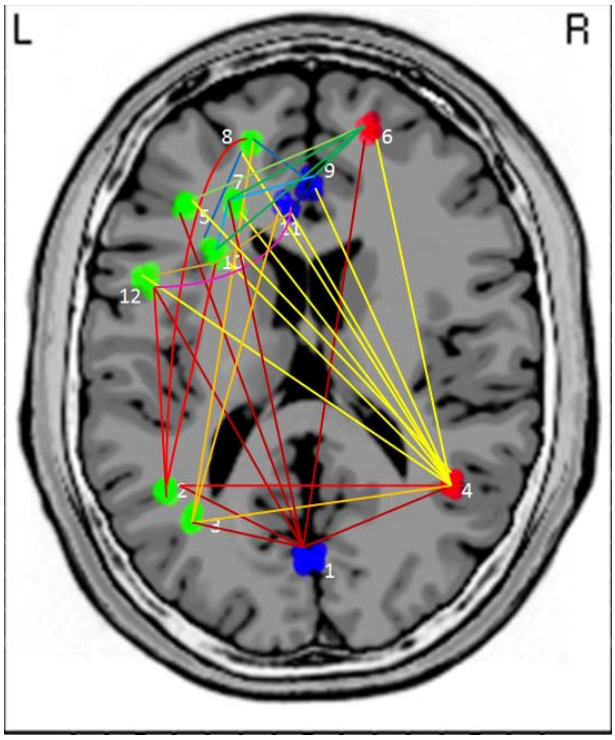
S1 6: EOB Delta



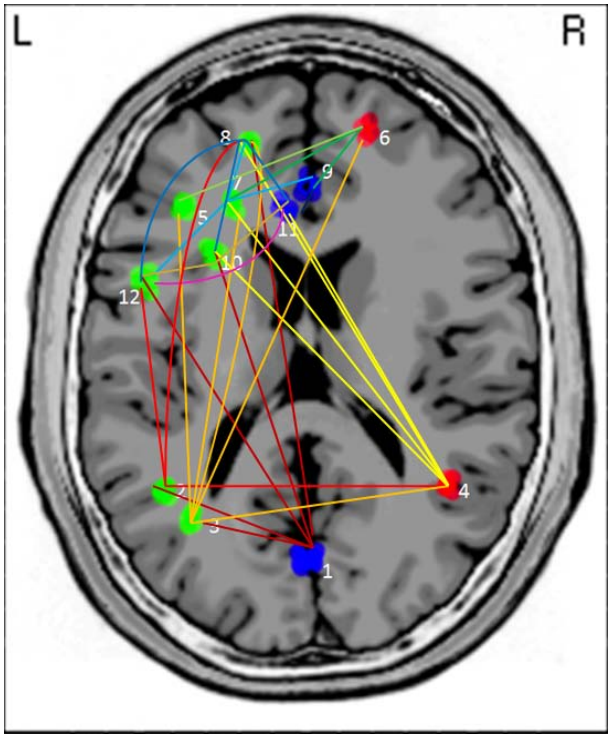
S1 7: EOB Theta



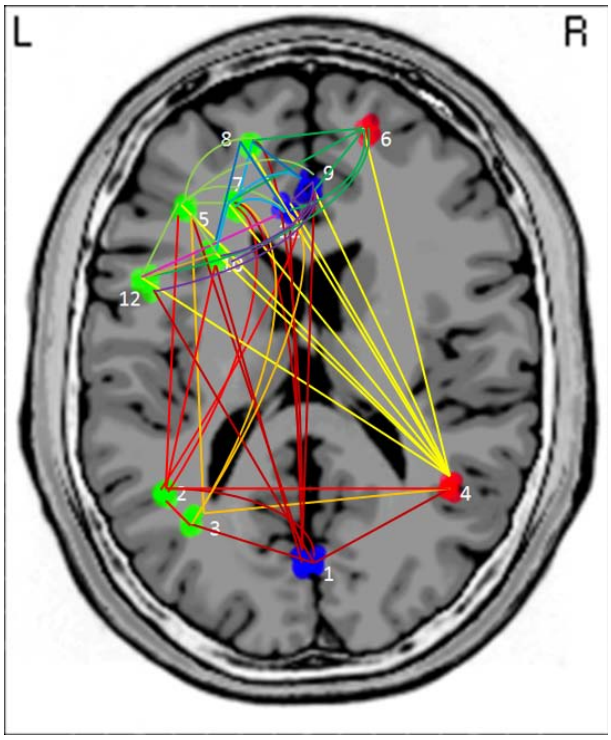
S1 8: EOB Alpha-1



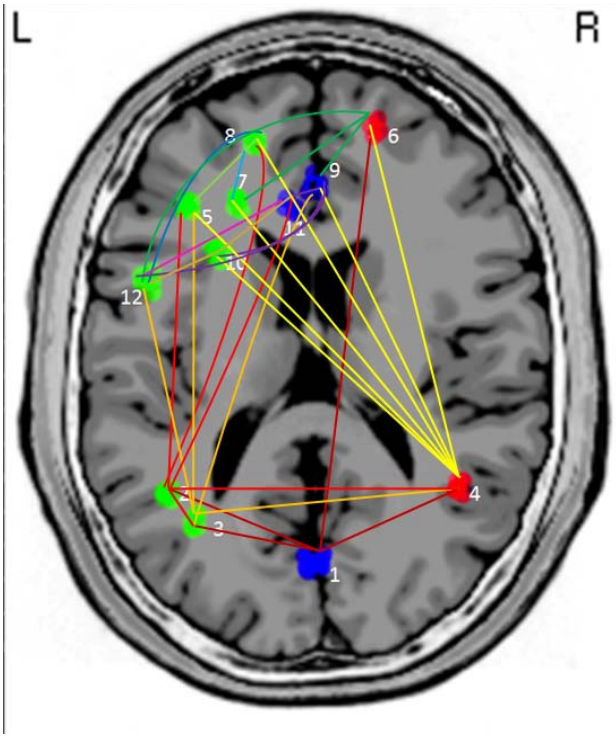
S1 9: EOB Alpha-2



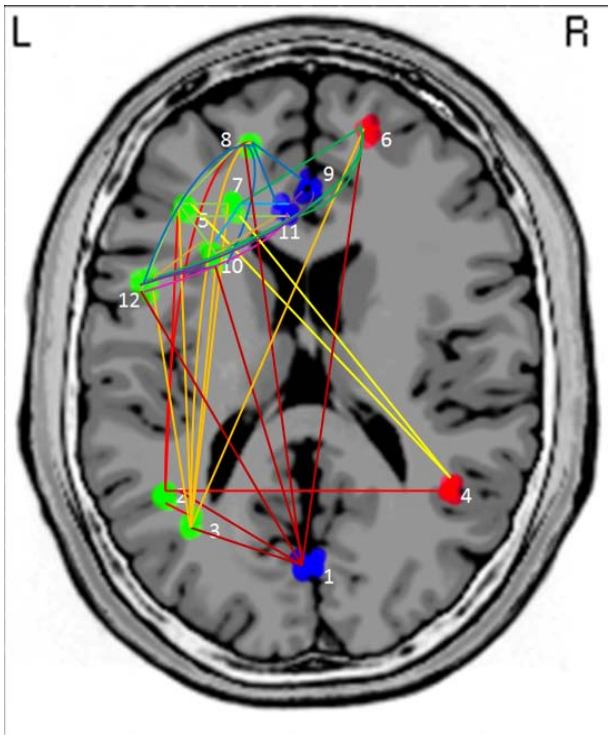
S1 10: EOB Beta



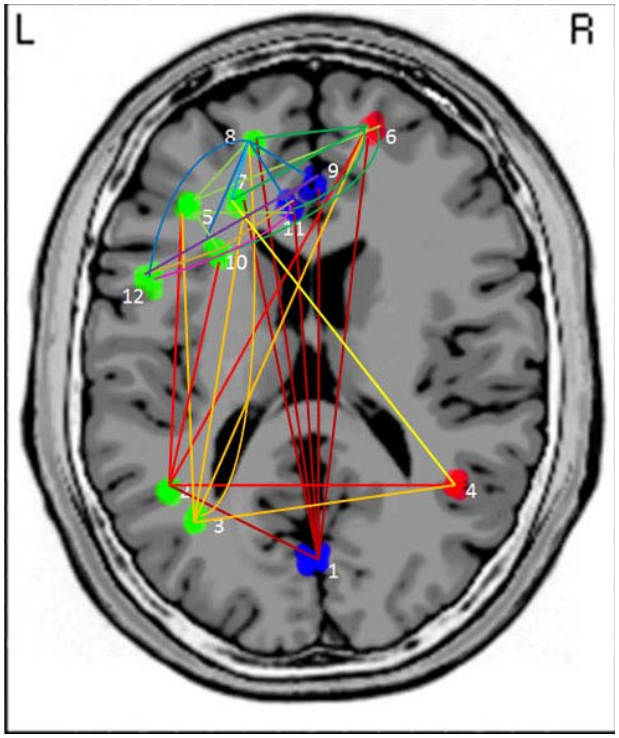
S1 11: ES Delta



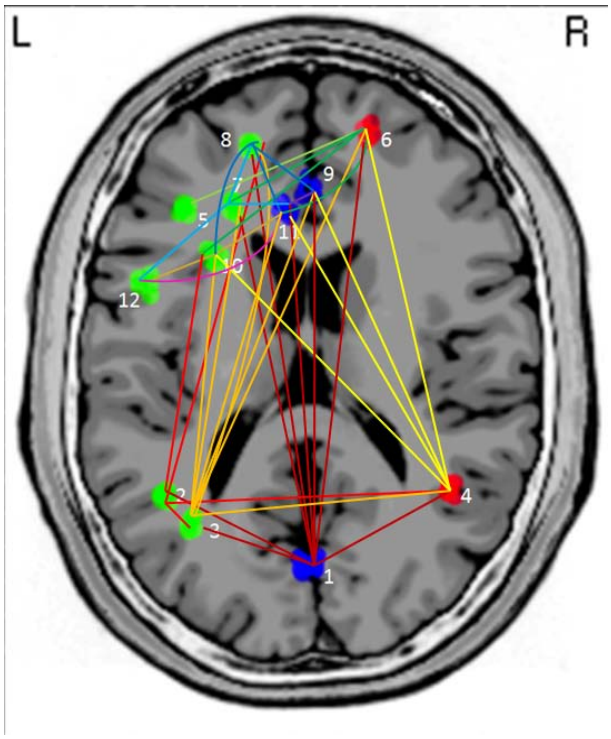
S1 12: ES Theta



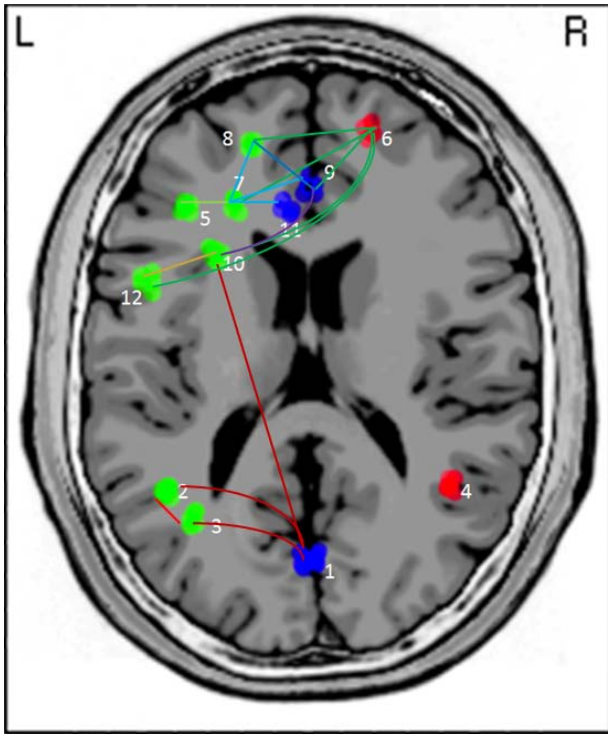
S1 13: ES Alpha-1



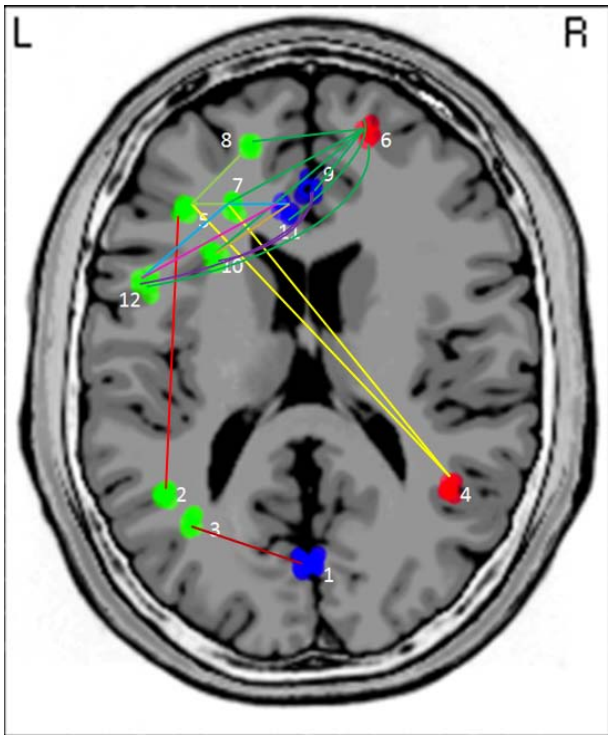
S1 14: ES Alpha-2



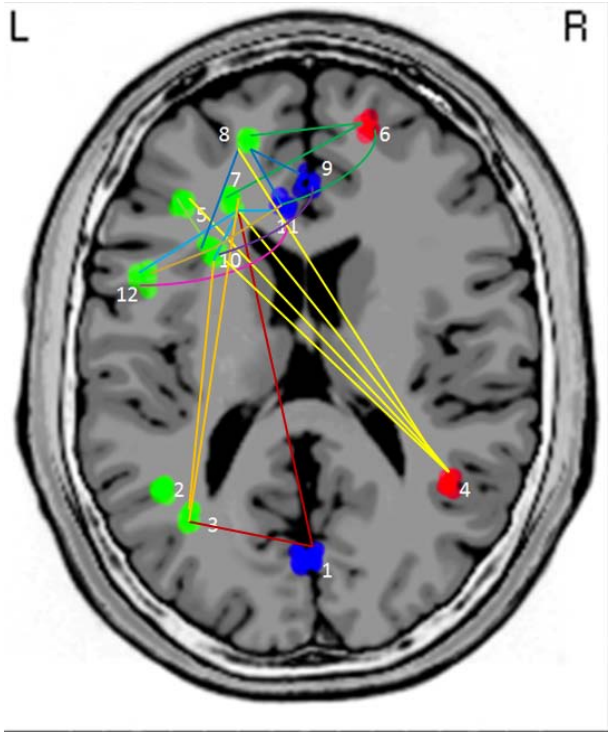
S1 15: ES Beta



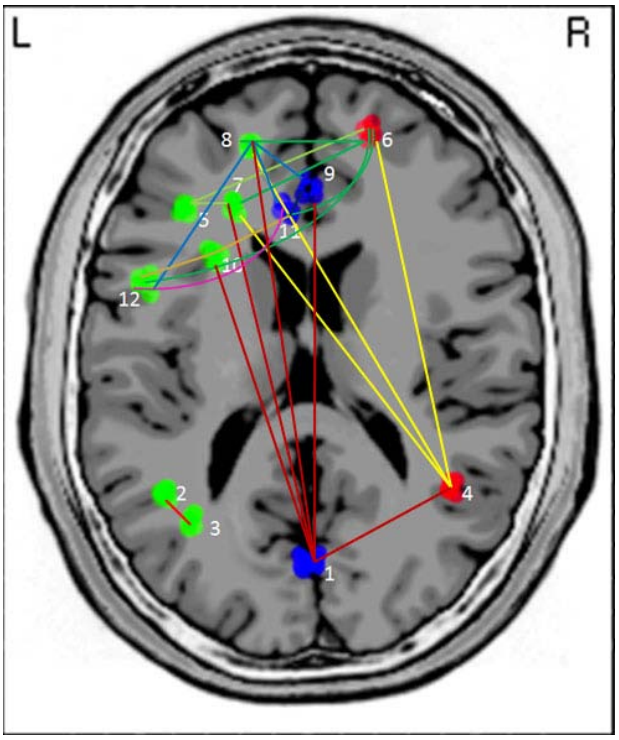
S1 16: SI Delta



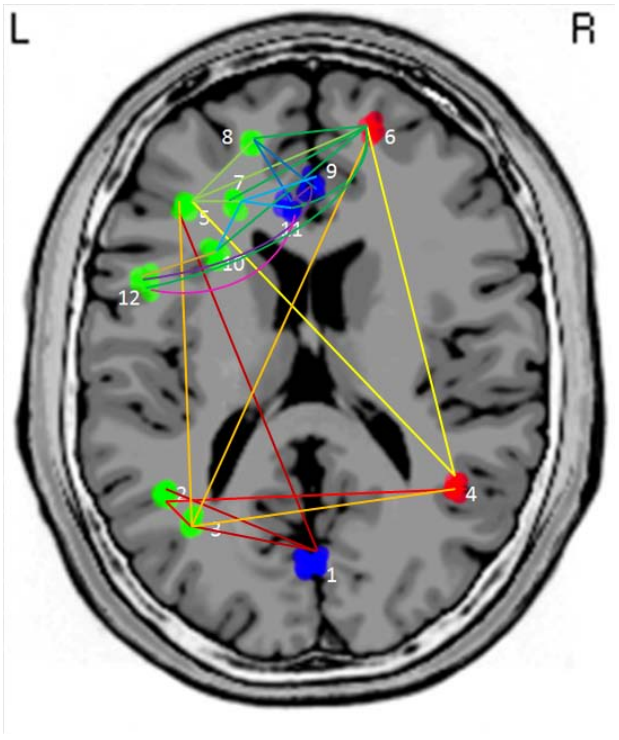
S1 17: SI Theta



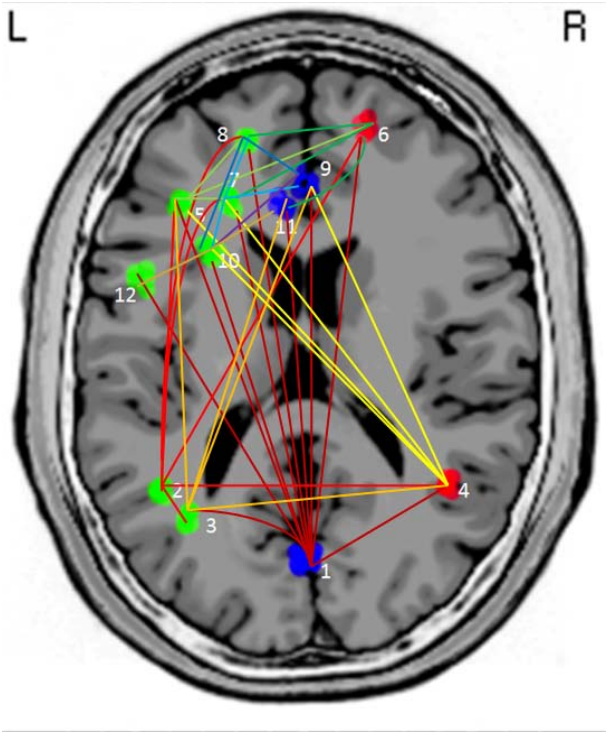
S1 18: SI Alpha-1



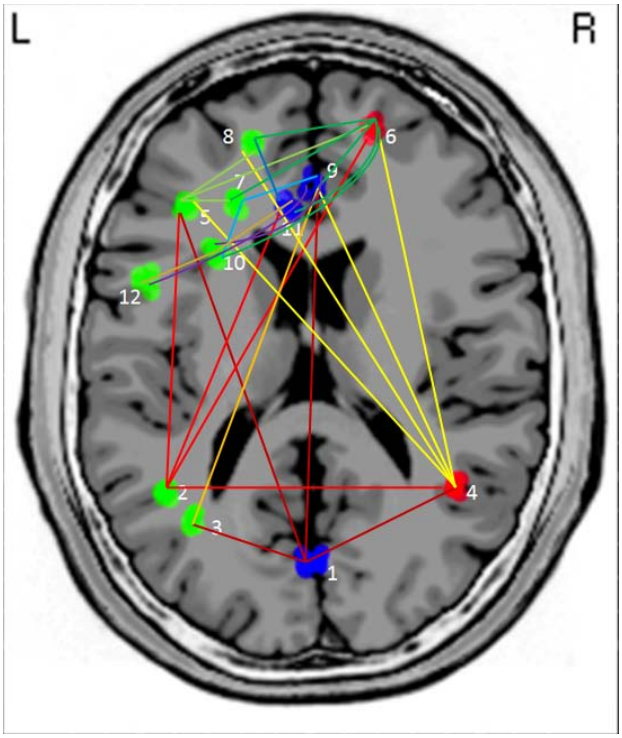
S1 19: SI Alpha-2



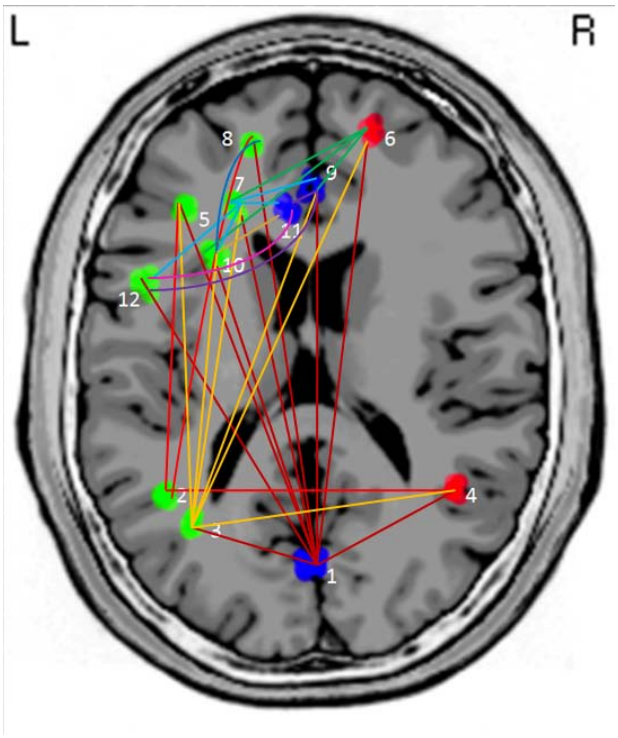
S1 20: SI Beta



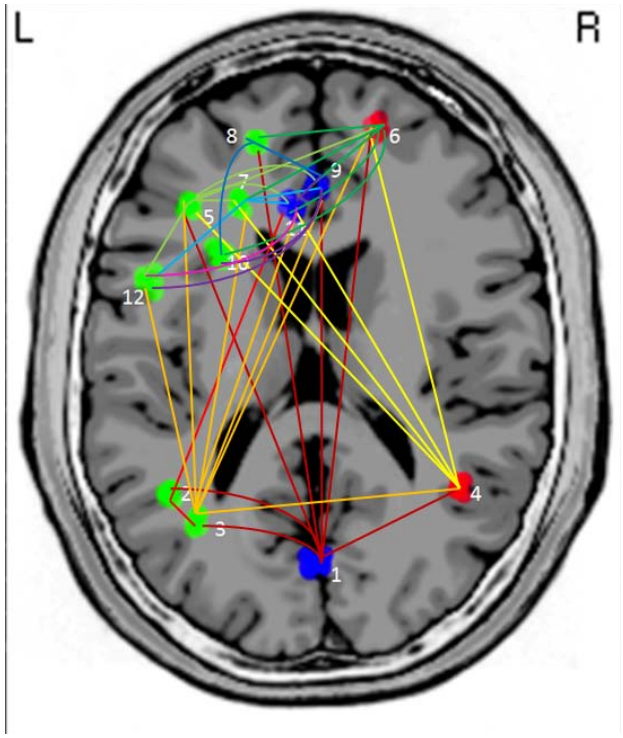
S1 21: BSI Delta



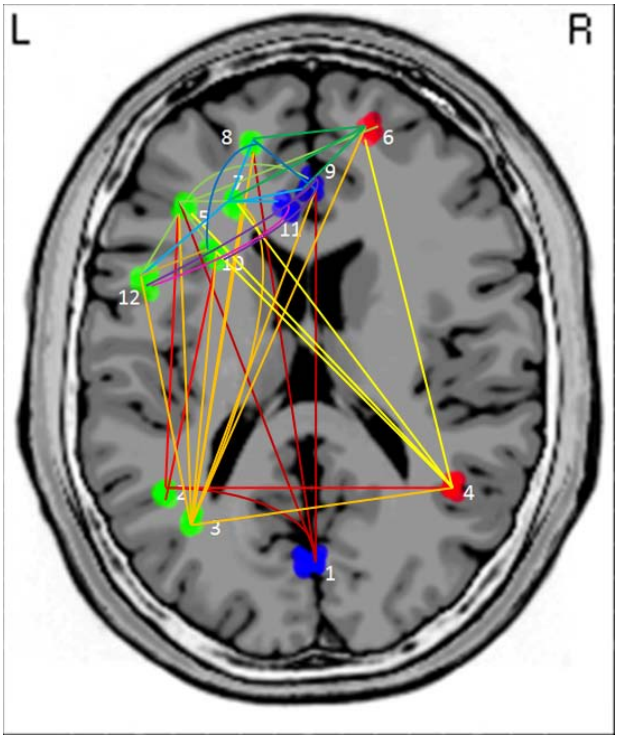
S1 22: BSI Theta



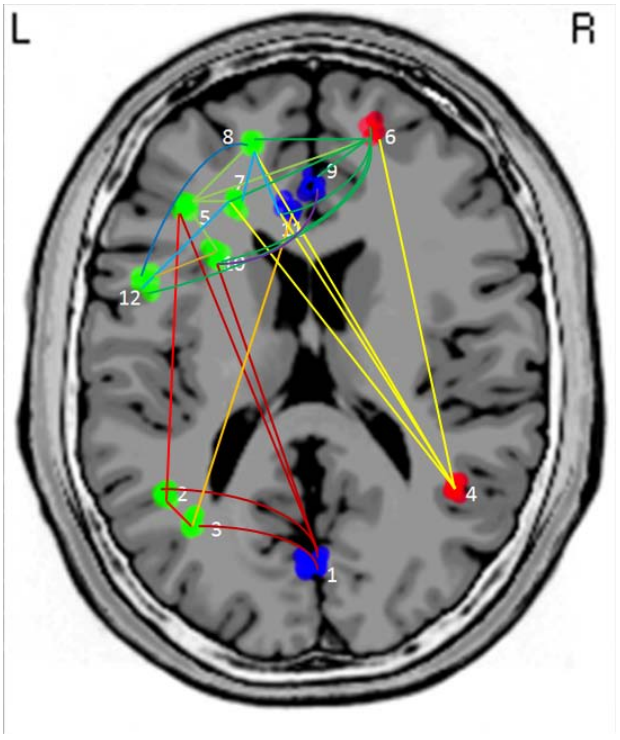
S1 23: BSI Alpha-1



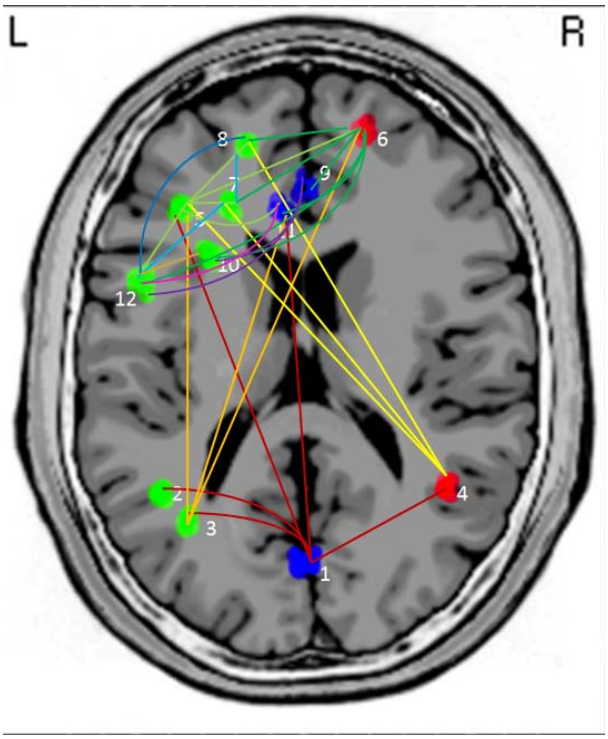
S1 24: BSI Alpha-2



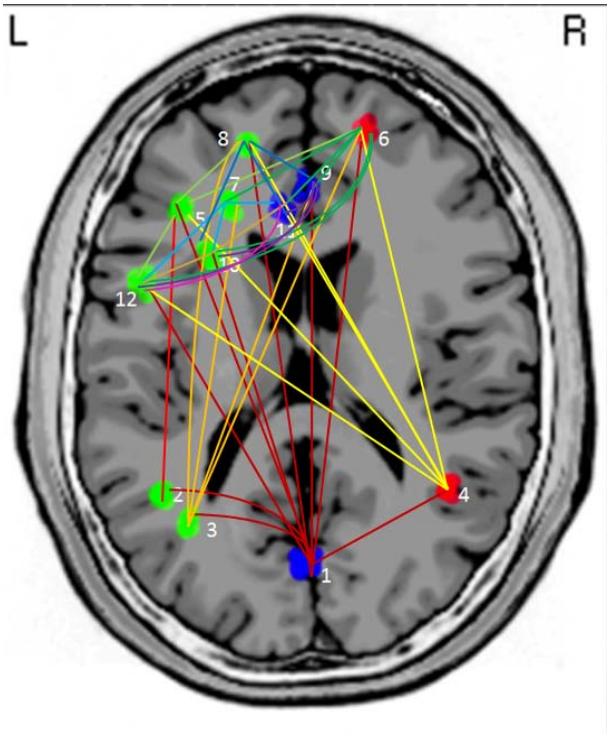
S1 25: BSI Beta



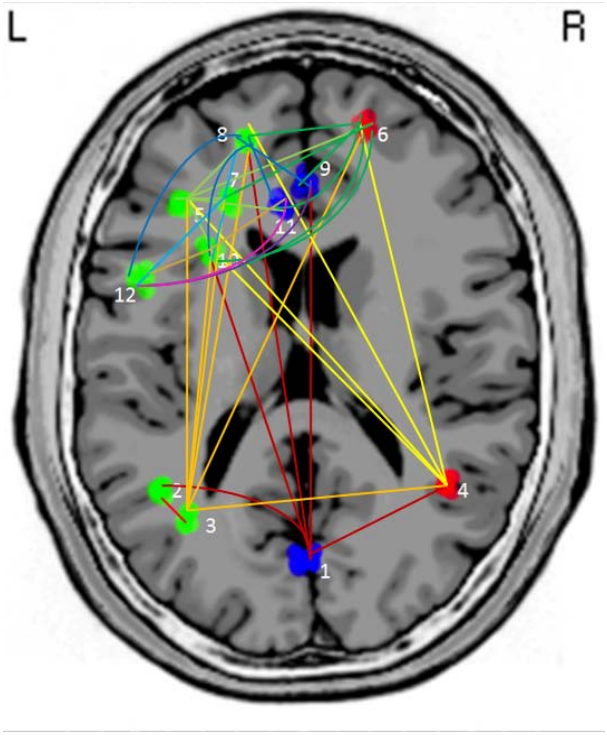
S1 26: TSCS Delta



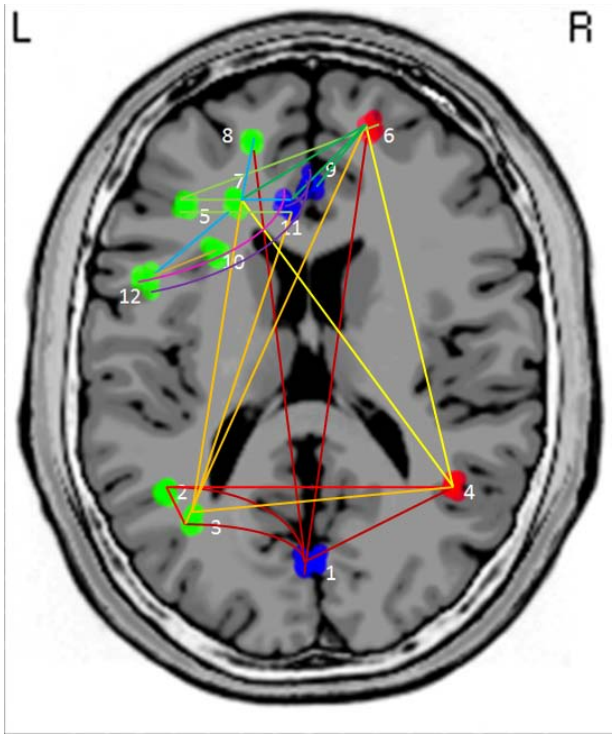
S1 27: TSCS Theta



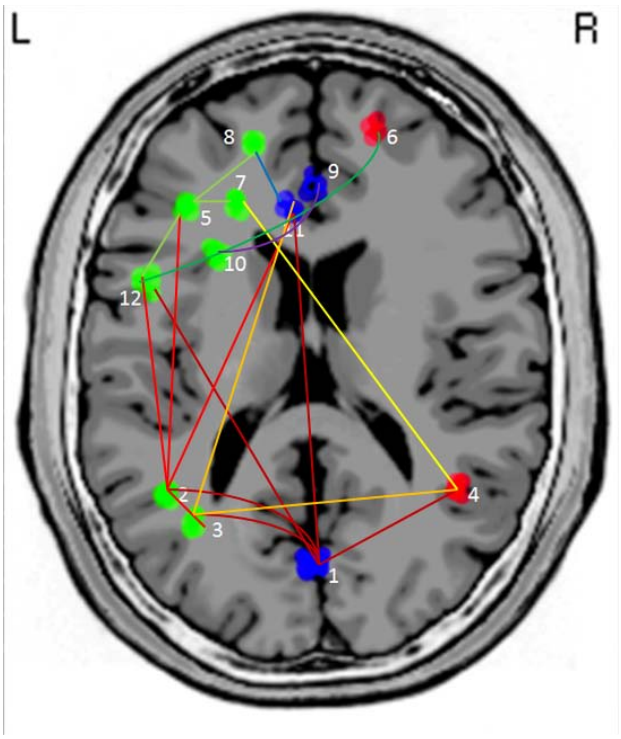
S1 28: TSCS Alpha-1



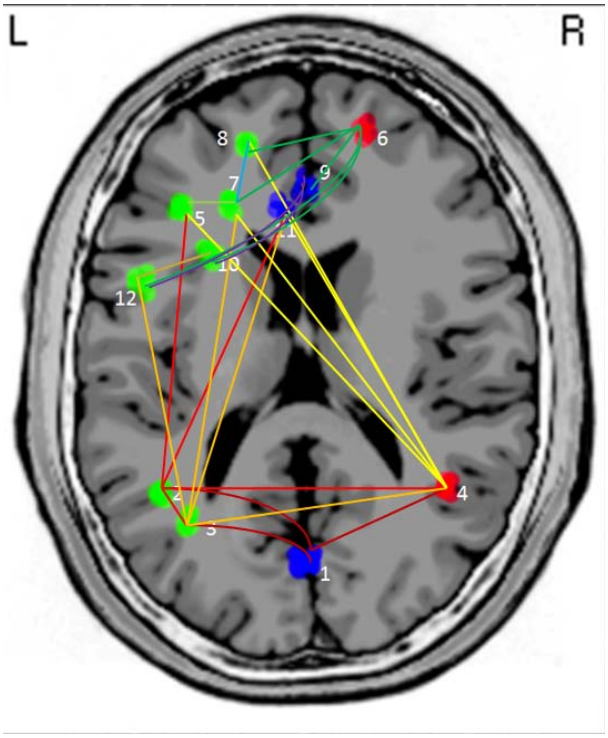
S1 29: TSCS Alpha-2



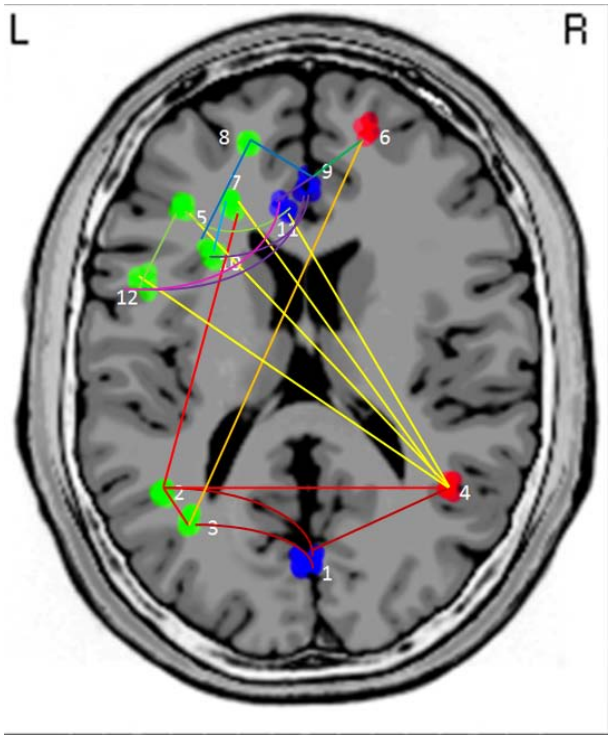
S1 30: TSCS Beta



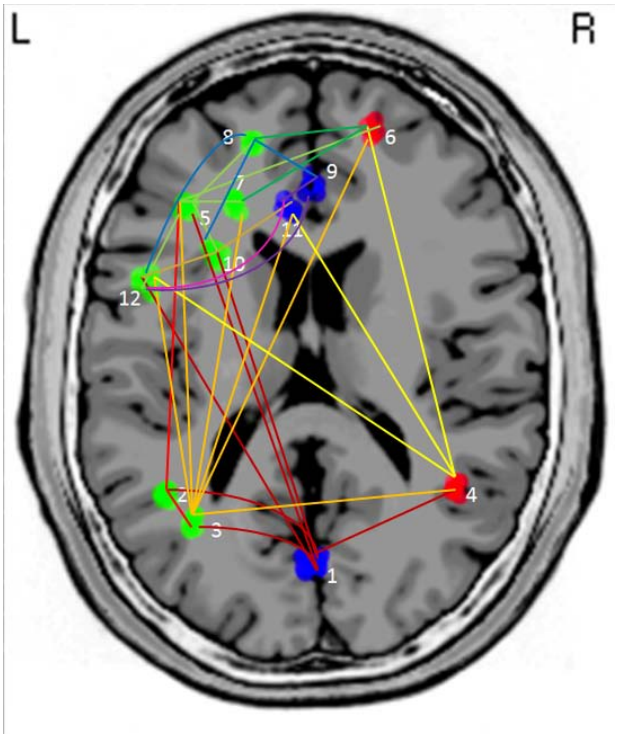
S1 31: Other Delta



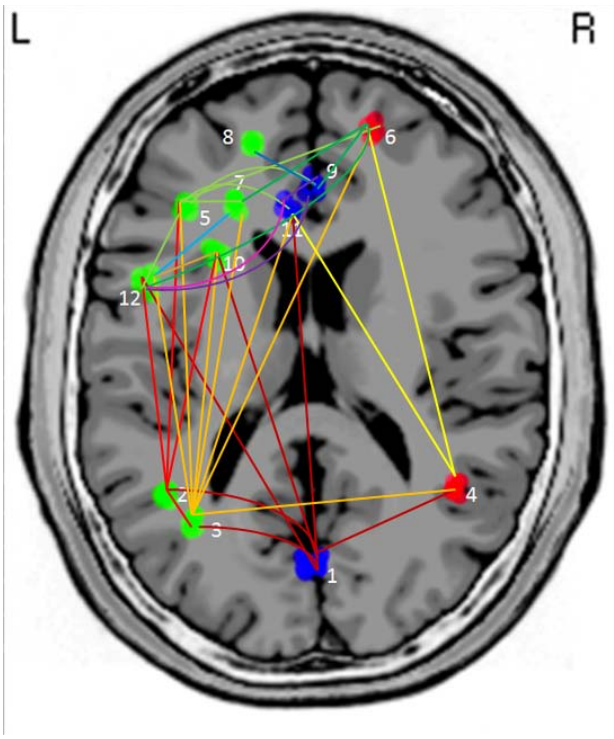
S1 32: Other Theta



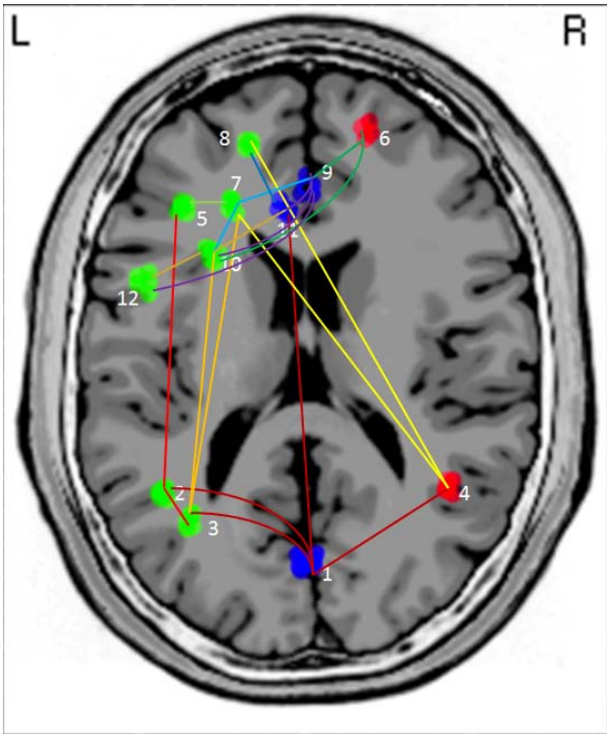
S1 33: Other Alpha-1



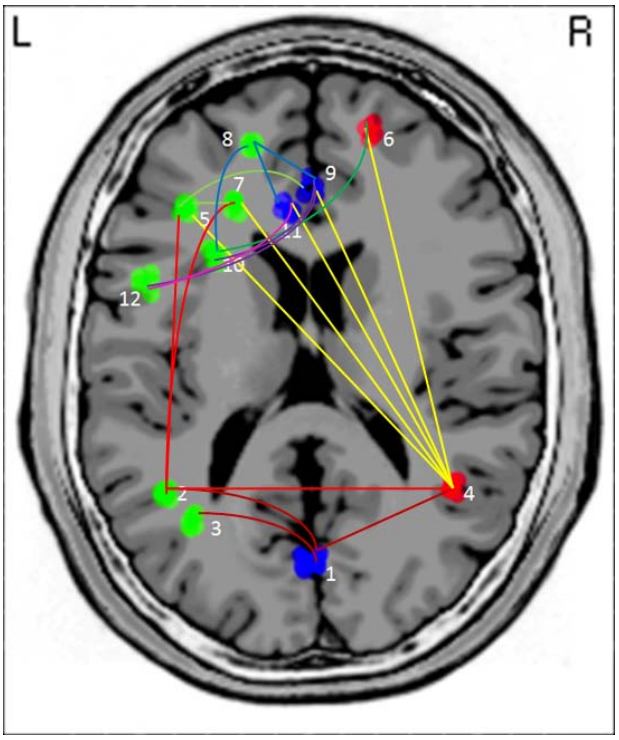
S1 34: Other Alpha-2



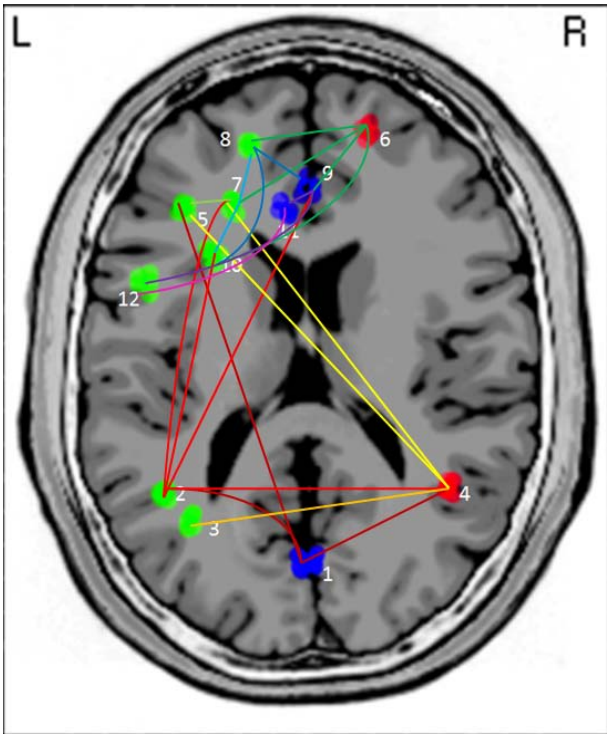
S1 35: Other Beta



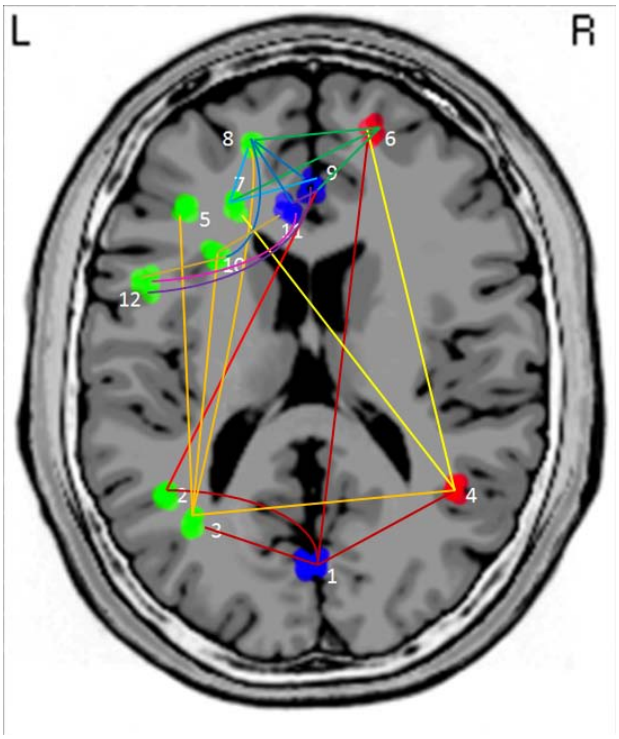
S1 36: Hammer Delta



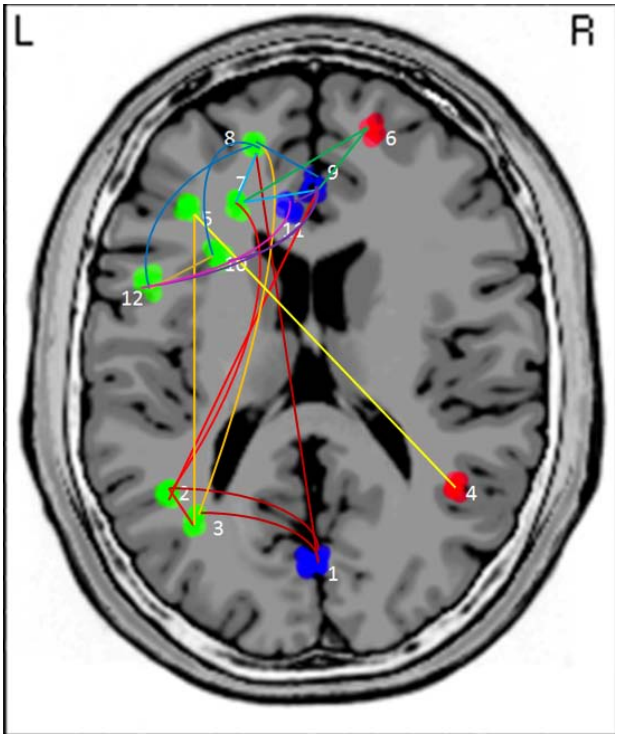
S1 37: Hammer Theta



S1 38: Hammer Alpha-1



S1 39: Hammer Alpha-2



S1 40: Hammer Beta

VITA

Rex Cannon was born in Portsmouth, Virginia. He was raised and lived in the Norfolk, Virginia beach area. He attended elementary and high school in both Virginia Beach and in Blount County, Tennessee. He received his Bachelor's Degree from The University of Tennessee in 2004 and his Master's Degree in experimental psychology with an emphasis in neuroscience and a minor in statistics in 2007. He worked in chemical dependency treatment centers throughout his undergraduate and graduate programs and has over 10,000 clinical hours. He has supervised both staff and clients and was appointed to several administrative positions.