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Personality traits, behavioral and psychological symptoms and cognitive decline in patients at an early stage of Alzheimer's disease

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THÈSE DE DOCTORAT
Présentée à la
FACULTÉ DE SCIENCES SOCIALES ET POLITIQUES
De l'Université de Lausanne
Pour l'obtention du grade de
Docteur en Psychologie
Par

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Faculté des sciences sociales et politiques

IMPRIMATUR

Le Conseil de la Faculté des sciences sociales et politiques de l'Université de Lausanne, sur proposition d'un jury formé des professeurs

- Jérôme ROSSIER, co-directeur de thèse, Professeur à l'Université de Lausanne
- Armin VON GUNTEN, co-directeur de thèse, Professeur à L'Université de Lausanne et au CHUV à Lausanne
- Dario SPINI, Professeur à l'Université de Lausanne
- Mathias ALLEMAND, Maître assistant à L'Université de Zürich

autorise, sans se prononcer sur les opinions de la candidate, l'impression de la thèse de Madame Cornelia POCNET, intitulée :

« Personality traits, behavioral and psychological symptoms and cognitive decline in patients at an early stage of Alzheimer's disease »

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Le Doyen de la Faculté

Professeur
Fabien Ohl

Summary

The aim of this doctoral thesis was to study personality characteristics of patients at an early stage of Alzheimer's disease (AD), and more specifically to describe personality and its changes over time, and to explore its possible links with psychological and symptoms (BPS) and cognitive level. The results were compared to those of a group of participants without cognitive disorder through three empirical studies.

In the first study, the findings showed significant personality changes that follow a specific trend in the clinical group. The profil of personality changes showed an increase in Neuroticism and a decrease in Extraversion, Openess to experiences, and Conscientiousness over time. The second study highlighted that personality and BPS occur early in the cours of AD. Recognizing them as possible precoce signs of neurodegeneration may prove to be a key factor for early detection and intervention. In the third study, a significant association between personality changes and cognitive status was observed in the patients with incipient AD. Thus, changes in Neuroticism and Conscientiousness were linked with cognitive deterioration, whereas decreased Openness to experiences and Conscientiousness over time predicted loss of independence in daily functioning. Other well-known factors such as age, education level or civil status were taken into account to predict cognitive decline.

The three studies suggested five important implications: (1) cost-effective screening should take into account premorbid and specific personality changes; (2) psycho-educative interventions should provide information on the possible personality changes and BPS that may occur at the beginning of the disease; (3) using personality traits alongside other variables in the future studies on prevention might help to better understand AD's etiology; (4) individual treatment plans (psychotherapeutic, social, and pharmacological) might be adapted to the specific changes in personality profiles; (5) more researches are needed to study the impact of social-cultural and lifestyle variables on the development of AD.

Résumé

L'objectif de cette thèse a été d'investiguer la personnalité chez des patients avec une maladie d'Alzheimer (MA) légére. Nous avons comparé, à travers trois études, ce groupe clinique à des participants sans troubles cognitifs, concernant l'évolution de la personnalité, son impact sur les symptômes comportementaux et psychologiques (SCP) ainsi que sur le niveau cognitif.

Dans la première étude, d'importants changements de personnalité, suivant une tendance spécifique, ont été observés uniquement dans le groupe clinique. Le profil de ces changements montre une augmentation du Névrosisme et une diminution de l'Extraversion, de l'Ouverture et de la Conscience au fil du temps. La deuxième étude souligne que les changements de la personnalité et les SCP surviennent tôt dans la MA. Les reconnaître comme des signes avant-coureurs de la maladie peut s'avèrer un facteur clé pour la détection et l'intervention precoce. Dans la troisième étude, une association significative entre l'évolution de la personnalité et le niveau cognitif a été observée chez les mêmes patients. Ainsi, les changements du Névrosisme et de la Conscience sont liés à la détérioration cognitive, tandis que la diminution de l'Ouverture et de la Conscience dans le temps prédit la perte d'autonomie quotidienne. Facteurs tels que l'âge, le genre, l'éducation et l'état civil ont été pris en compte pour prédire le déclin cognitif.

Ces études suggèrent cinq implications pratiques importantes: (1) un dépistage rentable de la MA devrait prendre en compte les traits premorbides et les changements spécifiques de la personnalité; (2) les interventions psycho-éducatives pourraient fournir des informations sur les changements de personnalité et SCP qui peuvent surgir tôt dans la MA; (3) des études sur la prévention sont nécessaires pour mieux comprendre l'étiologie de la MA; (4) le traitement individuel (psychologique, social, pharmacologique) pourrait être adapté aux changements spécifiques de la personnalité; (5) amples recherches sont requises afin d'étudier l'impact des variables socioculturelles et des styles de vie sur le développement de la MA.

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General Objectives

The significant increase of the number of elderly people in the world is accompanied by an increasing prevalence of people with either mild cognitive impairment or dementia. It is estimated that the number of individuals affected by dementia and in particular by Alzheimer's disease (AD) will double every twenty years (WHO, 2006); thus, the ageing psychology is expected to play an important role in the years to come.

So far, scientists agree that AD develops as a result of complex interactions among numerous factors, including age, genetics, environment and lifestyle, and coexisting medical conditions. The impacts of AD are multiple and affect different areas including cognitive functioning. Memory loss refers, undoubtedly, to the most famous dramatic consequence and evolve according to the progression of the disease. Beside memory deficits, AD affects other cognitive areas such as executive functions, defined as the ability allowing of the individual to adapt to its environment facing new and complex situations (Williams & Kemper, 2010). Thus, executive functions are involved in a wide variety of situations of daily life, and moreover their achievement is in large part responsible for the loss of personal autonomy. In addition, behavioral disorders play an important role in the symptomatology of AD. In this sense, Devanand and colleagues (Devanand, Marder, Michaels, Sackeim, Bell, Sullivan, Cooper, Pelton, & Mayeux, 1998) showed that 64% of AD patients had at least a psychological or behavioral disorder at the initial assessment. Cummings (2005) similarly found that neuropsychiatric symptoms accompanied AD in about 90% of cases. All psychological disorders, cognitive and behavioral problems associated with AD cause mental suffering to the person with the disease. It is also a source of suffering for those around who should bear the dependence of their proxy patient and the irreversible changes in his personality. They are also, in most cases, the reason for institutionalization (Kraus, Seignourel, Balasubramanyam, Snow, Wilson, Kunik, Schulz, & Stanley, 2008). At present,

no pharmacological treatment can neutralize permanently AD, although some drugs can slow the progression of decline and improve the quality of life of patients. The non-drug therapies remain thus very important aspects of the tratement of AD.

While researchers know AD involves progressive brain neuronal failure, many questions still remain unanswered. Today, studies focus on the discovery of additional risk factors that will deepen our understanding of why AD develops in some people and not others. In this respect, clinical experience suggests that personality characteristics, those most distinctive and stable in a person, may influence how individuals with dementia cope with difficulties. Moreover, some studies have observed that premorbid personality disorders were more common among AD patients than in control subjects suggesting that they may be risk factors for AD (Duchek, Balota, Storandt, & Larsen, 2007), although personality disorders were not well defined (Terracciano, McCrae, Brant, & Costa, 2005). In addition, other studies on this topic showed that premorbid personality traits were the only significant predictor of change for Neuroticism, Extraversion, Conscientiousness, and lower Openness to new ideas, fantasy, aesthetics, and values (Dawson, Welsh-Bohmer, & Siegler, 2000; Wilson, Schneider, Arnold, Bienias, & Bennett, 2007). Very early behavioural and personality changes are more easier detected by patient's family members as opposed to cognitive impairment (Carr, Gray, Baty, & Morris, 2000), hence, these may help in planning the disease management. Therefore, the interest in providing the link between AD and personality is multiple because it may involve other links, such as with behavioral and psychological symptoms and cognitive damages. However, research in this area is scarce despite the huge interest in personality in general.

The works of this doctoral thesis revolve around the concepts of personality and explore several hypotheses related to premorbid personality, changes of personality, and how these personality characteristics may have an effect on neuropsychiatric symptoms and global

cognitive functioning in AD patients. In order to achieve this, a comparative study between a group of patients in the earliest stage of AD and a group of mentally healthy people was conducted. Three main objectives were explored in our study. Firstly, *we examined differences of personality profiles in the earliest stages of dementia of the Alzheimer type relative to healthy ageing*. More precisely, we have tried to shed light on whether or not personality changes appear during the early stages of dementia and if so, to compare the magnitude of change with that of healthy control. Then, *we investigated the influence of premorbid personality and its changes over 5 years on behavioral and psychological symptoms (BPS)* also referred to as neuropsychiatric symptoms. Taking into account the multiple etiologies of BPS, *we have tried to clarify whether neuropsychiatric symptoms can be due to pathological processes linked to dementia, or whether certain personality characteristics can predispose to the occurrence of BPS*. Although certain preliminary studies suggest links between premorbid personality and cognitive decline in AD, the nature between these has yet to be determined. Furthermore, in the last chapter we have tried *to predict the loss of cognitive skills in patients at an early stage of AD through premorbid personality or its changes over five years*.

The first chapter of our work will focuse on a litterature review on the concept of personality and its description according to different perspectives emerged in the history of personality psychology. Then, AD and its psychological, behavioral, and cognitive consequences will be presented. In a third chapter a review of the available literature concerning the impact of personality characteristics on the clinical expression in neurodegenerative disorders will be presented. Chapters four, five, and six will present the results and their possible interpretations of three parts of our empirical study. The general conclusions with strenghts and shortcommings of this study, clinical implications, and new possible avenues of research will be discussed in a seventh and last chapter.

Up to date no effective therapy exists to cure or arrest the disease progression. Treatment efforts are focused on promoting quality of life for both patient and family, such as interventions strategies to deal with the distressing symptoms in both the patient and the family. The complexity of changing illness manifestations necessitates professional multidisciplinary collaboration throughout the course of the illness. Therefore, improving the understanding of impact of personality features on behavioural and psychological symptoms, and cognitive disorders is likely to influence our attitudes towards treating demented patients and to help alleviate difficulties both patients and their close ones experience.

Chapter 1. Personality Psychology

The aim of this first chapter is to introduce the concept of *personality* through *different approaches*. Then, I will focus particularly on the concept of *personality traits* and its *operationalizations*. Furthermore, I will discuss the *development and stability* of personality over time and across situations in normal subjects. This "normal" personality framework will be used as a reference to examine the personality and its possible impact on the development of AD in our empirical study.

1.1. Personality and characteristic adaptations

Over time, the personality psychology has put the human at the center of investigation examining relatively enduring component rather than fleeting and momentary characteristics of persons. To understand the person, the personality psychologist must take into account the biological, social, cultural, and historical context. Personality is usually conceived as a configuration of thoughts, feelings, and behavior that determine a person's unique pattern of adaptation (Costa & McCrae, 1992). Throughout history, the study of personality has generated many theories according to the choice of methods and views of the author. Each theroretical perspective is seen as offering its own principles of personality development and changes, and genereting its own hypothses of research.

1.1.1. Psychoanalytic and neo-analytic perspectives

Psychoanalysis is a curative method based on the verbalization of thoughts and association of ideas that appear in a context where what has been repressed may transpire. But the psychoanalysis is also a theorie of the psychic life developed from this experience. As a theory of the mind or personality, psychoanalysis takes into account the importance of unconscious, cognitive, affective, and motivational processes. According to Freud, among the phenomena that influence thought, feeling, and behavior can be listed: conflicting mental

processes, compromises among competing psychological tendencies that may be negotiated unconsciously, defense and self-deception, the influence of the past on current functioning, the effects of interpersonal patterns laid down in childhood, sexual and aggressive roles (Westen & Gabbard, 1999). Free associations and transference phenomena were of great methodological importance. Whereas Freud's first model is *topographic* and categorizes mental processes by their quality concerning consciousness, his last model is *structural* and categorizes mental processes by their functions or purposes. He introduces the *id*, *ego*, and *superego* to explain the conflicts between consciousness and unconscious. The *id* is the reservoir of sexual and aggressive energy. The *superego* is the conscience. The *ego* is the structure that must somehow balance the demands of desire, reality, and morality. To achieve this balance, the *ego* activates mechanisms of defense as well as creative compromises among competing forces (Freud, 1961). The major conflicts that produce anxiety in adults' lives are often the results of disagreements among these three different agents of the mind. Resolving conflicts, therefore, involves forging creative agreements that enable the three coexist with another in relative tranquillity. Therefore, psychoanalysis provides us a set of ideas that can be used in creative ways to explain how it is that people develop the particular traits and characteristics of adaptations that describe who they are (Hindle & Smith, 1999). Therefore, for Freud and the psychoanalytic theorists, human beings are fundamentally conflicted and driven by forces over which they have little control. The psychoanalytic research method of interpreting lives involves searching for hidden meanings in the manifest expression of everyday life. For example, Freud showed how dreams, slips of the tongue, symptoms, and indeed all aspects of human behaviour and experiences can be viewed. They exist as compromises among conflicting force (for dreams: wish fulfillments). Symptoms, dreams, and others human experiences are constructed according to the same principles through which a multitude of unconscious forces are synthetised into a manifest expression whose identity is

always disguised (Freud, 1953).

However, some weaknesses of psychoanalysis must be noted: 1. fuzzy concepts, difficult to "operationalize"; 2. subjective approach exclusively based on the case study method, generalization from a limited number of cases and the presumption of an universal character of concepts; 3. difficulty of analysts to assume the objectivity of their interpretative frames; 4. essentially "male" design of psychic functioning; 5. universality and particularity of the Oedipus complex concept.

Several authors who were influenced by Freud's psychoanalytic theory have come up with different neo-analytic personality theories. Grounded on it, they attributed an important role to the *id* and the influence of *social or cultural* dimensions. They rejected most of the psychoanalytic tenets such as the universality of the Oedipus complex and the preponderance of sexuality. An important contribution of the neo-analytic perspective is *Jung's theory*. One of the original contributions of Jung's theory in the psychology of personality is the idea that the unconscious is divided into two different entities: *the personal unconscious and the collective unconscious*. Jung also created some of the widely known psychological concepts, including the archetype, the complex, and synchronicity. According to Jung, the collective unconscious is inhabited by archetypes, which are universal patterns of experience that structure how people approach life. Common Jungian archetype includes the anima (a man's unconscious femininity), the animus (a woman's unconscious masculinity), and the shadow (reprehensible, primitive tendencies in all humans) (Jung, 1981). However, Jung's notion of the collective unconscious has proven to be very difficult to evaluate scientifically. In addition, the concepts of *introversion* and *extraversion*, very valuable in personality theorizing, have been used in many subsequent theories. Extraversion and introversion are typically viewed as being on a single continuum. Thus, to be high on one implies being low on the other. Jung (1981) provides an interesting model of personality development in the

adult years in term of individuation, or the full actualization and expression of the self. Each adult approaches the challenges of individuation from the standpoint of his or her particular psychological type, which is determined by the intersection of extraversion and introversion and four psychological functions (thinking, feeling, sensing, and intuiting). These features combined determine 8 personality types: extroverted thinking; introverted thinking; extroverted feeling; introverted feeling; extroverted sensing; introverted sensing; extroverted intuitive, and introverted intuitive (Jung, 1981).

Another significant contribution to the neo-analytic perspective is *Adler's theory*, which gave an important place to the *social dimension*. His theory claims that people tend *to compensate for their weakness and inferiority by a need to feel superior* (Adler, 1939). He was also an early supporter of feminism in psychology and the social world, believing that feelings of superiority and inferiority were often generated and expressed symptomatically in characteristic masculine and feminine styles. These styles could form the basis of psychic compensation and lead to mental health difficulties.

Horney (1942) developed a theory that focuses on the *neuroses*. Unlike previous theorists, she viewed the neuroses as a sort of coping mechanism that is a large part of normal life. She identified several neuroses, including the need for power, the need for affection, the need for social prestige, and the need for independence. Thanks to her many books, she gave normal people the means to understand their neurotic behavior and encouraged *self-analysis* (Horney, 1942). She limited her analysis to *normal personality*.

More recently, another representative of the neo-analytic approach was Erikson (1982) who promoted the idea that the *development of personality* does not stop at adolescence, but continues into adulthood. He basically formulated eight major stages of development, but after his death in 1994, his wife, Joan, published a revised version of his theory where she will add a ninth stage that describes very old age. Erikson's nine stages of personality

development are: trust vs. mistrust; autonomy vs. shame and doubt; initiative vs. guilt; industry vs. inferiority; identity vs. identity confusion; intimacy vs. isolation; generativity vs. stagnation; integrity vs. despair; despair vs. hope and faith that make us who we are as a person and explain why we are that way. Erickson believed humans had to resolve different conflicts as they progress through each stage of development in their life cycle. Thus, to explain the psychological and social complexities of human individuality during a particular period in the lifespan, he introduced the terms *identity* and *identity crisis.* According to Erikson, identity crisis is a time of "intensive analysis and exploration of different ways of looking at oneself " (Erikson, 1970). Identity has its own stages, and Erikson labeled them as *identity achievement*, *moratorium, foreclosure*, and *identity diffusion. Identity achievement* occurs when an individual has explored various identities and has made a commitment to one of them. *Moratorium* is the status of an individual actively involved in exploring identities, but who has not made a commitment. *Foreclosure* is when a person has already made a commitment without attempting to identify exploration. Lastly, *identity diffusion* occurs when there is either an identity crisis or commitment (Marcia, 1966). Identity crisis is present in many aspects of life and, through it Erikson was the first to formulate the concept of *lifespan development.* Taking social, cultural, and environmental factors into account, he contributed to our understanding of personality as it is developed and shaped over the course of our lifespan.

1.1.2. Learning perspective

According to the authors of learning perspective, such as Skinner or Bandura, our behavior will change constantly depending on life experiences, and our personality will change according to the new learning experiences. The environmental contexts of persons' lives, the roles of social learning and culture in the formation of personality were introduced by Skinner's theory, as part of the *stimulus-response psychology* (Skinner, 1957). The

environment determines most of our responses, and, in terms of their consequences, the responses will be reproduced or eliminated. In the first case, we speak of positive reinforcement, in the second situation of negative reinforcement. Skinner rejected subjective measures (self-report, questionnaires) and advocated an objective analysis of an *individual's reinforcers and punishers* (Skinner, 1971). Although Skinner's theory is based on scientifically reproducible evidence, its contribution, as part of the psychology of personality, is limited because it reduced personality to behavior, rejecting the influence of genetic and biological factors. In addition, it did not take thoughts, feelings and other mental phenomena into account.

The *neo-behaviorists*, such as Bandura, introduced *social and cognitive factors* in learning theory. Bandura believed that personality is influenced by external factors, particularly through the imitation of behaviors of others. He emphasizes the roles of observational learning, self-efficacy, and reciprocal determinism in human behavior. In 1986, Bandura advanced concepts of "triadic reciprocity" which determined the connections between human behavior, environmental factors, and personal factors such as cognitive, affective, and biological events, and of reciprocal determinism that governs the relations between these three factors. Bandura stresses that an individual's capacity of *self-organization* and *self-regulation* eventually give rise to his later work on *self-efficacy*. Self-efficacy is the belief that we are able to organize and produce behaviors for future actions. It is a kind of evaluation of our skills and our performance. This concept influences the choices we make, how we feel, and how we resist in the face of obstacles. In other words, the development of self-efficacy is a key mechanism whereby people are able to exercise control over threating events in the environment (Bandura, 1997). Bandura's social cognitive theory resulted in important empirical validation stemming from a solid experimental basis. Moreover, psychologists have documented the power of social learning in many different

areas of human functioning. An especially area in this regard is the study of aggression. Research documents the powerful role of observation in the formation and performance of aggressive responses.

1.1.3. Humanistic perspective

As an alternative to psychoanalysis and behaviorism, the humanistic perspective stems from two philosophies: *existentialism* and *phenomenology*. It appeared in the 1950s -1960s following the publication of several books by Maslow (1968) and Rogers (1961, 1969). This perspective emerged out of a desire to understand the conscious mind, free will, human dignity, and the capacity for self-reflection and development. Thus, the individual is considered as a whole. It is promotes creativity, intentionality, freedom of choice and spontaneity, and supports the idea that people have inner resources to solve their psychological problems. Among these resources are mentioned motives and goals. Motivation concerns the internal forces and factors that energize and direct human behavior, including wants, needs, and desires. So, humanistic perspectives centered on the idea that people control their lives. The self, personal growth, and development are emphasized. In connection with this, Maslow (1968) developed a humanistic theory of personality that underscored the motive for self-actualization and sustains that a hierarchy of needs is what motivates people. Basic needs must be met before higher ones can be satisfied:

- Physiological (satisfaction of hunger and thirst);
- Safety (security);
- Belongingness and love (being loved, avoiding loneliness);
- Esteem (achievement, recognition, self-esteem);
- Self-actualization (realization of one's full potential).

Maslow argued that self-actualizing tendencies are built on more basic needs for psychological equilibrium, safety and security, belonging and love, and self-esteem. He believed that the achievement of self-actualization is often marked by peak experiences, feelings of incredible peace and happiness in the course of life.

Carl Rogers (1961) used the theory of *self-concept*, which he defined as an organized pattern of perceived characteristics along with the values attached to those attributes. He also assumed that within each individual there is a biological drive toward the development of *self-concept*, which can ultimately lead to *self-actualization*. Rogers believed that while children's self-concept is developing, they might internalize conditions of worth, judgments about the kinds of behaviors that will bring approval from others. He felt that, to promote growth and development, parents and authority figures should give a child unconditional acceptance and love, allowing a child to develop *self-acceptance* and to achieve *self-actualization*. To help his clients get back on the road to self-actualization, Rogers developed a therapeutic approach called client-centered therapy, in which the therapist offers the client unconditional positive regard by supporting the client regardless of what is said. *Self-actualization* is a curative force in psychotherapy defined as a "man's tendency to actualize himself, to become his potentialities... to express and activate all the capacities of the organism" (Rogers, 1980). The important concepts of Rogers' theory are also empathy and warmth. These could lead the subject to free himself of distorted internalized representations of worth and to resume the self-actualization process. Nowadays, the links between *self-actualization,* personal developments, and vocational personality, and their results are used in professional counseling and interpersonal problems solving (Wiggins & Pincus, 1992; Gottfredson, Jones, & Holland, 1993).

Therefore, for Rogers, Maslow, and the humanistic theorists, a self-actualizing nature lies behind human individuality. They focused on the positive image of what it means to be human and on methods that allow fulfillment of potential.

1.1.4. Cognitive perspective

In the cognitive perspective, authors such as Kelly or Witkin focus on one particular internal aspect; cognitive processes are the dominant characteristics of personality. Social-cognitive adaptations are the characteristic personal constructs, cognitive styles, beliefs, expectancies, attributions, and the like that people draw upon in their efforts to meet the many demands of social life. Along with personal goals, social-cognitive adaptations help to regulate social behavior. So, Kelly's basic premise is that each individual decodes reality as an intuitive scientist who tries to understand, explain, predict, and control his or her immediate environment to adapt to it as best as he or she can. To do so, an individual has expectations that Kelly (1955) called *personal constructs.* Similarly, many psychologists of the 1950s and 1960s introduced the idea of a pattern of perceptual and intellectual activity to define *cognitive styles*. A pioneer of cognitive styles and learning styles theory was Witkin (1954). He found that personality could be revealed through differences in how people perceive their environment. He sustained that cognitive style is a stable and persistent personality dimension that influences attitudes, values, and social interactions. Moreover, cultures provide people with a range of cognitive styles that are appropriate for different cognitive tasks in different contexts. Psychologists have attempted to compare cognitive styles cross-culturally. Some have argued that the styles of individuals and of groups can be located on a continuum between a global style and an articulated style. People who use a global style tend to view the world holistically; first they see a bundle of relationships and only later the bits and pieces that are related. They are said to be field dependent. By contrast, people who use an articulated style tend to break the world up into small pieces, which can

then be organized into larger chunks. They also tend to see a clear boundary between their own bodies and the outside world. People using an articulated style are able to consider whatever they "happen to be paying attention to apart from its context and so are said to be field independent" (Cole & Scribner, 1974).

Many cognitivists have applied cognitive theory to psychological treatment, most notably Beck (1997). He is known for his research in psychotherapy, psychopathology, suicide, and psychometrics, which led him to contribute to the development of *cognitive therapy*. He also developed several assessment psychological instruments such as the Beck Depression Inventory (BDI) and the Beck Anxiety Inventory (BAI) to evaluate an individual's functioning. Particularly, his research led him to look for other ways of conceptualizing depression. Working with depressed patients, he found that they experienced streams of negative thoughts that seemed to pop up spontaneously. He termed these cognitions *automatic thoughts*, and discovered that their content fell into three categories: negative ideas about themselves, the world, and the future. Beck presented some key ideas in the *Cognitive Behavioral Therapy*, where he explained that different disorders were associated with different types of distorted thinking. He explained that frequent negative automatic thoughts reveal a person's core belief, formed over lifelong experiences. Some of his most recent work has focused on cognitive therapy for schizophrenia, borderline personality disorder, and for patients who are repeated suicide attempters.

1.1.5. Psychobiological perspective

While several previous theories were mainly descriptive, the psychobiological perspective offers a *causal model of individual differences*. The individual is genetically determined to behave in one-way or another, and the central nervous system and hormones strongly influence personality. However, this perspective did not exclude the influence of the environment.

Personality and temperament have long been considered as two separate concepts; today temperament is considered as part of the personality. The temperament theory has its roots in the ancient four humors theory of the Greek philisopher Hippocrates (460-370 BC), who believed certain human behaviors were caused by bodily fluids: lymph, black bile, yellow bile, and blood. He based his doctrine on the cosmology of Empedocles (440 BC) and therefore connected moods to the four elements (air, fire, water, and earth) and four qualities (cold, heat, humidity, and drought). Later, Galen (129-199) developed the first typology of temperament, and searched for the physiological reasons for different behaviors in humans. He observed that pairs of temperaments shared certain traits in common:

- *Phlegmatic*, apathetic, a longer response-delay, but short-lived response; link with water, balanced between cold and wet;
- *Sanguine*, optimistic, quick, impulsive, and relatively short-lived reactions; associated to air, balanced with hot and wet;
- *Melancholic,* sad, morose, long response time-delay, response sustained at length, if not, seemingly, permanently; related to earth, balanced with cold and dry;
- *Choleric*, irascible, strong and combative, short response time-delay, but response sustained for a relatively long time; in connection with fire, balanced with hot, and dry.

Much later, Pavlov (1952) theorized the four temperaments and conceived a modern theory of temperament. Studying conditioned reflexes, he hypothesized that certain properties of the central nervous system could explain individual differences such as speed, efficiency, accuracy, intensity, durability, and changeability of conditioned reflexes. These properties include *strength of excitation, strength of inhibition, the equilibrium of nervous processes,*

and their *mobility*. The combination of these properties constitutes nervous system types regarded as the physiological equivalent of temperament (Windholz, 1987).

After examining Pavlov's theory of higher nervous activity, with special reference to the typology of the nervous system, Strelau (1983) transferred his concepts into psychological constructs (traits) measured by the *Strelau Temperament Inventory* (STI) and by the *Pavlovian Temperament Survey* (PTI). In his *regulative temperament theory*, Strelau showed that temperament could have an impact on behavior independently from personality. For Strelau (1983) the biological basis of temperament is regarded as corresponding to neurobiochemical individuality. The different configuration of a diversity of biological mechanisms may determine different traits thus underlining individual differences (see Figure 1).

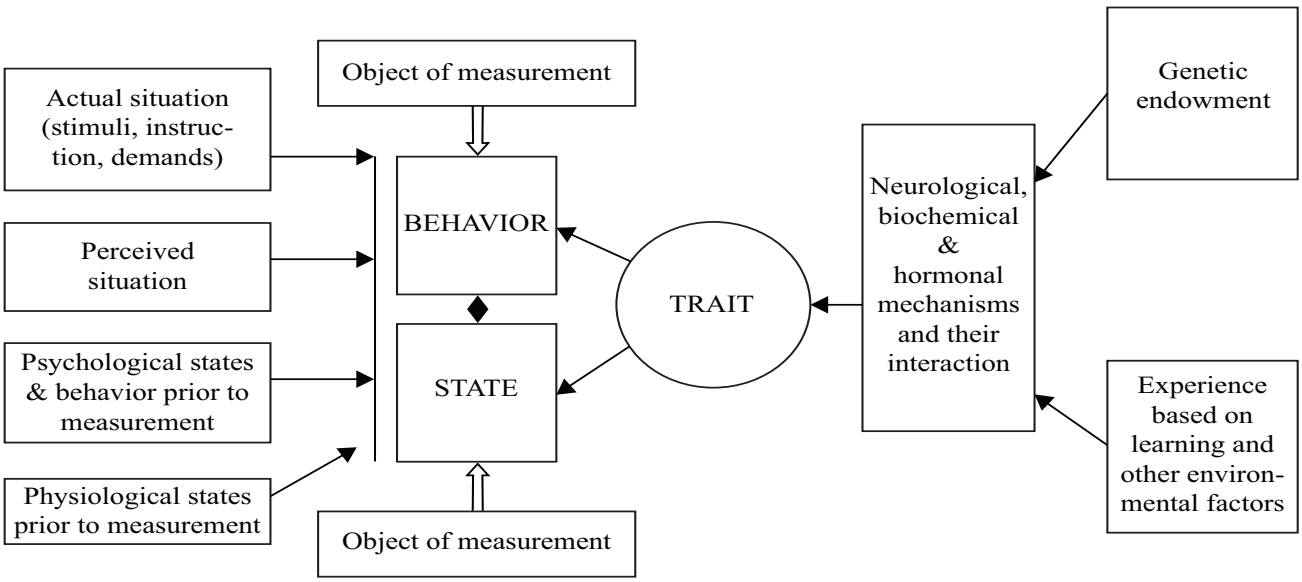

Figure 1. Theoretical status of temperament traits (Strelau, 2001). The hypothetical status of temperament traits includes determinants and ways of expression as well as variables, which mask, hamper or modify these expressions, and what we are measuring when we assess these traits.

Several authors investigated the relationship between the central nervous system's properties and temperamental traits or biologically determined personality. Among them, *Eysenc*k (1966) provided a detailed theory of the causes of personality. He conceptualized personality as three biologically based traits of temperament: *Extraversion, Neuroticism,* and *Psychoticism* (Eysenck & Eysenck, 1985). Neurotic behaviors are acquired but "unsuitable" and Eysenck offered a two-dimensional system aiming at distinguishing the various neurotic disorders. The first dimension opposes *Extraversion* to *Introversion*, while the second dimension opposes *Stability* to *Emotional Instability* (see Figure 2).

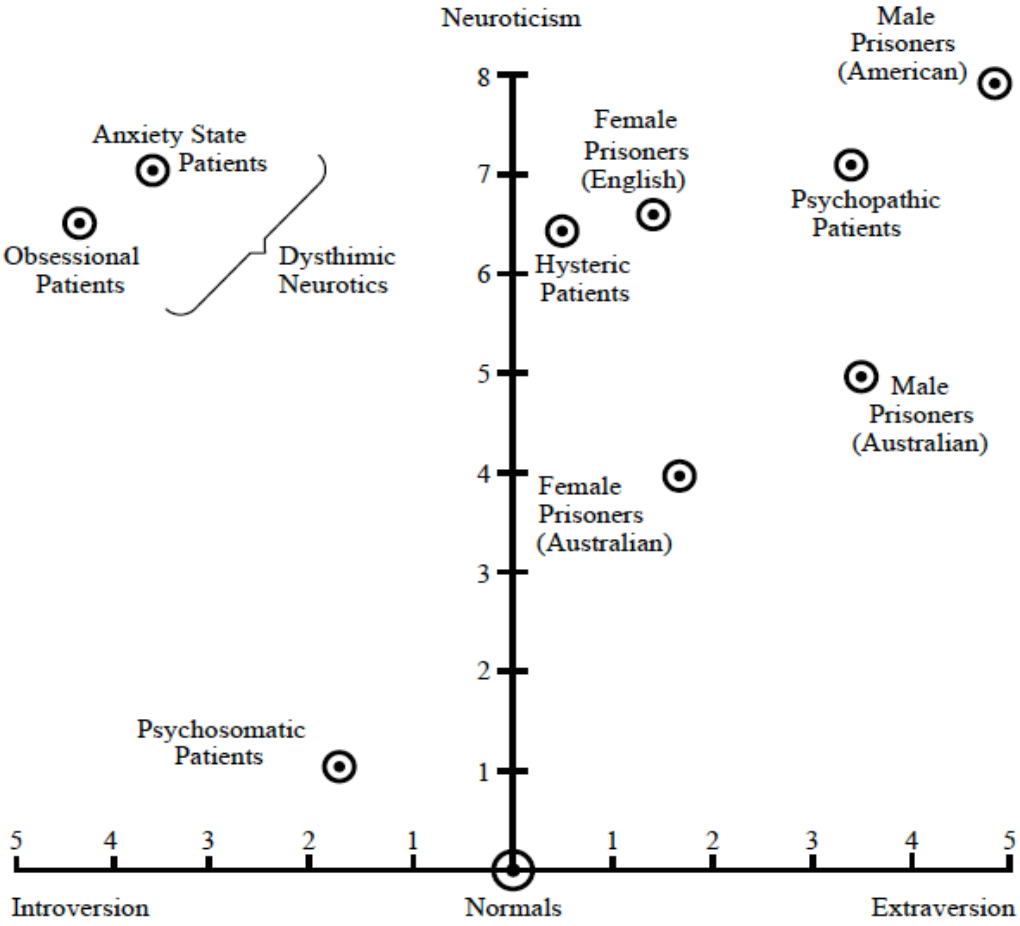

Figure 2. Organizational model of personality by Eysenck (1970). Extraversion vs introversion and neuroticism vs. emotional stability (normals) are the two main dimensions that define the direction of scale. On this scale, different secondary traits can take a certain value. Top left: dysthymia, anxiety, obsessional dependence (personality disorder, learning problems = neurotic disorders). Top right: hysteria, psychosis, antisocial personality (conduct disorder, learning process failure = psychotic disorders). Neuroticism: low threshold. Normal: high threshold.

According to Eysenck's arousal theory (1970), there is an optimal level of cortical arousal, and performance deteriorates as one becomes more or less aroused than this optimal level. Thus, extraverts are chronically under-aroused and bored and are therefore in need of

external stimulation to bring them up to an optimal level of performance. They seek to heighten their arousal to a more favorable level by increased activity, social engagement, and other stimulation-seeking behavior. Conversely, introverts are chronically over-aroused and jittery and are therefore in need of peace and quiet to bring them up to an optimal level of performance. The introvert seeks lower levels of stimulation. *Neuroticism*, according to Eysenck's theory, is based on activation thresholds in the sympathetic nervous system or visceral brain. This part of the brain is responsible for the fight-or-flight response in the face of danger. Neurotic people, who have low activation thresholds, experience negative affect in the face of relatively minor stressors, are easily upset. Emotionally stable people, who have high activation thresholds, experience negative affect only in the face of major stressors; they are calm under pressure compared to emotionally unstable people. According to Eysenck and Eysenck (1991), a high scorer on *Psychoticism* shows a solitary person, often troublesome, sometimes cruel, unempathic, aggressive, who has unusual tastes. The physiological basis suggested by Eysenck for psychoticism is testosterone, with higher levels of psychoticism associated with higher levels of testosterone. This dimension overlaps with concepts such as schizoid and antisocial personality disorders within the psychiatric sphere. The *Eysenck Personality Questionnaire* (EPQ) is the standard test to measure an individual's level of extraversion (vs. introversion) and neuroticism. This questionnaire has evolved through several different versions, the latest being the *Eysenck Personality Questionnaire-Revised* (EPQR) (Eysenck & Eysenck, 1991). Eysenck's theory has theoretical and practical value because it specifies some of the biological mechanisms believed to underlie personality traits that have been posited to be risk factors for substance use. According to him personality structure and characteristics represent the individual's capacity to function in a mentally healthy or pathological way. Given its social basis, normality is probably best defined as conformity to behaviors and customs typical of an individual's reference group or culture.

Pathology would then refer to behaviors that are uncommon, irrelevant, or alien to the individual's reference group. Thus, every personality type is also a coping style, a structure through which psychopathology should be understood.

Other noteworthy biological theories were inspired by Eysenck's theory, such as those of Gray (1987), Cloninger (1987), or Zuckerman (1984). All these theories converge on the importance of impulsivity sometimes using different names such as impulsivity like behavioral approach (Gray), novelty seeking and reward dependence (Cloninger), and sensation seeking (Zuckerman).

The *reinforcement sensitivity theory,* formulated by Gray (1970), and then refined over a series of articles (Gray, 1981, 1991), characterizes three systems that underpin individual differences in personality and psychopathology. Each of these three systems is assumed to correspond to a circumscribed set of neural pathways. First, the *Behavioral Approach System* (BAS) motivates behaviors that are intended to seek rewards. When this system is activated, individuals crave excitement, demonstrate remarkable persistence, and feel especially elated when they attain rewards. As a consequence, individuals become very sensitive to potential rewards. Dopaminergic fibers ascending from both the substantia nigra and ventral tegmental area, to innervate the basal ganglia, together with motor, sensorimotor, and prefrontal cortices, are assumed to underpin this system (Pickering & Gray, 1999). Second, the *Fight-Flight System* (FFS) motivates behaviors that are intended to avoid or escape aversive stimuli, often manifested as fear and panic. The periaqueductal grey, medial hypothalamus, amygdala, anterior cingulate, and prefrontal ventral stream are purported to underpin this system (Corr, 2004). Finally, the *Behavioral Inhibition System* (BIS) resolves conflicts among competing goals. When this system is activated, prepotent responses are inhibited, arousal rises, anxiety is experienced, and risks are assessed. The periaqueductal grey, medial hypothalamus, amygdala, septo-hippocampal system, posterior cingulated, and

prefrontal dorsal stream are supposed to underpin this system (Gray & McNaughton, 2000). Gray provided relations between the dimensions of personality and emotions. Thus, he argued that the interaction between BIS and BAS underlies Eysenck's extraversion and neuroticism factors, high BAS subjects being neurotic extraverts, and low BAS subjects stable introverts (Gray, 1970). Several BIS and BAS scales have been put forward, such as Carver & White's (1994).

Cloninger's theory of personality (1987) is based on a synthesis of information from family studies, studies of longitudinal development, and psychometric studies of personality structure as well as neuropharmacologic and neuroanatomical studies of behavioral conditioning and learning in human and animals. His revised biosocial model of personality posits seven domains of personality as measured by the *Temperament and Character Inventory* (TCI) (Cloninger, Przybeck, Svrakic, & Wetzel, 1994). The *temperaments* are genetically determined and are associated with specific biological variables. Specifically, temperament was conceptualized as corresponding to heritable biases in memory processing involved in presemantic perceptual processing and encoding of concrete visuospatial structural information and affective valence. These processes were hypothesized to be functionally organized as independently varying brain systems aligned to specific monoaminergic cell bodies which in turn are responsible for autonomic responses involved in the activation, maintenance, and inhibition of behavior (such as differences in classical conditioning, operant conditioning, and non-associative learning, i.e. sensitization and habituation (Cloninger et al., 1994). There are four temperaments*: novelty seeking* (activation), *avoidance of danger* (inhibition), *reward dependence* and *persistence* (maintenance). *Novelty seeking*, *harm avoidance* traits appear on conceptual grounds to be nearly equivalent to Gray's BAS, whereas the *reward dependence* appears to be nearly equivalent to Gray's BIS (Carver & White, 1994; Mardaga & Hansenne, 2007). The

characters correspond to learning and environmental effects and there are three of them: the *self-determination* (individual maturity), *cooperation* (social maturity), and *transcendence* (spiritual maturity). These dimensions were based on a synthesis of information about social and cognitive development and description of personality development in humanistic and transpersonal psychology (Cloninger et al., 1994). Specifically, the scales were designed to measure conceptual memory biases involved in the processing or conversion of sensory input into abstract symbols which translate into concepts of personal, social, and universal identity. *Self-determination* measures individual self-acceptance, *cooperativeness* measures acceptance of other people, while *self-transcendence* captures the degree to which an individual feels a part of nature and the universe at large. According to Cloninger's model, individuals with mature personalities are described as self-reliant, cooperative, and self-transcendent, in contrast to individuals with personality disorders who are troubled with self-acceptance, are intolerant or revengeful towards others and are unfulfilled (Cloninger, Svrakic, & Przybeck, 1993). Cloninger has stressed that the temperament and character domains, although distinct, are part of an "iterative epigenetic process" whereby each one interacts with the other in motivating behavior (Cloninger et al., 1993).

The TCI or the revised TCI (TCI-R) is a questionnaire of 226 items that has been used in several studies. Each temperament and character dimension has demonstrated good test-retest correlations irrespective of the sampled population (Cloninger et al., 1994). Recently, Rigozzi and Rossier (2004) using a short form for the TCI (TCI-56) in a study on smokers, a short form showing good psychometric proprieties and that seems to be valid and useful tool to assess personality differences. Confirming the results of others about the relation between addiction and personality, they found that smokers have significantly higher scores on *novelty seeking*, than non-smokers. Cloninger's model of personality was also successfully applied to describe clinic groups and, in particular, personality disorders.

In the early 1990s, Zuckerman reviewed the three factors proposed by Eysenck and developed *a monoaminergic and hormonal regulation model* that played an important role in personality research. More recently, he proposed an Alternative Five-Factor Model (AFFM), which was developed as the result of an attempt to define basic factors of personality of temperament (Zuckerman, Kuhlman, Teta, Joireman, & Kraft, 1993). Zuckerman conceived personality as a hierarchical structure where the features are grouped into super-traits. This Alternative of Five-Factor Model of personality is based on the claim that the structure of human personality traits is best explained by five broad factors called *impulsive sensation seeking*, *neuroticism-anxiety*, *aggression-hostility*, *sociability*, and *activity.* The model is based on the assumption that "basic" personality traits are those with a strong biological-evolutionary basis. Markers of "culture", "intellect", and "openness" were deliberately excluded on the basis that these traits are not present in non-human species. Zuckerman's theory rests on the assumption that there is an optimal level of arousal. According to his theory, the *sensation-seeking* trait is characterized by the "continuing necessity to experiment various, novel, and complex sensations" (Zuckerman, 1994). Sensation-seeking has been associated with all three groups of traits (impulsivity, aggression, and reward-seeking) related to three specific monoamine neurotransmitters, dopamine, neuropinephrine, and serotonin (Benjamin, Li, Patterson, Greenberg, Murphy, & Hamer, 1996). Sensation-seeking individuals tend to engage in behaviors that increase the amount of stimulation they experience. Such behaviors (e.g. interest in stimulating occupations, drug use, driving recklessly, etc.) involve seeking out arousal seeking. The activities to fulfill the preferred arousal vary in the amount of risk associated with them. Risk-taking is a correlate of sensation seeking but is not a primary motive in behavior. Sensation-seekers accept risk as a possible outcome of obtaining this arousal, yet do not seek out risk for its own sake (Zuckerman, 1994). The explanation is based on a model influenced by genetic, biological,

psychophysiological, and social factors, which influence certain behaviors, attitudes, and preferences (Zuckerman, 1991, 1994; Zuckerman & Cloninger, 1996).

He developed a questionnaire consisting in 99 true-false items *(Zuckerman-Kuhlman Personality Questionnaire* (ZKPQ, Zuckerman, 1991). Recently, a revised version of the AFFM and of the questionnaire was brought forward considering five slightly different main dimensions, each including four facets (Aluja, Kuhlman, & Zuckerman, 2010):

- *Aggression* includes physical aggression, verbal aggression, anger, and hostility;
- *Activity* includes work compulsion, general activity, restlessness, and work energy;
- *Extraversion* includes positive emotions, social warmth, exhibition, sociability;
- *Neuroticism* is composed of anxiety, depression, dependency, and low self-esteem.
- *Sensation seeking* includes thrill and adventure seeking, experience seeking, disinhibition, boredom, susceptibility or impulsivity.

Zuckerman and colleagues (1993) compared models with three to seven different factors. They found that both three and five factor solutions were acceptable, but argued that the five-factor solution was preferable due to greater specificity. The factors in the AFFM correspond to traits in Eysenck's three-factor model, and to four of the five traits in the Five-factor model. *Neuroticism-Anxiety* is basically identical to *Neuroticism*, while *Sociability* is very similar to *Extraversion* in Eysenck's model and five factor models. *Impulsive sensation seeking* is positively correlated with *Psychoticism* from Eysenck's model, and negatively with *Conscientiousness* in the Five-Factor Model. *Aggression-Hostility* is inversely related to *Agreeableness* in the Five-Factor Model. Zuckerman and colleagues noted that *Activity* is subsumed under *Extraversion* in some models of personality but argued that it should be

considered an independent dimension of temperament that is distinct from sociability. A later study (Aluja et al., 2003) comparing Zuckerman's model with the Five-Factor model using factor analysis found that *Activity, Sociability,* and *Extraversion* all loaded onto a single factor, suggesting that *Activity* and *Extraversion* are closely related. Zuckerman shows that particularly anxious people seem excessively excited and try to use behaviors and sometimes drugs to reduce their excitement. Other individuals seem to increase the excitement and search for sensations. As a result of his research on personality, Zuckerman (2002) observed that the link between personality and behavior is not linear and a relative stability depends on individual (history and biology) and environmental characteristics.

1.1.6. Personality traits

The personality traits approach assumes that human personality consists of predispositions (traits) that are expressed in a relatively stable way in a variety of situations and across time. Personality traits comprise a person's manner of thinking, feeling, perceiving, and relating to others. These traits have been evident since late childhood or adolescence and include what is unique about us and what we share with others. Over time, many studies have identified and assessed the main features of personality. So, from Allport (1937), Cattell (1950), Eysenck (1953) to the Big Five, traits are generally viewed as broad dimensions desribing individual differences and explicating interindividual consistency and continuity in behaviour, thought and feeling across situations and over time. The concept of personality traits has been refined and the language used to describe psychological traits has become more precise across autors and time. Thus, the trait theory has led to the development of a universal framework, used by various branches of personality psychology.

Historically, Allport (1937) was among the first prominent theorists that take the individual human being as the scientific unit analysis and assert the importance of *personality traits* as a theoretical concept. According to him (Allport, 1961), personality is the dynamic

organization within the individual of psychophysical systems that determine one's characteristic behaviors and thoughts. While recognizing that certain features are common to all individuals, others are much more specific, such as personal dispositions. His idiographic approach implied that individuals do not necessarily act the same in different contexts and it is not always possible to generalize from the behavior of individuals. Every individual is unique in a specific configuration of features. He defines six criteria for a mature personality: autonomy, warm relationship with others, frustration tolerance, realistic perceptions and skills, insight and humor, and self-determination. One of his early projects was to go through the dictionary and locate every term that he thought could describe a person. From this, he developed a list of 4,500 words referring to traits. This is similar to Goldberg's (1981) fundamental lexical hypothesis, or the hypothesis that, over time, humans develop widely used, generic terms for individual differences in their daily interactions. Allport reasoned that certain traits are more significant to one person than to another. He therefore divided traits into three levels: 1. *Cardinal trait*: this is the trait that dominates and shapes a person's behavior. These are the ruling passions, obsessions, such as a need for money, fame, etc. Only few people possess a cardinal trait but for those who do, this trait may be the ruling of the their personality. 2. *Central trait*: this is a general characteristic found to some degree in every person. These are the basic building blocks that shape most of our behavior although they are not as overwhelming as cardinal traits. An example of a central trait would be honesty. 3. *Secondary trait*: these are characteristics seen only in certain circumstances (Allport, 1931). Moreover, other people may not notice secondary traits unless they are very close acquaintances. They must be included to provide a complete picture of human complexity. Allport believed that by describing a person we could learn about him or her. To describe personality, traits may be very useful, but when explaining a person's behavior and

motivations, other theories come to complete this description. Allport's theory was one of the first humanistic theories, which later influenced many other authors.

Then, Cattell (1950) defined personality as the tendency to predict a person's behavior in a given situation. Stemming from the observation-based theory of traits, Cattell was interested in personality according to a mainly *factorial* and *lexical approach.* The lexical hypothesis rests on the assumption of the existence of a correspondence between descriptors (traits) of personality and adjectives of language to describe individuals. Using factor analysis, he concluded that the basic dimensions of personality are common to all individuals. Features, according to Cattell, are permanent entities that are inherited and which develop throughout an individual's life. Adopting the lexical approach and using factor analysis, Cattell (1947) identified 35 features (see Table 1), which are grouped into 16 surface features, and that gathered later in 5 original features (or of second order). Thus, behavior can be hierarchically organized and is quantifiable as a result. Initially, Cattell was particularly interested in describing concrete behaviors or traits. Only later did he try to combine traits into global scales to describe the structure of personality. The *Cattell's Sixteen Personality Factor Questionnaire* (16PF) describes 16 specific traits combined to enable a prediction of the behavior with multiple variations. This questionnaire was revised many times, and the latest edition (Cattell et al., 1993) comprises 185 items. To build this scale, Cattell adopted a hierarchical approach of personality, ranging from specific to general traits. This hierarchical structure was an *a posteriori approach,* using the *bottom-up method,* compared to other instruments that emerged later, and that followed the *top-down* method, such as the EPI, or NEO-Personality Inventory. These later instruments tried, first of all, to define the main dimensions, and only later were they able to identify subscales. The hierarchical structure was, for them, an *a priori way* of describing personality (Rossier, Meyer de Stadelhofen, & Berthoud, 2004).

Table 1. Cattell's (1947) 35 variables

Name of Bipolar Trait	
1. Ready to cooperate vs Obstructive	19. Hard, stern vs Kindly, soft-hearted
2. Emotionally stable vs Changeable	20. Insistently orderly vs Relaxed, indolent
3. Attention-getting vs Self-sufficient	21. Polished vs Clumsy, awkward
4. Assertive, self-assured vs Submissive	22. Prone to jealousy vs Not prone to jealousy
5. Depressed, solemn vs Cheerful	23. Rigid vs Adaptable
6. Frivolous vs Responsible	24. Demanding, impatient vs Emotionally mature
7. Attentive to people vs Cool, aloof	25. Unconventional, eccentric vs Conventional
8. Easily upset vs Unshakable, poised, tough	26. Placid vs Worrying, anxious
9. Languid, slow vs Energetic, alert	27. Conscientious vs. Somewhat unscrupulous
10. Boorish vs Intellectual, cultured	28. Composed vs Shy, bashful
11. Suspicious vs Trustful	29. Sensitively imaginative vs Pratical, logical
12. Good-natured, easygoing vs Spiteful, grasping, critical	30. Neurotic fatigue vs Absence of neurotic fatigue
13. Calm, phlegmatic vs Emotional	31. Esthetically fastidious vs Lacking artistic feeling
14. Hypochondriac vs Not so	32. Marked interest in opp. sex vs. Slight interest in opp. sex
15. Mild, self-effacing vs Self-willed, egoistic	33. Frank, expressive vs Secretive, reserved
16. Silent, introspective vs Talkative	34. Gregarious, sociable vs. Self-contained
17. Persevering, determined vs Quitting, fickle	35. Dependent, immature vs Independent-minded
18.Cautious, retiring, timid vs Bold, adventurous	

Note. Adapted from De Raad (2000).

1.1.7. Controversy about the respective importance of context vs. traits

Personality traits are individual differences on how to think, feel or behave. These traits are conceived as bipolar linear dimensions that capture general and stable dispositions of personality. However, the psychologists have disagreed about the technical nature of traits. So, there those who argue that traits are neuropsychic structures that exert a causal influence on the behavior of individual and those who suggest that traits are cognitive categories used

by observers to make sense of social life (McAdams, 2001). In other words, traits were hypothesized to exist within the person rather than the observable public sphere. Unlike behavior, traits could not be directly observed. To solve this dilemma, a number of personality and social psychologists was launched the person-situation debate. Therefore, the period of 1970-1980s is crossed by controversy about the importance of context vs. traits. The most important critique was that of Mischel (1968, 1973) that would shape a good deal of thinking in personality psychology today. While the concept of trait impliess some degree of cross-situational consistency in behavior, Mischel argued that human behavior is much more situationally specific than the concept of trait would suggest. According to social-learning theory, he maintained that behavior is shaped by the exigencies of a given context. Especially, he believes that the special meaning of a situation, a reward, or purpose largely determines the behavior of individuals. Supporters of Mischel's position (Mischel, 1977; Shweder & D'Andrade, 1979) brought data to buttress their "situationist" claims, often invoking finding from social psychology documenting the influence of situations on behaviour. They sustain that situation rather than traits drive and shape human behaviour, a fact that is clearest to see under well-controlled conditions of the laboratory experiment. Observed behavioral differences among persons in the same situation are small, unimportant, or the result of errors of biases on the part of observers, or methods of measurement. According to the dispositional approach, personality is a structured system of conducts (cognitions, emotions, and behaviors) that exhibit intra-individual consistency, temporal stability, and relative cross-situational consistency (Rolland, 2004). Mischel (1973) rejects cross-situational consistency, but accepts the temporal stability. He indicates that trait labels exist more in the minds of observers than in the actual personality of the person being observed, suggesting that may tell us more about how people think about other people's behaviour than they tell us about behavior itself. Thus, traits are convenient categories for our perceptions rather than real characteristics of the

person we perceive. Mischel argued that broad traits are mainly stereotypes in the minds of observers rather than dynamic forces in the lives of actors, that human behavior is situationaly specific than cross-situationally consistent, and that scores on traits scales are weak predictors of what people will actually do in particular situations. Furthermore, reviewing literature on such personality variables as honestity, dependency, aggression, rigidity, attitudes toward authority, Mischel (1977) showed that the correalations between personality-traits scores and actual behavior in a particular situation were generally low. This can suggests that trait scores fail to predict what a person will do in particular situations. However, defenders of traits (such as Block, 1977; Hogan, DeSoto, & Solano, 1977) argued that Mischel had i) misrepresented many trait theories and trait theorists; ii) selectively reviewed the empirical literature in an unfair way, and iii) overlooked many methodologically sophisticated studies that supported cross-situational consistency of behavior and the inner coherence of personality (McAdams, 2001). In the aftermath of Mischel's critique and the person-situation debate, many personality psychologists created the interactionist approach, a compromise position, which postulated that the behaviour is function of the person (and his or her traits) in interaction with the environment (Maddi, 1984; Krahe, 1992). This approach that "reconciles" the dispositional and situational views of personality (Shoda & Mischel, 1995) postulated that the inter-individual differences result of the encoding process, expectations, and self-regulatory processes. Mischel's critique and person-situation debate stimulated thought and research in the field of personality psychology. Therefore, after 1980s studies were developed to examine the longitudinal stability of traits over the life course, the origins of traits in genetic differences and environmental effects, the psychobiological underpinnings of traits. Although the critiques launced against the trait concept raised important issues in the field and helped to produce important advances (Kenrich & Funder, 1988) one of the big lessons learned from the person-situation debate was that personality psychology cannot get along without traits.

Not only did the concept of the trait survive the attaks, it emerged as stronger than ever before. The strong comeback stemmed from at least five major developments in the field of personality psychology. First, researchers conducted a number of studies showing that personality trait scores often do *predict* important differences in observed behavior at surprisingly strong statistical levels, especially when behavior is aggregated across different situations (Moskowitz, 1990). Although trait scores may prove to be but modest predictors of what a person will do in a single situation (laboratory-based) (Mischel & Peacke, 1982), traits generally work well in predicting behavioural trends across situations and over time (Costa & McCrae, 1997). They also prove to be robust predictors of important life outcomes like work performance and occupational success (Barrick & Mount, 1991), the quality of social relationships (Asendorpf & Wilpers, 1998), psychological well-being (Diener, Sandvik, Pavot, & Fujita, 1992), and even longevity (Friedman, Tucker, Tomlinson-Keasy, Schwartz, Wingard, & Criqui, 1993).

In addition, data from a number of longitudinal studies were published in the 1980s and 1990s showing long-term *stability* in individual differences for personality traits (Costa & McCrae, 1994; Roberts & Del Vecchio, 2000). Substantial continuity in trait scores has also been demonstrated between the childhood years and early adulthood (Caspi et al., 2003; Terracciano et al., 2005). Moreover, other studies showed substantial *heritability* for trait scores. Studies of twins have consistently produced heritability quotients around 50% for most personality traits (Bouchard, Lykken, McGue, Segal, & Tellegen, 1990). At least half of the variability in trait scores appears to be a result of genetic differences between people. Finally, research has begun to document links between certain traits and the functioning of the brain. Researchers have suggested that individual differences in *Extraversion,* for example, link up with a behavioral approach system (BAS) in the brain, a system conceptualized as regulating positive approach behavior, the pursuit of rewards and incentives, and positive

affect (Gray, 1987). Implicated in the complex functioning of the BAS are dopaminergic pathways in the brain (Depue, Luciana, Arbisi, Collins, & Leon, 1994), and the activation of the left frontal cortex (Sutton & Davidson, 1997). By contrast, *Neuroticism* may be associated with what has been called the behavioral inhibition system (BIS), conceptualized as regulating avoidance behavior and negative affectivity. The BIS may subsume certain aspects of the amigdala's functioning (Le Doux, 1996) and activation of the right frontal cortex. Although research on the neuroscience of traits is still in its infancy stage and results to date are still sketchy, there is every reason to believe that this area of study will yield many important findings in the coming years regarding the biological bases of basic personality traits. Therefore, the concept of personality traits seem to have emerged from the debate as a more powerful and useful concept than perhaps it has ever been before. It is hard today to imagine a personality psychology without traits. Nowadays, several theories and models of personality traits have emerged. Among them, the most influential and consensual is certainly the Five-Factor Model (FFM).

1.1.8. The Five-Factor Model of personality

The Five-Factor Model (FFM) posits that five independent dimensions can parsimoniously account for all personality traits. Although research on the FFM has become popular in the last two decades, the history of this approach can be traced back over 100 years to the work of Sir Francis Galton. Its history is grounded on what has come to be known as a lexical hypothesis (Goldberg, 1981, 1993). The basic premise of the lexical hypothesis is that all we need to know about personality is contained in natural languages. That is, the terms we commonly (and sometimes uncommonly) use to describe ourselves, and each other, contain all the information necessary to discern the fundamental dimensions of human personality. Then, also influenced by Allport, Cattell, and Eysenck's theories, the FFM provided an integrative descriptive model for personality research. Since the 1990s, there has been an

explosion of research with tools derived from the FFM and adapted in several languages and to different cultures. Although there continues to be disagreement about the number of dimensions necessary to account for all personality traits (Ashton, Lee, Perugini, Szarota, de Vries, & Di Blas, 2004; Eysenk, 1992; Goldberg, 1993), this model has been defended by several scientists (Costa & McCrae, 1985; 1990; Widiger, 2002; DeRaad, 1998; Digman, 1989; 1990). Research using the FFM has included studies of diverse populations (McCrae, Costa, del Pilar, Rolland, & Parker, 1998), often followed over decades (Costa & McCrae, 1992), employed multiple tools of assessment (Funder, Kolar, & Blackman, 1995), and case studies (Costa & McCrae, 1998). Some researchers indicate that the five dimensions of personality could have a biological base (McCrae, Jang, Livesley, Riemann, & Angleitner, 2001), may be generalized across several cultures (McCrae & Costa, 1997), be relatively gender invariant (Costa, Terracciano, & McCrae, 2001), and remain relatively stable across age, especially in middle and old age (Costa, Herbst, McCrae, & Siegler, 2000; McCrae, & Costa, 2006). In other words, the FFM is "the Christmas tree on which findings of stability, heritability, consensual validation, cross-cultural invariance, and predictive utility are hung like ornaments" (Costa & McCrae, 1993).

The FFM consists of the following bipolar trait dimensions: *Neuroticism* vs. *Emotional Stability, Extraversion* vs. *Introversion, Openness to experience* vs. *Closedness to experience, Agreeableness* vs. *Antagonism,* and *Conscientiousness* vs. *Negligence* (Costa & McCrae, 1990). Each of these broad dimensions includes six facets or lower-order traits (Digman, 1990; McCrae & Costa, 1999; De Raad, 2002). These five dimensions used to group 30 facets or traits (see Table 2):

Neuroticism is characterized by the tendency to experience distress and frequent negative emotions such as fear, anxiety, shyness, loss of control in difficult situations, sadness, depression, anger, and hostility (Costa & McCrae, 1992). People who *score low* in

this domain are usually characterized by emotional stability; they are relaxed most of the time, rarely get upset, and remain calm in stressful or dangerous situations; they do not worry about things that may happen in the future, and generally feel secure and self-satisfied. Individuals with *high scores* in this domain regularly present negative affects, a sense of insecurity, and self-awareness, are vulnerable to stress, sensitive to criticism and to failure. In the clinical situation, there is strong evidence for the relevance of Neuroticism in the assessment of personality disorders (Schroeder, Wormsworth, & Livesley, 1992). Neuroticism correlates significantly with various measures of illness (Costa & Mc Crae, 1987). There is evidence that neuroticism is involved in processes described in illness behavior models (Larsen, 1992). It is a strong predictor of psychological distress (Ormel & Wohlfarth, 1991), it predicts both positive and negative moods, and it is associated with higher interests in social comparison and with less favorable reactions in cancer patients (Van der Zee, Buunk, & Sanderman, 1998). Neuroimaging studies have found that Neuroticism is associated with brain activity at rest or in response to aversive or novel stimuli in brain regions associated with negative affect, including the amygdala, insula, and anterior cingulate cortex (Deckersbach, Miller, Klibanski, Fischman, & Rauch, 2006). High Neuroticism has been associated with lower levels of serotonergic function and with higher levels of the stress hormone cortisol. This association is consistent with the importance of the hypothalamic-pituitary adrenalin axis in response to threat and other stressors (McEwen, 1998).

Extraversion is associated with sociability, dynamism and the propensity to experience positive emotions (Costa & McCrae, 1992). The *extroverts* are communicative, expansive, sociable, warm, cheerful, enthusiastic, love to be in a group and be the leader, active, easily bored in the absence of external stimuli and tend to seek excitement. Extraversion is positively correlated with self-esteem (Costa, McCrae, & Dye, 1991), and is related to various health-related behaviors (Scheier & Carver, 1987). For example, it predicts subjective well-

being at midlife (DeNeve & Cooper, 1998). *Introverts* are reserved, calm, and independent. They are usually shy when meeting new people, but this is not an indication that they suffer from social anxiety. They are not as enthusiastic as extraverts are which, however, does not mean that they are pessimistic or unhappy. Several brain-imaging studies have demonstrated that Extraversion is predictive of brain activity in cortical areas influenced by dopamine during working memory task (Gray & Braver, 2002; Gray, Burgess, Schaefer, Yarkoni, Larsen, & Braver, 2005). Extraversion may also be related to the ways in which individuals are motivated to perform difficult cognitive tasks and even to how those tasks are processed in the brain (DeYoung & Gray, 2009).

Openness to experience refers to the tendency to dream, to the intuitive perception of the feelings of others or oneself, the taste of intellectual activities, as well as openness, and tolerance of different ideas and values. Qualifications from lexical studies describe this factor using terms such as originality, imagination, broad interests, and boldness. McCrae and Costa (1996) suggest that individuals with a high level on this dimension are intellectually and aesthetically sensitive. *Open* people tend to be cognitively flexible, curious, imaginative, score higher on intelligence tests, and pursue higher levels of education (McCrae, 1994). People who *score low* on this domain are usually characterized by conformism, resistance to novelty, and conventionality. In organizational settings, Openness to experience has been associated with increased creative behavior (George & Zhou, 2001) and job performance (Bing & Lounsbury, 2000), and it was negatively related to level of salary (Seibert & Kraimer, 2001). In addition, Aitken (2004) provided evidence of the relevance of Openness to experience for intercultural social efficacy. In clinical situations, aspects of Openness to experience seem to be related to several disorders (Costa & Widiger, 1994) and to high-risk health behavior (Booth-Kewley & Vickers, 1994). Moreover, Openness correlate positively with brain regions linked to working memory and attention (Sutin, Beason-Held, Resnick, &

Costa, 2009); the two executive functions have been consistently linked to fluid intelligence, the ability to solve novel problems (Gray & Thompson, 2004). However, Openness to experience is conceptually totally different from the construct of "intelligence" (McCrae & Costa, 1997). The neuropsychological model of Openness (DeYoung, 2006) implicates the dopaminergic system, specifically projections to the prefrontal cortex and the anterior cingulate cortex.

Agreeableness relates mainly to the attitude in interpersonal relationships and is the ability to easily get along with and trust others. Individuals whose level is *high* in Agreeableness are soft, gentle, friendly, pleasant, and have a tender heart (McCrae & Costa, 1987). Agreeable people are less likely to engage in risky health behaviors and are more optimistic about their future health risk (Vollrath, Knoch, & Kassano, 1999). These persons select tactics that minimize disruption during conflict episodes, and they continue to talk more with their conflict partners after conflict (Jensen-Campbell & Graziano, 2001). People who *score low* in this domain are usually characterized by intransigence, direct expression of disagreement, criticism. Agreeableness appears to reflect a tendency toward the maintenance of social stability, encompassing traits reflecting pro-sociality vs. anti-sociality: compassion, politeness, a general tendency to be interested in and considerate of the needs, desires and feelings of others and to refrain from aggressing or imposing one's will on others. In the interpersonal domain there are several correlates of Agreeableness, including more elevated ratings of peer performance on group exercises (Bernardin, Cooke, & Villanova, 2000), or interpersonal skills in teams (Neuman & Wright, 1999). Several fMRI studies using trait measures of empathy have reported findings that are directly relevant to the link between agreeableness and social information processing. In these studies, empathy was positively associated with activity in the mirror neuron system (Gazzola, Aziz-Zadeh, & Keysers, 2006). Other brain regions, beyond those typically identified as involved in social information

processing, have also been associated with trait measures of empathy. For example, Chakrabarti & Baron-Cohen, 2006) demonstrated that viewing different emotional expressions led to correlations of empathy with activity in brain regions functionally relevant to specific emotions, in particular happiness with a stronger activation of the ventral striatal reward system in participants with a high level of empathy.

Conscientiousness refers to the capacity to plan ahead, to delay gratification, and work steadfastly toward attaining goals (Costa & McCrae, 1992). *Conscientious* individuals are focused, task-oriented, reliable, dependable, careful, well organized, punctual, ambitious, and persevering (McCrae & Costa, 1987). They are also characterized by a sense of competence along with organizational skills, self-discipline, anticipation, and reflection. Equally, *Conscientiousness* appears to reflect the tendency to maintain motivational stability within the individual, to make plans and carry them out in an organized manner. In other words, Conscientiousness may represent the manifestation in personality of the ability and tendency to constrain immediate impulses in favor of longer-term goals. Contrariwise, people who *score low* in this domain are little concerned by organization, method; they improvise, and are frivolous, irresponsible, undependable, and forgetful. Thus, Heaven (1996) reported *Conscientiousness* to be negatively related to vandalism, and Clower & Bothwell (2001) found *Conscientiousness* to be negatively related to inmate recidivism. When considering research on the biological basis, the findings show that serotonin is associated with *Conscientiousness* (Manuck, Flory, McCaffery, Matthews, Mann, & Muldoon, 1998). Another biological factor that may be related to *Conscientiousness* is glucose metabolism. Glucose represents the basic energy source for the brain, and a number of studies indicate that blood glucose is depleted by acts of self-control (Galliot & Baumeister, 2007). The prefrontal cortex seems likely to be involved, given the central role in planning and voluntary control of

behavior, and given that consumption of glucose appears relatively high (Galliot & Baumeister, 2007).

Table 2. Facet scales of each domain of the Five-Factor Model

Neuroticism vs. Emotional Stability	Extraversion vs. Introversion	Openness vs. Closedness	Agreeableness vs. Antagonism	Conscientiousness vs. Negligence
Anxiety (fearful vs. relaxed)	Warmth (affectionate vs. cold)	Fantasy (imaginative vs. practical)	Trust (gullible vs. suspicious)	Competence (efficient vs. negligent)
Hostility (angry vs. even-tempered)	Gregariousness (sociable vs. withdrawn)	Aesthetics (aesthetic vs. unaesthetic)	Straightforwardness (straightforward vs. deceptive)	Order (organized vs. disorganized)
Depression (pessimistic vs. optimistic)	Assertiveness (forceful vs. unassuming)	Feelings (emotionally responsive vs. unresponsive)	Altruism (sacrificial vs. exploitative)	Dutifulness (dutiful vs. lax)
Self-Conscientiousness (timid vs. self-assured)	Activity (active vs. passive)	Actions (novelty-seeking vs. set in ways)	Compliance (compliant vs. oppositional or aggressive)	Achievement-Striving (ambitious vs. aimless)
Impulsivity (reckless vs. controlled)	Excitement-Seeking (adventurous vs. cautious)	Ideas (curious vs. pragmatic)	Modesty (self-effacing vs. arrogant)	Self-Discipline (industrious vs. hedonistic)
Vulnerability (fragile vs. stalwart)	Positive Emotions (high-spirited vs. placid)	Values (broad-minded vs. dogmatic)	Tender-Mindedness (sympathetic or empathic vs. tough)	Deliberation (thorough vs. careless)

Note. Illustrative trait adjectives associated with each facet are presented in parentheses (Adapted from Costa & McCrae, 1995).

The authors of the FFM (Costa & McCrae, 1992) argue that their model is a general framework for understanding personality and may guide research and gives a comprehensive representation of the differences in behavior, attitudes, and reactions that exist between

individuals. They advance four arguments in favor of this model. First, longitudinal studies conducted by several researchers showed that the five factors are real features that *occur specifically in certain situations*. Second, words or wordings related to the five factors are found in *everyday language* and in the main personality questionnaires. Third, the factors are found in different *cultures* and are *not influenced significantly by age and sex.* In keeping with this idea*, Neuroticism, Extraversion, and Openness to experiences* have all been reported to negatively correlate with age, while *Agreeableness* and *Conscientiousness* was related positively with age (McCrae & Costa, 2003). For example, college participants score half a standard deviation lower than adult participants (Costa & McCrae, 1994). Additionally, Roberts, Walton, & Viechtbauer (2006), examining standardized mean-level change over time, found significant increases up until the age of 60 for *Agreeableness, Conscientiousness,* and *Emotional Stability.* But these *changes do not signify any radical shift in personality* (Terracciano, Costa, & McCrae, 2006). Concerning gender, women have a higher level in Neuroticism and Agreeableness than men (Costa, Terracciano, & McCrae, 2001). Finally, they have a *biological basis*. The findings demonstrated that resilience is partly *heritable and that protective processes* operate through both *genetic and environmental effects* (Kim-Cohen, Moffitt, Caspi, & Taylor, 2004). It is known that *temperament* is a unique contributor to personality that forms the basis of the argument supporting *personality stability* (McCrae, 2000). The fact that temperaments observed at birth can be identified later in life, suggests that the extent of personality changes over the lifespan are limited (Shiner, 1998), and are due to intrinsic maturation, rather than environmental influences (McCrae et al., 2002; Teracciano, Costa, & McCrae, 2006). Therefore, the FFM is considered to be universal (Costa & McCrae, 1997) and this universality is observed through cross-observer agreement (McCrae, Costa, Hrebickova, Urbanek, & Martin, 2004). The validity of this model has been assessed mainly with adults but also with adolescents and children (Caspi, 2000; Kim-Cohen,

Moffitt, Caspi, & Taylor, 2004). Thus, consistent with other research, the study on children exposed to socioeconomic deprivation showed that maternal warmth, stimulating activities, and children's outgoing temperament appeared to promote positive adjustment in these children. Many studies of personality employing measures of the FFM argued that individuals could be characterized in terms of relatively enduring patterns of thoughts, feelings, and actions (McCrae & John, 1992). Therefore, this model postulates that five dimensions allow for an appropriate, economic and synthetic personality description.

1.1.9. The Five-Factor Theory of personality

According to the Five-Factor Theory (FFT) (McCrae & Costa, 1999), dimensions of the FFM are biologically rooted dispositions pointing to evidence that these dimensions and their structure are partly heritable (McCrae, Jang, Livesley, Riemann, & Angleitner, 2001). Figure 4 points to evidence that the dimensions of personality develop through the interaction of *biological (genetic)* with *environmental factors* (cultural norms, situations of life) giving rise to *observable behaviors* or *emotional reactions*. Between external influences and biological basis is a retroaction. It should be noted that there is no linear link between *traits* and *behavioral expression*, but a series of dynamic regulation processes (called *characteristic adaptations*) are involved. In other words, all our reactions are multi-determined by the environment and personality. An individual fixes goals and projects that allow him to organize his long-term action consistently with his personality traits. *External influences* in relationships with cultural norms, situations etc. interact with personality traits to shape, through dynamic processes, *characteristic adaptations*. Each individual adapts according to his or her knowledge and functions or mechanisms that are both universal and dynamic such as memory, attention, intelligence, and these mechanisms are influenced partially by personality. Although the role of the *self-concept* component of this scheme should be questioned, the FFT provides a framework for understanding the development and operation

of psychological mechanisms, behavior, and an individual's experience. Figure 3 can be interpreted cross-sectionally as a diagram of how personality operates at any given time, and also longitudinally to indicate personality development (in basic tendencies and characteristic adaptations) and the evolution of the life course (objective biography).

A synthesis of Cattell's and Eysenck's theories according to the nomothetic approach, the FFT showed that traits and dimensions, as described in the FFM, are present in all individuals, and are subject to a broad consensus. The nomothetic approach opposes the situational approach (the situation determines a behavior) relative to the idiographic perspective that stems from the idea that each and every single person has different traits. The FFT explains personality functioning as a universal personality system with defined categories of variables and classes of dynamic processes.

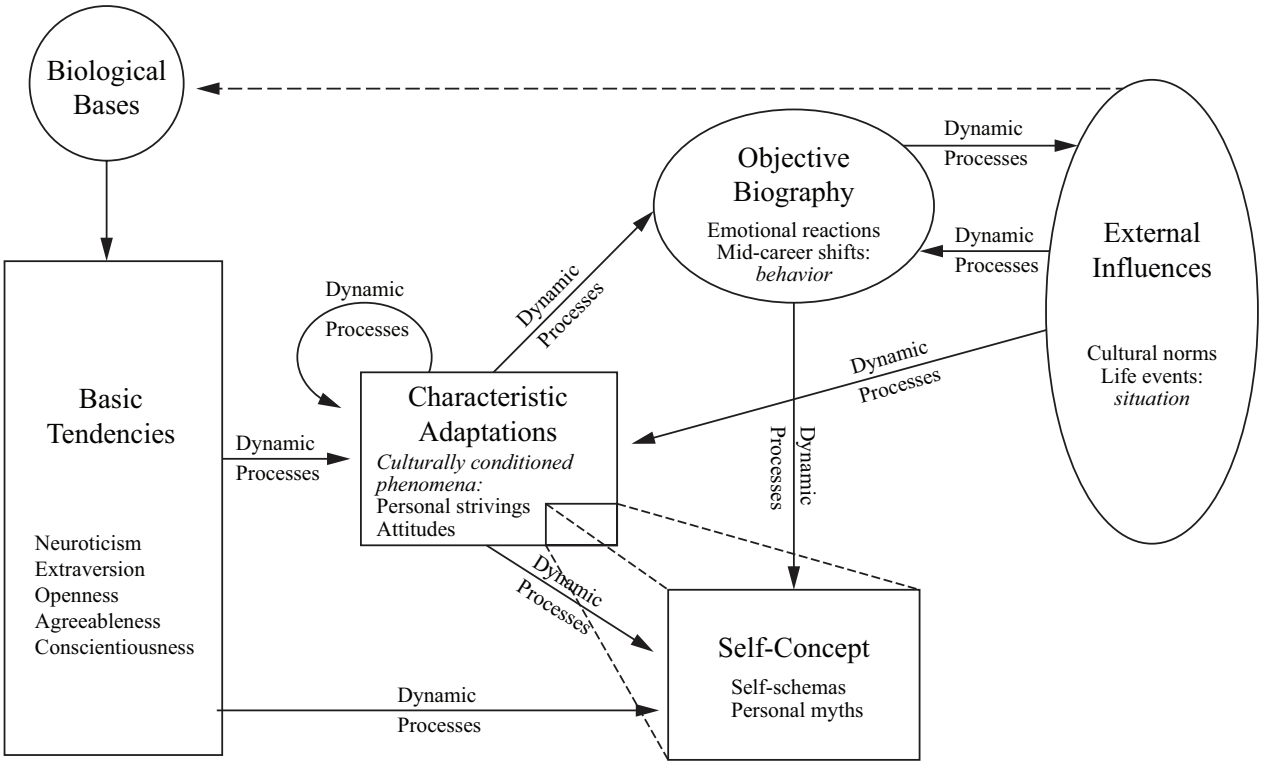

Figure 3. A representation of the Five-Factor Theory personality system according to the schema published by McCrae & Costa (1996).

1.2. Personality disorders

Personality disorders are a class of personality types and enduring behaviors associated with significant distress or disability, which appear to deviate from social expectations particularly in relation to human interaction. These disorders are included as mental disorders on Axis II of the diagnostic manual of the American Psychiatric Association and in the mental and behavioral disorders section of the ICD manual of the World Health Organization (WHO, 1993). According to DSM-IV-TR (2000), personality disorders are defined as distinct categories and enduring personality changes. They are described as ingrained patterns of inflexible and disabling responses that significantly differ from how the average person in a given culture perceives, thinks and feels, particularly in relation to others. The specific personality disorders are included in three clusters.

Cluster A (eccentric disorders) includes:

- *Paranoid personality disorder* that is characterized by irrational suspicions and mistrust of others;
- *Schizoid personality disorder* that is defined as a lack of interest in social relationships (these subjects see no point in sharing time with others), anhedonia, and introspection;
- *Schizotypal personality disorder* that is characterized by odd behavior or thinking.

Cluster B (dramatic, emotional or erratic disorders) includes:

- *Antisocial personality disorder* that is described as a pervasive disregard for the rights of others, lack of empathy, and (generally) a pattern of regular criminal activity;
- *Borderline personality disorder* that signifies extreme “black and white” thinking, instability in relationships, self-image, identity and behavior often leading to self-harm and impulsivity;

- *Histrionic personality disorder* that includes pervasive attention-seeking behavior including inappropriately seductive behavior and shallow or exaggerated emotions;
- *Narcissistic personality disorder* that is defined as a pervasive pattern of grandiosity, need for admiration, and lack of empathy. These people are characterized by self-importance, preoccupations with fantasies or beliefs that are special, including a sense of entitlement and a need for excessive admiration, and extreme levels of jealousy and arrogance.

Cluster C (anxious or fearful disorders) includes:

- *Avoidant personality disorder* that is characterized by pervasive feelings of social inhibition and social inadequacy, extreme sensitivity to negative evaluation and avoidance of social interaction;
- *Dependent personality disorder* that involves pervasive psychological dependence on other people;
- *Obsessive-compulsive personality disorder* (not the same as obsessive-compulsive disorder) that is characterized by rigid conformity to rules, moral codes, and excessive orderliness.

Of course, alternative categorization of personality disorders may exist and current classifications are bound to evolve, possibly including mixtures of different categories or dimensions.

The DSM-5 proposes a hybrid model, which incorporates both pathological symptoms and maladaptive traits combining into six specific personality disorders (antisocial, avoidant, borderline, narcissistic, obsessive-compulsive, and schizotypal). Unrelated to DSM-5, Widiger and Simonsen (2005) proposed a four-dimensional model, consisting of *Extraversion* vs. *Introversion, Antagonism* vs. *Compliance, Constraint* vs. *Impulsivity*, and *Emotional*

dysregulation vs. *Emotional stability*. These dimensions were based on extensive literature, showing robust associations between four higher order factors of the Five-Factor Model (Samuel & Widiger, 2008; Widiger & Trull, 2007) and similar models (Watson, Clark, & Harkness, 1994; Widiger & Simonsen, 2005) with personality pathology: *Introversion* (similar to *detachmen*t), *Antagonism*, *Emotional dysregulation* (*negative emotionality*), and *Impulsivity (disinhibition)*. The *Personality Inventory for the DSM-5* (PID-5) (Wright, Thomas, Hopwood, Markon, Pincus, & Krueger, 2012; Hopwood, Thomas, Markon, Wright, & Krueger, 2012), a 220-item questionnaire with a 4-point response scale (0, *Very false* or *often false*, to 3, *Very true* or *often true*), was used to measure the proposed *DSM-5* traits. The dimensional approach appears to be an alternative and possibly more suited approach given the heterogeneity of clinical situations although the most appropriate number and type of dimensions is still an object of controversy and debate.

1.3. Assessment of personality traits

Personality is assessed in a variety of different contexts, including clinical, educational, and occupational settings. The aim is to understand the unique personal circumstances that contribute to developing mental disorders or problematic behavior for example. Personality assessment using standardized questionnaires is typically an adjunct to a less formalized investigation; the trait scores of a subject are interpreted on the basis of clinical judgment. Many instruments based on the Five Factors Model have been developed to assess personality traits. Among them, we mention the NEO-Personality Inventory (NEO-PI), the Revised NEO-Personality Inventory (NEO-PI-R) or its short version, the NEO-Five-Factor Inventory (NEO-FFI) that has been translated and validated in many countries and languages and used extensively. Responses to item questions range from strong disagreement to strong agreement. *Form S* is used for self-reports and *Form R* for observer ratings. A 60-item short form, the NEO-FFI*,* or the Revised NEO-Five-Factor Inventory (NEO-FFI-R), or

its latest version (NEO-FFI-3; McCrae, Costa, & Martin, 2005) provides a quick, reliable, and accurate measure of only the five dimensions of personality. It is especially useful when assessment time is limited and global information on personality is considered sufficient. The NEO-FFI can help understand an individual's basic emotional, interpersonal, experiential, attitudinal, and motivational styles. The Structured Interview for the Five-Factor Model (SIFFM) (Trull & Widiger, 1997) is a semi-structured interview that assesses adaptive and maladaptive variants of traits of the Five-Factor Model.

1.3.1. Revised NEO Personality Inventory

The most common personality measurement based on the Five-Factor Model is the Revised NEO Personality Inventory (NEO-PI-R), initially published 1985. In 1992, a major revision was published introducing facet-scales for all five main dimensions (Costa & McCrae, 1992). This questionnaire is widely used in studies that examine personality features in diverse populations, including those of the elderly. It has been used extensively in both normal and clinical populations, for research and in clinical and industrial or organizational applications. Moreover, the model includes dimensions that can be found in the other models that were not developed according to a dimensional or statistical approach (Cloninger, 1998; Millon & Davis, 2000). The NEO-PI-R is a questionnaire that comprised 240 items grouped in 5 dimensions or factors. Each dimension is made up of six facets. Responses are made on a 5-point Likert-type scale, ranging from 1 (*strongly agree*) to 5 (*strongly disagree*). This instrument has been used in over a thousand published studies and has demonstrated longitudinal stability, predictive utility, and consensual validation. Self-peer correlations range from .34 to .73 (Costa & McCrae, 1992). NEO-PI-R factors have been related to most alternative measures of the FFM, and facet scales have shown specific validity of the five factors (Costa & McCrae, 1992). Internal consistency estimates for the domains range from .86 to .87; correlations between NEO-FFI and NEO-PI-R domains range from .77 to .92

(Costa & McCrae, 1992). Two-year retest reliabilities range from .83 to .91 for domains and from .64 to .86 for facets (McCrae, Costa, del Pilar, Rolland, & Parker, 1998). These inventories presented all have good cross-cultural validity and can be used in a variety of cultural settings.

1.3.2. The Structured Interview for the Five-Factor Model

The Structured Interview for the Five-Factor Model (SIFFM), Trull & Widiger, 1997) was developed to provide an interview-based measure of the Five-Factor Model of personality that evaluates the same main dimensions and the same 30 facets of the FFM. In contrast to the NEO-PI-R, it attempts to assess functional as well as dysfunctional variants of personality traits relevant to the FFM. Analyses of data, obtained from both non-clinical and clinical participants, have supported the reliability and validity of the structured interview. More particularly, SIFFM scores were reliable across judges, were internally consistent, and showed high convergent and discriminant validity. Further, the relationship between FFM personality constructs and Axis II personality disorders has been examined by a number of researchers (Wiggins & Pincus, 1989; Costa & McCrae, 1990). The results of these studies support the inclusion of FFM measures as the SIFFM in assessment batteries aimed at evaluating personality traits and personality pathology in patients (Widiger & Costa, 1994). There are a number of potential advantages offered by an interview-based assessment of personality and personality pathology. The interview method enables the clinician or researcher to tease apart and elicit additional information directly relevant to several major issues concerning personality traits and personality disorders. The additional aspects of personality assessment are crucial because, by definition, personality traits are long-standing and pervasive, and, if there is significant distress or maladaptivity associated with these traits, may be indicative of personality disorder (APA, 1994). Because it is shorter (120 items),

easier to apply, and more comfortable, this structured interview seems also adapted to people with cognitive deficits.

Translation, validation and reliabilities of the French-version of the SIFFM

The most widely used inventory to assess personality according to the Five-Factor Model (FFM) is the NEO-PI-R, a self-assessment questionnaire. However, a self-assessment questionnaire might not be adequate for elderly individuals suffering from memory deficits. For this reason, the Structured Interview for the Five-Factor Model (SIFFM) appears to be an interesting alternative. This instrument includes 120 questions assessing the five main personality domains. Each domain is made up of the 6 facets.

In order to validate our French-version (Pocnet, Rossier, & von Gunten, 2009), we collected data from 314 individuals (260 persons from the general population, aged 20 to 88 years, and 54 participants diagnosed with mild dementia of the Alzheimer type, aged 56 to 89 years). All subjects were assessed using the SIFFM and the NEO-PI-R (form R). The internal reliability of this structured interview was similar to those observed for the original version, ranging from .63 to .87. Concerning the varimax rotated principal components structure of the SIFFM, the eigenvalues of the first six principal components amounted to 5.01, 3.27, 2.53, 2.19, 1.58, and 1.14. Each component seemed to be correlated to one specific personality dimension. The factor structure was analyzed using a targeted factor analysis that suggested the results of the French-version of the SIFFM were in line with those observed for the English version. Varimax structure of the SIFFM and correlations between the components of the personality domains varies between .41 and .74. The correlations between the five dimensions assessed using the SIFFM and the NEO-PI-R were high and similar to those observed with the original English version of the structured interview. For each domain the coefficient is significant and equal or above .55 suggesting a satisfactory convergence between the two instruments. In order to further examine the underlying structure factors of

the SIFFM, a series of exploratory principal component analyses was conducted. Concerning factor analysis, the scores range from .68 to. 85 for SIFFM domains and from .69 to .87 for NEO-PI-R domains. These results showed that the five factors correspond to the five major dimensions of personality measured by the SIFFM and the NEO-PI-R, and, again, there is a neat correspondence between the structures for both administrations modes. Factor loadings are uniformly high, and suggest convergence between two instruments. In addition, we assessed the inter-rater reliability of the SIFFM scores. For this, 40 participants agreed to be filmed or to be assessed simultaneously by two investigators. Then, two types of coefficients were calculated. The *Pearson correlation* and *Intraclass Correlation Coefficients* (ICCs) ranged from .86 to .99 for the French version of the SIFFM domain and facet scores, and were equivalent to those of English version (range = .71 to .99). Thus, evaluators appear capable to assess the participants' responses to SIFFM very similarly showing that the SIFFM is accurate.

The analyses supported the French version's structure, validity, and reliability and its equivalence with the original English version. Moreover, our results showed that the SIFFM is an interesting alternative for assessing personality traits, especially for illiterate persons or those suffering from diseases affecting their ability to answer self-rating inventories (Pocnet et al., 2009).

1.4. Personality across the life course

One of the greatest challenges of personality psychology is to explain the *development of individual differences* that make each individual unique. *Lifespan perspectives* emphasize the inner organization of personality and sustain that behavior is consistent over time and situations. This concern has existed since ancient times. Thus, in his *Rhetoric* Aristotle describes the characteristics of individuals at different phases of their lives where he notes interesting continuities and discontinuities over time and across contexts. In classical and

contemporary theoretical formulations, two opposing views are generally placed at the front: the perspective of *change* and that of *change continuity*. Allport (1937) considered that several aspects of personality, its features, *change significantly and continuously* over a lifetime until the individual has become a "mature person". He (Allport, 1961) sustains that the individual's personality can change in adulthood, even into advanced old age. Inspired by the accumulation of results of cross-sectional and longitudinal studies, McCrae & Costa (2003) sustained that under normal circumstances, adult traits are largely stable, but individuals vary in terms of their intra-individual stability.

One persistent debate concerns the degree to which personality changes over time and whether these changes stem primarily from biological maturation or social experiences. Many patterns of behavior exist within our evolutionary heritage (Buss, 1991; 1995), determined by genes that play an essential role in the formation of personality, particularly with regard to the uniqueness of each individual (Caspi, 1999). So, quantitative genetic research indicates that phenotypic variance of personality traits is due to genetic factors (Riemann et al., 1997; Plomin & Caspi, 1998) that help to shape our similarities as human beings and our differences as individuals (Zuckerman, 1991). Identifying the specific genes responsible for the genetic variation can be an important way forward for research. This is evidenced by human *behavior-gene research* that has provided important insights into the etiology of individual differences in personality traits (Loehlin, 1992; Bouchard & Loehlin, 2001). These researches are based on studies of twins raised together in the same family, studies of twins who have been raised in different families, studies of adoptive families, and family studies analyzing the data of participants who are genetically related to varying degrees. All of these designs have their particular strengths and weaknesses, but firm conclusions regarding the etiology of individual differences are based on an integrative analysis of data based on all four designs (Loehlin, 1992). Across a range of traits, heritability estimates from twin studies lie in the

range .30 - .50. This is the result obtained for *Neuroticism, Extraversion, Conscientiousness,* and *Openness to experience*. *Sensation seeking* has been reported to have somewhat higher heritability, about .60 (Bouchard & Loehlin, 2001).

Traits are also associated with *environmental* exposure, as a consequence of proactive interactions with heritability factors (Caspi & Bem, 1990). Among the environmental determinants of personality, the individual will experience life through *cultural influences*. Each culture has its own institutionalized and approved processes of *learned behaviors, rituals,* and *beliefs*. The *status* of the individual*, education, role*, *responsibilities,* and *privileges* influence the way we respond to them. *Parental ties* are imported in the early development, whereas the *social group* helps the individual to adapt into accepting socially normative rules of behavior. The environment would serve thus as "dilution" of its hereditary potential (i.e. changing features), or a moderator for shaping the development of traits, or by crystallization (i.e. continuity of personality traits) (Morizot & Miranda, 2007). Therefore, both genetic and environmental factors contribute to development of personality traits through a series of transformations between individual and their social milieu and leads to unique adaptive variations. Nowadays various personality theorists stress the importance of *continuity of personality over time* (Caspi & Roberts, 1999) sustaining that personality characteristics and situations are becoming increasingly interdependent over time. Past, present, and future experiences have an important role in shaping personality. Hence, complex psychological adaptations are necessary to solve life problems adequately and to build a mature personality.

1.4.1. Personality development during childhood

Many researchers have argued that personality traits are already present at birth and further shaped throughout ontogeny and are the precursors of personality in adolescence and

adulthood (Caspi, 2000; Rothbart et al., 2000). Thus, the most *classical psychoanalytical theories* consider that an individual's personality is crystallized in childhood or early adolescence and that it remains stable throughout adulthood (Hindle & Smith, 1999). As opposed to this opinion, *radical behaviorists* believe that personality can change at any time of life depending on the learning and environmental stimuli to which a person is exposed (Skinner, 1971). According to theory of traits, the different dimensions of personality develop gradually from birth to early adulthood, from the early period of the discovery of bodily sensations to the stage when the individual acquires the ability to reflect on oneself and the world (Allport, 1961). For Cattell (1957), childhood is the period when personality changes the most as a result of the learning constraints imposed on the child. In accordance with the FFM, personality traits are the expressions of both heritability and intrinsic maturation (McCrae, Jang, Livesley, Riemann, & Angleitner, 2001). The interpretation as endogenous basic tendencies is consistent with their cross-cultural universality (McCrae & Terracciano, 2005). Several studies have investigated personality mean-level changes in childhood and adolescents. Thus, in a longitudinal, cross-sectional and cross-cultural study, McCrae and colleagues (McCrae, Costa, Ostendorf, Angleitner, Hrebickova, & Avia, 2000) found that adolescents between 12 and 18 years increased in *Openness to experience* and, for girls only, in *Neuroticism*. Mean levels of *Extraversion, Agreeableness,* and *Conscientiousness*, however, remained relatively stable during adolescence. In addition, Lamb and colleagues (2002) conducted a longitudinal study of 102 children assessed by adults (mothers and teachers) and followed them up over 2 to 15 years; they observed an increase in *Agreeableness* and *Conscientiousness* and a decline in *Extraversion.* Moreover, adolescents from the age of 14 years became more *tolerant* and *open to new ideas and experiences.* In a previous cross-sectional study, Rossier and colleagues (2007) observed higher internal consistencies at 11-12 years than 8-9 years and modest level differences between the age

groups. The results showed a small cross-sectional decline in *Extraversion* and *Imagination* for both girls and boys, and also a decline in *Emotional Stability* for girls. Another study that investigated personality in children aged 8-12 years is that of Quartier and Rossier (2008). In their study, children's self-perceptions were compared to parent's ratings. Their findings showed that children aged 11-12 years present higher structural congruence, higher reliabilities and higher mean correlation with their parents' descriptions than children aged 8-9 years. Mean levels were higher in younger children for *Imagination* in parents' ratings and for *Benevolence, Conscientiousness,* and *Imagination* in children's ratings. The predictive relation between the FFM personality traits using the *Five Factor Personality Inventory-Children* (FFPI-C) and degrees of risk-taking in preadolescents (ages 10 to 12) was studied in a sample of 50 fifth-graders (McGhee, Ehrler, Buckhalt, & Phillips, 2012). Results indicated that high *Extraversion* and *Openness to experience,* and low *Conscientiousness* were correlated with high risk-taking behavoir. From childhood to adolescence, the individual has to face necessary learning, social challenges, and developmental tasks, which may explain some changes of personality. During this period, the socialization process may foster or confronts certain limits of a person's capacity for assimilation, accommodation, and adaptation through a continuous process of learning (Piaget, 1958).

1.4.2. Changes vs. stability of personality during adulthood

Personality traits are conceptualized by many researchers to represent *stable* and *enduring patterns* of thinking, feeling, and behaving that become increasingly solidified throughout adulthood (Costa & McCrae, 1997). In support of this perspective are findings of increasing rank-order stability across all dimensions of personality from childhood through late adulthood (Roberts & DelVecchio, 2000). However, we may ask ourselves whether or not personality remains *stable and consistent over time and according to specific situations.* On the basis of the FFM, Rushton and colleagues (2008) consider that the dimensions of

Neuroticism, Conscientiousness, and *Agreeableness* refer to "stability", whereas *Extraversion* and *Openness to experiences* describe "plasticity". Together, the stability and plasticity constructs describe the general factor of personality and reflect individual differences in the emphasis on competence and capacity for meeting each of these two general needs in the ways characteristic of human beings (De Young, 2006). Longitudinal studies covering long periods of the lifespan provide important evidence of personality stability. Test-retest correlations suggested that individuals remain stable on almost all dimensions of personality. Thus, Costa and McCrae (1977) reported a ten-year stability coefficient for *Extraversion* ranging from .70 to .80, while those for *Anxiety* and *Neuroticism* fell between .58 and .69. However, personality stability can be evaluated from multiple perspectives. One of them is *structural stability* which implies that the positioning of traits relative to each other remains stable and is unaffected by ageing and age (Allemand, Zimprich, & Hendriks, 2008). Costa and McCrae (1994) argued that when an individual reaches the age of 30, his or her personality is almost fixed. Therefore, individual differences in personality traits are stable over long periods of time (Cattell, 1957, 1965; Eysenck 1981; Eysenck & Eysenck, 1985; McCrae & Costa, 2003; Allemand, Zimprich, & Hertzog, 2007; Roberts & DelVecchio, 2000) because they are believed to have a biological basis (McCrae et al., 2000) reflecting underlying neurobiological processes, some of which are mediated by genetic processes.

An alternative to stability is to conceptualize personality traits as developmental constructs that are subject to *change and adaptation* across the life span (Caspi, Roberts, & Shiner, 2005). Evidence to support this model includes significant mean-level changes for several personality traits during key development periods and indique a pattern of growth and maturity (Roberts, Walton, & Viechtbauer, 2006). This *maturity of personality* is defined as successful adjustment and adaptation to the demands of one's life, as well as the capacity to form healthy interpersonal relationships (Roberts, Capi, & Moffitt, 2001). Longitudinal

studies of transition from adolescence to adulthood indicated distinct patterns of stability and change for several dimensions of personality. Thus, the majority of personality changes occur before the age of 30; thereafter, individuals have attained a configuration of traits that will characterize them for years to come. These changes correspond to small decreases in *Neuroticism, Extraversion* and *Openness to experiences* and increases in *Agreeableness* and *Conscientiousness* from age 20 to 30 were observed (Terracciano et al., 2005). After a slight spike upward from adolescence to young adulthood, follow a plateau of the average level until the mid-fifties when there was a slight decline (Roberts et al., 2006). Other authors argued that there are variations of personality traits throughout life (Caspi & Roberts, 1999; Morizot & Le Blanc, 2003, 2005). In context of personality development, the intrinsic maturational in age-related personality changes are driven by biological processes (Caspi, Roberts, & Shiner, 2005), while the life course is due in particular to social roles and the life experiences that accompany them (Helson, Jones, & Kwan, 2002; Roberts et al., 2006; Figueredo, Sefcek, Vasquez, Brumbach, King, & Jacobs, 2000). Several sets of mechanisms may explain personality changes (Caspi et al., 2001; Roberts et al., 2006). Firstly, and perhaps most importantly, individuals are responsive to the *rewards and punishments* of a given setting and it is possible that long-term exposure to specific contingencies may produce lasting personality changes (Laub & Sampson, 2003). Secondly, *self-reflection* may lead to personality changes. It is possible that lasting personality changes may result from a considerable amount of deliberate attention to the self. Indeed, a belief in the power of self-reflection to promote change is the essence of insight-oriented psychotherapy (Rogers, 1961; 1980). Thirdly, *observing* others might serve as a catalyst for personality changes through *social learning* (Bandura, 1997). Finally, *perceptions by others or reflected appraisals* may create personality changes (Witkin, 1954). Thus, a strong *motivation* to change might be a necessary ingredient for the success of many of these mechanisms of personality changes. In

all cases, the experiences will have lasting effects on a person's *personality development*. According to the FFM, personality development may be described as a dynamic individual differences variable that exhibits both stability and change over the life course that results from the dynamic transactions between individuals and their environments (Costa et al., 2000; Caspi et al., 2005).

1.4.3. Continuity vs. changes of personality in old age

Does personality change or remains stable when we reach old age? Some studies report shifts in the revalence or intensity within the five-factor model frequently used to measure personality. For example, an age-related decrease in *Extraversion* and *Conscientiousness* as well as an increase in harm-avoidance has been reported. The increase in harm-avoidance could be part of an adaptative process to cope better with age-related morbidity and frailty (Srivastava, John, Gosling, & Potter, 2003). However, personality traits are considered conceptually as stable, even in old age. Indeed, the literature in this area suggests only moderate changes in personality features during ageing (Lautenschlager & Förstl, 2007). Johnson and colleagues (2005) presented the results of a prospective study on 833 twins from the Minnesota Twin Study of Adult Development and Aging. Participants self-rated their personalities twice: before and after 5 years. They had an average age of 59. 4 years at baseline and of 64,4 years at follow-up. The authors reported that the mean and standard deviations of scale scores of personality traits remained stable between the first and the second testing. The research group concluded that the high stability of personality traits even in old age is based on a strong underlying genetic component in combination with stable environmental effects. Others twin studies helped to estimate that approximately 40-60% of the variance in personality is genetically determined. It has been suggested that genes not only define temperament within the construct of personality but also keep influencing stability or changes of personality across the lifespan. Moreover, in their longitudinal study, Terracciano

and colleagues (2005) showed gradual personality changes. Their data were collected on 1944 participants, whose age ranged from 20 to 96 years. The hierarchical linear modeling analyses indicated a decline in *Neuroticism* up to age 80, stability and then decline in *Extraversion*, decline in *Openess*, increase in *Agreeableness*, and increase in *Conscientiousness* up to age 70. Although the individual differences in personality traits continue to be stable even in very old age, some researchs showed that the mean-level changes in personality traits accelerated in very old age (Mottus, Johnson, & Deary, 2011). There were no substantial changes in the beginning of the eighth decade but more pronounced changes within the ninth decade. This conclusion is consistent with the idea that effects on personality from the relatively changes in people's lives in later old age, such as deterioration of health and cognition, narrowing of social interaction and increasingly limited ability to function independently. On the other hand, some researchers have examined the role of relationships and gender-related and work experiences in shaping the developmental course of personality traits. For exemple, Costa et al. (2000) tested whether events such as marriage, divorce, widowhood, and death of parent or child had an effect on personality traits. They found effects of divorce and job change on personality traits, although it was not clear how enduring the effects might be. Further explorations of the possible effects on life events (Costa et al., 2000; Roberts et al., 2003) accompanied by the researches on possible biological causes of personality change should continue. This because the biological ageing process is highly variable from one individual to another, and psychological coping strategies with the ageing process are also highly variable depending on premorbid personality traits. However, the study of personality changes over time requires researches of considerable duration. Moreover, assessing personality might be sometimes difficult with older adults.

1.5. Personality and cognition

Recognizing the connections between personality and cognition and mental aptitudes is a major theme of recent research. The terms *cognition* (Latin: *cognoscere*, *to know*, *to conceptualize* or *to recognize*) refers to the faculty to process information, apply knowledge. *Cognition,* or *cognitive processes* are analyzed from different perspectives within different contexts. Cognition is studied in various disciplines such as psychology, philosophy, anthropology, linguistics, neurology, medicine, and computer science. In psychology, the term "cognition" is closely related to abstract concepts such as mind, intelligence, and is used to refer to mental functions, mental processes (thought), and states of intelligence. The mental processes include attention, language, perceiving, interpreting, encoding and retrieving information, solving problems, and making decisions. In cognitive science, cognition usually refers to an information processing view of an individual's psychological functions. It is also used in a branch of social psychology called social cognition to explain attitudes, attributions, and group dynamics. Individuals' behaviors, emotional expressions, and feelings, are expressed in accordance with circumstances but also under the indirect influence of basic tendencies regulated by the dynamic processes. In this case, we refer to *self-regulation* via cognitive monitoring and adjusting thoughts and behaviors (Ley & Young, 1998). These self-regulation processes are closely connected to processes of emotion regulation, and are important in order to express adapted behaviors that fit to the expectations of our social and cultural environments. People may regulate their emotions by selecting or altering emotion-eliciting situations, attentional deployment, cognitive change, or response modulation (De Young & Gray, 2009). With the emergence of self-awareness and internalized standards of behavior comes the capacity of self-regulation. People who routinely fail at self-regulation enjoy none of the psychological benefits that derive from a sense of psychological stability and control; they struggle with mild to severe forms of psychopathology. Moreover, among

the higher-order dimensions of personality, *Conscientiousness* is the most clearly relevant aspect related to self-regulation. Conscientiousness concerns the ways in which people characteristically manage their behavior. Its facets: competence, orderliness, dutifulness, achievement striving, self-discipline, and deliberation reflect different behavioral tendencies characteristic of successful self-regulation (Roberts, Chernyshenko, Stark, & Goldberg, 2005). Contrarily, *impulsivity*, a facette of *Neuroticism* dimension, is the tendency to act without thought or planning. People who are highly impulsive are prone to a host of high-risk behaviors characterized by poor self-control (Hoyle, 2006). Moreover, several researchers have examined the link between personality and cognition. The theoretical and empirical literature on personality and intelligence reflects two general approaches. The first approach, broad but unspecific, provides a rationale for investigators searching for *personality-intelligence relations* (Wechsler, 1950). The latter approach, more specific, involves a small set of personality traits that historically have been linked explicitly to *intellectual abilities* (e.g. Openness to experiences, intelligence, and anxiety) and provides a rationale for closer investigation of specific trait relations. Personality psychologists consider that *Openness to experiences,* as including flexiblity and creativity, embracing new ideas and taking on challenging intellectual or cultural pursuits, as one of the five major personality trait that is conceptualy related to cognitive abilities, unlike the other four traits (*Agreeableness, Conscientiousness, Neuroticism,* and *Extraversion*). According to Ackerman & Heggestad, (1997), these latter domains operate independently of a person's cognitive abilities. The cognitive abilities most often studied in investigations of personality predictors have been Horn-Cattell's first-order factors: *fluid reasoning* and *crystallized ability* (Horn, 1985). *Fluid reasoning* describes the ability to draw inferences and to solve problems. It is biologically anchored and sensitive to cerebral alterations due to aging and pathologies. *Crystallized ability* is defined as breadth and depth of knowledge with a cultural and educational anchor,

and depends on the learning opportunity and motivation. For Ackerman and Heggerstad, (1997) abilities, interests and personality coexist in the sense that ability levels and personality dispositions determine the probability of success in a particular task domain, and interests determine the motivation to attempt the task. Therefore, personality plays an important role in the adaptation of the individual in his or her environment since it allows to interpret the environment and to activate certain regulatory processes.

1.5.1. Memory and self-defining memories

Memory is the set of traces of past events. This set appears as a process that affects the feelings, thoughts, and actions. In this process, the information is *encoded, stored, and retrieved*. *Encoding* allows the perceived item of use or interest to be converted into a construct that can be stored within the brain and recalled later from long-term memory. *Storage* is the second memory stage or process, which entails that we maintain information over long periods of time. Finally, the third process is *retrieval* of information that we have stored (Schenk, Leuba, & Büla, 2004). Cognitive neuroscientists consider memory as the *retention, reactivation,* and *reconstruction* of the experience. One question that is crucial in cognitive neuroscience is: *how are information and mental experiences coded and represented in the brain?* Scientists have gained considerable knowledge about the neuronal codes from the studies of plasticity, but most of such research focused on simple learning in simple neuronal circuits. The neuronal changes involved in more complex examples of memory, particularly *declarative memory* that requires the storage of facts and events, are considerably less clear (Byrne, 2007).

Working memory (also called *short-term memory*) contains everything that we are conscious of working on right now. Information is held long enough to make a decision and then is either lost or sent on to storage for later use. If it is transferred to form a memory for

later use, it becomes *long-term memory*. Working memory is transient in nature and, unless processed and stored in long-term memory, will be lost after it is used (Smith, Petrrsen, Ivnik, Malec, & Tangalos, 1996). The phase in which working or short-term memory is transferred into long-term memory is called *memory consolidation*. This storage function allows us to bring information online for comparisons to other information contained in long-term memory, thereby enhancing problem solving and comprehension. Recent functional imaging studies detected *working memory* signals in both *medial temporal* (a brain area strongly associated with *long-term memory)*, and *prefrontal* cortex suggesting a strong relationship between working memory and long-term memory (Ranganath, Cohen, & Brozinsky, 2005). However, the substantially more working memory signals seen in the prefrontal lobe suggest that this area plays a more important role in working memory than the medial temporal lobe (Suzuki, 2007).

Short-term memory is temporary and subject to disruption, while *long-term memory* is persistent and stable. Consolidation of short-term memory into long-term memory at the cellular level presumably involves two processes: synaptic consolidation and system consolidation. The former involves a protein synthesis process in the medial temporal lobe and occurs within the first few hours after learning, whereas the latter transforms the medial temporal lobe-dependent memory into a medial temporal lobe-independent memory over months to years (Dudai, 2004). Recently, a third process has become the focus of research, reconsolidation, in which previously consolidated memories can be made labile again through reactivation of the memory trace (Tronson & Taylor, 2007).

1.5.2. Types of memories and their functioning

Memory may be the most important skill we have. It doesn't just allow us to reminisce about our experiences, but do everything that we had to learn at one point. Different types of

memories are stored in different regions of the brain. Thus, long-term memory is typically divided up into two major headings: *explicit memory* (declarative memory) and *implicit memory* (or procedural memory). *Explicit memory* or *declarative memory* refers to all memories that are consciously available; it is about the intentional and conscious recollection of an event or a piece of information. These memories are encoded by the hippocampus, entorhinal cortex, and perirhinal cortex, but consolidated and stored elsewhere (Schacter, Gilbert, & Wegner, 2011). The precise location of storage is unknown, but it is assumed to be in the temporal cortex. Declarative memory also has two major subdivisions: *semantic* and *episodic memories* (Adams, 2006). *Semantic memory* refers to knowledge about factual information, such as the meaning of words, memory elements relating to general knowledge organized into categories (objects, facts, rules, concepts, proposals). *Episodic memory* refers to memory for specific events in time and space (Tulving, 1983). A particular type of episodic memory is *autobiographical memory*, i.e. the ability to recall and describe events constituting one's own history. However, autobiographical memory is composed of different representations including general knowledge about one's past (semantic component) and specific personal events (episodic component) (Conway, 1996). Some old memories can remain very vivid because they are particularly important for the subject's identity. *Implicit memory* or *procedural memory* refers to mental or behavioral manifestations occasioned by the retention of non-conscious information. For example, the use of objects or movements of the body, such as how exactly to use a pencil, ride a bicycle, or drive a car is part of procedural memory. The cerebellum and the striatum presumably store this type of memory. There are various other categorizations of memory and types of memory. *Prospective memory* and *retrospective memory* are examples. They differ in the fact that retrospective memory emphasizes memory for events that have previously occurred, while prospective memory focuses on intended future events and is thus considered a form of memory for the future.

Retrospective memory involves the memory of what we know, containing informational content. Prospective memory focuses on when to act, without focusing on informational content (Schacter et al., 2011). Another type of memory is *emotional memory*, the memory for events that evoke a particularly strong emotion. Emotional memories can be consciously available, but elicit powerful, unconscious physiological reactions. They also have a unique physiological pathway that involves strong connections from the amygdala to the prefrontal cortex with weaker connections running back from the prefrontal cortex to the amygdala. The strength and longevity of memories is directly related to the amount of emotion felt during an event. Emotion and memory is a domain that can involve both declarative and implicit memory processes (Adams, 2006).

One of the key concerns of older adults is the experience of memory loss, and much of the current knowledge of memory has come from studying memory disorders (Tobiansky, Blizard, Livingston, & Mann, 1995). Understanding the mechanism of functioning of these types of memories can help the future of healthy and effective solutions to memory problems.

Chapter 2. Cognitive decline and Alzheimer's disease (AD)

In this chapter, I will describe both normal and pathological ageing. More specifically, I will characterize AD and how it evolves over time. Combining socio-demographic, psychological, biological, and psychiatric knowledge, this chapter offers a global picture to understand ageing and neurodegenerative diseases.

2.1. Successful ageing vs. pathological ageing

Although ageing represents an interesting field of research for theoretical and practical reasons, the boundaries delineating the manifestations of normal and pathological brain ageing remain as yet unclear. Aging is a complex notion involving intricate interweaving of its biological, psychological, and socio-cultural meanings. Ageing is determined by several factors as the changes occur over time regarding morphology, electrical operations, or the expression of genes. In normal ageing, plasticity is still possible, despite a certain degree of dendritic and synaptic loss, as dendrites may grow and synapses increase in size through compensatory phenomena, which allows maintaining large networks of connections (Baltes & Baltes, 1990). Normal ageing may still appear as a kind of extended maturation. It is accompanied by a continued diversity of adaptive capacities despite a decrease in functional reserves. Recently, the accumulation of research findings in geriatrics, psychology and social sciences led to a subtler picture contained in the *successful ageing* paradigm (Baltes & Baltes, 1990; Baltes & Smith, 2003). Successful ageing refers to a state of health in which there are measurable positive features across a spectrum of health measures. It extends beyond cognitive and functional definitions as it considers the value of self-related psychological wellbeing. In other words, successful ageing is a multidimensional construct that includes physical health, cognitive functioning, functional status, emotional adjustment, and social engagement (Ko, Berg, Uchino, & Smith, 2007). However, there is a considerable variability

among individuals as to their ageing trajectories and profiles. For example, in the framework of the Swiss Interdisciplinary Longitudinal Study on the Oldest Old, individuals' aged 80 to 84 at baseline were interviewed and followed longitudinally for 5 years (Clemence, Karmaniola, Green, & Spini, 2007). The findings showed that the positive impact of self-rated health reduced the negative effect of life events on well-being for long-term survivors, but not for those who died within five years. This suggests that survivors had better psychological resources for coping with disturbing life events, while the decreased lacked these resources, which buffered the impact of negative events. Although prior research on these individual differences in ageing has considered personality factors (Smith & Spiro, 2002), recent research elucidating the neurocognitive underpinnings of personality traits may further inform the nature of personality-ageing associations. Of particular interest are associations between personality factors and the constellation of cognitive processes such as executive functioning including working memory, cognitive flexibility, response selection, inhibition, initiation, set formation, and set maintenance (Suchy, 2009). Thus, some research shows that certain personality domains can be considered as protective factors against cognitive decline. For example, low *Neuroticism* has been associated with better episodic memory (Meier, Perrig-Chiello, & Perrig, 2002), while Pearson (1993) reported a positive correlation between *Neuroticism* and crystallized abilities in an older sample of women diagnosed with anxiety and depression. In addition, Jorm et al. (1993) found a negative correlation between *Neuroticism* and cognitive abilities in older adults. Ashton et al., (2000) found that *Openness to experiences, Conscientiousness,* and *Agreeableness* were positively related to performance on a number of cognitive tests assessing *crystallized* and *fluid abilities* in older adults. In general, models of successful ageing have tended to focus on goal setting and readjustment, as well as proactive coping (Ouwehand et al., 2006), which involve anticipation of future stressors (or losses) and engagement of preventive strategies (Aspinwall & Taylor, 1997).

Interestingly, all the psychological processes related to successful ageing (planning, goal setting and maintenance, anticipation of adverse future events) describe key aspects of executive functioning. Thus, individuals with better executive functioning will be better equipped to engage in cognitive and behavioral strategies that have been purported to characterize successful ageing (Williams & Kemper, 2010).

However, in parallel to the increase of life expectancy at birth, the whole old-age lifespan witnessed a growing gap between the *young-old* and the *old-old* (Neugarten, 1974) or *oldest-old* (Suzman, Willis, & Manton, 1992). Age is one established risk factor for cognitive impairment (Kawas, Gray, Brookmeyer, Fozard, & Zonderman, 2000). It is increasingly evident that some individuals start to experience cognitive changes years before deficits become obvious. Thus, some longitudinal studies showed that normal persons present a decline in cognitive performance over time (Driscoll, Resnick, Troncoso, An, O'Brien, & Zonderman, 2006). In this context, studies on ageing should strive for a better understanding of the factors that may account for the improvement of life conditions in the ageing population. Some categories of ageing individuals appear more fragile and vulnerable than others, among them women (Arber & Cooper, 1999), immigrants, and individuals belonging to lower socio-economic classes (Bolzman, Poncioni-Derigo, Vial, & Fibbi, 2004). Many aged individuals without neuropathologies present stable cognitive performances, suggesting that normal age-related cognitive decline is modest and, conversely, that more marked cognitive decline may represent incipient disease (Boyle, Buchman, Wilson, Leurgans, & Bennett, 2010). Cognitive impairment is an increasingly significant public health concern as it accompanies the growth of the older population. Previous attempts at characterizing cognitive changes intrinsic to normal ageing have produced several concepts under different headings such as senescent forgetfulness or age-associated cognitive decline (Levy, 1994).

2.2. Ageing and dementia

The various dementias are probably among the most significant clinical manifestations of pathological brain ageing. Dementia (taken from Latin, originally meaning *amentia*, for *without mind* or *craziness*) is a loss of global cognitive ability in a previously unimpaired person beyond what might be expected from normal ageing. Although dementia is far more common in the geriatric population, it can occur before the age of 65, in which case it is termed *early onset dementia* (Fadil, Borazanci, Yahyaoui, Korniychuk, & Minagar, 2009). Clinical research on the earliest signs of cognitive decline shows that mild cognitive impairment may include both pre-dementias states and states of memory impairment related to age (Petersen, 2003). The more precise characterization of factors discriminating these two subject groups and the evaluation of the effect of early intervention on their evolution are major issues of current clinical research. To get a comprehensive picture of cognitive impairment and dementia, a brief overview of the magnitude of occurence and course of these is given in the following. Thus, a set of disorders is grouped under the term *dementia* that involves the deterioration of intellectual functions, an alteration of coping skills, personality change, deterioration of emotional control (Petersen, 2003). These symptoms are considered as direct consequences of a general medical disorder (e.g. infectious or metabolic), the lingering effects of a substance (e.g. alcohol), a disease of the central nervous system (neurodegenerative disease, cerebro-vascular, etc.), or a combination of them (e.g. combined effects of cerebrovascular disease and AD) (Schenk et al., 2004). In other words, the dementing disease is a chronic disorder that gradually alters the patient's personality, social and personal functioning, implying a gradual dependence for acts of daily living (Petersen, 2003). It is important to distinguish the different origins (differential diagnosis) of cognitive impairment. The different types of dementia diagnostic criteria are now better standardized, taking into account the clinical aspects of each etiology. The construction of these criteria is

based on two levels of reliability of the clinical diagnosis: *possible diagnosis* vs. *probable diagnosis*, while certainty of diagnosis is only obtained by neuropathological examination. One of the main differential diagnoses of dementia is a major *depressive episode.* Indeed, dementia and depression share a number of symptoms within the affective (loss of interest, apathy), behavioral (slow down, loss of initiative), and cognitive (attention deficit disorder, memory) register (Persson, Berg, Nilsson, & Svanborg, 1991). Moreover, these two entities (*dementia* and *depression*) can coexist in the same individual. This is explained by the fact that cognitive impairment, especially memory, can occur in advanced age in the absence of any dementia pathology (Starkstein & Mizrahi, 2006). In the absence of dementia, the cognitive disorders are grouped under the term *Mild Cognitive Impairment* (MCI) for which the following diagnostic criteria were originally used: presence of memory complaint, no alteration of everyday activities, lack of objective memory function for age, and lack of diagnostic criteria for dementia. It should also be noted that there is an obvious continuity between MCI and dementia (Petersen, 2007). Thus, the annual rate of conversion of MCI to dementia (Alzheimer's or other) is about of 12-15%, with extremes ranging from 6-25% depending on the study. The study with the longest follow-up (6 years) observed a conversion rate of nearly 80% (Petersen, 2003). *Vascular dementia* is caused by reduced blood flow to the brain-usually from a stroke or series of strokes. The subtle and progressive decline in memory and cognitive functioning occurs when the blood supply carrying oxygen and nutrients to the brain is interrupted by a blocked or diseased vascular system (Battistin, & Cagnin, 2010). If blood supply is blocked for longer than a few seconds, brain cells can die, causing damage to the cortex - especially the area associated with learning, memory, and language. However, clinical, neuropsychological, and psychiatric manifestations vary depending on the size and topography of ischemic lesions that are at the origin. The most common type of vascular dementia is *multi-infarct dementia*, which is caused by a series of

small strokes, or mini-strokes, that often go unnoticed. These mini-strokes, also referred to as transient ischemic attacks, result in only temporary, partial blockages of blood supply and brief impairments in consciousness or sight. Over time, however, as more areas of the brain become damaged, the symptoms of vascular dementia begin to appear. The *Fronto Temporal Lobar Degeneration*-FTLD is a rather heterogeneous entity that includes: 1) frontotemporal dementias including *Pick's disease*, 2) primary *progressive aphasia,* and 3) *semantic dementia* (Snowden, Bathgate, & Varma, 2001). These conditions are the result of degeneration in the frontal and anterior temporal lobes, and display features, which include impairment of executive functions (attention, planning, abstraction, problem-solving) with relative maintenance of daily functioning and memory. Added to this are behavioral problems, motivation, and emotional expressiveness (indifference, depression, anxiety, and amimia). Physical neglect (hygiene), loss of control of social relations with disinhibition, mental rigidity, changes in feeding behavior associated with hyper-orality, and stereotypes are part of the diagnostic criteria for frontotemporal dementia (Snowden et al., 2001). *Dementia with Lewy Bodies*, characterized by clinical and neuropathological features include, besides the presence of cognitive disorders suggestive of dementia, the existence of extrapyramidal symptomatology and the frequent association with falls, fluctuations in vigilance, and psychiatric manifestations such as visual hallucinations (McKeith, Galasko, & Kosaka, 1996; Harrison & McKeith, 1995). *Parkinson's disease, progressive supranuclear palsy, corticobasal degeneration* are other dementing disaeases involving extrapyramidal syndromes.

Chronicity, progression of cognitive impairment, functional dependence, personality changes, emotions and behavioral disorders, and the impact on the environment impose severe suffering to patients and their families, and high costs to society. To ensure optimal care, diagnosis and management need to occur at the earliest possible stage.

2.3. Alzheimer's disease (AD)

According to the Word Health Organization (WHO) and its International Classification of Diseases, 10th edition, (CIM-10, 1993), the definition of Alzheimer's disease (AD) is: "Progressive deterioration of memory and thinking, significant enough to hamper the activities of daily life, appeared for at least 6 months and the presence of at least one disorder of the following: language, calculation, trial, impaired abstract thinking, praxis, gnosis or personality change". According to the DSM-IV-TR (2000), the essential characteristic in the dementia of AD type is the apparition of multiple cognitive deficits including the memory alteration and at least one of the following cognitive perturbations: aphasia, apraxia, agnosia or perturbation of the executive functions. The cognitive deficits must be severe enough to cause a significant alteration of the patient's professional or social functioning and have to present a decline in relation to their previous functioning level. The memory alteration, which is necessary for the diagnosis, is an early and predominant symptom. Personality and mental balance are altered. Moreover, dementia is associated with an organic etiology.

The disease course can be divided into several stages, with progressive patterns of cognitive and functional impairments. According to the criteria used, *preclinical AD* is defined as impairment in one or more cognitive domains (typically memory), or an overall mild decline across cognitive abilities that are insufficient to interfere with social and occupational functioning, as is required for a dementia syndrome. The first symptoms are often mistakenly attributed to ageing or stress (Waldemar, 2007). Many subjects remain stable or even revert to a normal cognitive state. Moreover, a psychiatric condition, particularly severe depression, is not classified as dementia, but in the *syndrome of depression* where cognitive impairment can be severe. Very often, it is difficult not only to diagnose the disorder with precision but also to establish it is beginning because deficits start insidiously and early symptoms are similar to the first signs of the normal ageing process. Often, several

years go by before a patient's family goes to see a physician and sometimes the patient is not aware of their difficulties and minimizes them. It all starts with small memory failures such as mild forgetfulness that can be bothersome in everyday life, or words that will not come to mind. Recent events have no hold on the memory. Answers to questions such as "What did you have for supper last night?" remain vague. On the other hand, old memories are preserved far longer. Motor skills are not altered at the early stage, and most patients are still independent to perform their daily activities. At this stage, apathy can be seen as the most persistent neuropsychiatric symptom in AD (Roberts et al., 2006). Over time, some symptoms may remain stable or even decrease. Around eight years before a patient fulfills the clinical criteria for AD neuropsychological testing can reveal mild cognitive difficulties (Linn, Wolf, & Bachman, 1995).

In the *mild or early Alzheimer's stage*, people may experience several symptoms that impair their everyday functioning. This sometimes hampers their social state at work and home. A significant inability to acquire new information (Kazui, Matsuda, & Hirono, 2005) has also been observed and subtle problems with the executive functions of attentiveness, planning, flexibility, and abstract thinking, or impairments in semantic memory (memory of meanings and concept relationship) (Spaan, Raaijmakers, & Jonker, 2003). The most noticeable deficit is memory loss and the diagnosis is confirmed when memory problems are increasing and when other cognitive functions deteriorate (language, object recognition, planning of complex movements, etc.). In the clinical diagnosis, language problems are mainly concerned with reduced speech fluency and decreasing vocabulary. This leads to the general difficulty regarding written as well as oral communication. At this stage, however, the patient is capable of successfully communicating his basic ideas to others (Becker & Overman, 2002). The patient may sometimes appear clumsy while performing fine motor tasks like coordination movements (apraxia) and may even face planning difficulties

(executive). These people may continue to perform many activities individually even with the progression of the disease, but require assistance regarding most cognitively challenging actions (Petersen, 2007).

Progression to a *moderate stage* is marked by increasing memory problems and a gradual reduction of the patient's autonomy. It becomes more and more difficult for the patient to follow a conversation with more than one person. Speech difficulties become evident due to an inability to recall vocabulary, which leads to frequent incorrect word substitutions (paraphasias). Reading and writing skills are also progressively lost (Benke, 1993). Additional disorders emerge such as the inability to think in a coordinated manner, to make judgments or even to self-orient in space or time. Disorientation in space and time becomes more and more obvious (difficulty remembering the day of the week, birthdays). During this phase, memory problems worsen, and patients gradually lose their capacity to recognize objects or even familiar faces. Long-term memory, which was previously intact, becomes impaired. Praxis impairment may complete the clinical picture. Therefore, complex motor sequences become less coordinated as time passes and AD progresses, so the risk of falling increases. Progressively, patients lose their self-sufficiency to such an extent that those simple actions such as lighting a candle, eating, or dressing become impossible (Förstl & Kurz, 1999). It is increasingly difficult for people to make choices, to manage their money and plan their daily activities. Between moderate and advanced stages, unusual behavior problems sometimes arise: for example, atypical or foul language, change of personality traits. Illusionary misidentification and other delusional symptoms also develop in almost 30% of patients with AD (Volicer, Harper, Manning, Goldstein, & Satlin, 2001).

In the *advanced stage* the patient loses his or her autonomy and becomes totally dependent for all activities of daily living, including food, which results in malnutrition. Ongoing monitoring or accommodation in a care center may be needed. Language is reduced

to simple phrases or even single words, eventually leading to complete loss of speech (Jelicic, Bonnebakker, & Bonke, 1995). Despite the losses of verbal language abilities, people can receive often understand and return emotional signals (Förstl & Kurz, 1999). It is quite important that family and friends maintain a close relation with their proxies' patients so that they can receive assistance and manage the day-to-day care if they are staying at home. Psychiatric problems occur, including hallucinations and paranoid delusions, exacerbated by severe memory loss and disorientation. Sleep problems are common. Patients neglect their personal hygiene, become incontinent and struggle to feed themselves. Due to increasing motor difficulties, the patient becomes bedridden. The death of these patients usually occurs after an infectious complication, caused by the related factors such as pneumonia and pressure ulcer (Gambassi, Landi, Lapane, Sgadari, Mor, & Bernabei, 1999).

To summarize, diagnosing the disease at an early stage is quite difficult. AD does not cure and it slowly renders the patients incapable of performing even simple tasks. Given life expectancy increase, AD could be considered as the disease of the century. There are four stages of the disease's development. The first one is predementia when a person faces difficulties performing normal daily functions. The second stage is the early dementia during which a patient experiences decrease in memory and faces learning problems. During the third stage, that is moderate dementia, the patient fails to recognize even his close relatives and at the final stage of the disease he is completely dependent upon his caregivers. These are arguments that explain the need to focus on the person and to investigate the risk, but also protective factors, facing this terrible disease.

2.3.1. Prevalence and incidence rates of dementia and Alzheimer's disease

The increasing number of elderly people in the world is accompanied by an increasing prevalence of people with mild cognitive impairment or dementia. In particular, AD develops over many years and its progression varies greatly from one person to another. As the age distribution of the world population shifts, AD is emerging as a major health problem. The assessment of prevalence and incidence of the disease provides crucial input for public health professionals in determining and allocating health care resources as well as identifying critical risk factors that may be amenable to preventive interventions. Many prevalence studies on dementia and AD have been conducted in various populations (Fratiglioni, De Ronchi, & Agüero Torres, 1999). Reported prevalence rates vary considerably and the variations are largely due to methodological differences, namely clinical diagnostic criteria, sampling strategies, and statistical analysis procedures. Despite the varying magnitude of the reported prevalence rates, all studies show a positive association between age and prevalence rates (Ferri, Prince, Brayne, Broadaty, Fratiglioni, & Ganguli, 2005). However, the association with age has been subject to considerable discussion. One view is that dementia and AD are age-dependent and, thus, inevitable consequences of the ageing process. This view predicts that if we live long enough, we will all become demented. The other view is that dementia and AD are age-related, as is cancer, where the relationship to age is the expression of other biological risk factors. This view implies that the disease can be separated from ageing and eliminated with the removal of the risk factors once they are known and treatable. However, prevalence studies have limitations. The changes in observed prevalence estimates with age cannot really answer the question about age dependency or age relatedness because prevalence is influenced by both survival and disease incidence (McGee & Brayne, 1998). *Incidence*, which is the rate of new cases in a population, is considered a better measure of disease risk. Since epidemiological studies on the incidence of dementia and AD can be expensive and

time-consuming, only a limited number of incidence studies have been published. All incidence studies reported a positive association between age and incidence rates of dementia. Concerning AD, there are two forms. The most common form affects people over the age of 65. The second form is hereditary and rare representing barely 5% of all AD patients. It is transmitted from one generation to the next and is therefore known as the "family" form of the disease. It can develop as early as the age of 30, but most cases start around the age of 40. Disease duration from the first manifestations to death varies considerably, between 8 and 12 years on average (Schenk, et al., 2004).

Results from a meta-analysis indicate that the increase in incidence rates of both dementia and AD slows down with increasing age, although the incidence rates themselves do not decline (Sujuan et al., 1998). For every 5-year increase in age, both dementia and AD incidence rates triple before age 64, double before age 75, and drop down to an increase of 1.5 times around age 85. This slowing down of age-related increase in incidence rates supports the hypothesis that both dementia and AD are age-related rather than age-dependent, with the hopeful corollary that it is possible that preventable risk factors can be identified. The relationship between gender and AD has been inconsistent across studies, although in many studies, women are reported to have higher rates of AD than men even after adjusting for differential survival. Significant differences between sexes usually occur, however, in the oldest age categories where there are few men and even fewer with AD, making estimates unreliable. The association between sex and AD assumes a greater significance as there is now increasing evidence that estrogen replacement therapy in postmenopausal women improves cognitive function and reduces the risk for both cognitive impairment and AD (Fratiglioni, Grut, Forsell, Viitanen, & Winblad, 1991; Schmidt, 1996). Due to the extension of life expectancy, it is estimated that within 20 years, the number of people affected by AD will double in the world. The World Health Organization (2006) estimated that in 2005, 0.38

% of people worldwide had dementia, and that the prevalence would increase to 0.44% in 2015 and to 0.56% in 2030. Other studies have reached similar conclusions (Ferri et al., 2005).

2.3.2. Alzheimer's disease and its impact on brain structures

Since the first description of AD more than a century ago, scientists have been studying all fronts to understand and combat it. In 1906 the German psychiatrist, neurologist, and neuropathologist Alois Alzheimer described the clinical disorders of a woman that he had gathered throughout her hospitalization. He also showed the damaged neurons and their processes, which he observed in the patient's brain, particularly in the cortex. This was the first description of both clinical and anatomical AD. The *phrenological model* proposed in 1808 by the German physician Gall was also confirmed. According to this model, cognitive functions are mainly organized in the cerebral cortex. Later, the German psychiatrist Kraepelin defined AD as a clinical entity. For the first time, a psychiatric disorder was associated with brain lesions. In fact, this discovery was also due to a new method of staining neurons that could reveal and identify the lesions. The development of microscopy and histological stains on tissue sections initiated the *nosological period* of pathology. The important consequence was that intellectual and behavioral disorders became associated with morphological changes of neurons in the cerebral cortex.

The discovery that dementia is a brain disease showed that each step in this knowledge was the result of parallel progress in the field of science and technology. Extensive research has expanded the understanding of cognitive impairment and dementia, in particularly AD, and has provided important knowledge on the origin and course of the disease, as well as advances in early detection and advances in medical treatments. Then, the *biochemical period* of AD began. Particularly, the *cholinergic hypothesis* emerged, which claimed that AD is caused by reduced synthesis of the acetylcholine neurotransmitter. Several researchers

observed a decrease of the *cholinergic innervation* in the cerebral cortex of patients who died of AD (Dickson, Crystal, Bevona, Honer, Vincent, & Davies, 1995). This is a decrease of neuronal release of the *acetylcholine neurotransmitter*. Whitehouse (1996) determined that this cortical cholinergic deficit is due to a loss of cholinergic neurons in the Meynert basal nucleus, situated at the base of the brain. The cholinergic hypothesis is not a sufficient explanation, largely because medications intended to treat acetylcholine deficiency have not been very effective. Other cholinergic effects have also been proposed. A 2004 study found that deposition of amyloid plaques does not correlate well with neuron loss (Schmitz, Rutten, Pielen, Schafer, Wirths, & Bayer, 2004). This observation supports the *tau hypothesis*, the idea that tau protein abnormalities initiate the disease cascade (Mudher & Lovestone, 2002). In this model, hyperphosphorylated tau begins to pair with other threads of tau. They may form neurofibrillary tangles inside nerve cell bodies. When this occurs, the microtubules disintegrate, collapsing the neuron's transport system (Sandbrink, Hartmann, Masters, & Beyreuther, 1996). This may result first in malfunctions in biochemical communication between neurons and later in the death of the cells (Chun & Johnson, 2007). Another hypothesis is the *amyloid hypothesis,* which postulated that amyloid beta peptide (Aβ) is the fundamental cause of the disease (Hardy & Allsop, 1991; Mudher & Lovestone, 2002). Support for this postulate came from the location of the gene for the amyloid beta precursor protein (APP) on chromosome 21, together with the fact that people with trisomy 21 (Down Syndrome) who have an extra gene copy almost universally exhibit AD by 40 years of age (Nistor, 2007). Further evidence came from the finding that transgenic mice that present a mutant form of the human APP gene develop fibrillar amyloid plaques and Alzheimer-like brain pathology with spatial learning deficits (Games, Adams, Alessandrini, Barbour, Borthelette, & Zhao, 1995). An experimental vaccine was found to clear the amyloid plaques in early human trials, but it did not have any significant effect on dementia (Holmes, Boche,

Wilkinson, Yadegarfar, Hopkins, & Bullok, 2008). Moreover, researchers have been led to suspect *non-plaque Aβ oligomers* as the primary pathogenic form of Aβ. These toxic oligomers bind to a surface receptor on neurons and change the structure of the synapse, thereby disrupting neuronal communication (Lacor, Buniel, Furlow, Clemente, Velasco, & Klein, 2007). One receptor for Aβ oligomers may be the *prion protein*, the same protein that has been linked to mad cow disease and the related human condition, Creutzfeldt-Jakob disease, thus potentially linking the underlying mechanism of these neurodegenerative disorders with that of AD (Lauren, Gimbel, Nygaard, Gilbert, & Strittmatter, 2009). In 2009, this theory was updated, suggesting that a close relative of the beta-amyloid protein, and not necessarily the beta-amyloid itself, may be a major culprit in the disease. The theory holds that an amyloid-related mechanism to neuronal connections in the brain in the fast-growth phase of early life may be triggered by ageing-related processes in later life to cause the neuronal withering of AD (Nikolaev, McLaughlin, O'Leary, & Tessier-Lavigne, 2009). In this model, beta-amyloid plays a complementary role by depressing synaptic function. In summary, the *amyloid peptide* and *tau protein* were used to guide research into new therapeutic avenues: enzymes that inhibit the production of amyloid peptide, or molecules that prevent pathogenic tau changes, and various types of vaccines. But these *biological models* and the hopes raised are not confirmed by the *procholinergic treatments* either in clinical trials or in clinical practice. At the same time, the first mutation of this gene was identified in a familial form of the disease. Thus, mutations in two other genes (*presenilin 1* and *presenilin* 2) were discovered. When a person expresses one of these mutations, he or she systematically develops the disease.

In addition, isolating the genetic mutations responsible for AD, scientists are developing animal models of the disease. Several transgenic mice models have been created that can be used for testing the efficacy of newly developped molecules. The injection of

amyloid peptides leads to a reduction of senile plaques in mouse brains and prevents their appearance when the injection is performed early. This prophylaxi*s* is explained by the production of antibodies against the peptide injected into the blood passing through the brain and degrading the abnormal amyloid beta peptide produced by the brain. Unfortunately, clinical trials in humans are not convincing, and many people develop brain inflammation (encephalitis). It was necessary to explore other ways.

Then, the *anatomical period* of AD began, during which researchers focused on a particular area of the brain called the entorhinal cortex, the gateway to the hippocampus, for two reasons. First, the hippocampus receives many cholinergic connections, and second the hippocampus is affected early in AD. It is known that this is a key brain region involved in memory. The lesions were visualized directly on the brain of patients with "biomarkers". Studies using magnetic resonance imaging (MRI) and positron emission tomography (PET) have documented reductions in the size of specific brain regions in people with AD as they progressed from MCI to AD, and in comparison with similar images from healthy older adults. These studies lead to the concept of a relatively homogeneous disease, corresponding to a *progressive amnestic dementia*. This anomaly is linked to disorders of episodic memory characteristics of AD, the hippocampal type amnestic syndrome (Wenk, 2003; Moan, 2009). Other hypotheses have been proposed.

Herpes Simplex Virus type 1 (HSV1) has also been suggested to play a causative role in people carrying susceptible versions of the ApoE gene (Itzhaki & Wozniak, 2008). The characteristics of the virus consist in the action of a genetic factor-modulating outcome of infection. There are various possible ways in which HSV1 might lead to the development of AD: its up-regulation of various enzymes and in particular certain kinases, its effect on the cell cycle, on autophagy, and its inflammatory and oxidative effects. Another hypothesis asserts that the disease may be caused by age-related *myelin breakdown* in the brain. Iron

released during myelin breakdown is hypothesized to cause further damage. Homeostatic myelin repair processes contribute to the development of proteinaceous deposits, such as amyloid-beta and tau (Bartzokis, Lu, & Mintz, 2007). *Oxidative stress and dyshomeostasis of biometal* metabolism may be significant in the formation of the pathology (Su, Wang, Nunomura, Moreira, Lee, Perry, Smith, & Zhu, 2008). AD individuals show 70% loss of *locus coeruleus* cells that provide *norepinephrine* (in addition to its neurotransmitter role) that locally diffuses from "varicosities" as an endogenous *anti-inflammatory* agent in the microenvironment around the neurons, glial cells, and blood vessels in the neocortex and hippocampus. Norepinephrine stimulates mouse microglia to suppress Aβ-induced production of cytokines and their phagocytosis of Aβ. This suggests that degeneration of the locus coeruleus might be responsible for increased Aβ deposition in AD brains (Heneka, O'Banion, Terwel, & Kummer, 2010). Other factors unrelated to the ageing process may, in the future, be amenable to therapeutic intervention by way of estrogen replacement therapy for postmenopausal women, anti-inflammatory drug therapy and reducing vascular risk factors. Advanced age, however, remains the major established risk factor for AD, although environmental variables may also have some role in disease expression. Today, researchers are focusing on the epidemiological aspects of AD giving an idea of the importance of the disease in terms of public health.

Lately the pace of discovery has rapidly accelerated and AD is now associated with increasing numbers of clinical, biochemical, and histological markers. But a key point, personality, will be developed in the following studies, which could be the piece of the "AD puzzle" that will serve to better explain the link between many current hypotheses.

In the 3rd, 4rd, 5rd and 6rd chapters, after a review of the impact of personality characteristics on the clinical expression in neurodegenerative disorder, *we examined different hypotheses* through several empirical studies. Thus, we focused on *the relationship* between *personality characteristics, behavioral* and *psychological symptoms,* and *cognitive decline in the earliest stages of dementia of the Alzheimer type relative to healthy aging*.

Chapter 3. The impact of personality characteristics on the clinical expression in neurodegenerative disorders: A review[1]

3.1. Introduction

Neurodegenerative disorders cause progressive cognitive decline. A substantial body of literature also sustains that dementia gives rise to behavioral and psychological symptoms (BPS) as well as personality changes during dementia. The number of elderly people is rising steeply in both the economically developed and developing world (Ferry et al., 2005). And so does the number of people with dementia and of course precursor stages of the dementias. It is estimated that the number of demented people will double every 20 years and amount to more than 80 million people worldwide by 2040 with about 70% of them living in low and middle income countries (Ferry et al., 2005). Clinical experience suggests that longstanding personality characteristics as a person's most distinctive features of all are likely to play a role in how someone with dementia copes with his increasing deficiencies. Thus, personality characteristics may have a pathoplastic effect on BPS. Personality characteristics may even have an impact on how cognition declines. Thus, the conceptual links between dementia and premorbid personality characteristics appear to be manifold. However, research findings in this area remain scarce despite a huge literature on personality in general.

Personality is usually explored mainly according to two major approaches. The nomothetic approach of personality constructs comprises category versus dimensional approaches on the one hand and theory-driven versus statistical approaches on the other hand. Within the dimensionally and statistically driven approaches, the Five-Factor Model (FFM)

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[1] This chapter has been previously published as a scientific article (von Gunten, Pocnet, & Rossier, 2009).

has acquired the status of a reference model (McCrae et al., 2005). This hierarchical model is based on an empirical generalization about the covariation of personality traits and postulates that five broad dimensions named *Neuroticism*, *Extraversion, Openness to experience*, *Agreeableness,* and *Conscientiousness* adequately map these personality traits (Digman, 1990; McCrae & Costa, 1985; McCrae et al., 1992). A large consensus exists about the FFM, these five dimensions are similar to the Big Five identified in numerous lexical studies (De Raad, 2000; Rossier, Dahourou, & McCrae, 2005) and two of them were already included in *Eysenck's Psychoticism-Extraversion-Neuroticism* (PEN) model (Eysenck, 1990). According to this model, these dimensions are biologically rooted, pointing to evidence that these main personality dimensions and their structure are heritable (McCrae et al., 2001). Several empirical studies also confirmed the universal replicability of the FFM (McCrae et al., 2005; Rossier et al., 2005). Moreover, personality as described by the FFM is known to be consistently associated with some psychiatric disorders, such as depression or personality disorders (Quilty, Meusel, & Bagby, 2008; Rigozzi et al., 2009; Rossier & Rigozzi, 2008). Grounded on this observation, some authors claim that normal and abnormal personality should be studied conjointly and that abnormal personality might be seen as an extreme trait level of a normal personality dimension or as a dysfunction associated with specific personality profiles (Wiggins & Pincus, 1989) as already suggested by Eysenck (1953) many years ago. Moreover, personality is likely to have an impact on the treatment outcome of some psychiatric disorders such as major depressive disorder and might thus be considered as a mediator of treatment response (Quilty et al., 2008). The most commonly used operationalization of the FFM is the NEO personality inventory revised (McCrae et al., 1992). It is of note that some of the dimensions of the FFM are similar to dimensions postulated by other theory-driven approaches (Cloninger, 1998; Millon & Davis, 2000). Neurobiological approaches to personality and its changes, driven by modern neuroimaging and genetic

methods, are steadily catching up with the amount of previously predominant studies that had been framed within psychological and social theories (De Young & Gray, 2009). Personality is usually seen as the result in a young adult of their psycho-affective development throughout childhood and adolescence and considered to remain stable to a very large extent. How personality evolves, however, into old age is a largely understudied field. The existence of a considerable agreement between different personality measurements is a remarkable observation (Depue & Collins, 1999). However, assessing personality may be complicated in patients with cognitive disorders (Holst, Hallberg, & Gustafson, 1997). Reports from the patients themselves are of little value when their memory is severely reduced. However, cognitive impairment in mild cognitive impairment (MCI) is not severe and personality assessment in MCI patients may be comparable to that of normal individuals. The same statement cannot be made for more severely impaired individuals with AD or front-temporal dementia (FTD). Few or no studies address this potential bias.

Considering briefly the possibility that personality exert an effect on cognition in healthy subjects we shall then focus on the main issue of this paper and review what is know about the influence of personality characteristics on BPS as well as cognitive performance and cognitive decline considering MCI, AD, and FTD.

3.2. Effects of personality characteristics on cognition

The idea that cognitive information processing is related to personality characteristics is intriguing and, if confirmed, of potentially major importance when examining cognition in the demented, let alone in those suffering from precursor stages of the various dementias. According to the FFM, personality can be adequately mapped using five dimensions, each being made up of six facets. For example, extraversion is composed of the facets warmth, gregariousness, activity, excitement seeking, and positive emotions. Specific lower level traits fall within the same larger dimension because they are supposed to share some common

underlying cause. However, the five main personality dimensions are regularly intercorrelated and some authors suggested that a higher order factor structure should be considered. Thus, *Neuroticism* (reversed), *Agreeableness*, and *Conscientiousness* from one higher order factor or metatrait, labeled α or stability, and *Extraversion* and *Openness*/*intellect* from another factor, labeled β or plasticity (De Young & Gray, 2009). The two metatraits are supposed to have genetic origins (Jang, Livesley, & Vernon, 1996). Evidence is accumulating that stability is related to serotonin whereas plasticity may be more related to dopamine (De Young, 2006). Plasticity appears to reflect a general exploratory tendency, with extraversion representing a more behavioral mode of exploration and openness/intellect a more cognitive mode. The role of dopamine in exploratory behavior and cognitive flexibility is well established, making it a plausible biological substrate for plasticity. A growing body of evidence indicates that extraversion is partly a function of dopaminergic activity (Deary, Peter, Austin, & Gibson, 1998). Additionally, variation in the catechol-O-methyltransferase gene (COMT), which regulates levels of dopamine in the prefrontal cortex, has been associated with intellect/imagination in a sample of healthy older adults (Harris, Wright, Hayward, Starr, Whalley, & Deary, 2005). How far these personality characteristics determine specific cognitive abilities remains, however, speculative, as little research has been carried out in this domain.

Supposing that personality traits influence information processing, we may ask how do they do it. In clinical psychology, the idea of dysfunctional cognitive schemata was put forward to explain specific psychopathological states, in particular depression (Beck, 2009). Similarly, stemming from observations of psychopathological states, pervasive personality traits reflecting highly organized stable sets of self-beliefs and attitudes may be associated with specific cognitive schemata that are themselves highly stable over time.

Psychobiological theories laid out a rationale for treating personality traits as expressions of brain systems. *Extraversion* was linked to arousability of cortico-reticular circuits, and neuroticism to arousability of the limbic system that regulates emotions (Eysenck, 1991). A number of studies found correlations between extraversion and some standard information processing tasks such as attention, memory, speeded response, motor skills, problem solving, and strategy choice. Extraverts tend to show superior performance than introverts on demanding tasks requiring divided attention, resistance to distraction or to interference. Extraversion effects are frequently context-dependent and extraverts may have advantages in verbal information processing that support their sociability and thus serve an adaptive purpose. Good language skills as well as high resistance to distraction and speed of response are adaptive and support sociability, one of the primary characteristics of extraversion (Matthews & Gilliand, 1999). Introvert superiority is most pronounced on higher workload tasks. However, introverts had worse working memory performance (Gray & Braver, 2002). Extraversion tended to be detrimental to performance on long-duration tasks placing high demands on visual perception, but the trait tended to facilitate performance on shorter duration tasks requiring symbolic processing. Personality may affect specific information processing functions such as working memory or selective attention. In accordance with cognitive neuroscience approaches, focused attention is supported by left hemisphere structures, such as the left posterior cingulate cortex, whereas right hemisphere involvement produces a wider focus. A number of studies on stress show that *Neuroticism* relates to over estimation of threats, underestimation of personal coping and personal agency, to ineffective forms of emotion-focused coping such as self-criticism and maladaptive meta-cognition that perpetuate awareness of negative self-beliefs and lead to perseverative and unproductive worry (Wells & Matthews, 1994; Matthews & Zeidner, 2004). In the interpersonal realm,

neuroticism appears to be linked to hostile appraisals of and reactions towards others that deteriorate the quality of one's relationship.

Overall, our understanding is moving on from linking state dependent emotion to context-dependent cognition towards discriminating more specific cognitive mechanisms or information processing that may be interrelated with both trait emotions or personality traits as well as with increasingly better defined brain subsystems. Personality traits result from the subtle co-evolution and adaptive interplay between emotion and cognitive information processing sanctioned by the adaptive outcome as modelized in the adaptive triangle (Matthews, Zeidner, & Roberts, 2002). Moreover, taking into account simultaneously the different levels of personality structure-the metatraits, the first and second order personality traits-might help describe more precisely the relationship between personality characteristics and cognition, and more specifically the relationship between personality characteristics and cognitive decline of the various dementias.

3.3. Personality changes or BPS?

BPS includes affective, psychotic, and behavioral disorders. Affective disorders refer to anxiety, depression, emotionalism, apathy, or elation. Psychotic disorders refer to delusions, hallucinations, and misidentification syndromes, while behavioral disorders refer to aggressiveness, irritability, eating disorders, wandering, hoarding, and others (Cummings, Mega, & Gray, 1994). Some further dimensions can be added and may comprise suspiciousness, aloofness, indifference, extraversion, submissiveness, and others. BPS are more essential determinants of patients distress and caregiver burden than cognitive impairment and the most important reason for premature institutionalization (Burgio, 1996; Steele, Rovner, Chase, & Folstein, 1990). The frequency of BPS is high although much controversy remains as there are major discrepancies regarding prevalence rates. As an example, estimations of prevalence of depression among patients with AD range from 0% to

86% (Knesevish, Martin, & Berg, 1983; Merrian, Aaronson, & Gaston, 1988) from 11% to 25% for the diagnosis of major depressive episode and from 27% to 30% for the diagnosis of dysthymia and minor depressive episode, respectively (Migliorelli, Teson, Sabe, Petracchi, Leiguarda, & Starkstein, 1995; Ballard, 2001; Cummings, 2003;). Discrepancies between studies may be due to methodological bias secondary to variations as to sample size or the instruments used to assess depressive symptoms, and the source of information (Mackenzie, Robiner, & Knopman, 1989; Migliorell et al., 1995; Weiner, Svetlik, & Risser, 1997).

It must be emphasized that there are no clear-cut boundaries between BPS. Indeed, whether or not these latter changes are pervasive changes of a patient's personality or merely ephemeral BPS remain an issue to be investigated. Thus, it is unclear how persistent personality changes are over time in neurodegenerative disorders. In other words, it remain unclear whether or not such changes are modifications in the fundamental personality structure defining a new stable personality pattern different from a person's longstanding previous personality traits. The most common personality changes reported were diminished enthusiasm or energy and stability while tenderness and goodness remained stable over time. Personality modifications are a consistent aspect of the phenomenology of AD as suggested by findings of yet other studies (Cummings, Hill, & Shapira, 1988; Chatterjee, Strauss, Smyth, & Whitehouse, 1992; Siegler, Dawson, & Welsh, 1994; Aitken, Simpson, & Burns, 1999; Petry, Purandare, Bloom, Page, Morris, & Burns, 2002). Scarce studies report BPS in MCI or patients with mild AD and include, beside depression and anxiety, features like irritability, disinhibition, reduced initiative, or apathy (Cummings et al., 1994; Rubin, Kinscherf, & Morris, 1989; Rubin, Morris, Storandt, & Berg, 1989; Lyketsos, Lopez, Jones, Fitzpatrick, Breitner, & DeKosky, 2002). These features may be referred to as personality disturbances or petsonality changes in such studies. These changes in incipient dementia are usually assumed to correspond to a de novo genesis of heterotypic (acquisition of new

characteristics) or hypotypic (loss of some traits) personality characteristics (Ware, Fairburn, & Hope, 1990; Chatterjee et al., 1992; Kolanowski & Whall, 1996; Geda, Smith, Knopman, Boeve, Tangalos, & Ivnik, 2004). Others interpret these changes as homotypic (accentuations of premorbid personality traits) leading some researchers to consider that demented patients retain much of their former personalities (Kolanowski & Whall, 1996; Balsis, Carpenter, & Storandt, 2005), which argues against the emergence of a universal *Alzheimer personality* (Balsis et al., 2005).

What the concomitants of possible personality changes in dementia are remains under investigated. However, in a group of 52 AD and 15 control subjects using an Italien version of Brooks' and McKinlay's Personality Inventory, reliance on others, liking company, irritability, unhappiness, energy, enthusiasm, contact with reality, maturity, kindness, being reasonable and stable were influenced by the severity of cognitive, functional, and behavioral complaints rather than age, gender, education, and disease duration (Talassi, Cipriani, & Bianchetti, 2007).

3.4. Pathoplastic effect of personality characteristics on BPS in neurodegenerative disorders

BPS does not define the whole spectrum of personality dimensions. The use of an all encompassing personality model is needed to assess the effect of other personality traits not usually considered in studies on BPS, such as *Extraversion* or *Neuroticism*, on clinical characteristics of these patients. Besides the scarcity of studies in this field, several conceptual parameters may explain differences between study conclusions. First, trait markers of personality are rarely taken into account and assessed grounded on a dimensional approach of personality. Second, variations of the length of observation periods or attrition rates at follow-up participation are other factors explaining contradicting study conclusions. Finally, there are no or few longitudinal studies investigating the role of personality characteristics in patients

with neurodegenerative disorders. Indeed, studies relying on a retrospective design to track personality changes are limited by systematic biases in personality perception and recall. However, we shall explore whether or not specific clusters of BPS in neurodegenerative disorders are dependent on premorbid personality traits or premorbid psychological symptoms.

3.4.1. Affective BPS

Whether or not premorbid anxiety determines anxiety disorders, as BPS later on in dementia is largely unknown. However, *premorbid Neuroticism* is linked to premorbid anxiety and may also be associated with anxiety later on in dementia (Strauss, Lee, & DiFilippo, 1997).

Depression has been more extensively studied. Thus, a correlation between a high level of premorbid neuroticism (Chatterjee, et al., 1992) and a weak tolerance of frustration (Meins, Frey, & Thiesemann, 1998) with later depression in dementia has been reported; this corroborates the observation that *Neuroticism* often co-occurs with depression or predicts depression in the non-demented (Kendler, Neale, Kessler, Heath, & Eaves, 1993; Jang et al., 1996). However, *premorbid Neuroticism* did not appear to be associated with depression in AD in another study (Archer, Brown, Reeves, Boothby, & Lovestone, 2007). In a rare longitudinal investigation, depressive symptoms were predominant in mean with previously lower levels of openness, who possible experienced more distress when confronted to increasing dependence, as well as reduced *Agreeableness*; this held true for overt incipient AD as opposed to the prodromal phase of AD (Wilson, Arnold, Beck, Bienias, & Bennett, 2008). Anxiety was correlated with depression in dementia, but neither with the duration nor with the severity of dementia (Orrell & Bebbington, 1995). Depressive as well as suicidal antecedents are considered to be risk factors for depression in the demented (Katz, 1998). It has been suggested that major depression may be related to biological factors, whereas

depressive symptoms would be an emotional response to progressive cognitive impairment (Chemerinski, Petracca, Sabe, Kremer, Sergio, & Starkstein, 2001). In the first group, the depressive episode often starts before cognitive impairment; it does not appear to be associated with cognitive deficits, but it is related to cerebral perfusion deficits in specific brain areas. In the second group, depressive symptoms are more prevalent at the start of the disease and are related to the preservation of awareness of cognitive impairment. Previous personal and family histories of depression were risk factors related to the presence of depressive symptoms in dementia (Pearlson, Ross, & Lohr, 1990).

Higher rates of negative affect and lower rates of positive affect in dementia have been associated with premorbid hostility in one study (Magai, Cohen, Culver, Gomberg, & Makatestsm, 1997). Greater affective disturbance in dementia was found in those with higher premorbid agreeableness (Low, Brodaty, & Draper, 2002). AD patients were generally characterized as having had a more neurotic premorbid personality and, thus, as more emotionally labile and tense when demented than patients with Parkinson's disease (Meins, Frey, & Thiesemann, 2000). A cross-sectional study of 58 nursing homes residents with dementia as well as depression and/or psychosis found that a higher degree of openness predicted an affective disorder (Low et al., 2002).

3.4.2. Psychotic BPS

Positive psychotic symptoms such as delusions and hallucinations are associated with other psychopathological disturbances such as agitation, aggressiveness, insomnia, and depression (Ballard et al., 2001). However, these authors conclude that the aetiology of psychotic symptoms is not currently understood although a number of associations have been reported, mostly with little consistency. Of course, psychotic symptoms are multifactorial in their origin, and cognitive and personality characteristics may predispose to the emergence of hallucinations in the demented (Whitehouse et al., 1996), but no study investigates delusions

and their correlations with premorbid psychotic traits. Likewise, misidentification syndromes are phenomenologically and etiologically tremendously complex and sometimes accompanied by delusions or persecutory feelings (Whitehouse et al., 1996), although this is by far not always the case. Higher neuroticism was predictive of delusions, and higher agreeableness of hallucinations in nursing homes residents with dementia as well as depression and/or psychosis (Low et al., 2002). We have speculated that premorbid characteristics may give a specific flavour to the content of a misidentification syndrome (von Gunten, Giannakopoulos, & Duc, 2005).

3.4.3. Alterations of self-awareness

Many patients with dementia have anosognosia or denial that may concern their cognitive deficits and both their BPS and their personality changes. Dissociation may occur as a patient may have anosognosia regarding their activities of daily living, but may retain insight into their deficits on cognitive tests (Starkstein, Sabe, Chemerinski, Jason, & Leiguarda, 1996). Behavioral and personality changes and lack of insight are considered hallmarks of FTD, but they are also frequent in AD although these latter patients are often able to cover up cognitive deficits and maintain socially appropriate behavior for some time during their illness. In one study, the frequency of anosognosia increased from very mild (10%), mild (31%), moderate (50%) to severe AD (57%) (Starkstein & Mizrahi, 2006). The authors also found a significant association between anosognosia and disinhibition; therefore, the question arises whether impaired frontal lobe function may represent a common cause for both these changes in personality and behavior. Only 3% of the patients over-estimated their impairment with overestimation being associated with the presence of minor or major depression. Studies on anosognosia in AD do not usually consider the awareness of personality characteristics or changes and focus mostly on awareness of cognitive deficits. To our knowledge, one single study investigated this issue comparing patients with FTD and

with AD. While FTD patients as a group showed the greatest magnitude of error in the largest number of personality dimensions, the AD group showed accurate self-awareness in all personality dimensions studied except submissiveness and extraversion (Rankin, Baldwin, Pace-Savitsky, Kramer, & Miller, 2005). Patients with FTD tended to overestimate positive personality dimensions and to underestimate the presence of negative feature while healthy controls rather underestimated their positive personality dimensions. Interestingly, for both patients with FTD and AD, self-awareness was most reduced for those personality dimensions that had changed the most when comparing premorbid and present personalities. These results are particularly interesting as self-awareness of only some of the personality dimensions measured are altered in AD suggesting that complex differential mechanisms might be at play in this disorder whereas FTD is accompanied by a global change of awareness. In this study, the preservation of some insight in AD may be due to the fact that the patients were in early stage of the disease, the level of insight decreasing with disease progression (McDaniel, Edland, & Heyman, 1995; Rankin et al., 2005). Another study explored the cerebral correlates of self-assessment and perspective taking in patients with mild AD as well as elderly and young volunteers (Ruby, Collette, D'Argembeau, & Péters, 2009). All subjects assessed relevance of personality traits adjectives for self and a relative, taking either their own or their relative's perspective, during a functional imaging experiment. The comparison of subjects and their relative's answers provided congruency scores used to assess self-judgment and perspective taking performance. The self-judgment "accuracy" score was diminished in AD. When the patients assessed adjectives for self-relevance, they predominantly activated bilateral intra-parietal sulci. Previous studies associated intra-parietal sulci activation with familiarity judgment, which AD patients would use more than recollection when retrieving information to assess their own personality. When taking a third-person perspective, patients activated prefrontal regions (similarly to young volunteers), while elderly controls recruited

visual associative areas (also activated by young volunteers). This suggests that mild AD patients relied more on reasoning processes than on visual imagery of autobiographical memories to take their relative's perspective. This strategy may help AD patients to cope with episodic memory impairment even if this does not prevent them from making some mind-reading errors.

Patients with early and medium-stage dementia often experience a significant amount of stress related to their relationships with family and friends, feelings about losses, and attempts to manage losses (Ostwald, Duggleby, & Hepburn, 2002). Those who are highly conscientious and reserved in their emotional expressions may be more likely to use defensive denial (Weinstein, Friendland, & Wagner, 1994). Those who are highly conscientious and reserved in their emotional expressions may be more likely to use defensive denial (Weinstein et al., 1994). Those with what Weinstein called a "prototypical denial personality" may find the experience of dementia particularly distressing when they are faced with the disintegration of order and control, and a lowering of standards. Such individuals may have an increased need to defend themselves against the threat of dementia using defensive denial, thus showing reduced awareness. In another study, *Conscientiousness,* attitudes towards emotional expression, and avoidant behavioral coping did not significantly influence the awareness level after controlling for disease severity, duration of symptoms, depression, and anxiety (Seiffer, Clare, & Harvey, 2005). In contradiction to Weinstein et al.'s study, those with negative attitudes towards emotional expression were neither found to show reduced awareness nor did the use of behavioral avoidant coping strategies influence the level of awareness. However, considering a person's awareness, personality style, use of defense mechanisms and coping strategies on an individualized level are pivotal when considering clinical interventions for people facing the threat of dementia.

3.4.4. Other BPS

Irritability and *aggressiveness* in the demented were correlated with male gender (Marx, Cohen-Mansfield, & Werner, 1990), psychotic symptoms (Deutsch, Bylsma, & Rovner, 1991), and premorbid family relationships (Hamel, Gold, Andres, Reis, Dastoor, & Grauer, 1990). Lower *premorbid Agreeableness* was associated with *agitation* and *irritability* in AD and also predicted an *agitation/apathy* syndrome (Archer et al., 2007). An association with depression and possibly with premorbid functioning has been reported (Cohen-Mansfield & Werner, 1998). *Aggressiveness* might correspond to the exaggeration of premorbid personality traits (Kurtz, Lee, & Sherker, 1999). A high level of *premorbid Neuroticism* in AD patients was significantly associated with current troublesome behavior (Meins et al., 1998). There are no studies on catastrophic reactions or oppositional behavior in the context of premorbid traits, but these behaviors may be related to *persecutory ideas* or *depression*. A similar association has been reported for *wandering* or related behaviors among a series of other confounding factors with wanderers sometimes being people used to go for long walks by habit or to face a stressing situation before they developed a dementia syndrome. Symptoms of passivity, agitation, and self-centeredness were more prevalent among non-demented individuals with memory problems than among controls (Rubin et al., 1989). *Shadowing, Godot's syndrome* and other repetitive or magnetic behaviors were seen to be more frequent in those with *anxiety* and *depression* (Reisberg, Borstein, Franssen, Salob, Steinberg, & Chulman, 1987), but no direct link with premorbid characteristics has so far been reported. *Stereotypies* and *hoarding behavior* are related to frontal damage, but no study examined the relationship with premorbid obsessions or compulsions. *Vocally disruptive behavior* is etiologically very heterogeneous (von Gunten, Anlawaqil, Abderhalden, Needham, & Schüpbach, 2008) but it has been linked to premorbid introversion, psychic rigidity, and strict control over one's emotions (Holst et al., 1997). *Sexually inappropriate*

behavior has many confounding factors although it may depend on manifest or latent disorders of sexuality preceding incipient dementia (Philo, Richie, & Kaas, 1996). To our knowledge, no studies investigate *eating disorders* such as bulimia, *PICA syndrome* and others and their relationship to pre-existing alimentary habits. The same seems to hold true as to *apathy*. *Sleeping disorders* are extremely frequent in the elderly, in particular in the demented, and they are related to depression and anxiety or stress (Hohagen, Käppler, Schramm, Rink, Riemann, & Berger, 1994; Reifler, Larson, Teri, & Poulson, 1986). However, there are no studies investigating premorbid sleeping habits in those who suffer from dementing disorders.

3.5. Studies using more classically personality-oriented concepts

Most of the above reported changes are quite clear-cut and incisive while more subtle changes of personality are rarely reported. As mentioned, only few studies have investigated personality in demented patients using standard personality assessments or based on specific personality theories. However, in patients suffering from mild dementia, personality components like *Openness*, *Agreeableness*, *Neuroticism*, and *Extraversion* were reported to remain stable. One study found no relationship between premorbid personality and subsequent BPS (Low et al., 2002). In 68 patients with dementia, premorbid inhibited character was associated with irritability and social retreat when they became demented while this association was less prominent in those with independent personalities (Gould & Hyer, 2004). Another study on 66 demented subjects suggested a moderate link between high *Neuroticism* and later personality change as well as between a low degree of tolerance towards frustration and later depression (Meins et al., 1998) an investigation conceptually related to Holst et al.'s (1997) study mentioned earlier. A study using the Interpersonal Adjectives Scales filled in by a caregiver found changes in AD early in the disease. They were, however, clearly less pronounced than those in patients with either fvFTD or tvFTD

(Rankin, Kramer, Myhack, & Miller, 2003). This study further showed that patients with fvFTD had extreme loss of social dominance (and became more docile) but only mild to moderate loss of nurturance and affiliation compared to controls while those with tvFTD showed the inverse pattern (and became less compliant and cold-hearted) which is reminiscent of the Klüver-Bucy syndrome. This may not surprise as FTD is mainly defined as a disorder of behavioral and personality change progressing to a global dementia syndrome in the later stages of the illness with reported misdemeanour in 50% of the patients including shoplifting, trespassing into other people's homes, verbally or physically threatening spouses, relatives, and strangers (Diehl, Ernst, & Krapp, 2006).

Although the subjective view people with cognitive disorders take of themselves, as a part of their personality and innermost intra-personal space must not be neglected, auto-evaluation may not be sufficient. Personality assessment by first-degree relatives of patients with dementia has been shown to have very good inter-rater reliability (Heinik, Keren, & Vainer-Benaiah, 1999; Kurtz et al., 1999; Strauss et al., 1997). However, the information given by a close relative about a patient's previous personality may be biased to some extent as a result, e.g. of the idealization of the patient and their previous relationship as well as of the stress endured as a consequence of the change of their relationship (Aitken et al., 1999). When caregivers retrospectively described their demented proxy's personality comparing their previous and current personality they obtained lower scores for Openness, Conscientiousness, and Extraversion and higher scores for Neuroticism (Chatterjee et al., 1992; Siegler et al., 1994; Dawson et al., 2000). AD patients were rated lower on current than premorbid Agreeableness (Chatterjee et al., 1992).

In short, the review on BPS shows that only few studies have used longitudinal designs to examine personality changes well before and after clinical diagnosis of neurodegenerative diseases and this undoubtedly adds to the uncertainty of our current

knowledge in the field (Petry et al., 1988; Rubin et al., 1989). This is regrettable as knowing a person's premorbid personality trait might be helpful in the differential diagnosis of the various neurodegenerative disorders (Mychack et al., 2001). At that, as personality changes often occur before clinical diagnosis of dementia is made they may aid in the early detection of dementia which would facilitate early treatment (Balsis et al., 2005; Feldman, Scheltens, & Scarpini, 2004). This is remarkable and appears to be a more recent and emerging research focus that aims at investigating BPS in older adults diagnosed with MCI (Feldman et al., 2004; Huang, Wahlund, Svensson, Winbald, & Julin, 2004) while investigations with personality as their focus are still lacking. Furthermore, little or nothing is known about possible treatments of personality changes in AD. Cholinergic treatment may have a positive effect on personality changes in some patients (Purandare et al., 2002). However, such studies are hampered by the difficulty to differentiate permanent personality changes from BPSD.

3.6. Pathoplastic effect of personality characteristics on cognition in neurodegenerative disorders

Premorbid personality might be related to cognitive functioning (cf. above) as well as patterns of cognitive impairment. Indeed, premorbid neuroticism was associated with the level of episodic memory impairment in clinically diagnosed AD patients (Wilson, Fleischman, & Myers, 2004). In this study, 363 participants' cognitive performance and premorbid personality characteristics along five dimensions, one of which was the tendency to experience psychological distress, were assessed at baseline by a knowledgeable informant. Cognitive tests included measures of episodic memory, visouconstruction, repetition, and naming. The results suggest that premorbid proneness to experience psychological distress is related to level of impairment in episodic memory in persons with AD. The authors suggest that the remarkably stable distress-proneness throughout adulthood can serve as an indicator in older persons of the level of negative emotional states experienced during someone's life

span. The hippocampal formation is especially vulnerable to chronic stress, with resulting structural changes and impairment of forms of learning and memory mediated by the hippocampus. An implication of this hypothesis is that persons who are more prone to experience psychological distress may be at increased risk of developing AD compared with those who are less distress-prone possibly because less AD pathology would be needed to cause clinical dementia.

3.7. Personality characteristics and their association with cognitive decline

The prevalence of BPS in MCI lay between that of normal and AD subjects (Geda et al., 2004). Comparing 514 healthy controls with 54 MCI and 87 AD patients 95% of the controls were free of neuropsychiatric symptoms, whereas only 65% of patients with MCI and 20% patients with AD showed no neuropsychiatric symptoms. Thus, the presence of specific BPS in MCI may be associated with an increased risk of converting to AD and therefore be of potential predictive value. However, whether or not premorbid personality characteristics, as opposed to early BPS, are associated with further cognitive decline must be treated as a separate topic. Known clinical predictors of future cognitive decline in MCI comprise age, longitudinal cognitive decline (including verbal memory impairment, working memory, visuo-spatial perception, delayed auditory verbal recall, category fluency), decline of olfaction, subtle motor deficits, and a low premorbid IQ (Devenand, Sano, Tang, Taylor, Gurland, & Mayeux, 1996; Collie & Maruff, 2000; Bennett, Wilson, Schneider, Evans, Beckett, & Bach, 2002; Artero, Tierney, Touchon, & Ritchie, 2003; Cummings, 2003; Aggarwal, Wilson, Beck, Bienias, & Bennett, 2005; Fleisher, Sowell, Taylor, Gamst, Petersen, & Thal, 2007). However, these models are too imprecise for routine clinical use (Tian, Bucks, Haworth, & Wilcock, 2003) and other factors contribute to further cognitive decline. Among these factors, personality characteristics must be considered. A review article on psychiatric aspects of MCI concluded that an improvement in identifying and classifying

the various neuropsychiatric entities in MCI might help better unravel the underlying causes of MCI and with this improve clinical management options (Crocco & Loewenstein, 2005).

A few studies in AD patients found that premorbid psychiatric syndromes are possible risk factors for cognitive decline in the elderly. As there is a frequent co-occurrence of psychiatric features and personality characteristics, the evidence emerging from these studies may shed light on which parameters may be the more predominant predictors of further cognitive decline in MCI or cognitively normal subjects. Thus, in previous studies, persecutory ideation, late-onset anxiety, and mood disorders predicted future dementia (Agbayewa, 1986; Alexopoulos, Meyers, Young, Mattis, & Kakuma, 1993; Baker, Kokmen, Chandra, & Shoenberg, 1991; Buntinx, Kester, Bergers, & Knottnerus, 1996; Devenand et al., 1996; Kral & Emery, 1989; Rabins, Merchant, & Nestadt, 1984; von Gunten et al., 2005). Chronic stressful experience may link anxiety and mood disorders and future cognitive decline as it has been associated with structural changes in the hippocampus and with impairment in forms of learning and memory mediated by the hippocampus (Shelin, Wang, Gado, Csernansky, & Vannier, 1996; Lupien, Gaudreau, & Tchiteya, 1997; von Gunten, Fox, Cipolotti, & Ron, 2000).

Only a few studies looked at premorbid personality traits as possible predictors of cognitive decline (Holst et al., 1997). However, some studies have observed that premorbid personality disorders were more common among AD patients than controls suggesting that they may be a risk factor for AD although personality disorders were not well defined (Kokmen, Beard, Chandra, Offord, Schoenberg, & Ballard, 1991). Physical under-activity, that could be considered as the expression of a life-time personality characteristic, was more common among AD patients than matched controls (Broe, Henderson, Creasey, McCusker, Jorm, & Anthony, 1990). Psychological distress or proneness to psychological distress may be associated with higher risk of AD, independently of pathologic markers of AD, a finding

suggesting that in these patients less AD pathology might be needed to reach the clinical threshold of dementia (Lupien, Nair, & Briere, 1999; Rasmusson, Shi, & Duman, 2002; Wilson, Evans, Bienias, Mendes De Leon, & Schneider, 2003). Basic writing and composition abilities in nuns that possibly reflect personality and their mode of expression were predictive of dementia several decades later as opposed to a more research style of composition (Snowdon, Kemper, Mortimer, Greiner, Wekstein, & Markesbery, 1996). In another study, premorbid proneness to experience psychological distress was related to the level of impairment in episodic memory in persons with AD, but neither distress-proneness nor other personality traits were related to disease progression (Wilson et al., 2004). Within the realm of the Religious Orders Study, the relation of distress-proneness or neuroticism to risk of AD was investigated (Wilson et al., 2003). Those with the highest life-long distress-proneness (90^{th} percentile) had twice the risk of developing AD than those who were lowest in distress-proneness (10^{th} percentile). However, in those who died, distress-proneness was not related to the extent of AD pathology. It is tempting to regard distress-proneness as a cofactor leading to dementia in AD (Snowdon et al., 1996). The association of dementia with neuroticism, if confirmed, should provoke a major research interest. An obvious candidate mechanism is the well-known effect of glucocorticoids on hippocampal neurons (McEwen, 2000). Distress-prone people are vulnerable to depression, which in turn is associated with hypercortisolemia patients with AD show sizable increases in neuroticism scores and regardless of whether or not elevated neuroticism scores are an independent antecedent of AD or one of its early signs, distress-proneness predicts an increased risk of clinical AD in an elderly population (Breitner & Costa, 2003).

Most studies reported above have a retrospective design. However, one prospective study reported that personality changes in undiagnosed people predicted dementia after a 2-year follow-up (Smith-Gamble, Baiyewu, Perkins, Gureje, Hall, & Ogunniyi, 2002). Another

recent prospective study examined personality changes reported by a collateral source on the blessed dementia scale in people who were nondemented when they entered a longitudinal study (Balsis et al., 2005). Of the 108 participants examined, 68 received a clinical diagnosis of no dementia and 14 receveid a neuropathological diagnosis of AD. The results indicate that initial personality changes often occur early, even before clinical diagnosis. Individuals without a clinical diagnosis who had AD at autopsy experienced personality changes comparable with those of individuals who had received a clinical diagnosis. In a longitudinal clinicopathologic cohort study with up to 12 years of annual follow-up of a total of 997 older Catholic nuns, priests, and brothers without dementia at enrolment, of whom 176 developed AD over time, a high conscientiousness score was associated with an 89% risk reduction of AD compared with a low score. Conscientiousness was also associated with decreased incidence of MCI and reduced cognitive decline. In those who died and underwent brain autopsy, conscientiousness was, however, unrelated to neuropathologic measures (Wilson et al., 2008).

Subjective memory complaint or decline (SCD) is frequent in the community and increases with increasing age (Tobiansky, Blizard, Livingston, & Mann, 1995; Jonker, Launer, Hooijer, & Lindeboom, 1996). Most studies suggest that SCD can be persistent, but they differ in their views as to whether the symptom predicts the development of dementia. In one study, SCD was reinvestigated 2 years after the initial examination (Tobiansky et al., 1995). Of those who initially had subjective memory complaints, 79% either reported similar complaints or had lost them 2 years later; 13% were depressed, and 7% were demented, one subject had both depression and dementia. On the whole, SCD was not found to be useful for screening for dementia or depression. Another large community study re-examined 2,114 subjects, with no dementia and a MMSE score of at least 24 at baseline, 4 years later. Of these individuals, 131 had developed dementia at follow-up and they had more SCD at baseline

relatively to the non-demented. The authors suggested that subjective memory impairment might be a useful marker for the development of dementia and/or depression. However, this was not confirmed in another study (Flicker, Ferris, & Reisberg, 1993). Conversion to cognitive impairment or dementia of those with SCD is uncertain. It could be proportional to the intensity of the complaint and be as high, in those after 75 years of age, as one third for cognitive decline and a further third for AD (Palmer, Bäckman, Small, & Fratiglioni, 2006).

However, as SCD may be a predictor of future cognitive problems, it is worthwhile looking at possible associations, in the context of this review, between SCD and psychiatric and personality factors. Indeed, elderly individuals with SCD demonstrated a significantly higher score on the depression scale in comparison to the individuals without SCD (Zandi, 2004). When comparing a younger (mean age 41 years) and an older patient group (mean age 70 years) all of whom had an episode of severe major depression, subjective cognitive abilities showed little relationship with objective dysfunction in the older patients (Tarbuck & Paykel, 1995). In a population-based sample of 85-year olds with major depression or dysthymia (Palson, Johannsson, Berg, & Skoog, 2000), SCD rated as absent, mild or moderate/severe did not correlate with the scores of any of the memory, executive and visuo-spatial tests used. SCD decreased in frequency according to the diagnostic group; 60% of schizophrenics and 50% of patients with cognitive disorders complained about their memory. They were followed by those with affective disorders (34%) and those with adjustment and anxiety disorders (both 28%). When determining the agreement between SCD and recall performance, only patients belonging to the anxiety and affective disorder categories correctly judged their own performance as compared with the other groups. Other studies have also reported an association between SCD and anxiety (Corcoran & Thompson, 1993; Hanninen, Reinikainen, Helkala, Koivisto, Mykkanen, & Laakso, 1994; Smith, Petersen, Ivnik, Malec, & Tangalos, 1996), schizophrenia, and in 1st-degree relatives of AD patients (McPherson, La

Rue, Fitz, Matsuyama, & Jarvik, 1995) although this latter finding remains controversial (Small et al., 1994). Improvement in depressive symptoms was significantly related to a decrease in SCD (Plotkin et al., 1985). Thus, in a sample of 403 individuals between 67 and 78 years of age, those most prone to emphatically complain of memory loss had also greater tendencies towards somatic complaining, higher feelings of anxiety about their physical health, and more negative feelings of their own competence and capabilities than those who did not have SCD (Hanninen et al., 1994). This study suggests that some personality traits are related to the occurrence of SCD in late life.

In general, studies suggest that a combination of risk factors rather than a single factor might enhance prediction of cognitive decline in patients with psychiatric disorders. Thus, late-onset depression in association with ApoE4 was found to be a risk factor for or a prodromal symptom of AD either alone or in association with psychotic features (Krishnan et al., 1996; Steffens et al., 1997; Zubenko et al., 1996). Depressive symptoms did not increase during prodromal AD (Wilson et al., 2008) although depression is now often considered to increase the risk for dementia (Buntinx et al., 1996; von Gunten, 2005). A recent prospective study showed that persons with depressive symptoms at baseline had an increased risk of MCI, an association independent of underlying vascular disease (Barnes, Alexopoulos, Lopez, Williamson, & Yaffe, 2006). Similarly, within the realm of a prospective study of 2,551 community-dwelling people aged between 60 and 64 years, 26 subjects had MCI that was the best predicted by fewer years of education and higher depression scores (Kumar, Parslow, Jorm, Rosenman, Maller, & Meslin, 2006). Depression among cognitive measures, racial and constitutional factors, cerebrovascular disease and ApoE4 was associated with the amnesic type of MCI (Lopez et al., 2003). Depressive symptomatology, in particularly loss of interest, contributed significantly to the prediction of both MCI and dementia (Stepaniuk, Ritchie, & Tuokko, 2008). However, the presence of depressive symptoms in patients with

AD did not affect the course of cognitive impairment at 12 months (Gare-Olmo, Lopez-Pousa, Vilalta-Franch, & Touron-Estrada, 2003). To our knowledge, no studies using standard personality assessments focused on direct investigations of the possible influence of personality traits on cognitive decline.

Psychotic symptoms have most commonly been associated with a more rapid disease progression (Stern et al., 1997). However, this association refers to psychotic features that occur once dementia is clinically present and, similarly, the significance of psychotic symptoms in prodromal AD or long before AD becomes clinically manifest, is not clear. Most studies have focused on depression and found that mild depressive symptoms (e.g., decreased energy, decreased interest, decreased concentration, and depressed mood) are common in non-dement individuals with memory problems (Berger, Fratiglioni, Forsell, Winblad, & Backman, 1999; Geerlings et al., 2000; Rubin et al., 1989). However, it remains controversial whether these symptoms predict more rapid cognitive decline or a future diagnosis of AD (Bassuk, Berkman, &Wypij, 1998; Chen et al., 1999; Devenand et al., 1996; Yaffe, Blackwell, Gore, Sands, Reus, & Browner, 1999). In a 3-year follow-up study of 112 MCI and 32 normal control subjects symptoms of personality change, i.e., agitation and passivity, were associated with a more rapid increase in functional difficulty over time and those who developed AD, whereas depressive symptoms were not (Copeland et al., 2003). Similarly, the effect of premorbid personality traits in the evolution of SCD in dementia disorders is poorly understood. Although passive, agitated, and self-centered behavioral changes were noted on initial evaluation in one to two thirds of AD patients, the prevalence of these behaviors increased substantially over a 50-month follow-up period (Rubin et al., 1987). However, the presence of personality changes at a mild stage of dementia did not predispose subjects to more rapid progression towards a more advanced stage of illness (Rubin et al., 1987).

3.8. Structural brain changes and genetic markers

Numerous neuroimaging and genetic studies have been carried out in the field of the dementias including their possible association with cognitive decline in neurodegenerative disorders. However, there is only rare evidence linking BPS or personality profiles with neuroimaging and genetic data. Some of these studies carried out in individuals with neurodegenerative disease or related disorders will be reviewed below with special emphasis on limbic brain areas and on serotoninergic neurotransmission as promising candidate topics.

3.8.1. Structural brain changes

Some studies suggest that AD patients with BPS represent a neurobiologically distinct subgroup of patients with greater involvement of paralimbic and frontal cortex (Cummings, Ross, & Absher, 1995). Various dynamic and structural neuroimaging as well as neuropathological correlation studies linked BPS in AD to frontal and temporal areas (Farber et al., 2000; Holland et al., 1985; Johnson et al., 1999; Sultzer et al., 1995; von Gunten et al., 2005). Changes in the orbito-frontal and anterior cingulated cortex (ACC) may be of particular importance (Mentis, et al., 1995). Indeed, the ACC is a major brain region involved in controlling behaviors and providing motivational context. Among cognitive, motor, and autonomic functions, its most anterior sections (BA25, BA33, and rostral BA24) play a crucial role in affective and social regulations in part through connections with the amygdala and the periaqueductal grey (Devinsky & D'Esposito, 2004). A long line of observations shows that affective and emotional states such as sadness or happiness, recognizing the emotional content in a facial expression, aggressiveness, and others are associated with the ACC (Ballantine, Flanagan, & Marino, 1967; Devinsky, Morrell, & Vogt, 1995; Veit et al., 2002; Keightley et al., 2003). Permanent changes reminiscent of minor sociopathic personality disorder are reported after ACC lesions (Devinsky et al., 1995; Mega, Cummings, Fiorello, & Gornbein, 1996; Rubin et al., 1989; Tow & Whitty, 1953). The ACC is part of the

prefrontal network sustaining personal and social behavior together with the orbitofrontal and dorsolateral regions (Devinsky & D'Esposito, 2004). The orbitofrontal cortex, is particular through its posterior agranular limbic region, is well known to mediate social and drive behaviors to environmental stimuli (Devinsky & D'Esposito, 2004) and its anatomical connections largely parallel those of the ACC. Alterations in ACC or orbito-frontal cortex have been observed in mild dementia or mild cognitive impairment (Benoit et al., 2002; Huang et al., 2002). A few preliminary studies point out associations between personality characteristics and cortical limbic areas. Most of them use functional neuroimaging in non-demented cohorts (Stenberg et al., 1990; Ebmeier et al., 1994; Johnson et al., 1999; Canli et al., 2001; Stepaniuk et al., 2008). Regional cerebral blood flows in the resting state correlated with each personality dimension, i.e. novelty seeking, harm avoidance, and reward dependence and was consistent with that of the assumed monoaminergic projections for each personality dimension (Sugiura, Kawashima, Nakagawa, Okada, Sato, & Goto, 2000). Harm avoidance, as another personality trait, showed a significant inverse correlation with in vivo 5-HT2A receptor binding in the frontal and left parietal cortex but not in the basal ganglia (Moresco, Dieci, Vita, Messa, Gobbo, & Galli, 2002). Furthermore, personality may influence limbic-cortical interactions during sad mood induction which was shown for the ACC, thus contradicting the general assumption that emotion-related activation patterns are similar across people (Keightley et al., 2003). A single study using a structural approach looked at trait personality characteristics and associated brain changes in patients with FTD. It found a significant positive correlation between the agreeableness personality dimension and the right orbito-frontal volume as well as a negative correlation with the left orbito-frontal volume (Rankin et al., 2004).

3.8.2. Genetic markers

BPS in AD were found to be associated with ApoE4 and less so ApoE3 genotypes (Zubenko et al., 1991; Krishnan et al., 1996; Ramachandra et al., 1996; Müller-Thomsen et al., 2002; Monastero et al., 2006) although some studies contradict such findings (Heidrich, Thome, & Rosler, 1997; Gabryelewicz et al., 2002). Findings of correlation studies focusing on BPS may point to genetic markers and related parameters involved in emotion regulation and mediation of personality characteristics. Thus, BPS may be secondary to the disruption of different neurotransmitter systems (Cummings et al., 1995), in particular the serotoninergic system as a large body of evidence suggests that the dysfunction of this system plays a pivotal role in the pathogenesis of suicide impulsivity, and aggression (Lesch et al., 1996; Constantino, Morris, & Murphy, 1997; Coccaro, 1998; Malafosse, 2005; Mann, 2003) as well as major depressive disorder (Levinson, 2006). These results are corroborated by similar findings in AD suggesting a reasonable correlation between serotonin dysfunction and various BPS, an emerging evidence based on the use of both genetic and neuropathological methods (Palmer at el., 1988; Brane, Gottfries, & Blennow, 1989; Zubenko et al., 1991; Förstl, Burns, & Luthert, 1992; Victoroff et al., 1996; Holmes et al., 1998; Nacmias et al., 2001; Sukonick et al., 2001). Linking psychiatric features (such as depression) predictive of future cognitive decline with the serotoninegic system suggests that the latter may itself be a predictor of further cognitive decline. For the same reason, it is useful to consider whether or not serotoninergic markers are related to premorbid personality traits. Premorbid personality characteristics were found to be associated with serotoninergic markers in studies investigating community samples or psychiatric cohorts. The correlation between indices of low serotonin turnover and several behaviors are among the most robust findings in biological psychiatry (Mann, 2003). These studies were initiated by the seminal observation of a bimodal distribution of the concentration of 5-hydroxyindolacetic acid (5-HIAA, the

serotonin metabolite) in the cerebrospinal fluid (CSF) of unipolar depressed patients (Asberg, Traksman, & Thoren, 1976). Patients with the lowest CSF 5-HIAA concentrations were most likely to attempt or commit suicide using violent means and to present personality traits such as propensity to feel or to express anger (for a review see Courtet, Jollant, Castelnau, Buresi, & Malafosse, 2005). More recently, molecular genetic studies of serotonin-related candidate genes further supported these results (Courtet, Baud, & Abbar, 2001; Bellivier, Chaste, & Malafosse, 2004). Associations between the serotoninergic gene polymorphism and impulsivity and expressing anger independently of the Axis I diagnosis were also reported (Courtet et al., 2001, 2005). The second most commonly studied gene codes for the serotonin transporter (5-HTT) of which a specific polymorfism was associated with anxiety-related traits as well as suicide attempt (Lesch et al., 1996; Courtet et al., 2005). Increased serotoninergic function should be associated positively with agreeableness and conscientiousness and negatively with neuroticism as low levels of serotonin are associated with aggression, poor impulse control, depression, and anxiety, and drugs that boost serotoninergic function are often used successfully to treat of these problems. A combined behavior genetic and genomic study demonstrated that the correlation between neuroticism and agreeableness has a genetic basis and that variation in the serotonin transporter gene accounted for 10% of the correlation (Jang et al., 1996). A pharmacological manipulation that promotes serotonin release and inhibits reuptake has demonstrated that both low neuroticism and high conscientiousness are associated with increased serotoninergic responsiveness (Manuck, Flory, & Ferrell, 1999). Variation in the monoamine oxidase-Agene, which affects levels of serotonin, is associated with defferences in agreeableness and conscientiousness. Stressful life events predicted suicide ideation or attempt among individuals carrying this specific allele (Caspi et al., 2003). Within this view, we might hypothesize that BPS, as frequent concomitants of incipient dementia might be the expression, among other factors, of

susceptibility genes involved in serotonin metabolism in individuals who have always had a tendency to react over-emotionally to stressful life events. Indeed, stressful life events are environmental risk factors for mental disorders and they may be associated with premorbid personality and be risk factors for personality changes in the demented. However, whether or not genetic factors related to premorbid personality traits promote cognitive decline is unknown and no such studies exist to our knowledge. A number of potential pitfalls exist for such studies and comprise false positive or false negative findings, mismatch of patients and control subjects, under-powering of studies, the fact that there may be a high number of low risk genes, the etiological heterogeneity of MCI, and the lack of longitudinal studies (van Duijn, 2004). Nevertheless, there is indirect evidence for the possibility the genetic factors related to personality traits predict future cognitive decline. Thus, major depression is recognized as a predictor of future dementia (see above) and, as shown more recently, for future MCI (McEwen, 2000; Barnes, Alexopoulos, Lopez, Williamson, & Yaffe, 2006). Moreover, major depression is quite robustly predicted by high premorbid neuroticism, i.e., premorbid personality traits (Kendler, Kuhn, & Prescott, 2004). It is estimated that 55% of the genetic risk for major depressive disorder is shared with neuroticism (Kendler et al., 1993), the heritability of which is considered to be as high as 40-50% (Jang et al., 1996). Thus, it can be hypothesized that genotype influences stress reactivity rather than depression alone with stress reactivity being linked genetically to future dementia and, analogously, to MCI conversion. Evidence supporting this idea comes from studies of candidate genes in that the 5-HTTLPR (serotonin transporter gene linked polymorphic region) genotype influenced stress reactivity (Mithchell, Wilhelm, & Parker, 2004). An association between this gene and neuriticism has been suggested (Levinson, 2006). Depression and neuroticism linkage findings point to a series of chromosomal sites (Fullerton, Cubin, Tiwari, Wang, Bomhra, & Davidson, 2003; Holmans et al., 2004; Nash et al., 2004; Camp, Lowry, Richards, Plenk,

Carter, & Hensel, 2005; Neale, Sullivan, & Kendler, 2005) and a similar suggestion was raised with regard to harm avoidance (Cloninger, 1991; Cloninger et al., 1998). CREB1 (cyclic adenosine monophosphat (cAMP) responsive element binding protein 1) was hypothesized to be a plausible candidate gene for depression (Laifenfeld, Karry, Klein, & Ben-Shachar, 2005), but no studies exist on a possible link with personality characteristics. Taken together, as yet rare studies and indirect evidence suggest that cortical limbic regions, in particular in the ACC and orbitofrontal cortex, as well as serotoninergic markers may be associated with personality characteristics or BPS and predict further cognitive decline in MCI patients.

3.9. Conclusions

Cognitive disorders accompanied by BPS are a tremendous burden for both the patient and their proxies and a challenge for the clinician eager to help. The steeply rising number of elderly people with such disorders adds a public health dimension to the problem. Therefore, every effort is needed to disentangle the complex interplay of the many factors potentially responsible for BPS and cognitive decline. Premorbid personality is a candidate factor. A growing field of research is interested in the links not only between quite short-lived emotional states and cognitive processes, but also between longstanding personality traits and cognition. Much is to be expected from such studies even more so as they start linking personality traits and cognitive information processing to identifiable brain system. As an example, extraversion may be associated with increased resistance to cognitive interference and, possibly, the dopaminergic neurotransmitter system. Grounded on such findings scientific curiosity quite naturally prods our questioning about the possible influence of personality traits on the clinical phenomenology observed in cognitive disorders. However, our review shows the dearth of studies on a possible pathoplastic effect of personality characteristics on cognition in neurodegenerative disorders. One of the most important

shortcomings that hampers so far the progress of our understanding in these domains is the confusion in the literature between longstanding premorbid personality traits and transient personality changes. Further clarification is needed as to whether personality changes refer to premorbid personality traits, thereby constituting a risk factor for specific BPS in neurodegenerative diseases, or whether or not they are merely an early "pre"-clinical sign. Few studies have based their assessments on accepted personality theories and carefully investigated premorbid personality traits in patents with cognitive disorders, although defining premorbidity may be controversial. Nevertheless, it is becoming increasingly clear that premorbid personality is a co-determinant of BPS in cognitive disorders despite the need for further clarification as no strong links have so far emerged. A few studies in AD patients found that premorbid psychiatric syndromes are possible risk factors for cognitive decline in the elderly. Similarly, some studies have observed that premorbid personality traits such as distress-proneness or low conscientiousness were more common among AD patients than controls suggesting that they may be a risk factor for neurodegenerative diseases. This is particularly promising field of personality research in particular when concomitantly using neurobiological approaches, in particular structural brain imaging and genetic studies. Indeed, as yet rare studies and indirect evidence suggest that morphological changes in cortical limbic regions, in particular in the ACC and orbitofrontal cortex, may be associated with BPS and further cognitive decline in patients with early neurodegenerative disease. Similarly, genetic markers, e.g. serotoninergic or dopaminergic markers may be associated with personality characteristics and with BPS, or predict further cognitive decline in MCI patients. For this reason, further studies should be conducted taking into account not only personality characteristics but also the variability of possible genetic and neuroanatomial markers. It also seems very important to conduct longitudinal studies in this field, which might be combined with a retrospective approach. Concerning personality several sources of information might

be considered such as personality self-assessment, peer-reports, or even personality relevant information obtained using an experimental approach. It might be especially informative to compare self-and peer-reports, knowing that many patients with dementia suffer from alterations of self-awareness. Finally, some other psychological dimensions or processes, which are considered by the authors of the FFM to mediate the relationship between personality and behavior and which are crucial for situational adaptations, might also be considered in further studies such as self-regulation or motivation. Improved understanding of premorbid personality characteristics as determinants of BPS or cognitive capacities or decline is likely to influence our attitudes towards the treatment of demented patients and ultimately to help alleviate a patient's and their proxies' burden.

Chapter 4. Personality changes in patients with beginning Alzheimer's disease[2]

4.1. Introduction

Alzheimer's disease (AD) is a leading cause of cognitive decline in old age. It is also accompanied by behavioral and psychological symptoms and personality changes. The few existing studies on the topic suggest that personality changes occur early in the disease and may aid in early detection and diagnosis (Balsis et al., 2005). A better understanding of personality traits on disease susceptibility and risk or the interaction between personality change and the disease process may further both early detection of AD and more appropriate care. Research into current and premorbid personality traits or disorders as early markers of AD has been neglected (von Gunten, Pocnet, & Rossier, 2009). Further, experimental and clinical work strains to prove clear links between personality factors and features of AD, a difficulty owing, at least in part, to the complexity and multitude of the causal factors involved in the development of AD and the many facets of personality itself. At that, only few studies have systematically investigated personality changes in patients with AD. However, some studies (Chatterjee et al., 1992; Welleford, Harkins, & Taylor, 1995; Dawson et al., 2000) have examined changes in personality traits among patients with AD using ratings from close relatives asked to compare current with retrospective personality. These studies show that premorbid personality traits were the only significant predictor of change for *Neuroticism* (particularly higher anxiety, depression, and vulnerability facets), *Extraversion* (lower assertiveness and activity facets), and lower *Openness* to new ideas, fantasy, aesthetics, and values. In a 12-year annual follow-up study, using a standard 12-item measure of

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[2] This chapter has been previously published as a scientific article (Pocnet, Rossier, Antonietti, & von Gunten, 2011).

Conscientiousness, Wilson et al. (2007) demonstrated an association between lower levels of *Conscientiousness* and the incidence of AD.

Although these studies provide a consistent and plausible picture, they reflect evaluation by close caregivers and often ignore the personality description by the patients themselves. The information given by a close relative about a patient's previous personality may be biased to some extent as a result (for example, the idealization of the patient and their previous relationship as well as the stress endured as a consequence of the change in their relationship (Aitken et al., 1999). Thus, personality self-assessment may be a useful piece of information in addition to the evaluation by a close caregiver. Moreover, the interaction between personality and dementia development might be especially sensitive and informative at the onset of this disease.

Whether or not personality changes during beginning dementia is unclear. Given the dearth of information and the controversies in this research domain, we preferred not to make specific assumptions. In our study, we wished to compare both current and retrospectively assessed previous personality traits in patients with incipient AD and mentally healthy control subjects, using both structured interviews of current personality as well as an evaluation by proxies of a patient's current and previous personality traits.

4.2. Method

4.2.1. Sample

Fifty-four patients diagnosed with mild AD were selected from patients attending an old-age psychiatric memory clinic, and 64 control subjects were recruited by journal announcements and "word of mouth".

4.2.2. Procedure

All the patients had a comprehensive medical, psychiatric, neuropsychological, and psychosocial evaluation. Most often, they also had cerebral magnetic resonance imaging as well as numerous standard laboratory tests. This investigation yielded an International Classification of Disease, 10th Edition, diagnosis (Word Health Organization, 1993) and the National Institute of Neurological and Communicative Disorders and Stroke, and the Alzheimer's Disease and Related Disorders Association (McKhann et al., 1984) criteria for AD were established.

More specifically, and for the purpose of the study, AD patients had the Hospital Anxiety and Depression scale (Zigmond & Snaith, 1983) and the Mini-Mental Status Examination (Folstein, Folstein, & McHugh, 1975). Observer-report by family members was obtained through the Neuropsychiatric Inventory (Cummings et al., 1994), the Activities of Daily Living (Katz, 1998), the Instrumental Activities of Daily Living scales (Lawton & Brody, 1969), and the Informant Questionnaire on Cognitive Decline in the Elderly (Jorm & Jacomb, 1989). The control subjects had an identical assessment.

Participation in our study was proposed to the patients, the control subjects, and their proxies. The goals of the project were explained and written consent was obtained. The completion of the clinical research battery took about 2.5 hours for the patient, 2 hours for the participants in the control group, and 1 hour and forty minutes for the family member. To minimize the subjects' fatigue, they were seen in 1 or 2 sessions with not more than one week between sessions. Our study did not present any particular risks for the patients. The Ethics Committee of the Biology and Medicine Faculty of the University of Lausanne approved this project (Protocol 85/2008).

4.2.3. Personality assessment

Personality traits were assessed according to the Five-Factor Model (FFM) that is currently the most common dimensional approach to personality (Costa & McCrae, 1992; Digman, 1990). This model claims that personality can be described along five main independent dimensions called *Neuroticism*, *Extraversion, Openness to experience, Agreeableness,* and *Conscientiousness*. Each of these dimensions is composed of six lower-level personality facets (Rossier et al., 2004). Costa & McCrae (1990) have suggested that the extremeness of scores on the dimensions of the FFM could differentiate normal personality from pathological personality or that dysfunction might be associated with some specific personality profiles according to another study (Rossier et al., 2008).

Two mutually compatible tools based on the Five-Factor Model (FFM) were used. The French version (Pocnet et al., 2009) of the *Structured Interview for the Five-Factor Mode* (Trull & Widiger, 1997) appears as a well-suited instrument for the assessment of personality traits in patients with AD who may be unable to complete a questionnaire. It is composed of 120 questions. The *NEO Personality Inventory Revised*, Form R (Costa & McCrae, 1992) is a questionnaire composed of 240 items and used for peer ratings. For our study, proxies assessed both the current and the previous personality of the patients with AD. The previous period was defined as the time from young adult age to 5 years prior to the beginning of cognitive decline. Thus, family members completed the NEO-PI-R twice, once to evaluate the participants' current personality and the second time to assess personality traits as they were remembered to be 5 years earlier.

4.2.4. Statistical Analysis

The data were analyzed using SPSS, version 18 (SPSS Inc, Chicago, IL) and R (R Development Core Team, 2009). Descriptive statistics were used to characterize demographic and clinical characteristics by the two groups: patients with AD and control subjects.

Comparison of current personality characteristics between patients with AD and normal controls were performed calculating ANCOVAs to control for demographic variables, in particular age, which differed between the two groups. Gender distribution was similar across the two groups. Previous personality traits in patients with Alzheimer's disease and healthy subjects were compared using also ANCOVAs with control for age. Comparisons of current and previous personality traits in patients with AD were done using ANOVAs for repeated measures. We also calculated the effect size for each comparison. To further examine the effect of generalized interaction, a MANCOVA was carried out. Correlations between current self-assessment of personality traits and observer-description of current and previous traits for the clinical group were also computed.

4.3. Results

The AD and control groups had significantly different mean age but gender distributions were similar. As expected, the clinical group scored higher than the control group on the clinical depression scale (HAD), the IQCODE, and on the NPI for symptom severity, and had lower scores on the MMSE, and the ADL and IADL scales (see Table 3).

Table 3. Demographics and descriptive statistics

	Patients AD, *n* = 54		Healthy controls, *n* = 64		
Variables	*Mean*	*SD*	*Mean*	*SD*	*p*
Age, years	76.9	8.5	69.3	8.7	< .001
Gender	39 female, 15 male		35 female, 29 male		.050
MMSE	23.7	3.0	29.2	1.0	< .001
HAD: Anxiety	4.1	2.7	4.4	2.2	.444
HAD: Depression	4.2	2.7	2.3	1.6	< .001
ADL	5.1	1.1	6.0	0.0	< .001
IADL	3.9	2.1	8.0	0.0	< .001
IQCODE	4.0	0.5	3.0	0.1	< .001
NPI-Q: Severity	7.6	4.1	0.7	2.1	< .001

Note. AD = Alzheimer disease; MMSE = Mini-Mental State Examination; HAD = Hospital Anxiety and Depression scale; ADL = Activities of Daily Living; IADL = Instrumental Activities of Daily Living; IQCODE = Informant Questionnaire on Cognitive Decline in the Elderly; NPI-Q = Neuropsychiatric Inventory.

4.3.1. Current personality profiles in patients with AD, compared with control subjects

Concerning evaluation through the structured interview for FFM of Personality (Pocnet et al., 2009), the mean personality profile for patients with AD was very different from that of the healthy controls subjects. Some of the differences reported below were associated with large effect sizes ($d \geq 0.80$) (Cohen, 1994). After controlling for age, the AD group presented significantly higher scores on *Neuroticism* owing to differences, especially on the *vulnerability* facet scale. The significantly lower scores of the AD group on *Extraversion* were mainly due to differences on the *gregariousness*, *assertiveness*, *activity*, *excitement seeking*, and *positive emotions* facet scales. Equally, the significantly lower scores of the AD group on *Openness to experience* were due to differences on the *fantasy*, *esthetics*, *action*, *ideas*, and *values* facet scales. The significantly lower scores of the AD group on *Conscientiousness* resulted from differences on the *competence*, *dutifulness*, *achievement-striving*, and *self-discipline*, facet scales. No significant difference between the two groups was observed for *Agreeableness* (see Table 4).

Table 4. Current personality profiles in patients with AD, compared with control subjects

	AD patients, *n* = 54		Healthy controls, *n* = 64				
Variables SIFFM	*Mean*	*SD*	*Mean*	*SD*	*F**	*d*	*p-value*
Neuroticism	14.1	5.6	12.5	4.7	2.42	0.17	.433
Anxiety	2.5	1.8	1.9	1.4	2.18	0.27	.077
Hostility	1.8	1.1	1.7	1.1	0.99	0.01	.753
Depression	2.6	1.6	2.5	0.7	1.76	0.15	.187
Self-Consciousness	2.1	1.2	2.0	1.4	2.03	0.20	.127
Impulsiveness	1.7	1.0	1.9	1.1	1.56	0.10	.156
Vulnerability	3.4	1.4	2.4	1.4	5.16	0.85	< .001
Extraversion	19.2	4.9	29.5	4.6	11.38	1.41	< .001
Warmth	4.0	1.6	4.7	1.4	4.60	0.76	< .001
Gregarious	3.5	1.2	5.2	1.1	6.58	1.01	< .001
Assertiveness	2.9	1.4	5.0	1.7	9.79	1.24	< .001
Activity	3.1	1.1	5.5	1.2	5.92	0.92	< .001
Excitement-seeking	1.7	1.1	3.6	1.0	5.16	0.86	< .001
Positive emotions	4.0	1.1	5.5	1.1	4.20	0.57	< .001
Openness	16.3	4.0	23.5	4.2	8.26	1.14	< .001
Fantasy	1.8	1.1	2.8	1.0	2.99	0.07	< .001
Aesthetics	3.0	1.0	4.6	1.3	5.16	0.86	<. 001
Feelings	5.3	0.9	5.7	1.1	2.93	0.06	.499
Action	1.6	0.9	2.7	1.4	6.46	1.00	< .001
Ideas	1.9	1.3	3.9	1.6	8.28	1.15	< .001
Values	2.8	0.9	3.9	1.3	5.47	0.89	< .001

Continued

Table 4. Current personality profiles in patients with AD, compared with control subjects (continued)

	AD patients, n = 54		Healthy controls, n = 64				
Variables SIFFM	*Mean*	*SD*	*Mean*	*SD*	*F**	*d*	*p-value*
Agreeableness	29.4	3.4	29.3	3.7	0.78	0.14	.434
Trust	4.0	1.3	5.1	1.1	2.10	0.04	.372
Straightforwardness	5.4	0.8	5.3	1.0	0.76	0.13	.423
Altruism	4.0	0.9	4.7	1.1	2.74	0.05	.273
Compliance	5.2	1.2	4.7	1.2	2.89	0.06	.367
Modesty	4.5	1.6	3.8	1.5	4.21	0.51	.001
Tender- Mindedness	6.2	1.2	5.6	1.2	2.77	0.05	.341
Conscientiousness	28.1	4.0	33	4.2	6.57	1.03	< .001
Competence	4.3	1.1	5.8	0.9	6.60	1.02	< .001
Order	4.1	1.5	4.2	1.3	1.04	0.04	.507
Dutifulness	5.7	1.1	6.3	0.9	3.45	0.60	< .001
Achievement-striving	4.6	0.8	5.2	0.9	2.61	0.48	< .001
Self-discipline	4.6	1.2	6.5	1.3	8.28	1.17	< .001
Deliberation	4.9	1.2	5.0	1.4	4.34	0.71	< .001

Note. * ANCOVAs to control for age; *df* =1,115.

The current observer ratings, using NEO-PI-R, indicate significant differences between the two groups for the same 4 domains: for the AD patients we found a higher score on *Neuroticism* (t (115) = 7.73, p < .001, d = 1.13), and a lower score on *Conscientiousness* (t (115) = 14.72, p < .001, d = 1.48), in comparison with personality self-description. The results on *Extraversion* (t (115) = 10.56, p < .001, d = 1.33), and on *Openness to experience* (t (115) = 8.81, p < .001, d = 1.19) remain as high as in self-assessment; similarly, *Agreeability* scores

are also unchanged (t (115) = 0.76, p = .45, d = 0.14). Facets description follows the same consistent trend, but they are more pronounced.

4.3.2. Previous personality profiles in patients with AD, compared with control subjects

Comparisons of the previous personality traits in patients with AD and healthy subjects show significant differences for 4 domains: higher scores on *Neuroticism* for patients with AD (t (115) = 4.10, p < .001, d = 0.70), and lower scores on *Extraversion* (t (115) = 6.42, p < .001, d = 1.00), *Openness to experiences* (t (115) = 6.87, p < .001, d = 1.03), and *Conscientiousness* (t (115) = 4.82, p < .001, d = 0.80). These results were mainly due to differences on the following facet scales: for *Neuroticism*, *depression* (d = 0.73), *self-consciousness* (d = 0.79), and *vulnerability* (d = 0.78); for *Extraversion*, *warmth* (d = 0.85), *gregariousness* (d = 0.61), *assertiveness (d = 0.*96*),* and *activity (d* =0.66); for *Openness to experiences*, *esthetics* (d = 0.68), *actions* (d = 0.96) *ideas* (d = 1.21), and *values* (d = 0.80); for *Conscientiousness*, *competence* (d = 0.88), *achievement striving* (d = 0.74), and *self-discipline* (d = 0.80). No significant difference between the two groups was observed for *Agreeableness* (t (115) = 0.28, p = .78, d = 0.05). Several differences between the two groups are thus associated with a large effect size ($d \geq 0.80$). Moreover, for the AD group there was a significant and positive association between current self-assessment of personality traits and observer-description of previous traits for *Neuroticism*, *Extraversion*, *Openness to experiences*, and *Agreeableness*, but not for *Conscientiousness* compared with the control group (see Table 5).

Table 5. Correlation between current self and observer-ratings, both concurrent and retrospective personality traits, in the two groups

	NEO-PI-R previous personality					NEO-PI-R current personality				
SIFFM	N	E	O	A	C	N	E	O	A	C
					AD group					
Neuroticism	.40 **	-.22	.07	-.08	-.05	.40 **	-.25	.06	-.16	-.01
Extraversion	-.14	.40 **	.22	.15	.30 *	-.03	.20	.12	.02	.21
Openness	-.13	.13	.60 ***	.05	.19	-.09	.12	.60 ***	.07	.13
Agreeableness	-.03	-.22	-.16	.29 *	-.01	.14	-.31 **	-.14	.26	-.10
Conscientiousness	.07	.14	.23	.09	.18	.09	.25	.23	.13	.28 *
					Control group					
Neuroticism	.34 **	-.07	.00	-.19	-.09	.34 **	-.04	.00	-.20	-.08
Extraversion	.05	.38 **	.06	-.11	-.13	.03	.35 **	.05	-.11	-.10
Openness	.00	.18	.51 ***	-.08	-.11	-.03	.17	.50 ***	-.08	-.09
Agreeableness	-.06	.26 *	.30 *	.47 **	.06	-.05	.28 *	.30 *	.48 **	.06
Conscientiousness	-.15	-.18	-.13	.00	.37 **	-.15	-.18	-.10	.00	.34 **

Note. FFM = Five-Factor Model; NEO-PI-R, = NEO Personality Inventory Revised; N = Neuroticism; E = Extraversion; O = Openness; A = Agreeableness; C = Conscientiousness. *$p < .05$; ** $p < .01$; *** $p < .001$.

4.3.3. Evolution of personality characteristics between previous and current traits in patients with AD.

Current personality traits, as assessed by the proxies of the patients with AD, were clearly distinct from previous traits with some of the differences being associated with large effect sizes. Although the correlations between current and previous traits for the clinical group are significant and very high, incipient AD was accompanied by a highly significant increase on *Neuroticism*, a decrease on *Extraversion*, *Openness to experiences*, and *Conscientiousness*, while *Agreeability* scores remained unchanged. These results were mainly due to changes on the following facet scales: for *Neuroticism*, *depression*, *activity, impulsiveness*, and *vulnerability*; for *Extraversion*, *warmth*, *gregariousness*, *assertiveness*, *activity*, *excitement-seeking*, and *positive emotions*; for *Openness to experiences*, *fantasy*, *aesthetics*, *feelings*, and *ideas*; for *Conscientiousness*, *competence*, *order*, *dutifulness*, *achievement striving*, *self-discipline,* and *deliberation* (see Table 6).

Table 6. Evolution of personality characteristics between previous and current traits in patients with AD

NEO-PI-R (previous and current)	*r*	*p*	*F**	*d*	*p*
Neuroticism	.73	< .001	9.78	1.33	< .001
Anxiety	.63	< .001	2.77	0.38	.008
Hostility	.75	< .001	3.29	0.48	.002
Depression	.79	< .001	9.48	1.29	< .001
Self-consciousness	.77	< .001	3.14	0.43	.003
Impulsiveness	.56	.001	4.53	0.59	.001
Vulnerability	.57	.001	13.10	1.78	< .001
Extraversion	.66	< .001	9.57	1.30	< .001
Warmth	.73	< .001	6.46	0.88	< .001
Gregariousness	.71	< .001	3.83	0.52	.001
Assertiveness	.59	< .001	9.19	1.25	< .001
Activity	.57	.001	9.44	1.28	< .001
Excitement-seeking	.77	.001	4.90	0.67	.001
Positive emotions	.66	.001	4.20	0.57	.001
Openness to experiences	.87	< .001	7.35	1.00	< .001
Fantasy	.67	< .001	5.16	0.70	< .001
Esthetics	.89	< .001	7.43	1.01	< .001
Feelings	.84	< .001	3.24	0.44	.002
Actions	.49	.001	2.55	0.35	.010
Ideas	.80	< .001	10.45	1.42	< .001
Values	.67	< .001	1.44	0.20	.160

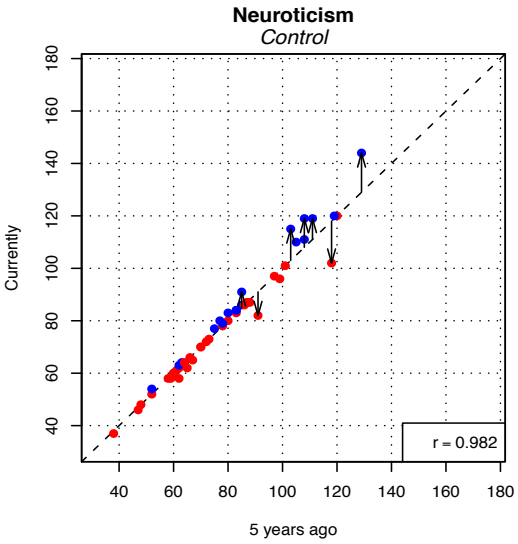
Continued

Table 6. Evolution of personality characteristics between previous and current traits in patients with AD (continued)

NEO-PI-R (previous and current)	*r*	*P*	*F**	*d*	*p*
Agreeableness	.93	< .001	2.06	0.28	.040
Trust	.90	< .001	2.61	0.36	.010
Straightforwardness	.95	< .001	0.82	0.11	.420
Altruism	.69	< .001	4.82	0.66	.005
Compliance	.82	< .001	0.99	0.13	.330
Modesty	.86	< .001	4.11	0.56	.001
Tender-mindedness	.82	< .001	1.82	0.25	.080
Conscientiousness	.47	.001	17.83	2.48	< .001
Competence	.59	< .001	14.92	2.03	< .001
Order	.47	.001	15.35	2.09	< .001
Dutifulness	.46	.001	15.49	2.10	< .001
Achievement striving	.58	< .001	12.85	1.75	< .001
Self-discipline	.46	.001	16.37	2.23	< .001
Deliberation	.67	< .001	13.48	1.83	< .001

Note. * ANCOVAs - Adjusted for age; *df* = 1,53.

These results were confirmed by an overall MANCOVA. Comparing current and previous personality of patients with AD and healthy control subjects, this analysis showed a significant and very large interaction effect between repeated measures, personality domains and group (F (4,113) = 89.35, p < .001, η^2 = 0.76). Figure 5 enables the identification of significant differences regarding the evolution of personality characteristics in the last 5 years between the 2 groups.


Neuroticism
Control
Currently
5 years ago
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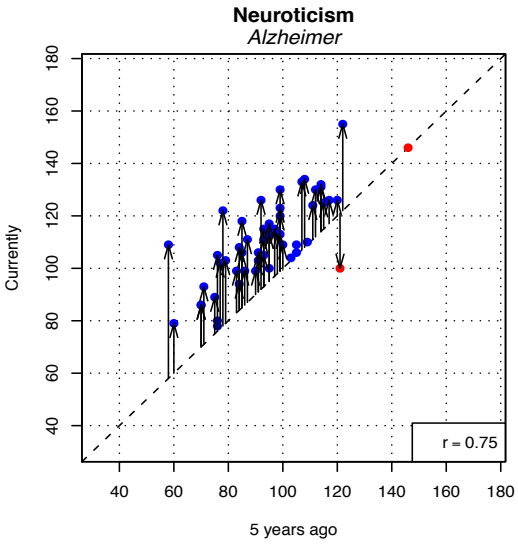
Neuroticism
Alzheimer
Currently
5 years ago
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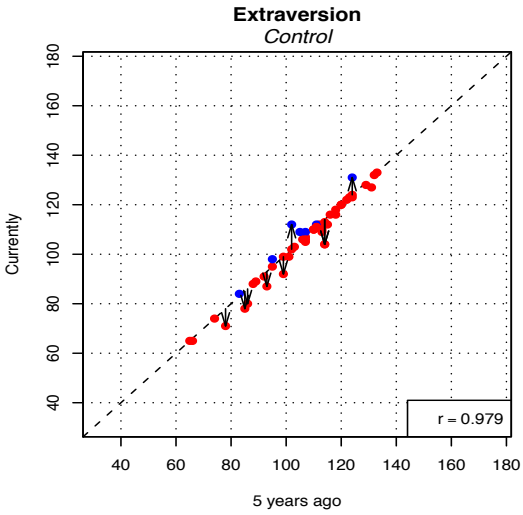
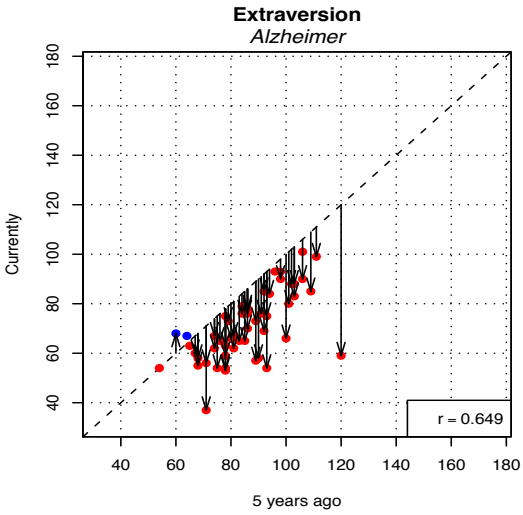

Extraversion
Control
Currently
5 years ago
r = 0.979


Extraversion
Alzheimer
Currently
5 years ago
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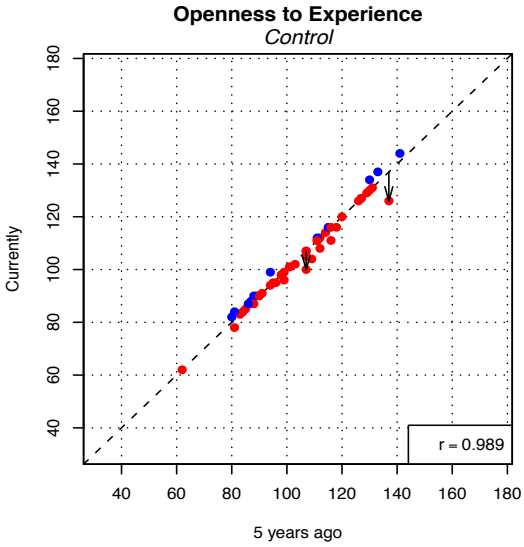
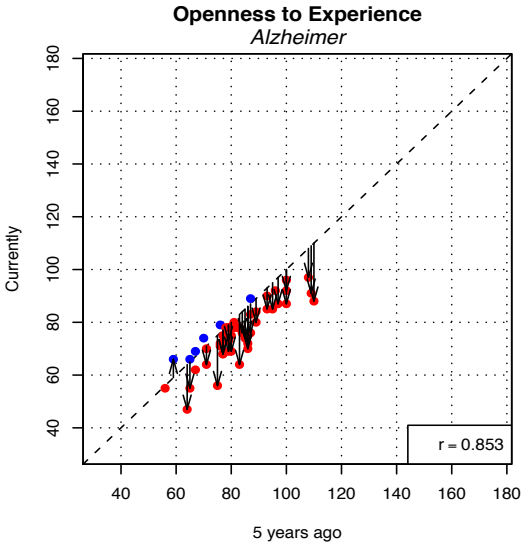

Openness to Experience
Control
Currently
5 years ago
r = 0.989


Openness to Experience
Alzheimer
Currently
5 years ago
r = 0.853

Continued

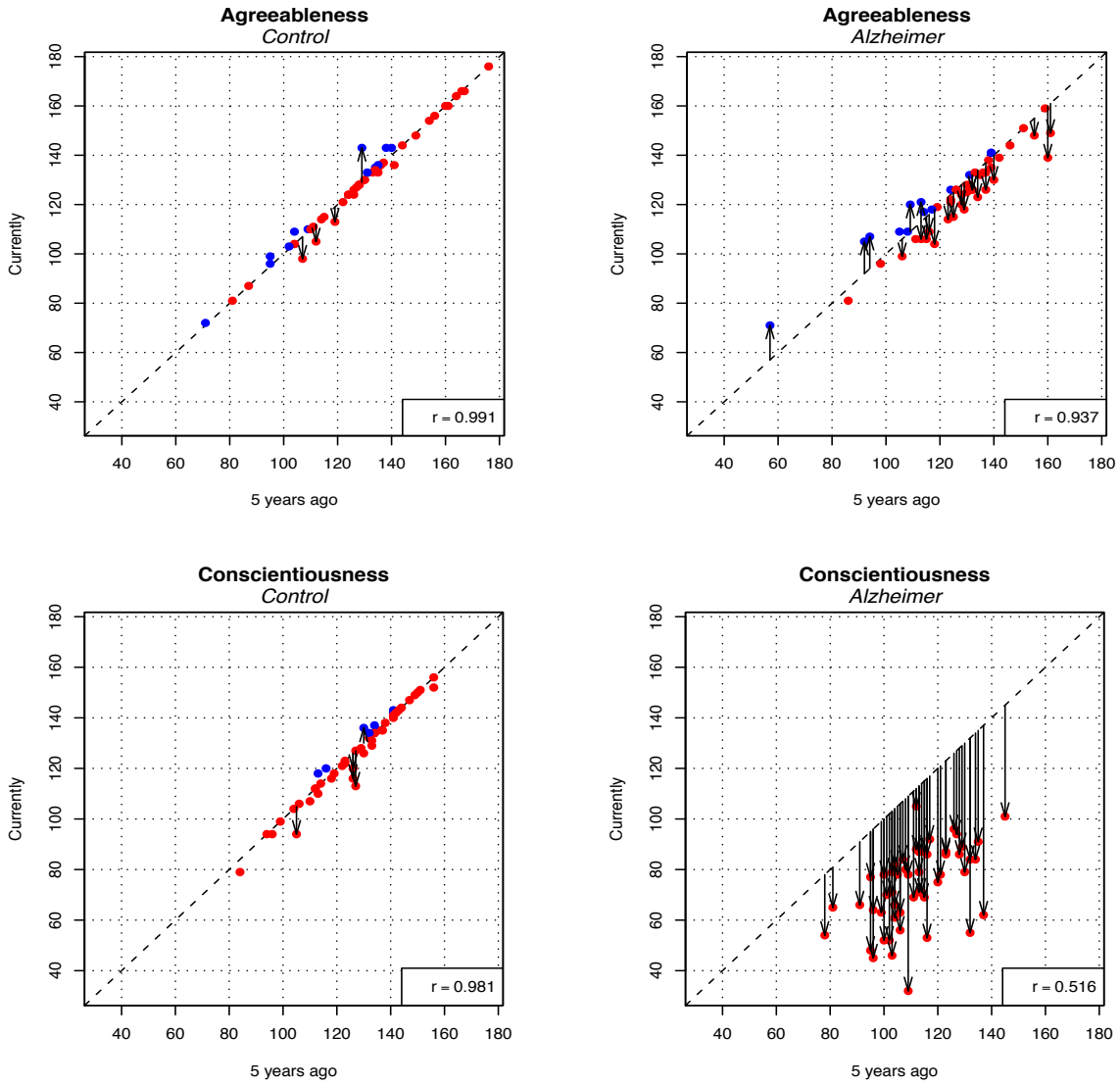


Figure 4. The scatter diagram shows the evolution of personality dimensions during the last 5 years as assessed by their proxies, in patients with AD and control groups. "↓" and "↑" emphasize the direction of the evolution of personality traits with blue upwards directed arrows indicating increase, and red downwards directed arrows decreased scores on the various personality dimensions (scores indicate absolute values on the NEO-PI-R).

4.4. Discussion

Our study shows that current personality features of patients with beginning AD are different, compared with those in normal healthy subjects. Patients with incipient AD have higher mean scores on *Neuroticism* and lower mean scores on *Extraversion, Openness to experiences*, and *Conscientiousness*, while no significant difference was observed on *Agreeableness*. Importantly, there is major convergence between the description given by the subjects themselves as to their current personality traits and the evaluation made by their proxies. However, the differences between patients and controls appear to be much larger in current observer ratings compared to self-report. This suggests that patients with AD evaluate their former personality when asked to evaluate their current personality traits and that self-perception in patients with AD does not evolve parallel to personality changes as observed by third parties. In Rankin et al. (2005), patients with dementia may fail to update their self-image once affected by the disease.

The same differences were already present, although to a lesser degree, 5 years earlier to the current assessment. This profile was observed when considering personality traits as the patients' proxies remembered them. Moreover, the findings about the evolution of personality characteristics in patients with AD were convergent with the current differences between the patients and the control subjects and concerned the same four domains. Thus, patients with AD undergo significant personality changes, which contrasts with the overall stability of personality traits observed for the healthy subjects of our study and which has been reported by others (Costa & McCrae, 1992; Rossier et al., 2004). Overall, patients with AD seem to become more vulnerable to stress, more dependent, hopeless, and reserved, somewhat gregarious, as well as more compulsive. Their conservativeness and conventionality in their views and behaviors increase; these patients prefer situations they are familiar with, and their

novelty seeking and emotional responses are somewhat blunted. Their general interest is decreased and indifference in the pursuit of their goals becomes evident.

According to Terraciano et al. (2005), personality traits of people in good mental health remain relatively stable during their whole life, small changes occur slowly and gently and not as quickly and significantly as observed in our clinical group. Our findings are in line with those of other studies reporting personality change in AD and suggest that personality change is a consistent aspect of the phenomenology of AD (Talassi et al., 2007). Current personality traits in patients with AD could correspond to systematic shifts of previous personality traits, or specific personality changes affecting subtypes of patients as postulated by some authors (Chatterjee et al., 1992). In agreement with the literature (Rankin et al., 2005) in patients with AD, the personality changes are dissociated; that is our findings suggest reproducible patterns of personality changes either through accentuation or attenuation of specific personality traits over time following a consistent trend. We interpret these changes as a uniform direction of change whatever the previous personality traits were before. Thus, there seems to be a specific change but not a specific AD personality. This interpretation is also in line with that of some researchers, who consider that demented patients retain much of their former personalities and argue against the emergence of a specific *Alzheimer personality* (Balsis et al., 2005).

The strengths of our study result from the use of well-validated instruments allowing comparing self- and observer assessment of personality traits in a well-characterized sample of patients with incipient AD. However, measuring personality changes using retrospective assessment by proxies may have introduced some memory bias and the heterogeneity of the proxies interviewed may figure among the more important study limitations. Although the analyses were adjusted for significant age differences findings ought to be replicated with

more similar groups. However, in general, our findings appear to clearly show that important personality changes occur in patients with incipient AD.

4.4.1. Conclusions

Patients with incipient AD have different personality profiles, compared with healthy control subjects, as they undergo significant personality change with an increase on neuroticism, and a decrease on *Openness, Extraversion,* and *Conscientiousness.* These changes are likely to occur early during the course of AD and their observation may help in the early detection of dementia. Our study does not further the debate as to whether or not the existence of specific premorbid personality traits may constitute a risk factor either for AD, for future cognitive decline in AD or patients with mild cognitive impairment, or, the occurrence of specific behavioral and psychological symptoms of dementia. Future studies should attempt to detect these early personality changes using long-term prospective designs. A better understanding of such links may ultimately suggest novel strategies for delaying the occurrence of symptoms of AD and help patients and their proxies more efficiently.

Chapter 5. Personality traits and behavioral and psychological symptoms in patients at an early stage of Alzheimer's disease[3]

5.1. Introduction

Alzheimer's disease (AD) is often associated with behavioral and psychological symptoms (BPS) and personality changes. The prevalence of BPS is high and impacts substantially on the quality of life of both the demented and those who support them. Neuropsychiatric symptoms of dementia take on many forms and can be grouped into affective, psychotic, behavioral, and personality disorders or changes (Cummings, 2003).

Behavioral and psychological symptoms (BPS) in people with AD are commonly seen as a consequence of brain degeneration, a vantage point assuming a direct causal relationship between neuropathology and behavior. However, this biologically orientated level of explanation appears to have only partial theoretical and empirical support (Bird & Moniz-Cook, 2008) and ignores both the individual experience of the demented and their socio-cultural context (Cheston & Bender, 1999). AD phenomenology resulting from interactions between the neurological, psychological and social factors receives increasing attention in research (Downs, Clare, & Anderson, 2008) and so does the potential influence of personality on BPS (Ballard et al., 2001; von Gunten et al., 2009). Indeed, individual personality structure may both influence how a person experiences AD and be causal to the occurrence of BPS.

Some researchers consider that demented patients retain much of their former personalities (Kolanowski & Whall, 1996; Balsis et al., 2005), and personality changes, which appear with the evolution of disease, are interpreted as accentuations of premorbid personality traits. These personality changes are a consistent aspect of the phenomenology of AD as

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[3] This chapter has been previously published as a scientific article (Pocnet, Rossier, Antonietti, & von Gunten, 2013).

suggested by findings of yet other research work (Siegler et al., 1994; Aitken et al., 1999; Purandare et al., 2002).

Certain studies have suggested that BPS in subjects with AD reflect an individual's longstanding personality traits (Kolanowski & Whall, 1996). Thus, *premorbid Neuroticism* was a significant positive predictor of depression in dementia (Gilley et al., 2004), and life-long predisposition towards negative emotions may be associated with increased vulnerability to distress once AD has occurred (Wilson et al., 2003). *Premorbid Extraversion* was a negative predictor of wandering during dementia (Song & Algase, 2008). Lower *premorbid Agreeableness* was associated with agitation and irritability in AD and predicted an *agitation/apathy* syndrome (Archer et al., 2007). Further associations between personality traits and neuropsychiatric symptoms in dementia were reported and included the following: higher *premorbid Neuroticism* with increased depression, and behavioral disturbance, lower *premorbid Extraversion* and frustration tolerance with increased depression, higher premorbid hostility with delusions, and higher *Openness* with hallucinations (Chaterjee et al., 1992; Strauss et al., 1997; Meins et al., 1998; Meins, 2000). In nursing home residents, Low et al. (2002) found that higher *premorbid Neuroticism* was predictive of delusions, higher *Agreeableness* of hallucinations, aggressiveness, affective disturbance and overall behavioral disturbance, and, finally, higher openness of affective disorder. Therefore, Duchek, Balota, Storandt and Larsen (2007) suggest that premorbid personality may be an additional element in the discrimination between individuals with early stage AD and healthy subjects. However, other studies have failed to demonstrate links between premorbid personality and specific BPS (Lebert, Pasquier, & Petit, 1995; Swearer et al., 1996; Holst et al., 1997; Kolanowski, Strand, & Whall, 1997; Brandt et al., 1998; Kolanowski & Garr, 1999; Clark et al., 2000).

Given the controversial findings to date, the aims of this study were to explore the relationship between both premorbid personality and its changes over 5 years with BPS in patients with mild AD.

5.2. Method

5.2.1.Sample

Fifty-four patients diagnosed with mild AD were selected from patients attending an old-age psychiatric memory clinic (39 women, 15 men, M_{age} = 76.9 years, SD_{age} = 8.5 years), and 64 control subjects (35 women, 29 men, M_{age} = 69.3 years, SD_{age} = 8.7 years) were recruited in the community through newspaper advertisement and by word of mouth.

5.2.2. Procedure

All the patients had a comprehensive medical, psychiatric, neuropsychological, and psychosocial evaluation made by a multidisciplinary team. Most often, they also had a cerebral magnetic resonance imaging as well as a number of standard laboratory tests. Among these tests, the standard clinical assessment included the Informant Questionnaire on Cognitive Decline (IQCODE; Jorm and Jacomb, 1989), the Mini Mental State Examination (MMSE; Folstein, Folstein, and McHugh, 1975), the Activities of Daily Living (ADL; Katz, 1998), and the Instrumental Activities of Daily Living (IADL; Lawton and Brody, 1969) scales to evaluate the cognitive level and functioning of daily living. This investigation yielded a diagnosis of AD according to the International Classification of Diseases, 10th edition (World Health Organization, 1993), and the criteria edited by the National Institute of Neurological Communicative Disorders and Stroke and the Alzheimer's Disease and Related Disorders Association (NINCS-ADRDS) (McKhann et al., 1984). Only patients with a Clinical Dementia Rating (CDR) (Morris, 1993) score of 1 were included. Three inclusion criteria were mandatory: age greater than 55 years, inclusion diagnoses, and the patients

accompanied by a family member (adult child or spouse caregivers). Four exclusion criteria were considered: anxiety or depression as defined by a score equal or higher than 10 on either of the two sub-scales of the HAD scale (Zigmond & Snaith, 1983); a physically or mentally unstable illness that could put the patient at risk, school education of less than 5 years, and refused consent by the patient or by his relative. A non-decompensate psychiatric diagnosis did not exclude a patient with the exception of schizophrenic disorders or brain disorders other than AD. This research project is a prospective pilot study. The individuals with AD were selected from the patients seeking help at the Memory Clinic of the Old-Age Psychiatry Service of the Lausanne University Hospital. Patients were recruited over a 1-year period. Participation in our study was proposed to the patients, the control subjects, and their proxies. The goals of the project were explained and written consent was obtained. The completion of the clinical research battery took about 2.5 hours for the patient, 2 hours for the participants in the control group, and 1.5 to 2 hours for the family member. To minimize the subjects' fatigue they were seen in one or two sessions with not more than 1 week between the sessions. We have not collected any demographic information on the caregivers. The only requirement for proxies was that they were family members (child or spouse) living nearby taking care of their demented proxies' needs. Control subjects had an identical clinical assessment. The control group was constituted to distinguish the influence of premorbid personality characteristics from the evolution of normal personality, the latter being generally characterized by a wide stability (McCrae & Costa, 1987).

5.2.3. Personality assessment

Personality traits were assessed according to the Five-Factor Model (FFM), which is currently the most common dimensional approach to personality (Digman, 1990; Costa & McCrae, 1992). This model claims that personality can be described along five main independent dimensions called *Neuroticism, Extraversion, Openness to experience*,

Agreeableness, and *Conscientiousness.* Each of these dimensions is comprised of six lower-level personality facets (Rossier et al., 2004). Costa and McCrae (1990) have suggested that the extremeness of scores on the dimensions of the FFM could differentiate normal from pathological personality or that dysfunction might be associated with some specific personality profiles (Rossier et al., 2008).

The NEO Personality Inventory Revised, Form R (NEO-PI-R; Costa & McCrae, 1992), a tool based on the Five-Factor Model (FFM), was used. This questionnaire is composed of 240 items and used for peer ratings. For this study, proxies assessed both the current and previous personality of the AD patients. The previous period was defined as the time from young adult age to 5 years prior to the perceived beginning of cognitive decline. Thus, family members completed the NEO-PI-R twice, once to evaluate the participants' current personality and the second time to assess personality traits as they were remembered to be 5 years earlier.

5.2.4. Assessment of behavioral and psychological symptoms

The Neuropsychiatric Inventory Questionnaire (NPI-Q) was used, as it is a well-validated and reliable tool to assess current BPS in AD (Cummings, 1997). It contains 12 BPS domains (delusions, hallucinations, agitation, depression, anxiety, euphoria, apathy, disinhibition, irritability, aberrant motor behavior, sleep disturbance, and eating disorders) and allows a 3-level severity assessment for each BPS. Summing up the 12 domain scores yields a total NPI-Q score (maximum 36). Additional information was collected on patient anxiety and depression using the self-administered 14-item Hospital Anxiety and Depression scale (HAD) (Zigmond & Snaith, 1983).

5.2.5. Statistical Analyses

The data were analyzed using SPSS, version 19 (SPSS Inc, Chicago, IL) and R (R Development Core Team, 2009). Descriptive statistics were used to describe demographic and clinical characteristics of both the clinical and control group. As the scores for the various NPI-Q domains were not normally distributed, comparisons were carried out using the non-parametric Mann-Whitney test. So as to determine whether or not premorbid personality traits have an impact on BPS, binomial logistic regressions were used. Then we attempted to identify possible links between personality changes and BPS, using the Student *t* test (Welch form, given that the assumption of homogeneity of variance is not satisfied). To do so, the domain indices of change were first calculated, and all variables of the NPI-Q dichotomized.

5.3. Results

The AD patients were significantly older than the control subjects (t (116) = -4.75, $p <$ .001), but gender distribution was similar (χ^2 (1) = 3.85, $p >$ .05). As expected, the clinical group scored higher than the control group on the NPI-Q for symptom severity scale and the Informant Questionnaire on Cognitive Decline and had clearly lower scores on the MMSE, Activity of Daily Living, and Instrumental Activities of Daily Living scales. After controlling for age, the personality characteristics in patients with AD, both for the current and premorbid evaluation, differed markedly from those in the healthy controls (see Table 7)

Table 7. Clinical characteristics of the study participants

	AD patients, n = 54		Healthy controls, n = 64		
Variables	*Mean*	*SD*	*Mean*	*SD*	*t or Z statistic, p value*
			Current personality		
Neuroticism	110.8	16.4	79.7	22.8	$t(116) = 8.58$, $p < .001$
Extraversion	70.6	13.8	104.2	17.1	$t(116) = 11.79$, $p < .001$
Openness	76.5	12.5	104.6	17.2	$t(116) = 10.28$, $p < .001$
Agreeableness	122.3	16.7	127.4	20.8	$t(116) = 1.48$, $p = .150$
Conscientiousness	73.5	16.2	126.7	18.5	$t(116) = 16.67$, $p < .001$
			Premorbid personality		
Neuroticism	94.5	16.9	79.2	21.4	$t(116) = 4.35$, $p < .001$
Extraversion	85.6	13.9	104.8	16.2	$t(116) = 6.92$, $p < .001$
Openness	82.9	12.9	104.6	17.1	$t(116) = 7.86$, $p < .001$
Agreeableness	124.5	20.0	127.1	20.6	$t(116) = 0.68$, $p = .498$
Conscientiousness	111.4	14.0	127.3	17.7	$t(116) = 5.43$, $p < .001$
			Current behavioral and psychological symptoms		
NPI-Q total score	7.6	4.1	0.7	2.2	$Z = 8.29$, $p < .001$
			Current cognitive status and daily living functioning		
ADL score	5.1	1.1	6.0	0.0	$Z = 6.36$, $p < .001$
IADL score	3.9	2.1	8.0	0.0	$Z = 9.63$, $p < .001$
IQCODE score	4.0	0.5	3.0	0.1	$Z = 14.79$, $p < .001$
MMSE score	23.7	3.0	29.2	1.0	$Z = 12.90$, $p < .001$

Note. ADL = Activities of Daily Living; IADL = Instrumental Activities of Daily Living; IQCODE = Informant Questionnaire on Cognitive Decline in the Elderly; MMSE = Mini-Mental State Examination; t = Student t-test for independent samples; Z= non-parametric test U of Mann-Whitney.

Thus, the clinical group presented significantly higher scores than normal controls on current *Neuroticism*, and significantly lower scores on current *Extraversion*, *Openness*, and *Conscientiousness*, whereas no significant difference was observed for *Agreeableness*. Group comparison and retrospective personality evaluation were convergent. Significant personality changes followed a specific trend in AD patients as described in an earlier paper (Pocnet, Rossier, Antonietti, & von Gunten, 2011).

5.3.1. BPS in patients with AD as compared to healthy controls

Neuropsychiatric symptoms were rarely present in normal control subjects. There was a large variability of the different NPI scores in the patients with AD. Some BPS occurred extremely often in AD patients. Thus, some degree of apathy occurred in most AD patients whereas about one out of two patients featured anxiety, depression, irritability, and agitation (see Figure 5).

The AD and control groups differed significantly as to agitation ($W = 3185$, $Z = -4.76$, $p < .001$), depression ($W = 3128$, $Z = -4.61$, $p < .001$), anxiety ($W = 3052$, $Z = -5.36$, $p < .001$), apathy ($W = 2326$, $Z = -9.35$, $p < .001$), disinhibition ($W = 3500$, $Z = -2.91$, $p = .003$), irritability ($W = 3197$, $Z = -4.27$, $p < .001$), sleep disturbance ($W = 3436$, $Z = -3.16$, $p = .002$), eating disorders ($W = 3372$, $Z = -3.56$, $p < .001$), and the NPI-Q total behavioral score ($W = 2341$, $Z = -8.29$, $p < .001$), the values being systematically higher in the AD patients (see Figure 5).

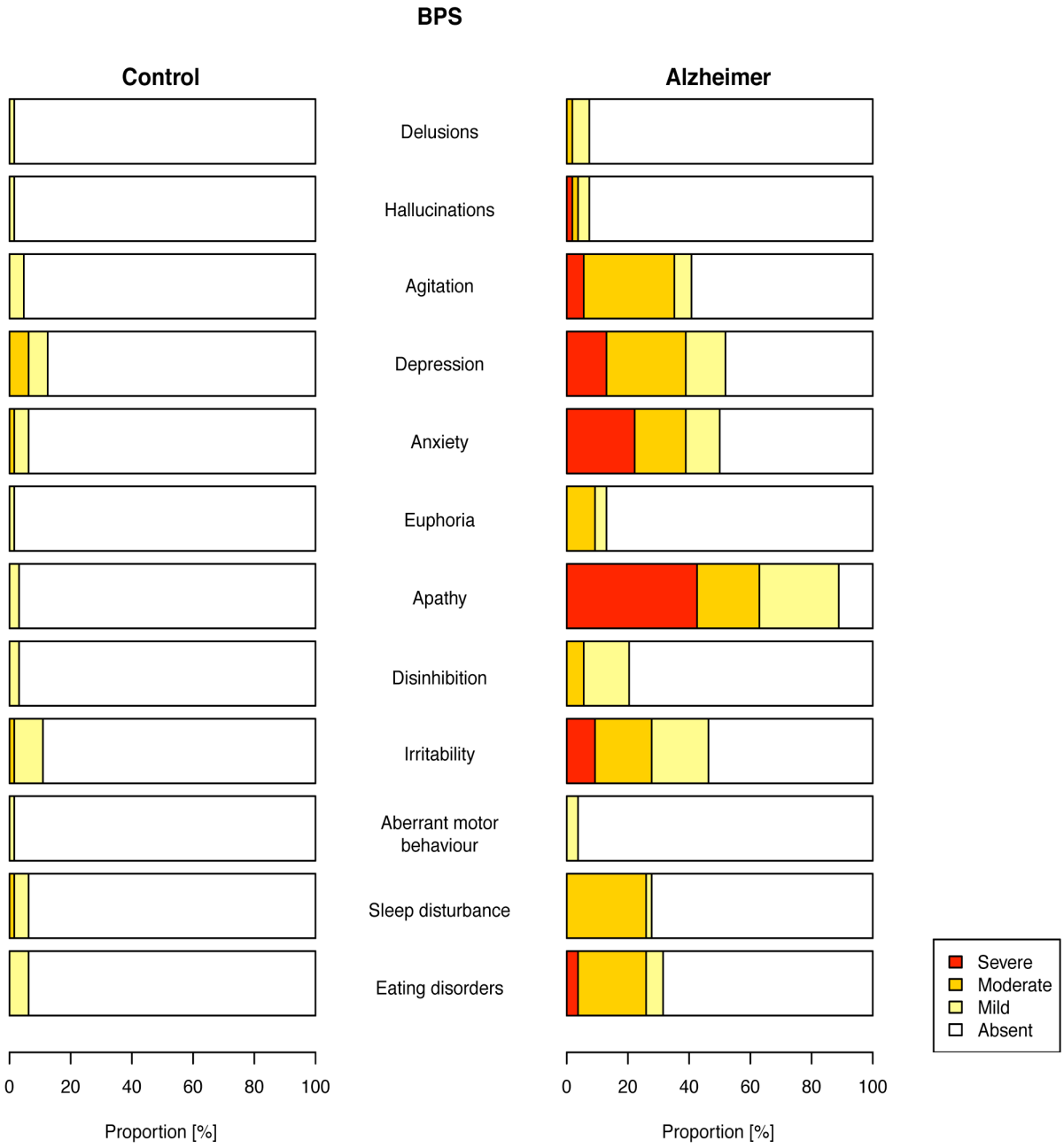

Figure 5. The distribution of behavioral and psychological symptoms (BPS) in the two groups.

5.3.2. Premorbid personality dimensions and BPS

Analyses were first performed for the AD and control group lumped together. *Premorbid Neuroticism* was significantly and positively associated with agitation ($\chi^2(1) = 4.19$, $p < .01$), anxiety ($\chi^2(1) = 10.44$, $p = .001$), apathy ($\chi^2(1) = 7.99$, $p = .005$), irritability ($\chi^2(1) = 4.16$, $p < .05$), and the total NPI-Q score ($\chi^2(1) = 12.48$, $p < .001$), whereas a significant and negative association appeared between *premorbid Openness to experiences* and depression ($\chi^2(1) = 7.05$, $p < .01$), apathy ($\chi^2(1) = 19.79$, $p < .001$), and the total NPI score ($\chi^2(1) = 17.33$, $p < .001$). There was an association between low *premorbid Extraversion* and agitation ($\chi^2(1) = 4.42$, $p < .05$) as well as irritability ($\chi^2(1) = 4.14$, $p < .05$). However, when considering the AD and control group separately, these effects disappeared, most likely due to both a significant difference of distribution of the scores of premorbid personality and neuropsychiatric symptoms between the two groups and a high intra-group homogeneity. This observation is illustrated in Figure 6.

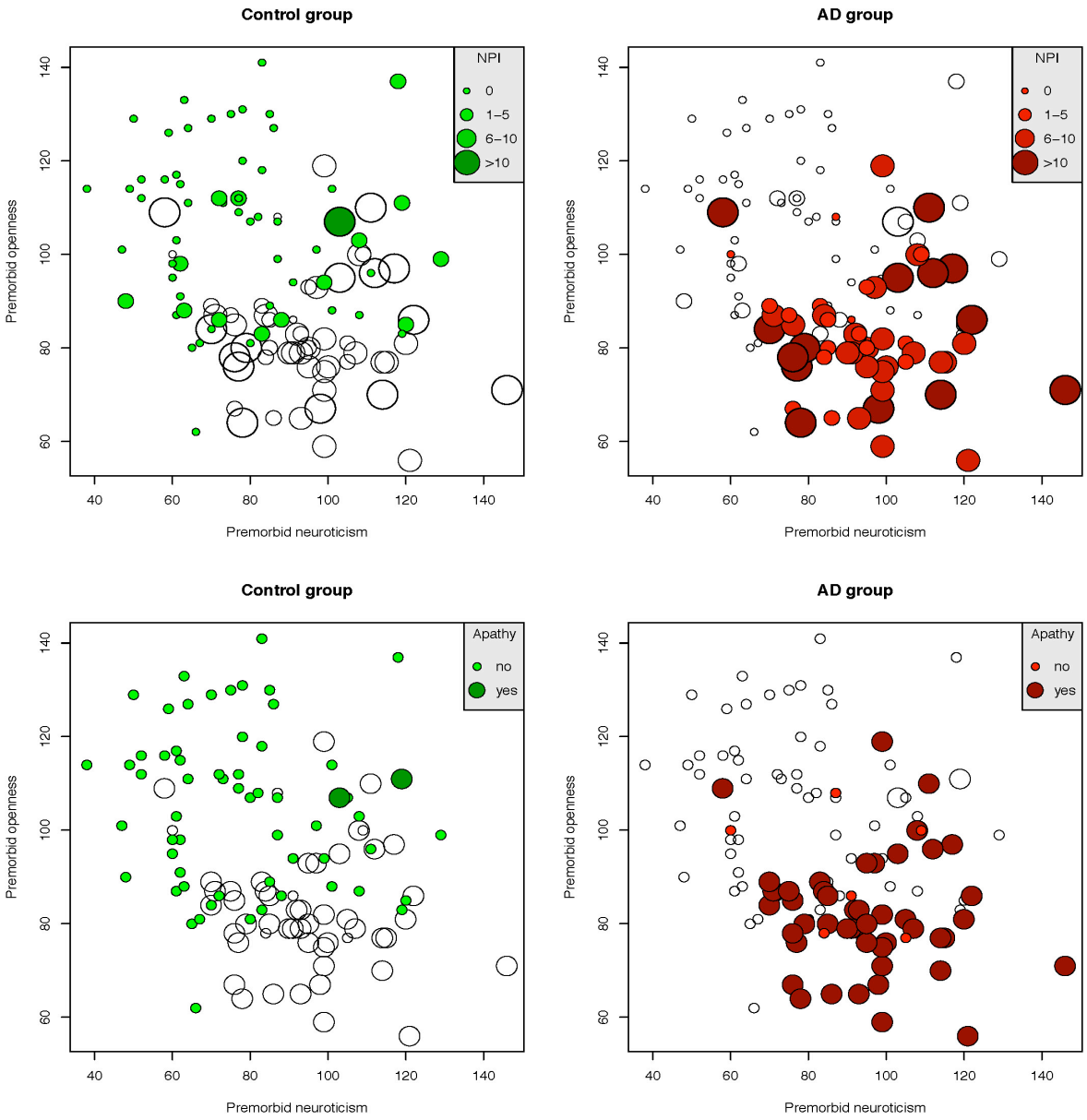

Figure 6. Distribution of premorbid neuroticism and openness to experience and BPS scores (NPI total scores and Apathy) in the two groups (AD group and Control group). *Neuroticism* and *Openness* are dimensions of personality that best explain the results of the NPI total score and of apathy. The individuals in the two groups are represented in a plane defined by the variables: premorbid *Neuroticism* and premorbid *Openness*. To specify the value of the BPS variable (i.e. NPI total scores, and Apathy), colors and sizes of different points were used: Red = AD group; Green = Control group; white circles allow comparison of the positions of the two groups, that is, of AD group in the control group chart and vice versa.

Figure 6 graphically shows the relationship, for the AD and control group, between premorbid *Neuroticism* and *Openness* as well as the total NPI score and apathy as examples of clinical features observed in this sample. The diagrams allow the identification of large differences between the two groups on *Neuroticism* and *Openness to experience* as well as apathy and the total psychiatric symptoms scores (see Figure 6).

5.3.3. Personality changes and BPS

There were significant associations between personality changes and specific behavioral symptoms, mainly when considering both groups together. The links were positive for changes on *Neuroticism*, and negative for changes on *Openness to experiences*, *Extraversion*, and *Conscientiousness*. However, when considering the AD group alone, only (i) changes in *Extraversion* and sleep disorders as well as aberrant motor behavior; (ii) changes in *Openness* and aberrant motor behavior; and (iii) changes in *Conscientiousness* and delusions were significantly interrelated (see Table 8).

Table 8. Relationship between personality changes and BPS in the AD and control groups

Behavior NPI-Q Domains	Neuroticism changes	Extraversion changes	Openness changes	Agreeableness changes	Conscientiousness changes
Delusions	1.57/NO	0.71/NO	-0.34/NO	-1.52/NO	**-3.01***/NO
Hallucinations	-0.86/NO	0.47/NO	1.00/NO	-0.78/NO	0.28/NO
Agitation	-0.61/0.56	0.63/-0.36	0.34/-0.19	0.14/-0.28	-0.02/-0.82
Depression	0.47/-0.06	-0.50/-0.69	1.17/-0.79	-0.38/-0.45	-0.38/0.45
Anxiety	0.50/-0.01	-1.23/0.42	0.80/-0.39	-0.66/0.59	0.01/-0.07
Euphoria	1.17/NO	0.97/NO	0.51/NO	-1.47/NO	0.66/NO
Apathy	0.58/0.11	-1.11/1.29	0.13/0.02	-0.66/0.38	-0.87/-0.92
Disinhibition	0.52/0.42	-1.01/0.53	0.98/-0.69	0.29/0.38	-0.55/-0.40
Irritability	-0.36/0.20	0.70/0.38	-0.16/-0.08	1.29/0.13	-0.82/-0.45
Aberrant motor behavior	-0.90/NO	**-2.17***/NO	**-3.39***/NO	-0.17/NO	-0.01/NO
Sleep disturbance	1.32/0.95	**2.52***/-0.20	-1.99/-0.41	-0.27/-0.22	-0.46/-0.31
Eating disorders	0.84/0.54	-0.40/0.03	-0.61/-0.30	0.07/-0.78	-0.68/-0.80
Total score	0.55/0.52	-0.35/0.38	1.94/2.24	0.06/-0.52	0.03/-0.47

Note: *p* value is significant at **p* < .05; Student *t* test (Welch form). The first value for each intersection shows the association for the AD group, the second value for the control group; NO means that the trait is not manifested.

5. 4. Discussion

This study shows that personality changes significantly in AD patients as opposed to control subjects when comparing premorbid and current traits. Similarly, AD patients frequently present with BPS unlike normal subjects. As AD patients have significantly different premorbid personality traits in this study, the hypothesis that premorbid traits may be related to current BPS is straightforward and was actually confirmed by a number of previous studies (Chatterjee et al., 1992; Kitwood, 1993; Strauss et al., 1997; Meins et al., 1998; Meins, 2000; Ballard et al., 2001; Gilley et al., 2004). However, this hypothesis was not supported by our findings as premorbid personality traits did not predict BPS in the AD group, although clear correlations were observed when the AD and control groups were lumped together, an artifact due to the combination of two clinically clearly distinct and per se homogeneous groups. Similarly, other studies found no relationship between premorbid personality traits and BPS in AD patients (Swearer et al., 1996; Holst et al., 1997; Brandt et al., 1998). Thus, the impact of premorbid *Neuroticism* on the occurrence of depression in mild AD as suggested by some studies (Chatterjee et al., 1992; Strauss et al., 1997; Meins et al., 1998; Gilley et al., 2004) was not supported by our findings, although depression and *Neuroticism* scores were quite high in these patients. The absence of any impact of premorbid *Neuroticism* on current depression scores may indicate that depression in AD is mostly related to biological changes, as suggested by Zubenko et al. (1991) or Archer et al. (2007). However, the NPI may not be an appropriate measure for depression in AD patients as it is an indicator of the possible presence of depression rather than a diagnostic tool.

Both personality changes and BPS seem to occur in parallel in early AD, which is in keeping with the line of thought considering that they are both directly related to brain degeneration (Bird & Moniz-Cook, 2008). However, although personality change and BPS may occur in parallel, they may not be interdependent. Thus, whilst personality changes

appear to occur according to a specific and predictable pattern in AD patients (Pocnet et al. 2011), the occurrence of BPS does not seem to be harmonious and predictable across patients who show a large variability of neuropsychiatric symptoms. Nevertheless, despite of the low number of occurrences of some of the specific BPS observed, we found a significant correlation between the following: (i) a change in *Extraversion* and current sleep disorders and aberrant motor behavior; (ii) a change in *Openness* and current aberrant motor behavior; and (iii) a change in *Conscientiousness* and current delusions. Although these associations have never been reported before and must be considered as entirely preliminary, they still suggest that some personality changes may be more often accompanied by some specific BPS relative to others. This idea clearly deserves and requires larger-scale studies.

5.4.1. Limitations

Some shortcomings of this study must be mentioned. Among the more significant limitations is the use of retrospective personality ratings subjecting our findings to possible inaccuracies of recall of premorbid personality characteristics. In addition, the heterogeneity of the proxies interviewed may have introduced another bias as their descriptions depend on different filters. Finally, the sample size of this study was small which reduces its statistical power compared to larger samples (Wilson et al., 2003). Replication of this study in a larger and more representative sample is advisable.

The strengths of this study result from the use of well-validated instruments allowing the comparison of a group of well-characterized individuals at an early stage of AD with a group of healthy older controls free of any cognitive impairment.

5.4.2. Conclusion and perspective

Our results suggest a diachronic relationship between personality changes and BPS. However, this development may not be entirely interdependent as personality changes seem

to occur according to a more predictable pattern than BPS. Furthermore, our findings do not definitely exclude our hypothesis of a relationship between premorbid personality and BPS that may, however, be more difficult to establish as the occurrence of BPS appear to be less predictable than the personality changes that accompany early AD. It will be advisable to study the longitudinal development of both personality changes and BPS as they develop. The role of premorbid personality in the development of BPS in the demented is not well established, but it is likely that the possible relationship between the two is complex and non-linear. However, both personality and behavior changes occur early in the course of AD and recognizing them as possible early signs of neurodegeneration may prove to be a key factor for early detection and intervention.

Chapter 6. Personality features and cognitive level in patients at an early stage of Alzheimer's disease[4]

6.1. Introduction

According to the International Classification of Diseases, 10th edition (WHO, 1993), preclinical Alzheimer's disease (AD) is defined as impairment in one or more cognitive domains (typically memory) that are insufficient to interfere with social and occupational functioning. The first symptoms are correctly attributed to something else than AD (ageing or stress). Detailed neuropsychological testing can reveal mild cognitive difficulties up to eight years before a person fulfills the clinical criteria for diagnosis of AD. Thus, subtle problems with the executive functions of attention, planning, flexibility, and abstract thinking, or impairments in semantic memory (memory of meanings, and concept relationships) can also be symptomatic of the early stages of AD (Bäckman, Jones, Berger, Lukka, & Small, 2004). In this case, personality changes and language deficits (word-finding problems) are the first signs noticed by relatives. However, it is difficult to specify a date for the beginning of these additional changes because deficits settle insidiously. The evolution is characterized by a gradual onset and continuing decline marked by the memory alteration and other cognitive perturbations as aphasia, apraxia, agnosia, disorders of executive functions, and a progressive reduction of patient autonomy to its immediate environment (DSM - IV- TR, 2000).

The possible link between personality traits and cognitive decline in dementia such as AD has been little studied. Nevertheless, some authors suggest that *premorbid personality characteristics* may represent a risk factor for AD, and for this reason premorbid personality might differ between AD patients and controls (von Gunten, Pocnet, & Rossier, 2009). In

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[4] This chapter is currently under consideration publication in a scientific journal (Pocnet, Rossier, Antonietti, & von Gunten, 2013)

particular, *Neuroticism* as characterized by frequent negative affect and vulnerability to stress may be a risk factor for cognitive impairment. Thus, Wilson et al., (2003) found a link between "proneness to distress" and increased risk for AD. They measured proneness to distress prospectively at baseline by using the Neuroticism scale from the NEO Five-Factor Inventory (Costa & McCrae, 1992) in a sample of healthy control individuals from the Religious Orders Study. Individuals with the highest distress proneness were twice as likely to develop AD, as were individuals with the lowest distress proneness, when other risk factors were controlled for such as age, education, and depressive symptoms. Therefore, high neuroticism in older adults could be viewed as an indicator of brain exposure to chronic stress (Wilson et al., 2006) that may produce functional and structural changes to the hippocampal formation (Baker & Kim, 2002), leading to the erosion of episodic memory and to cognitive decline (Wilson et al., 2005). Depression is linked to premorbid *Neuroticism* and also considered a risk factor of AD, either because patients experience it personally (Kokmen, Beard, Chandra, Offord, Schoenberg, & Ballard, 1991), or because there is a family history of it (Tsolaki, Fountoulakis, Chantzi, & Kazis, 1997). Other studies found an association between premorbid *Neuroticism* and cognitive impairment (Crowe, Andel, Pedersen, Fratiglioni, & Gatz, 2007) or dementia (Persson, Berg, Nilsson, & Svanborg, 1991).

Moreover, people with AD often score lower than age-matched controls in the premorbid personality domains of *Openness*, *Extraversion*, and *Conscientiousness*. Generally, *Extraversion* is associated with the use of more effective coping strategies and more efficient utilization of social support (Wang et al., 2009). Living in a rich social environment or having an active lifestyle was found to be associated with a reduced risk of dementia (Fratiglioni, Paillard-Borg, & Winbald, 2004). Low *Neuroticism* in combination with high *Extraversion* was related to the lowest dementia risk (Wang et al., 2009). Conversely, other studies (Von Dras & Siegler, 1997; Seidler, Bernhardt, Nienhaus, & Frölich, 2003) associate low

Extraversion with poor social activity and support, and with a higher risk of AD. Wilson, Scherr, Schneider, Li, & Bennett, (2007) reported that subjects who developed AD scored lower on *Extraversion*. However, *Extraversion* is not an independent predictor of AD risk in multivariate analyses, perhaps because of its associations with *Neuroticism* or *Conscientiousness*. Higher openness was linked with cognitive activity and engagement (Costa & McCrae, 1992) and low *Openness* with an increased risk for AD, even after accounting for the level of education (Duberstein et al., 2011). *Conscientiousness* refers to the capacity to plan ahead, delay gratification, and work steadfastly toward attaining goals (Costa & McCrae, 1992). High levels of *Conscientiousness* were associated with an 89% risk reduction of AD compared with a low *Conscientiousness* score in a longitudinal clinico-pathologic cohort study with up to 12 years follow-up of 997 nuns and priests of whom 176 developed AD over time (Wilson, Schneider, Arnold, Bienias, & Bennett, 2007).

Moreover, specific *changes in personality profiles* have been reported as preclinical symptoms of AD (Balsis, Carpenter, & Storandt, 2005) that reflect the impact of progressive brain damage. In this prospective, longitudinal study of non-demented older adults evaluated annually, substantial personality changes associated with dementia were observed. The most common personality changes in this group were increased rigidity, growing apathy, increased egocentricity, and impaired emotional control. These results add to prior research that has documented personality changes in dementia through retrospective reports by informants (Chatterjee, Strauss, Smyth, & Whitehouse, 1992; Siegler, Dawson, & Welsh, 1994; Strauss & Pasupathi, 1994; Smith-Gamble, Baiyewu, Perkins, Gureje, Hall, & Ogunniyi, 2002; Pocnet, Rossier, Antonietti, & von Gunten, 2011). Other studies suggest that *Conscientiousness* and *Neuroticism* are the personality domains that exhibit the most changes (Robins-Wahlin & Byrne, 2011) and may precede cognitive decline in AD (Ducheck, Balota, Storandt, & Larsen, 2007). Kolanowski and Whall (1996), in a review of studies on

personality changes, note that, although there are systematic personality changes in subjects with dementia, the individuals appear to maintain their model of premorbid personality traits. In other words, patients with dementia maintain models of adaptation they used in the past.

Given the controversial findings to date, the aim of this study was to investigate the possible relation between both premorbid personality and its changes over 5 years and global cognitive level in patients at an early stage of AD.

6.2. Material and Methods

6.2.1. Participants

Fifty-four patients diagnosed with mild AD were selected from patients attending an old-age psychiatric memory clinic (39 women, 15 men, M_{age} = 76.9 years, SD_{age} = 8.5 years), and 64 control subjects (35 women, 29 men, M_{age} = 69.3 years, SD_{age} = 8.7 years), without cognitive impairment, were recruited in the community through newspaper announcements and by word of mouth.

6.2.2. Personality assessment

Personality traits were assessed according to the Five-Factor Model, which is currently the most common dimensional approach to personality (Costa & McCrae, 1992; Digman, 1990). This model claims that personality can be described along five main independent dimensions called *Neuroticism, Extraversion, Openness to experience, Agreeableness,* and *Conscientiousness*. Each of these dimensions is composed of six lower-level personality facets. To assess personality, the *NEO Personality Inventory Revised* (NEO-PI-R, Form R) (Costa & McCrae, 1992), was used. It is a questionnaire composed of 240 items used for peer ratings. The NEO-PI-R is the result of extensive research on personality change and stability, and has well-established reliability and validity data in older population (McCrae & Costa, 1987). For this study, proxies assessed both the current and previous

personality of the participants. People with dementia often cannot inform reliably about their own personality due to amnestic difficulties. In addition, in the early clinical course of dementia insight and judgment are often impaired and self-reflective capacity reduced (Bozeat, Gregory, Ralph, & Hodges, 2000). Moreover, it may be difficult for people with dementia to be able to complete a lengthy questionnaire (Seiffer, Clare, & Harvey, 2005). Hence, we used the proxy rating according to many studies (Siegler et al., 1994; Kolanowski & Garr, 1999). In our study, family members completed the NEO-PI-R (Form R) twice, once to evaluate the participants' current personality and again to assess their personality as it was remembered to be 5 years prior to the beginning of the cognitive decline.

6.2.3. Assessment of cognitive status and daily living functioning

The cognitive functioning status was evaluated using the following two well-validated tests or questionnaires: 1) The *Mini Mental State* (MMSE; Folstein, Folstein, & McHugh, 1975) permits a quick screening of the patient's cognitive deficits and the determination of the global cognitive level. It is composed of 30 questions that explore memory (time and space orientation, immediate and delayed memory of 3 words), attention and calculation, language and the reproduction of a drawing. 2) The *Informant Questionnaire on Cognitive Decline* (IQCODE; Jorm & Jacomb, 1989) evaluates a subject's cognitive and functional level change. It is a 16-item scale filled out by a relative. The meaning of scores in the two instruments is opposite. Thus, lower scores in MMSE and higher scores in IQCODE demonstrate cognitive dysfunction.

Daily living was evaluated using the following 2 scales: 1) The *Activities of Daily Living* (ADL; Katz, 1998), a hierarchical scale of 6 activities: bathing, dressing, going to the toilet, transferring, continence, and feeding. Good reliability and construct validity of this scale were reported. 2) The *Instrumental Activities of Daily Living* (IADL; Lawton & Brody, 1969) is an 8-item scale evaluating the patient's dependency level for activities including

shopping, using the public transportation system, cooking, house cleaning, doing laundry, using the phone, taking medication or managing the budget. Relatives completed the both scales.

6.2.4. Procedure

All the patients had a comprehensive medical, psychiatric, neuropsychological and psychosocial evaluation. Most often, they also had a cerebral magnetic resonance imaging as well as a number of standard laboratory tests. This investigation yielded a diagnosis of AD according to the International Classification of Diseases, 10th edition (WHO, 1993) and the National Institute of Neurological and Communicative Disorders and Stroke, and the Alzheimer's Disease and Related Disorders Association (NINCS-ADRDS) criteria (McKhann, 1984). Only patients with a Clinical Dementia Rating scale (CDR) score of 1 were included (Morris, 1993). Three inclusion criteria were considered: age greater than 55 years, inclusion diagnoses, and patients accompanied by family members (adult child or spouse caregivers). Four exclusion criteria were considered: anxiety or depression as defined by a score equal or higher than 10 on either of the two sub-scales of the HAD scale (Zigmond & Snaith, 1983); a physically or mentally unstable illness that could put the patient at risk (a non-decompensated psychiatric diagnosis does not exclude a patient with the exception of schizophrenic disorders or brain disorders other than AD); school education of less than 5 years, and refused consent by the patient or by his relative. Both the patients and the control subjects were assessed identically concerning personality, cognitive status, and daily living functioning.

This research project consists of a prospective pilot study. The individuals with AD were selected from the patients seeking help at the Memory Clinic of the Old-Age Psychiatry Service of the Lausanne Hospital. Participation in our study was proposed to the patients, the control subjects, and their proxies. The only requirement for proxies was that they were

family members (child or spouse) living nearby and took care of their demented proxies' needs.

This study was approved by the Ethics Committee of the Faculty of Medicine of the University of Lausanne (Protocol 85/2008) and complies with the ethical code of the Swiss Psychological Society.

6.2.5. *Statistical Analyses*

The data were analyzed using SPSS, version 20, and R (R Development Core Team, 2009). Descriptive statistics taking into account effect size calculations (Cohen, 1988) were used to characterize clinical and control groups. To identify the effects of premorbid personality and its changes on cognitive level and daily living functioning, a series of hierarchical regressions was conducted. Furthermore, the domain indices of change were calculated.

6.3. Results

The patients with AD were significantly older than the control subjects (t (116) = -4.75, $p < .001$), but gender distribution was similar ($\chi^2(1) = 3.85$, $p = .05$). Regarding education distribution, the clinical group is characterized by elementary study or vocational diploma (t (116) = 7.15, $p < .001$), whereas the control group has more often a vocational diploma or university degree. There are significant differences as to civil status (χ^2 (1) = 6.05, $p = .014$). The personality characteristics in people with AD differed markedly from those in the healthy controls. The patients presented significantly higher scores than normal subjects on premorbid *Neuroticism*, and lower scores on premorbid *Extraversion*, *Openness*, and *Conscientiousness,* while no significant difference was observed for *Agreeableness*. Current personality assessment again showed significant differences between the two groups for the same four domains with important personality changes during the last 5 years only for the AD

group (see Table 9). More information about these comparisons can be found in Pocnet et al., (2011).

Table 9. Descriptive Statistics

	AD patients, *n* = 54		Healthy controls, *n* = 64		
Variables of personality	*Mean*	*SD*	*Mean*	*SD*	*d*
		Current Personality			
Neuroticism	110.8	16.4	79.7	22.8	1.57
Extraversion	70.6	13.8	104.2	17.1	-2.16
Openness	76.5	12.5	104.6	17.2	-1.87
Agreeableness	122.3	16.7	127.4	20.8	-0.27
Conscientiousness	73.5	16.2	126.7	18.5	-3.06
		Premorbid Personality			
Neuroticism	94.5	16.9	79.2	21.4	0.79
Extraversion	85.6	13.9	104.8	16.2	-1.27
Openness	82.9	12.9	104.6	17.1	-1.43
Agreeableness	124.5	20.0	127.1	20.6	-0.13
Conscientiousness	111.4	14.0	127.3	17.7	-0.99
		Current Cognitive Status and Daily Living Functioning			
ADL score	5.2	1.0	6.0	0.0	-1.13
IADL score	3.9	2.1	8.0	0.0	-2.76
IQCODE score	3.9	0.4	3.0	0.1	3.08
MMSE score	23.7	3.0	29.2	1.0	-2.46

Note. ADL = Activities of Daily Living; IADL = Instrumental Activities of Daily Living; IQCODE = Informant Questionnaire on Cognitive Decline in the Elderly; MMSE = Mini-Mental State Examination; *d* = effect size.

Concerning cognitive status and daily living functioning, the clinical group scored higher than the control group on the IQCODE and had clearly lower scores on the MMSE, ADL, and IADL scales. As expected, there was a clearly larger variability of scores in the patients with AD as compared to those in the healthy subjects (see Table 9).

6.3.1. Personality characteristics, cognitive Status, and daily living functioning

A series of hierarchical regressions were computed to determine whether or not premorbid personality traits mediated by demographic variables have an impact on cognitive level and daily living functioning. Analyses were performed for the AD and control group combined. These regressions considered in a first step age, education, gender, and civil status in order to control for these demographic variables that have an effect on some of the scales used (MMSE, IQCODE, ADL, IADL). In a second step, the five main premorbid personality dimensions were examined in order to assess their contribution in predicting cognitive level and daily living functioning. Thus, after controlling for age, education, gender, and civil status, premorbid personality explained 14% of the variance of the total MMSE score, 14% of the IQCODE score, 7% of the ADL score, and 12% of the IADL scores. The high scores of IQCODE are mainly predicted by low premorbid *Extraversion* (β = -.20, $p < .05$) and low premorbid *Openness to experience* (β = -.24, $p < .05$). As for the score of the MMSE, 14% of the total variance was predicted by premorbid *Conscientiousness* (β = .17, p = .07) and *Openness* (β =. 18, p = .08). In addition, 12% of the total variance explaining the IADL score was attributable to premorbid *Extraversion* (β = .18 p = .06) and Openness (β = .19, p = .07). These results indicate a moderate association between premorbid personality features and the total IQCODE score and trends with regard to MMSE and IADL scores. As to ADL scores no link emerged with premorbid personality domains.

Moreover, a series of hierarchical regressions showed that there were significant links between personality changes having occurred during the last 5 years and both cognitive status

and daily living functioning, when considering both groups together. Thus, *Neuroticism* changes were related positively to the total MMSE score and negatively to the IQCODE total score. *Openness* changes were associated with the total ADL and IADL scores. Finally, the changes on *Conscientiousness* were related to MMSE, IQCODE, ADL, and IADL scores. However, these personality changes were not independent predictors, but associated with educational level, civil status, and/or age (see Table 10).

Table 10. Predicting cognitive status and daily living functioning using personality changes

Predictor		MMSE β	IQCODE β	ADL β	IADL β
Step1.	Age	-.31***	.38***	-.31***	-.42***
(Ref: Male)	Gender	-.11	.08	.03	.01
	Education	.47***	-.36***	.26**	.40***
(Ref: Married)	Civil status	.15	-.06	.29**	.23*
Step 2.	Age	-.14	.14*	-.17	-.18**
	Gender	-.07	.05	.03	.02
	Education	-.33***	-.14*	.13	.16*
	Civil status	.13	-.04	.24**	.20**
Neuroticism changes		.37**	-.24*	.13	.14
Extraversion changes		.06	-.06	-.17	.01
Openness changes		-.05	.05	-.25*	-.25**
Agreeableness changes		-.08	.02	.15	.04
Conscientiousness changes		.80***	-.85***	.73***	.96***
Adjusted R^2		.55	.62	.31	.68
ΔR^2		.22***	.34***	.17***	.37***
F		17.07***	22.47***	6.81**	28.75***

Note. *p <.05 ; **p <.01; ***p <.001;

However, when considering the AD and control group separately, these effects disappeared, most likely due to both a significant difference of distribution of the scores of premorbid or personality changes and cognitive and daily living between the two groups and a high intra-group homogeneity.

Interaction diagrams enabled the identification of significant differences regarding the two groups as to the scores on *premorbid Conscientiousness* and *Conscientiousness changes* as well as cognitive level and daily functioning (see Figure 7).

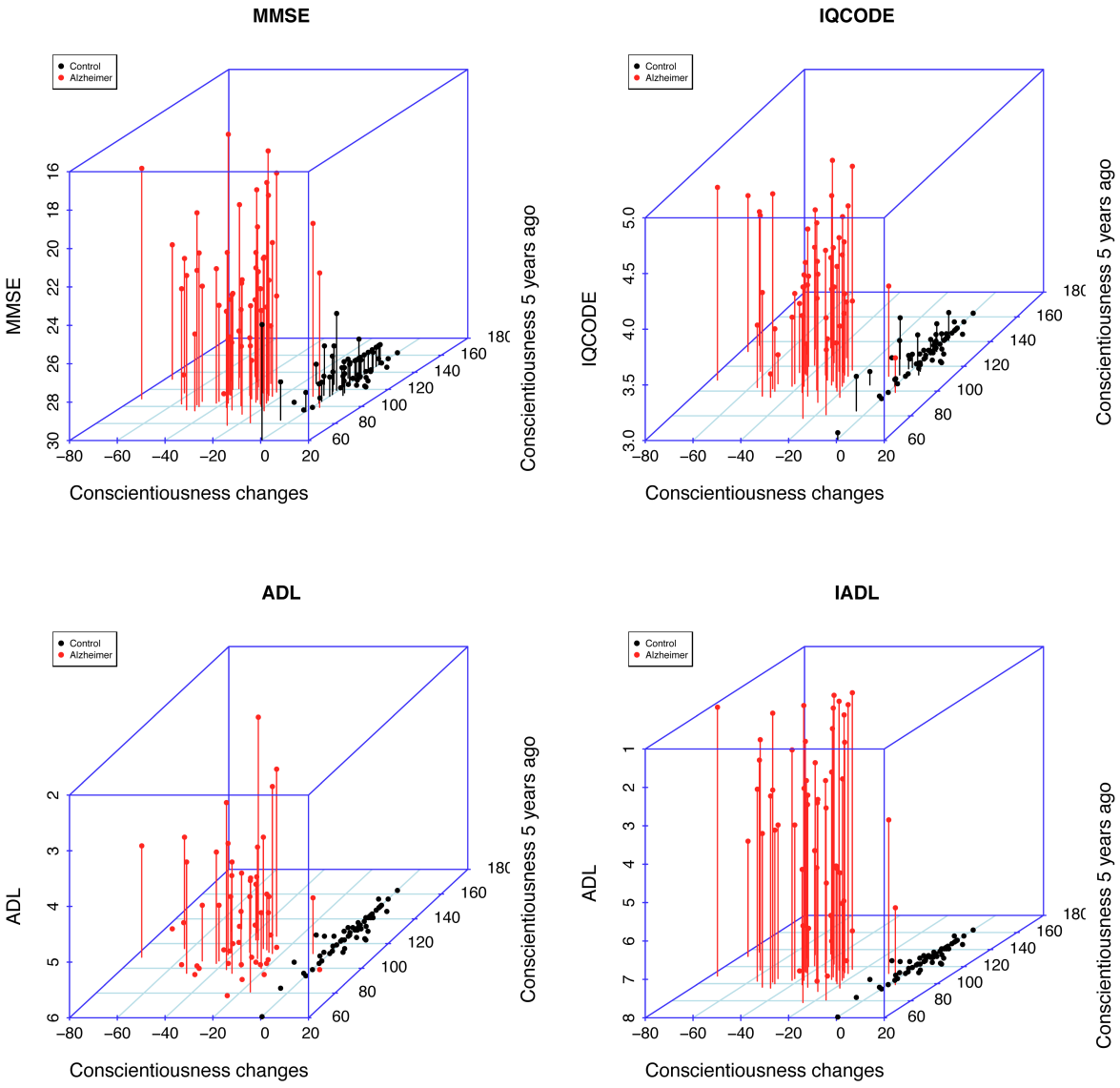

Figure 7. Differences of the scores in the two groups (AD group and Control group) regarding *premorbid Conscientiousness* and *Conscientiousness changes* as well as cognitive level and daily living functioning. *Conscientiousness* is the dimension that best explains the results of MMSE, IQCODE, ADL and IADL scores. The individuals in the two groups are represented in a plane defined by the variables *premorbid Conscientiousness* and *Conscientiousness changes*. The color dots (AD group = red; Control group = black) represent the position of the two groups depending on the cognitive level or daily living functioning.

6.4. Discussion

Our study shows a significant diachronic relationship between both cognitive status and daily living functioning, and personality changes having occurred over a period of 5 years. With regard to the impact of premorbid personality traits on cognitive deterioration, we observed moderate links. In particular, *Extraversion* and *Openness to experience* have a moderate effect on IQCODE scores, and a low effect on instrumental activity daily living, while *Conscientiousness* and *Openness* have a small influence on MMSE scores. However, the effects of premorbid personality on cognitive decline are mediated significantly by demographic variables including age, education, gender, and civil status. This suggests that premorbid characteristics could be a non-cognitive risk factor of AD.

Currently, this topic is controversially discussed in the literature (Dawson, Welsh-Bohmer, & Siegler, 2000; Low, Brodaty, & Draper, 2002; Wilson et al., 2003, 2006). The absence of significant correlations in our study concerning premorbid personality features may be due to the small sample size. This may have reduced the statistical power compared to results obtained in larger cohorts (Wilson et al., 2003, 2007; Wang et al., 2009; Duberstein et al., 2011). Furthermore, different results may be due to the fact that our sample comprised of patients diagnosed with mild cases of AD unlike other studies, which contain data collected in the non-demented older adults community (Fratiglioni et al., 2004; Crowe et al., 2007), or in older catholic clergy members (Wilson et al., 2003, 2005). Among these people, who underwent annual clinical evaluations according to the clinical classification of AD, some develop the disease and some not. In longitudinal studies, the authors observed the possible risk or protective factors of the disease related to personality.

However, our study reveals significant links between *personality changes* as opposed to *premorbid characteristics,* and cognitive status and daily living functioning. Thus, personality changes having occurred during the last 5 years such as *Neuroticism* and

Conscientiousness changes could influence the cognitive deterioration measured by the IQCODE and the MMSE. Moreover, changes on *Openness* and *Conscientiousness* over time might predict decrease of autonomy in AD patients. Of course, other well-known factors such as age, education level, or civil status must be taken into account to predict cognitive decline. Personality changes could be interpreted as an early "pre"-clinical sign of AD, converging then in a diachronic relationship with cognitive alterations, unlike what other studies that focused on synchronous links have found.

The strengths of this study result from the use of well-validated instruments allowing a comparison of a group of well-characterized individuals in an early stage of AD with a group of healthy older controls free of any cognitive impairment. Some shortcomings of this study must be mentioned. Among the more significant limitations is the use of retrospective personality ratings subjecting our findings to possible inaccuracies of recall of premorbid personality characteristics. Hence, longitudinal studies are more suitable to better understand the course of personality changes and their possible influence on cognitive decline. In addition, the heterogeneity of the proxies interviewed may have introduced another bias as their descriptions may depend on different filters. The two groups differed slightly according to different demographic variables that were therefore considered in a first separate step in the regressions analyses. Finally, the small size of our sample explains the reduced statistical power. Replication of this study in a larger and more representative sample is advisable.

6.4.1. Conclusion

Our study suggests that premorbid traits can be considered as a latent element linked to the neuropathology underlying the AD process. Moreover, neurodegeneration (measured by MMSE and IQCODE) is associated with personality changes that are the likely consequence of the pathological process. Prospective studies including the follow-up of personality traits

are required to clarify the dynamic temporal interplay of the numerous factors leading to cognitive decline and have implications for the design of intervention studies.

Chapter 7. Overall discussions

The relationship between personality and psychopathology is complex in AD, and it is through the dismantling of this complexity that we can better understand some mechanisms of behavioural changes in AD. Our results illustrate the need for a theoretical and practical understanding of the dynamics of personality changes in patients with AD. We focused our assumptions on the importance of personality traits as a non-cognitive indicator of early stage AD and their possible links with neuropsychiatric symptoms and level of cognitive functioning. Clinical experience suggests that *longstanding personality characteristics* as a person's most distinctive features are likely to play a role in how someone with dementia copes with their increasing deficiencies. Some studies suggest that premorbid personality characteristics are co-determinants of BPS in cognitive disorders (Low et al., 2002; Gilley et al., 2004), but much effort is needed to clarify whether or not specific premorbid personality traits are associated with specific BPS, as no strong links have so far emerged (von Gunten et al., 2009). A growing field of research is interested in the links between quite *short-lived emotional states* and cognitive processes. However, the associations between *longstanding personality traits* and cognition in both healthy individuals and patients with neurodegenerative disorders have not been investigated enough. Although some studies exist, few found that specific premorbid personality traits may be risk factors for neurodegenerative diseases.

Research findings in this area remain scarce despite the considerable amount of literature on personality and cognitive functioning in general. An important shortcoming that hampers our understanding of progress in these domains is the confusion in the literature between longstanding *premorbid personality* traits and *personality changes* observed in neurodegenerative diseases. Few studies have based their assessments on accepted personality theories and carefully investigated premorbid personality traits in patients with cognitive

disorders, perhaps because assessing personality may be complicated in these patients (Bozeat et al., 2000; Seiffer et al., 2005).

7.1. Evolution of personality characteristics in patients with Alzheimer's disease

Although it is generally accepted that personality has a biological basis and that its evolution in AD patients reflects the impact of progressive brain damage, other factors seem to come into play. While some dementia symptoms arise from brain pathology, others may be generated and perpetuated by a person's environment and long-standing characteristics. Hence, an integrative theoretical approach to personality in dementia that balances the influence of both biology and environment would be suitable. In keeping with this idea, a *life-span* perspective on personality would make an important contribution through assessments of personality in retrospective and longitudinal studies that capture personality processes over course of the disease. In this perspective, our data included only the reports of close informants regarding premorbid personality. The longitudinal data are not included in this thesis given that database was incomplete at completion time of my thesis. Their valorisation will be made during my research work.

In our study, personality traits of 54 AD patients compared to those of 64 mentally healthy control subjects were investigated using both *self* and *observer reports, currently* and *retrospectively*. We found considerable differences in current personality traits in both *self-reports* and *informant reports* in the healthy controls versus mild AD group. Regarding *self-reports*, the clinical group presented significantly higher scores than normal control subjects on current *Neuroticism* and significantly lowers scores on current *Extraversion, Openness to experiences,* and *Conscientiousness*, while no significant difference was observed on *Agreeableness*. Concerning *observer ratings,* a similar profile was noted, although self-perceptions were less accentuated. Specifically, family members perceived their patients as *more neurotic, less extraverted, less open, and less conscientious* than patients saw

themselves at the time of rating. The *informant reports* were consistent with the literature (Siegler et al., 1994). In our study, a good agreement between *self-report* and *observer ratings* of personality at the same time frame was observed (i.e. current self vs. current observer: *r* between .34 and .50 for the healthy control group, and *r* between .20 and .60 for the AD group). Interestingly, the correlations between current assessments done by self and observer are similar to the correlations of the assessments with different time frames (i.e. current self vs. previous observer). A possible explanation for this phenomenon is that AD patients seem to view themselves as they were in the past, as if the update of their behavioral changes in their mind's eye had not occurred. Several phenomena can occur, such as the denial of illness, or the anosognosia (lack of awareness of the loss of their capacities), or that the encoding of new information, including their behavior changes, is disturbed. Therefore, an important aspect of the present study is that the differences between the two groups are based on both *self-report* and *informant-reports*, compared to those reported in the literature, where only *informant-reports* were used (Balsis et al., 2005; Dawson, Welsh-Bohmer, & Siegler, 2000). This is important because the two descriptions converge, although the patient's own description is less pronounced.

Moreover, *diachronic personality* assessment showed significant differences between the two groups for the same four domains, with important personality changes only for the AD group. These detailed informations regarding facets of personality changes and their degree of change seems very indicative of dementia. Specifically, relatives reported that AD patients became *more neurotic* over time, i.e. more hostile, depressed, impulsive, and vulnerable. They were observed to be *less extroverted*, particularly less warm, gregarious, assertive, active, and less focused on positive emotions. Within the domain of *Openness to experience*, close ones perceived their proxies as becoming less intellectually curious, aesthetic, and less open to ideas, actions or feelings, but developing more vivid imaginations.

All the patients were believed to become *less conscientious*. The *Conscientiousness* factor is composed of items that are related to setting and accomplishing goals, being organized, following through tasks, and being dependable and reliable. Or in the clinical group, these characteristics are reduced. This shows that, in the last five years, *patterns of personality change* appear only in AD patients. The similarity of both the *magnitude* and *direction of change* was particularly striking. This suggests that these shifts occur predictably from premorbid to current scores across most patients, compared with the control group. Personality changes emerge following a *clear, consistent,* and *systematic pattern*, i.e. considerably increased *Neuroticism* and substantial decline in *Extraversion, Openness,* and *Conscientiousness*. This contrast with the *stability* generally observed in mentally healthy people in their personality profile throughout their lives and also during ageing (Terracciano et al., 2005). It should be noted that these *systematic changes* do not suggest that individuals with AD converge towards a unified personality. Rather this reflects real and predictable changes that the informant observed at an early stage of the disease, and which is consistent with existing literature of personality changes in dementia (Welleford et al., 1995; Duchek et al., 2007; Robins, Wahlin, & Byrne, 2011). In interviews with family members of AD patients, we found evidence for the *continuity of patients' normal behavior patterns*. Thus, linking current behaviors to those in the past helps family members understand what patients were communicating through their behavior. In this regard, the personalities of patients with AD appear to reflect *adaptive behavior that served them in the past*. This correspondence between pre-and post-morbid profiles was also found in other studies (i.e. Petry et al., 1988). In short, patients with incipient AD present systematic and predictable shifts in their personality, maintaining at the same time their unique relative configuration of personality traits or pattern of personality. Personality changes in AD may correspond *to accentuations of premorbid personality* as previously postulated by others (Charttejee et al., 1992).

Personality changes occur early in the illness and may be useful early markers of dementia as they may precede measurable cognitive decline. Over time, the skills of emotional regulation of AD patients seem to decrease. Therefore, they change in ways that may appear as negative relative to their former selves. Yet, they still retain features that are distinct across individuals, an observation that argues against the appearance of a universal *Alzheimer personality* (Balsis et al., 2005). We emphasize the fact that personality changes emerged with the onset of the illness, and may continue revealing the diminution, intensification, and increased frequency of the previous behaviors. However, the question of whether personality characterization through retrospective personality assessment 5 years before the current status corresponds to early signs of AD or real premorbid personality differences in people, who later develop AD would require long-term prospective designs.

7.2. Personality and behavioral and psychological symptoms in AD patients

As a result of the emergence of psychological approaches to dementia, research regarding neuropsychiatric symptoms has widened to include multiple causal factors. A very interesting factor is personality as it may influence not only how someone experiences dementia but also be causal to behavioral and psychological symptoms. For example, some studies reported a significant relationship between premorbid personality and BPS, supporting thus the inclusion of personality as a factor contributing to behavior in AD (Archer et al., 2007).

Focusing on individual personality structure, we explored the relationship between premorbid personality and its changes over 5 years, and BPS in the same patient group versus healthy controls. Our results concur with previous studies (Mega et al., 1996) showing that patients with beginning AD frequently present a large variability of behavioral and psychological symptoms, in particular apathy, depression, anxiety, and agitation unlike normal subjects in whom they are rare. Research suggests that some aspects of BPS are a

result of unsuccessful adaptation to the environment or unmet needs, or variations in the physical environment (Stokes, 2000; Bird & Moniz-Cook, 2008).

However, the hypothesis that *premorbid personality traits* may be related to BPS, shown by a number of previous studies (Meins et al., 1998; Chatterjee et al., 1992), was not supported by our findings. We are in line with Swearer et al., (1996) who found that premorbid personality might not predispose patients to changed or disruptive behaviors. This could be explained by a significant difference of distribution of the scores of premorbid personality and neuropsychiatric symptoms between the two groups as well as a high intra-group homogeneity. For instance, despite our expectations, there was no significant association between premorbid *Neuroticism* and *depression*. This suggests that depression in AD is linked to the nature of neuropathological changes occurring during the disease course which override influences of premorbid personality as suggested by others (Zubenko et al., 1991; Archer et al., 2007). In our study, depression was measured using a symptom rating scale (NPI-Q), and the results do not indicate to clinically relevant depression. In other words, the instrument used might have been inadequate to measure the depression, as defined by the ICD-10 classification. Therefore, although premorbid personality was not associated with BPS in early stage of AD in our study, complex and non-linear relationships between the two are not excluded.

Unlike premorbid personality, *changes of personality* can modify the phenomenology of BPS as suggested by our studies. In AD patients, personality changes appear to develop according to a specific and predictable pattern unlike the evolution of BPS. However, this hypothesis should be tested in longitudinal studies. Nevertheless, we found some correlations between a change in *Extraversion* and current *sleep disorders,* and *aberrant motor behavior*. Similarly, *Openness change* is linked to current *aberrant motor behavior*, and *Conscientiousness* with current *delusions*. These associations have never been reported before and these findings must be considered as entirely preliminary and interpreted with caution.

Personality traits clearly change in the course of beginning AD and this change seems to develop jointly with BPS as early signs of AD. The direction of prediction is difficult to know at present. Larger studies that involve several social and biological variables and using a longitudinal design are needed to clarify this aspect.

Given the multiple etiologies of BPS, its complexity and diversity, it is important to take into account person-centered models of BPS as suggested by our findings and to consider people's past emotional and psychological histories, cognitive status, environment, lifestyle, and mental health when attempting to understand BPS (Ballard et al., 2001).

7.3. Personality and cognitive functioning in AD patients

The clinical group scored higher on the IQCODE and had significantly lower scores on the MMSE, ADL and IADL scales than the control group. Furthermore, concerning cognitive status and daily living functioning, our study clearly confirms a larger variability of scores of AD patients compared to those of healthy subjects.

Regarding the clinical group, we observed the slight links between their *premorbid personality* and cognitive status. This suggests that premorbid features can be considered as latent traits associated to the neuropathology underlying the disease process. Therefore, *premorbid personality* might constitute an important non-cognitive risk factor.

Moreover, significant links between *personality changes and cognitive level* were observed in the patient group. Thus, increasing *Neuroticism* and decreasing *Conscientiousness* over time were associated with cognitive deterioration, whereas decreased *Openness to experience* and *Conscientiousness* over time predicted loss of independence in daily functioning in the clinical group. This suggests that the magnitude of *personality change* may confer a risk for poorer global cognitive functioning and therefore is a plausible mental health predictor. For instance, personality changes such as heightened *Neuroticism* and

lowered *Conscientiousness* could influence the cognitive deterioration measured by the IQCODE and the MMSE. The finding that *Neuroticism* was associated with global cognitive functioning, consistent with previous work (Jorm et al., 1993; Wilson et al., 2005), might reflect the effects of chronic experience of emotional stress, as stress-associated glucocorticoid activity may result in hippocampus atrophy, a brain structure that is pivotal for learning and memory (McEwan, 2000; Wilson et al., 2003; 2006). *Conscientiousness* refers to an individual's tendency to control impulses, to be self-disciplined, scrupulous, purposeful, and goal-directed (Digman, 1990; Costa & McCrae, 1992) suggesting that this personality trait is linked to the capacity for self-regulation, which allows people to alter or inhibit behaviors. Therefore, *Conscientiousness* has a general role in health maintenance. Conversely, the association between low *Conscientiousness* and global cognitive disability may reflect a poor capacity for self-regulation in people with AD. Moreover, *lower Conscientiousness* and *Openness to experience* over time might predict AD patients' decrease of autonomy. Consequently, loss of intellectual curiosity and of independence of judgment (as descriptors of the Openness domain of personality) may explain the daily difficulties. In addition, the reduction of regulation processes including emotional regulation that modify the expression of some personality traits (changes of Conscientiousness and Openness) could result in the deterioration of daily functioning. Of course, other variables such as age and education level must be taken into account, as they are well-established predictors of cognitive decline. Finally, further studies might also look into other psychological dimensions or processes such as *self-regulation* or *motivation*, which are considered by the authors of the FFM to moderate the relationship between personality and behavior and which are crucial for situational adaptations.

7.4. Strengths and Shortcomings

The current study appears to be unique in that it provides a comparison of a group of *well-characterized individuals* at an early stage of AD with a group of healthy controls, without cognitive impairment. Moreover, we have used *well-validated instruments*. In particular and for the first time, a *semi-structured interview* was used which helped to describe both "normal" and maladaptive features of personality. In our study, the discrepancies between the two groups are highlighted using *both self-assessment* and *informant reports*, unlike other studies that used only the descriptions by the relatives of AD patients. Furthermore, the structure of the study gives a global *overview of the articulation* between personality, affective and psychotic symptoms, and cognitive functioning.

An important limitation of this study is that we assessed premorbid personality traits *retrospectively* by asking an informant to describe the person 5 years before the onset of AD. It is possible, therefore, that the ratings were biased by the informants' inaccurate memory. The length of the preclinical phase of AD is unknown. Even if evidence indicates that the neuropathologic characteristics of AD develop several years before detection (Ohm et al., 1995), careful identification of the probable onset of the first signs of dementia is essential (Meins, 2000). Hence, it is important to adequately define the premorbid period. In this study, the period of 5 years before diagnosis represents premorbidity. Our choice (definition of premorbidity) is justified as too long a time frame, which may lead to inaccurate recall by the informants. Therefore, our findings warrant longitudinal studies so as to avoid this bias and to better understand the course of personality changes and their possible influence on BPS and cognitive decline.

Different *characterstics of the informants* such as closeness with the patient, age, gender, civil status, or level of education could have biased their reports about demented individuals. In future studies, it may be appropriate to take into account caregiver

characteristics. However, the cognitive functioning awareness is compromised in dementia subjects. Thus, amnestic difficulties, insight and judgment are often impaired, and self-reflective capacity is reduced. Therefore, people with dementia often cannot reliably inform about their own personality (Bozeat, Gregory, Ralph, & Hodges, 2000). For these reasons, family members are a most important source of information in connection with personality changes of their ill relatives. Using proxy rating is in accord with many studies that support the reliability and validity of informant reports (Richman, 1988; Costa & McCrae, 1988; Chatterjee et al., 1992; Strauss et al., 1993; Siegler et al., 1994; Heinik et al., 1999; Kolanowski & Garr, 1999). An alternative procedure could consist in introducing the personality descriptions of dementia patients by two informants (e.g. evaluation of both the primary caregiver and another relative or friend) and evaluating observer bias and observer concordance for descriptions of personality changes in dementia.

The AD and control groups differed slightly according to different *demographic variables*. To mitigate this limitation, we adjusted for these variables in the analyses. In futur studies, including groups that are better matched for age, gender, civil status, or level of education is advisable.

Finally, the *small size* of our sample reduces statistical power and, therefore, replicating of this study in a larger representative sample is required.

7.5. Clinical implications and perspectives

Our findings contribute to the emerging literature on personality adding to prior research that has documented personality changes in dementia (Aitken et al., 1999; Balsis et al., 2005; Petry et al., 1987). In addition, our results have significant public health implications.

Firstly, they highlight the importance of *personality assessment* in the purpose of both prevention and screening. Given that AD has an insidious evolution several years before detection, the development of *epidemiological studies* including personality assessment in groups of young people (for example, from 40 years) is suggested. Similarly, in clinical psychiatry, personality assessment should be included in the *initial evaluation of MCI and AD, through both self- and observer reports.* Moreover, a cost-effective screening should take into account premorbid traits and specific personality changes that may occur at the beginning of the disease. This might help to better discriminate the healthy control individuals from the MCI or very mild AD subjects. Other authors have made the same suggestion, given that early detection of AD could facilitate early treatment (Duchek et al., 2007).

Secondly*, psycho-educative interventions* may provide information on the personality changes and disruptive behaviors. Supportive activities could aim to use dialogue among family members and patients (e.g. teaching the caregiver skills applicable to the patient such as pleasant event planning, cognitive stimulation). However, psycho-educative interventions regarding personality changes can focus on the *relative stability of personality traits* (Allemand, Steiger, & Hill, 2013). Based on scarce research that suggests that individuals are able to perceive their trait changes (Robins et al., 2005), they can learn how their personality repertoire fits within the difficult life experiences, or aging, given that this period is associated with increased loss in control and autonomy as well as physical and cognitive decline. The aim is to describe causes and consequences of possible changes in the individual in order to develop active exercises to stabilize personality. That way, they learn to retain their dispositions through tumultuous periods. Promoting stability during these periods of change can be beneficial, because it helps individuals to retain a consistent and coherent picture of themselves despite external and internal changes (Allemand et al., 2013).

Thirdly, *preventive interventions* for AD may use personality characteristics alongside other variables to identify individuals who would best benefit from treatment. Knowledge of personality style has been used to modify the treatment of olders that develop psychogeriatric problems (Harrison & McKeith, 1995). Thus, researchers and clinicians who take into account a patient's premorbid personality may be in a better position to understand and respond to changed or disruptive behaviors. These findings have implications for *prevention research and the conceptualization of AD's etiology*.

Fourthly, specific changes in personality profiles have been reported as early, preclinical symptoms of AD. In addition, increase in neuropsychiatric symptoms and decreases of cognitive functioning have also been reported. Hence, understanding personality change as a correlate of both neuropsychiatric symptoms and cognitive decline in AD may help in the research design of trials and/or help establish *individual treatment plans (psychotherapeutic, social, and pharmacological treatments)*. We found that personality is a reliable predictor of adaptation or coping, and clinical observations may link personality to the outcome of different types of therapy. As successful interventions for AD rely upon early diagnosis, it is important to understand the factors influencing dementia treatment. However, longitudinal studies are needed to understand how personality changes in dementia occur and to better capture patterns that are continuous with earlier ones.

Fifthly, relying on a lifespan perspective would not only enhance individualized care for AD patients but also and advance *theory development* in future research. The key message is to focus on the person, not the disease. We hope our results will be confirmed in *future, longitudinal studies* aimed at explaining the etiological mechanisms of AD. For example, consider the family characterstics, social or cultural context factor may be mediators between personality and cognitive functioning. *Socio-cultural* and lifestyle variables may also influence the symptomatic expression of the disease. *Cultural difference*s may impact on how

early people with dementia are diagnosed, the type of care they receive and how long they live as well as the way families of AD patients cope with their difficulties (Karim et al., 2010; Lim et al., 2012; Dilworth-Anderson & Gibson, 2005). Although personality traits are supposed to be the same across cultures (McCrae et al., 2005), the expression of personality, and by extension of a neurodegenerative disease, could be moderated by cultural factors (McCrae & Costa, 1996; Matsumoto, 2007) that may vary between and within ethnic groups. For the time being, it is unclear how these socio-cultural factors may interact with personality traits. Identifying possible cultural differences in personality changes may help develop culturally sensitive instruments for appropriate diagnostic and caregiving interventions. Similarly, this knowledge could lead to better management strategies of behavioral disorders in AD and, as a consequence, slow down the evolution of the disease. Understanding the purpose of behavior is the first step in developing effective interventions. Understanding the context, the nature, and natural history of the non-cognitive, psychiatric changes of AD or other dementias is essential when analyzing the efficacy of therapies, be they psychotherapeutic, social or pharmacological.

7.6. Conclusions

AD is a devastating, irreversible clinical syndrome characterized by a wide spectrum of progressive impairments in cognitive, behavioral, and functional abilities. Personality changes and neuropsychiatric sypmtoms accompany these cognitive changes. Determining when AD actually begins is a difficult task as symptoms occur gradually. Although limited due to the small sample size, our study highlighted personality profile differences between AD patients and healthy controls. Specifically, higher scores for *Neuroticism*, and lower score in *Extraversion*, *Openness to experiences,* and *Conscientiousness* characterized patients concerning *premorbid personality*. These personality traits evolve differently over time in the two groups. Thus, the *pattern of personality change* that occurs early in the clinical course of

AD might be a useful early clinical marker of dementia due to AD. Moreover, our findings showed a marked variability in the occurrence of neuropsychiatric features in patients with AD as compared to cognitively healthy controls. Additionally, our results highlight a lower global cognitive level and an increased dependence for daily activities in the same patients. Nevertheless, *the role of premorbid personality* in the development of BPS in the demented is not well established. Similarly, the exact links between premorbid personality and cognitive decline remain difficult to specify. Improved understanding of premorbid personality characteristics as risk factors for both BPS and cognitive decline is likely to influence our attitudes towards the treatment of demented patients. However, we observed the links between *specific personality changes* and specific symptoms, as well as between low cognitive functioning and specific personality changes. Therefore, our study confirms that personality alterations are an important and consistent aspect of AD phenomenology.

In conclusion, the findings of this research highlight the need to better understand the role of personality in the pathogenesis of cognitive disorders as AD patients. Further longitudinal studies should examine the diachronic relationship between personality, BPS, and cognitive outcomes to better inform models of pathogenesis and to identify the subjects at greatest risk of cognitive decline. Studying the impact of personality characteristics in patients with cognitive disorders is an especially promising field of research. Combining concomitant analysis of genetic, neurological data, biographical and cultural information could contribute improving shortcomings of our study.

References

Ackerman, P. L., & Heggestad, E. D. (1997). Intelligence, personality, and interests: Evidence for overlapping traits. *Psychological Bulletin*, *121*, 219-245.

Adam, S. (2006). Le fonctionnement de la mémoire épisodique dans la maladie d'Alzheimer. In C. Belin, A.-M. Ergis, O. Moreaud (Ed.), *Actualités sur les Démences: Aspects cliniques et Neuropsychologiques* (pp. 135-165). Marseille, France: Solal.

Adler, A. (1930). Individual psychology. In C. Murchison (Ed.), *Psychologies of 1930* (pp. 395-405). Worcester, MA: Clark University Press.

American Psychiatric Association. (2000). *Diagnostic and statistical manual of mental disorders: DSM-IV-TR* (4th Ed. Text Revision). Washington, DC: American Psychiatric Publishing, Inc.

Agbayewa, M. O. (1986). Earlier psychiatric morbidity in patients with Alzheimer's disease, *American Journal Geriatrics Sociology, 34*, 561-564.

Aggarwal, N. T., Wilson, R. S., Beck, T. L., Bienias, J. L., & Bennett, D. A. (2005). Mild cognitive impairment in different functional domains and incident Alzheimer's disease. *Journal of Neurology, Neurosurgery & Psychiatry, 76*, 1479-1484.

Aitken, L., Simpson, S., & Burns, A. (1999). Personality change in dementia. *International Psychogeriatrics, 1*, 263-271.

Aitken, H. J. (2004). Measure intelligence, achievement, openness to experience and creativity. *Personality & Individual Differences*, *36*, 913-930.

Alexopoulos, G. S., Meyers, B. S., Young, R. C., Mattis, S., & Kakuma, T. (1993). The course of geriatric depression with "reversible dementia": A controlled study. *American Journal Psychiatry, 150*, 1693-1699.

Allemand, M., Zimprich, D., & Hertzog, C. (2007). Cross-sectional age differences and longitudinal age changes of personality in middle adulthood and old age. *Journal of Personality*, *75,* 323-358.

Allemand, M., Zimprich, D., & Hendriks, A. A. J. (2008). Age differences in five personality domains across the life span. *Development Psychology*, *44,* 758-770.

Allemand, M., Steiger, A.E., & Hill, P.L. (2013). Stability of personality traits in adulthood: Mechanisms and implications. *Journal of Gerontopsychology and Geriatric Psychiatry*, *26,* 5-13.

Allport, G. W. (1931). What is a trait of personality? *Journal of Abnormal and Social Psychology, 25,* 368-372.

Allport, G. W. (1937). *Personality: A psychobiological interpretation*. New York, NY: Holt.

Allport, G. W. (1961). *Pattern and growth in personality*. New York, NY: Holt.

Aluja, A., Kuhlman, M., & Zuckerman, M. (2010). Development of the Zuckerman-Kuhlman-Aluja Personality Questionnaire (ZKA-PQ): A factor/facet version of the Zuckerman-Kuhlman Personality Questionnaire (ZKPQ). *Journal of Personality Assessment, 92*, 416-431.

Arber, S. & Cooper, H. (1999). Gender differences in health in later life: A new paradox? *Social Science and Medicine, 48,* 61-76

Archer, N., Brown R. G., Reeves S. J., Boothby, H., Nicholas, E., … Lovestone, S. (2007). Premorbid personality and behavioral and psychological symptoms in probable Alzheimer's disease. *American Journal Geriatric Psychiatry, 15,* 202-213.

Artero, S., Tierney, M. C., Touchon, J., & Ritchie, K. (2003). Prediction of transition from cognitive impairment to senile dementia: A prospective, longitudinal study. *Acta Psychiatrica Scandinavica*, *107*, 390-393.

Asberg, M., Traksman, L., & Thoren, P. (1976). 5-HIAA in the cerebrospinal fluid: A biochemical suicide predictor? *Archives of General Psychiatry, 33*, 1193-1197.

Asendorpf, J. B., & Wilpers, S. (1998). Personality effects on social relationships. *Journal of Personality and Social Psychology*, *74*, 1531-1544.

Ashton, M. C., Lee, K., & Son, C. (2000). Honesty as the sixth factor of personality: Correlations with machiavellianism, primary psychopathy, and social adroitness. *European Journal of Personality, 14*, 359-368.

Ashton, M. C., Lee, K., Perugini, M., Szarota, P., de Vries, R. E., Di Blas, L…. De Raad, B. (2004). A six-factor structure of personality-descriptive adjectives: Solutions from psycholexical studies in seven languages. *Journal of Personality and Social Psychology, 86,* 356-366.

Aspinwall, L. G., & Taylor, S. E. (1997). A stitch in time: Self-regulation and proactive coping. *Psychological Bulletin, 121,* 417- 436.

Baker, F. M., Kokmen, E., Chandra, V., & Schoenberg, B. S. (1991). Psychiatric symptoms in cases of clinically diagnosed Alzheimer's disease. *Journal Geriatric Psychiatry and Neurology, 4*, 71-78.

Baker, K. B., & Kim, J. J. (2002). Effects of stress and hippocampal NMDA receptor antagonism on recognition memory in rats. *Learning & Memory*, *9,* 58-65.

Bäckman, L., Jones, S., Berger, A. K., Laukka, E. J., & Small, B. J. (2004). Multiple cognitive deficits during the transition to Alzheimer's disease. *Journal of Internal Medicine*, *256,* 195-204.

Ballantine, H. T., Flanagan, N. B., & Marino, R., Jr. (1967). Stereotaxic anterior cingulotomy for neuropsychiatric illness and intractable pain. *Journal of Neurosurgery, 26,* 488-495.

Ballard, C., O'Bbrien J., James I., & Swann A. (2001). *Dementia: Management of behavioural and psychological symptoms*. Oxford, UK: Oxford University Press.

Balsis, S., Carpenter B. D., & Storandt, M. (2005). Personality changes precede clinical diagnosis of dementia of the Alzheimer type. *Journal of Gerontology: Psychological Sciences*, *60*, 98-101.

Baltes, P. B., & Baltes, M. M. (1990). *Successful aging: perspectives from the behavioral sciences*. New York, NY: Cambridge University Press.

Baltes, P. B. & Smith, J. (2003). New frontiers in the future of aging: From successful aging of the young old to the dilemmas of the fourth age. *Gerontology*, *49*, 123-135.

Bandura, A. (1977). *Social learning theory.* Englewood Cliffs, NJ: Prenctice-Hall.

Bandura, A. (1997). *Self-efficacy: The exercice of control.* New York, NY: Freeman.

Barrick, M. R., & Mount, M. K. (1991). The Big Five personality dimensions and job performance: A meta-analysis. *Personnel Psychology*, *44*, 1-26.

Barnes, D. E., Alexopoulos, G. S., Lopez, O. L., Williamson, J. D., & Yaffe, K. (2006). Depressive symptoms, vascular disease, and mild cognitive impairment. *Archives General Psychiatry*, *63*, 273-280.

Bartzokis, G., Lu, P. H., & Mintz, J. (2007). Human brain myelination and amyloid beta deposition in Alzheimer's disease. *Alzheimer's & Dementia*, *3*, 122-125.

Bassuk, S. S., Berkman, L. F. & Wypij, D. (1998). Depressive symptomatology and incident cognitive decline in an elderly community sample, *Archives of General Psychiatry*, *55*, 1073-1081.

Battistin, L. & Cagnin, A. (2010). Vascular cognitive disorder: A biological and clinical overview. *Neurochemical Research*, *35*, 1933-1938.

Beck, A. T. (1997). The past and future of cognitive therapy. *Journal of Psychotherapy Practice and Research, 6*, 276-284.

Beck, A. T., & Alford, B. A. (2009). *Depression: Causes and treatment*. Philadelphia, PA: University of Pennsylvania Press.

Becker, J. T., & Overman, A. A. (2002). The semantic memory deficit in Alzheimer's disease. *Revista de Neurologia, 35,* 777-783.

Bellivier, F., Chaste, P., & Malafosse, A. (2004). Association between the TPH gene A218C polymorphism and suicidal behavior: A meta-analysis. *American Journal of Medical Genetics B: Neuropsychiatry Genetics, 124*, 87-91.

Benke, T. (1993). Two forms of apraxia in Alzheimer's disease. *Cortex, 29*, 715-25.

Bennett, D. A., Wilson, R. S., Schneider, J. A., Evans, D. A., Beckett, L. A., Aggarwal, N. T., … Bach, J. (2002). Natural history of mild cognitive impairment in older persons. *Neurology, 59*, 198-205.

Benjamin, J., Li, L., Patterson, C., Greenberg, B. D., Murphy, D. L., & Hamer, D. H. (1996). Population and familial association between the D4 dopamine receptor gene and measures of novelty seeking. *Nature Genetics, 12,* 81-84.

Benoit, M., Koulibaly, P. M., Migneco, O., Darcourt, J., Pringuey, D. J., & Robert, P. H. (2002). Brain perfusion in Alzheimer's disease with and without apathy: A SPECT study with statistical parametric mapping analysis. *Psychiatry Research*, *114*, 103-111.

Berger, A. K., Fratiglioni, L., Forsell, Y, Winblad, B., & Backman, L. (1999). The occurrence of depressive symptoms in the preclinical phase of AD: A population-based study. *Neurology, 53*, 1998-2002.

Bernardin, H. J., Cooke, D. K., & Villanova, P. (2000). Conscientiousness and agreeableness as predictors of rating leniency. *Journal of Applied Psycholo*gy, *85,* 232-236.

Bing, M. N., & Lounsbury, J. W. (2000). Openness and job performance in U.S.-based Japanese manufacturing companies. *Journal of Business and Psychology, 14*, 515-523.

Bird, M., & Moniz-Cook, E. (2008). Challenging behavior in dementia: A psychosocial approach to intervention. In R. Woods & L. Clare (Ed.), *Handbook of the Clinical Psychology of Aging* (pp.549-571). West Sussex, UK: John Wiley.

Block, J. (1977). Advancing the psychology of personality: Paradigmatic shift or improving the quality of research? In D. Magnusson & N. S. Endler (Ed.), *Personality at the crossroads: Current issues in interactional psychology.* Hillsdale, NJ: Lawrence Erlbaum.

Bolzman, C., Poncioni-Derigo, R., Vial, M., & Fibbi, R. (2004). Older labour migrants' well-being in Europe: The case of Switzerland. *Ageing & Society, 24,* 411-429.

Booth-Kewley, S., & Vickers, R. R. (1994). Association between major domains of personality and health behavior. *Journal of Personality*, *62*, 281-298.

Bouchard, T. J., Jr., Lykken, D. T., McGue, M., Segal, N. L., & Tellegen, A. (1990). Sources of human psychological differences: the Minnesota study of twins reared apart. *Science, 250*, 223-228.

Bouchard, T. J., Jr., & Loehlin, J. C. (2001). Genes, evolution, and personality. *Behavior Genetics*, *31*, 243-273.

Bozeat, S., Gregory, C. A., Ralph, M. A., & Hodges, J. R. (2000). Which neuropsychiatric and behavioural features distinguish frontal and temporal variants of frontotemporal dementia from Alzheimer's disease? *Journal of Neurology, Neurosurgery & Psychiatry, 69*, 178-186.

Boyle, P., Buchman, A. S., Wilson, R. S., Leurgans, S. E., & Bennett, D. A. (2010). Physical frailty is associated with incident mild cognitive impairment in community-based older persons. *Journal of the American of Geriatrics Society*, *58,* 248-255.

Brane, G., Gottfries, C. G., & Blennow, K. (1989). Monoamine metabolites in cerebrospinal fluid and behavioral ratings in patients with early and late onset of Alzheimer's disease. *Alzheimer Disease & Association Disorders*, *3*, 148-156.

Brandt, J., Campodonico, J. R., Rich, J. B., Baker, L., Steele, C., Ruff, T., … Lyketsos, C. (1998). Adjustment to residential placement in Alzheimer's disease patients: Does premorbid personality matter? *International Journal of Geriatric Psychiatry, 13,* 509-515.

Breitner, J. C. S., & Costa, P. T. (2003). Neuroticism and dementia. *Neurology*, *61*, 1468-1469.

Broe, G. A., Henderson, A. S., Creasey, H., McCusker, A. E., Jorm, A. F., Longley, W., … Anthony, J. C. (1990). A case-control study of Alzheimer's disease in Australia. *Neurology, 40*, 1698-1707.

Buntinx, F., Kester, A., Bergers, J., & Knottnerus, J. A. (1996). Is depression in elderly people followed by dementia? A retrospective cohort study based in general practice. *Age Ageing, 25*, 231-233.

Burgio, L. (1996). Interventions for the behavioral complications of Alzheimer's disease: Behavioral approaches. *International Psychogeriatrics*, *8*, 45-52.

Buss, M. D. (1991). Evolutionary personality psychobiology. *Annual Review of Psychology, 42*, 459-492.

Buss, M. D. (1995). Evolutionary psychology: A new paradigm for psychobiological science. *Psychobiological Inquiry, 6,* 1-49.

Byrne, P., Becker, S., & Burgess, N. (2007). Remembering the past and imagining the future: A neural model of spatial memory and imagery. *Psychological Review, 114*, 340-375.

Camp, N. J., Lowry, M. R., Richards, R. L., Plenk, A. M., Carter, C., & Hensel, C. H. (2005). Genome-wide linkage analyses of extended Utah a pedigree identifies loci that influence recurrent, early-onset major depression and anxiety disorders. *American Journal of Medical Genetic, 135*, 85-93.

Canli, T., Zhao, Z., Desmond, J. E., Kang, E., Gross, J., & Gabrieli, J. D. E. (2001). An FMRI study of personality influences on Brain reactivity to emotional stimuli. *Behaviour Neurosc*ience, *115,* 33-42.

Carr, D. B., Gray, S., Baty, J., & Morris, J. C. (2000) The value of informant versus individual's complaints of memory impairment in early dementia. *Neurology*, *55*, 1724-1726.

Carver, C. S., & White, T. L. (1994). Behavioural inhibition, behavioural activation, and affective responses to impending reward and punishment: The BIS/BAS scales. *Journal of Personality and Social Psychology, 67*, 319-333.

Caspi, A., & Bem, D. J. (1990). Personality continuity and change across the life course. In L. A. Pervin (Ed.), *Handbook of personality: Theory and Research* (pp. 549-575). New York, NY: Guilford Press.

Caspi, A., & Roberts, B. W. (1999). Personality continuity and change across the life course. In L. A. Pervin & O. P. John (Ed.), *Handbook of personality: Theory and research* (2nd Ed., pp. 300-326). New York, NY: Guilford.

Caspi, A. (2000). The child is the father of the man: Personality continuities from childhood to adulthood. *Journal of Personality and Social Psychology*, *78,* 158-72.

Caspi, A., & Roberts, B. W. (2001). Personality development across the life course: The argument for change and continuity. *Psychological Inquiry*, *12*, 49-66.

Caspi, A., Sugden, K., Moffitt, T. E., Craig, I. W., & Harrington, H. (2003). Influence of life stress on depression: Moderation by a polymorphism in the 5-HTT genes. *Science, 301,* 291-293.

Caspi, A., Roberts, B. W., & Shiner, R. L. (2005). Personality development: Stability and change. *Annual Review of Psychology, 56*, 453-484.

Cattell, R. B. (1947). Confirmation and clarification of primary personality factors. *Psychometrika, 12*, 197-220.

Cattell, R. B. (1950). *Personality: A systematic theoretical and factual study.* New York, NY: McGraw Hill.

Cattell, R. B. (1957). *Personality and motivation structure and measurement.* New York, NY: World Book.

Cattell, R. B. (1965). *The scientific analysis of personality.* Baltimore, MD: Penguin.

Cattell, R. B., Cattell, A. K., & Cattell, H. E. (1993). *16PF Fifth Edition Questionnaire.* Champaign, IL: Institute for Personality and Ability Testing, Inc.

Chakrabarti, B., & Baron-Cohen, S. (2006). Empathizing: Neurocognitive developmental mechanisms and individual differences. *Progress in Brain Research*, *156*, 403-417.

Chatterjee, A., Strauss, M. E., Smyth, K. A., & Whitehouse, P. J. (1992). Personality changes in Alzheimer's disease. *Archives of Neurology, 49,* 486-491.

Chemerinski, E., Petracca, G., Sabe, L., Kremer, J., Sergio E., & Starkstein, M. D. (2001). The specificity of depressive symptoms in patients with Alzheimer's disease. *The American Journal of Psychiatry*, *158,* 68-72.

Chen, P., Ganguli, M., Mulsant, B. H., & DeKosky, S. T. (1999). The temporal relationship between depression symptoms and dementia: A community-based prospective study. *Archives of General Psychiatry, 56*, 261-266.

Cheston, R. & Bender, M. (1999). *Understanding dementia: The man with the worried eyes.* London, UK: Jessica Kingsley Publishers Ltd.

Chun, W. & Johnson, V. W. (2007). The role of tau phosphorylation and cleavage in neuronal cell death. *Frontiers in Bioscience, 12*, 733-756.

Clark, L. M., Bosworth, H. B., Welsh-Bohmer, K. A., Dawson, D. V., & Siegler, I. C. (2000). Relation between informant-rated personality and clinician-rated depression in patients with memory disorders. *Neuropsychiatry, Neuropsychology and Behavioural Neurology, 1*, 39-47.

Clémence, A., Karmaniola, A., Green, E. G. T., & Spini, D. (2007). Disturbing life events and well-being after 80 years-of-age: A longitudinal comparison of survivors and the deceased over five years. *Ageing & Society*, *27*, 195-213.

Cloninger, C. R. (1987). A systematic method for clinical description and classification of personality variants. *Archives of General Psychiatry*, *44,* 573-588.

Cloninger, C. R., Przybeck, T. R., & Svrakic, D. M. (1991). The tridimensional personality questionnaire: U.S. normative data. *Psychological Reports*, *69*, 975-990.

Cloninger, C. R., Svrakic, D. M., & Przybeck, T. R. (1993). A psychobiological model of temperament and character. *Archives of General Psychiatry, 50,* 975-990.

Cloninger, C. R., Przybeck, T. R., Svrakic, D. M., & Wetzel, R. D. (1994). *The Temperament and Character Inventory (TCI): A guide to its development and use.* Washington, DC: Center for Psychobiology of Personality.

Cloninger, C.R. (1998). The genetics and psychobiology of the seven-factor model of personality. In K. R. Silk (Ed.), *Biology of personality disorders* (pp. 63-92). Washington, DC: American Psychiatric Press Inc.

Clower, C. E., & Bothwell, R. K. (2001). An exploratory study of the relationship between the Big Five and inmate recidivism. *Journal of Research in Personality*, *35,* 231-237.

Coccaro, E. F. (1998). Neurotransmitter function in personality disorders. In Silk K. R. (Ed.), *Biology of personality disorders* (pp. 1-25). Washington, DC: American Psychiatric Press Inc.

Cohen-Mansfield, J., & Werner, P. (1998). Predictors of aggressive behaviours: A longitudinal study in senior day care centers. *Journals of Gerontology, 53*, 300-310.

Cohen, J. (1988). *Statistical power analysis for the behavioral sciences,* (2nd Ed.). Hillsdale, NJ: Erlbaum.

Cohen, J. (1994). The earth is round ($p < .05$). *American Psychologist, 49,* 997-1003.

Cole, M., & Scribner, S. (1974). *Culture and thought: A psychological introduction*. New York, NY: Wiley.

Collie, A., & Maruff, P. (2000). The neuropsychology of preclinical Alzheimer's disease and mild cognitive impairment. *Neuroscience Biobehavioral Rev*iews, *24,* 365-374.

Constantino, J. N., Morris, J. A., & Murphy, D. L. (1997). CSF 5-HIAA and family history of antisocial personality disorder in newborns. *American Journal of Psychiatry, 154*, 1771-1773.

Conway, M. A. (1996). Autobiographical Memory. In E. L. Bjork & R. A. Bjork (Ed.), *Memory* (pp.443-490). San Diego, CA: Academic Press.

Copeland, M. P., Daly, E., Hines, V., Carol, M. M., Gunther, J., & Albert, M. (2003). Psychiatric symptomatology and prodromal Alzheimer's disease. *Alzheimer Disease & Association Disorders*, *17,* 1-8.

Corr, P. J. (2004). Reinforcement sensitivity theory and personality. *Neuroscience and Biobehavioral Reviews, 28,* 317–332.

Corcoran, R., & Thompson, P. (1993). Epilepsy and poor memory: Who complains and what do they mean? *British Journal Clinical Psychology*, *32*, 199-208.

Costa, P. T., & McCrae, R. R. (1977). Age differences in personality structure revisited:

Studies in validity, stability, and change. *Age and Human Derelopment, 8*, 261-275.

Costa, P. T., & McCrae, R. R. (1985). *The NEO personality inventory manual*. Odessa, FL: Psychological Assessment Resources.

Costa, P. T., & Mc Crae, R. R. (1987). Neuroticism, somatic complaints, and disease: Is the bark worse than the bite? *Journal of Personality*, *55,* 299-316.

Costa, P. T., & McCrae, R. R. (1990). Personality disorders and the five-factor model of personality. *Journal of Personality Disorders, 4*, 362-371.

Costa, P. T., Jr., McCrae, R. R., & Dye, D. A. (1991). Facet scales for agreeableness and conscientiousness: A revision of the NEO Personality Inventory. *Personality and Individual Differences, 12*, 887- 898.

Costa, P. T., & McCrae, R. R. (1992). *Revised NEO Personality Inventory (NEO-PI-R) and NEO-Five-Factor (NEO-FFI) professional Manual*. Odessa, FL: Psychological Assessment Resources.

Costa, P. T., & McCrae, R. R. (1993). Bullish on personality psychology. *The psychologist, 6,* 302-303.

Costa, P. T., & McCrae, R. R. (1994). Set like plaster? Evidence for the stability of the adult personality. In T. F. Heatherton & J. L. Weinberger (Ed.), *Can personality change?* (pp. 21- 40). Washington, DC: American Psychological Association.

Costa, P. T., & Widiger, T. A. (1994). *Personality disorders and the five-factor model of personality.* Washington, DC: American Psychological Association.

Costa, P. T., & McCrae, R. R. (1995). Domains and facets: Hierarchical personality assessment using the revised NEO Personality Inventory. *Journal of Personality Assessment*, *64,* 21-50.

Costa, P. T., & McCrae, R. R. (1997). Longitudinal stability of adult personality. In R. Hogan, J. A. Johnson, & S. Briggs (Ed.), *Handbook of Personality Psychology* (pp.269-290). San Diego: Academic Press.

Costa, P. T., & McCrae, R. R. (1998). Trait theories of personality. In D. F. Barone, M. Hersen, & V. B. V. Hasselt (Ed.), *Advanced personality* (pp.103-121). New York, NY: Plenum Press.

Costa, P. T., Jr., Herbst, J. H., McCrae, R. R., & Siegler, I. C. (2000). Personality at midlife: Stability, intrinsic maturation, and response to life events. *Assessment*, *7*, 365-378.

Costa, P. T., Jr., Terracciano, A., & McCrae, R. R. (2001). Gender differences in personality traits across cultures: Robust and surprising findings. *Journal of Personality and Social Psychology, 81*, 322-331.

Courtet, P., Baud, P., & Abbar, M. (2001). Association between violent suicidal behaviour and the low activity allele of the serotonin transporter gene. *Molecular Psychiatry*, *6,* 338-341.

Courtet, P., Jollant, F., Castelnau, D., Buresi, C., & Malafosse, A. (2005). Suicidal behaviour: Relationship between phenotype and serotonergic genotype. *American Journal of Medical Genetics*, *133*, 25-33.

Crocco, E. A., & Loewenstein, D. A. (2005). Psychiatric aspects of mild cognitive impairment. *Current Psychiatry Reports, 7,* 32-36.

Crowe, M., Andel, R., Pedersen, N. L., Fratiglioni, L., & Gatz, M. (2007). Personality and risk of cognitive impairment 25 years later. *Psychology and Aging*, *21*, 573-580.

Cummings, J. L., Mega, M., & Gray, K. **(**1994). The neuropsychiatric inventory: Comprehensive assessment of psychopathology in dementia. *Neurology, 44,* 2308-2314.

Cummings, J. L., Ross, W., & Absher, J. (1995). Depressive symptoms in Alzheimer's disease: Assessment and determinants. *Alzheimer Disease & Association Disorders*, *9*, 87-93.

Cummings, J. L. (1997). The neuropsychiatric inventory: Assessing of psychopathology in dementia patients. *Neurology*, *48*, 10-16.

Cummings, J. L. (2003). Neuropsychiatric symptoms. In R. C. Petersen (Ed.), *Mild cognitive impairment: Aging to Alzheimer's disease* (pp. 41-61). Oxford, UK: Oxford University Press.

Cummings, J. L. (2005). Behavioral and neuropsychiatric outcomes in Alzheimer's disease. *International Journal of Neuropsychiatric Medicine, 10*, 22-27.

Dawson, D. V., Welsh-Bohmer, K. A., & Siegler, I. C. (2000). Premorbid personality predicts level of rated personality change in patients with Alzheimer's disease. *Alzheimer Disease & Association Disorders*, *14*, 11-19.

Deary, I. J., Peter, A., Austin, E., & Gibson, G. (1998). Personality traits and personality disorders. *Brain of Journal Psychol*ogy, *89*, 643-661.

Deckersbach, T., Miller, K. K., Klibanski, A., Fischman, A., & Rauch, S. (2006). Regional cerebral brain metabolism correlates of neuroticism and extraversion. *Depression and Anxiety*, *23*, 133-138.

DeNeve, K. M., & Cooper, H. (1998). The happy personality: A meta-analysis of 137 personality traits and subjective well-being. Chicago, IL: Aldine.

Depue, R. A., Luciana, M., Arbisi, P., Collins, P., & Leon, A. (1994). Dopamine and the structure of personality: Relationship of agonist-induced dopamine activity to positive emotionality. *Journal of Personality and Social Psychology*, *67,* 485-498.

Depue, R. A., & Collins, P. F. (1999). Neurobiology of the structure of personality: Dopamine, facilitation of incentive motivation, and extraversion. *Behavior Brain Science, 22*, 491-569.

De Raad, B. (1998). Five big, Big Five issues: Rationale, content, structure, status, and crosscultural assessment. *European Psychologist*, *3,* 113-124.

De Raad, B. (2000). *The big five personality factors: The psycholexical approach to personality*. Göttingen, Germany: Hogrefe & Huber Publishers.

De Raad, B., & Perugini, M. (Ed.). (2002). *Big five assessment*. Kirkland, WA: Hogrefe & Huber.

Deutsch, L. H., Bylsma, F. W., & Rovner, B. W. (1991). Psychosis and physical aggression in probable Alzheimer's disease. *American Journal of Psychiatry*, *148,* 1159-1163.

Devenand, D. P., Sano, M., Tang, M. X., Taylor, S., Gurland, B. J., Wilder, D. E., Stern, Y., & Mayeux, R. (1996). Depressed mood and the incidence of Alzheimer's disease in the elderly living in the community. *Archives of General Psychiatry, 53,* 175-182.

Devanand, D. P., Marder, K., Michaels, K. S., Sackeim, H. A., Bell, K., Sullivan, M. A., Cooper, T. B., Pelton, G. H. & Mayeux, R. (1998). A randomized, placebo-controlled dose-comparison trial of haloperidol for psychosis and disruptive behaviors in Alzheimer's disease. *American Journal of Psychiatry*, *155,* 1512-1520.

Devinsky, O., & D'Esposito, M. (2004). *Neurology of cognitive and behavioral disorders.* New York, NY: Oxford.

Devinsky, O., Morrell, M. J., & Vogt, B. A. (1995). Contributions of anterior cingulate cortex to behaviour. *Brain*, *118*, 279-306.

De Young, C. G. (2006). Higher-order factors of the Big Five in a multi-informant sample. *Journal of Personality and Social Psychology, 91*, 1138-1151.

De Young, C. G., & Gray, J. R. (2009). Personality neuroscience: explaining individual differences in affect, behavior, and cognition. In P. J. Corr & G. Matthews (Ed.), *The Cambridge handbook of personality*. Cambridge, UK: University Press.

Dickson, D. W., Crystal, H. A., Bevona, C., Honer, W., Vincent, I., & Davies, P. (1995). Correlations of synaptic and pathological markers with cognition of the elderly, *Neurobiological Aging*, *16*, 285-304.

Diehl, J., Ernst, J., & Krapp, S. (2006). Misdemeanor in frontal dementia. *Neurological Psychiatry*, *74,* 203-210.

Diener, E., Sandvik, E., Pavot, W., & Fijita, F. (1992). Extraversion and subjective well-being in U.S. probability sample. *Journal of Research in Personality*, *26*, 205-215.

Digman, J. M. (1989). Five robust trait dimensions: Development, stability, and utility. *Journal of Personality, 57, 195-214.*

Digman, J. M. (1990). Personality structure: Emergence of the five-factor model. *Annual Review of Psychology*, *41*, 417-440.

Dilworth-Anderson, P., Brummett, B. H., Goodwin, P., Williams, S. W., Williams, R. B., & Siegler, I. C. (2005). Effect of race on cultural justifications for caregiving. *Journal of gerontology, 60*, 257-262.

Downs, M., Clare, L., & Anderson, E. (2008). Dementia as a biopsychosocial condition: implications for practice and research. In R.Woods & L. Clare (Ed.), *Handbook of the clinical psychology of aging* (pp. 549-571). West Sussex, UK: John Wiley & Sons Ltd.

Driscoll, I., Resnick, S. M., Troncoso, J. C., An, Y., O'Brien, R., & Zonderman, A. B. (2006). Impact of Alzheimer's pathology on cognitive trajectories in nondemented elderly. *Neurology, 60,* 688–695.

Duberstein, P. R., Chapman, B. P., Tindle, H. A., Sink, K. M., Bamonti, P., Robbins, J., Jerant, A. F., & Franks, P. (2011). Personality and risk for Alzheimer's disease in adult 72 years of age and older: A 6-year followup-up. *Psychology and Aging, 26*, 351-362.

Duchek, J. M., Balota, D., Storandt, M., & Larsen, R. (2007). The power of personality in discriminating between healthy aging and early-stage Alzheimer's disease. *Journal of Gerontology: Psychological Sciences,* 62, 353-361.

Dudai, Y. (2004). The Neurobiology of Consolidations, or, How Stable is the Engram? *Annual Review of Psychology, 55*, 51–86.

Ebmeier, K. P., Deary, I. J., O'Carroll, R. E., Prentice, N., Moffoot, A. P. R., & Goodwin, G. M. (1994). Personality associations with the uptake of the cerebral blood flow marker 99mTc-exametazime estimated with single photon emission tomography. *Personality and Individual Differences*, *17*, 587-595.

Erikson, E. H. (1982). *The Life Cycle Completed: A Review.* New York, NY: W.W. Norton.

Erikson, E. H. (1970). Reflections on the dissent of contemporary youth. *International Journal of Psychoanalysis, 51,* 11-22.

Eysenck, H. J. (1953). *The Structure of human personality.* London, UK: Methuen.

Eysenck, H. J. (1966). Personality and experimental psychology. *Bulletin of the British Psychological Society, 19*, 1-28.

Eysenck, H. J. (1970). *The structure of human personality,* (3rd Ed.). London, UK: Methuen.

Eysenck, H. J. (1981). *A model for personality.* New York, NY: Springet.

Eysenck, H. J., & Eysenck, M. W. (1985). *Personality and Individual differences*. *A natural science approach.* New York, NY: Plenum.

Eysenck, H. J. (1990). Biological dimensions of personality. In L. A. Pervin (Ed.), *Handbook of personality: Theory and research* (pp. 244-276). New York, NY: Guilford.

Eysenck, H. J. (1991). Dimensions of personality: 16, 5, or 3? Criteria for a taxonomic paradigm. *Personality and Individual Differences*, *12,* 773-790.

Eysenck, H. J., & Eysenck, M. W. (1991). *Manual for the EPQR-R.* Sevenoaks, England: Hodder & Stoughton.

Fadil, H., Borazanci, A., Yahyaoui, M., Korniychuk, E., & Minagar, A. (2009). Early onset dementia, *International Review of Neurobiology*, *84*, 245-262.

Farber, N. B., Rubin, E. H., Newcomer, J. W., Kinscherf, D. A., Miller, J. P., Morris, J. C., Olney, J. W., & McKeel, D. W. (2000). Increased neocortical neurofibrillary tangle density in subjects with Alzheimer's disease and psychosis. *Archives Geneneral of Psychiatry*, *57*, 1165-1173.

Feldman, H., Scheltens, P., & Scarpini, E. (2004), Behavoiural symptoms in mild cognitive impairment. *Neurology*, *62*, 1192-1201.

Ferri, C. P., Prince, M., Brayne, C., Broadaty, H., Fratiglioni, L., & Ganguli, M. (2005). Global prevalence of dementia: A Delphi consensus study. *Lancet, 366,* 2112-2117.

Figueredo, A. J., Sefcek, J. A., Vasquez, G., Brumbach, B. H., King, J. E., & Jacobs, W. J. (2000). Evolutionary personality psychology. In D. M. Buss (Ed.), *Handbook of evolutionary psychology* (pp. 851-877). Hoboken, NJ: Wiley.

Fleisher, A. S., Sowell, B. B., Taylor, C., Gamst, A. C., Petersen, R. C., & Thal, L. J. (2007). Clinical predictors of progression to Alzheimer's disease in amnestic mild cognitive impairment. *Neurology, 68,* 1588-1595

Flicker, C., Ferris, S. H., & Reisberg, B. (1993). A longitudinal study of cognitive function in elderly persons with subjective memory complaints. *American Journal of Geriatric Sociology, 41*,10-32.

Folstein, M. F., Folstein, S. E., & McHugh, P. R. (1975). Mini-mental state: A practical method for grading the cognitive state of patients for clinicians. *Journal of Psychiatry Research, 12*, 189-198.

Förstl, H., Burns, A., & Luthert, P. (1992). Clinical and neuropathological correlates of depression in Alzheimer's disease. *Psychological Medicine*, *22*, 877-884.

Förstl, H., & Kurz, A. (1999). Clinical features of Alzheimer's disease. *European Archives of Psychiatry and Clinical Neuroscience, 249*, 288-290.

Fratiglioni, L., Grut, M., Forsell, Y., Viitanen, M., & Winblad, B. (1991). Prevalence of Alzheimer's disease and other dementias in an elderly urban population: Relationship with age, sex, and education. *Neurology, 41,* 1886 -1892.

Fratiglioni, L., De Ronchi, D., & Agüero Torres, H. (1999). Worldwide prevalence and incidence. *Drugs & Aging, 15*, 365-375.

Fratiglioni, L., Paillard-Borg, S., & Winblad, B. (2004). An active and socially integrated lifestyle in late life might protect against dementia. *Lancet Neurology*, *3*, 343-353.

Freud, S. (1953). *The interpretation of dreams*. In Vols 4 and 5 of *the standard edition*. London, England: Hogarth.

Freud, S. (1961). *The ego and the id.* In Vol 19 and 5 of *the standard edition*. London, England: Hogarth.

Friedman, H. S., Tucker, J. S., Tomlinson-Keasy, C., Schwartz, J. E., Wingard, D. L., & Criqui, M. H. (1993). Does childhood personality predict longevity? *Journal of Personality and Social Psychology*, *65*, 176-185.

Fullerton, J., Cubin, M., Tiwari, H., Wang, C., Bomhra, A., & Davidson, S. (2003). Linkage analysis of extremely discordant and concordant sibling pairs identifies quantitative-trait loci that influence variation in the human personality trait neuroticism. *American Journal of Human Genetics, 72*, 879-890.

Funder, D. C., Kolar, D. W., & Blackman, M. C. (1995). Agreement among judges of personality: Interpersonal relations, similarity, and acquaintanceship. *Journal of Personality and Social Psychology, 69,* 656-672.

Gabryelewicz, T., Religa, D., Styczynska, M., Peplonska, B., Pfeffer, A., & Wasiak, B. (2002). Behavioural pathology in Alzheimer's disease with special reference to apolipoprotein E genotype. *Dementia and Geriatric Cognitive Disorders*, *14*, 208-212.

Galliot, M. T. & Baumeister, R. F. (2007). The physiology of power: Linking blood glucose to self-control. *Personality and Social Psychology Review*, *11*, 303-327.

Games, D., Adams, D., Alessandrini, R., Barbour, R., Borthelette, P., & Zhao, J. (1995). Alzheimer-type neuropathology in transgenic mice overexpressing V717F β-ameloyd precursor protein. *Nature, 373*, 523-527.

Gambassi, G., Landi, F., Lapane, K. L., Sgadari, A., Mor, V., & Bernabei, R. (1999). Predictors of mortality in patients with Alzheimer's disease living in nursing homes. *Journal of Neurology, Neurosurgery, and Psychiatry, 67*, 59-65.

Garre-Olmo, J., Lopez-Pousa, S., Vilalta-Franch, J., & Touron-Estrada, A. (2003). Evolution of depressive symptoms in Alzheimer's disease: On year follow-up. *Archives of Women's Mental Health, 17,* 77-85.

Gazzola, V., Aziz-Zadeh, L., & Keysers, C. (2006). Empathy and the somatotopic auditory mirror system in humans. *Current biology*, *16*, 1824-1829.

Geda, Y. E., Smith, G. E., Knopman, D. S., Boeve, B. F., Tangalos, E. G., & Ivnik, R. J. (2004). De novo genesis of neuropsychiatric symptoms in mild cognitive impairment (MCI). *International Psychogeriatric, 16,* 51-60.

Geerlings, M. I., Schoevers, R. A., Beekman, A. T. F., Jonker, C., Deeg, D. J. H., & Schmand, B. (2000). Depression and risk of cognitive decline and Alzheimer's disease:

Results of the two prospective community-based studies in the Netherlands. *British Journal of Psychiatry, 176,* 568-575.

George, J. M., & Zhou, J. (2001). When openness to experience and consciencientiousness are related to creative behavior: An interactional approach. *Journal of Applied Psychology, 86*, 315-324.

Gilley, D. W, Wilson, R. S., Bienias, J. L., Bennett, D. A., & Evans, D. A. (2004). Predictors of depressive symptoms in persons with Alzheimer's disease. *Journal of Gerontology: Psychological Sciences*, *59*, 75-83.

Goldberg, L. R. (1981). Language and individual differences: The search for universals in personality lexicons. In L.Wheeler (Ed.), *Review of Personality and social psychology*, (pp.141-165). Beverly Hills, CA: Sage.

Goldberg, L. R. (1993). The structure of phenotypic personality traits. *American Psychologist, 48*, 26-34.

Gottfredson, G. D., Jones, E. M., & Holland, J. L. (1993). Personality and vocational interests: The relation of Holland's six interest dimensions to five robust dimensions of personality. *Journal of Counseling Psychology*, *40,* 518-524.

Gould, S. L. & Hyer, L. A. (2004). Dementia and behavioral disturbance: Does premorbid personality really matter ? *Psychological Reports*, *95*, 1072-1078.

Gray, J. A. (1970). The psychophysiological basis of introversion-extraversion. *Behaviour Research and Therapy, 8,* 249-266.

Gray, J. A. (1981). A critique of Eysenck's theory of personality. In H. J. Eysenck (Ed.), *A model for personality* (pp. 246-276). Berlin, Germany: Springer.

Gray, J. A. (1987). *The psychology of fear and stress* (2nd ed.), Cambridge, England: Cambridge University Press.

Gray, J. A. (1991). The neuropsychology of temperament. In J. Strelau & A. Angleitner (Ed.), *Explorations in temperament: International perspectives on theory and measurement. Perspectives on individual differences* (pp. 105-128). New York, NY: Plenum.

Gray, J. A., & McNaughton, N. (2000). *The neuropsychology of anxiety.* Oxford, England: Oxford University Press.

Gray, J. R., & Braver, T. S. (2002). Personality predicts working memory related activation in caudal anterior cingulate cortex. *Cognitive Affective & Behavioral Neuroscience*, *2,* 64-75.

Gray, J. R., & Thompson, P. M. (2004). Neurobiology of intelligence: Science and ethics. *Nature Reviews Neuroscience, 5*, 471-482.

Gray, J. R., Burgess, G. C., Schaefer, A., Yarkoni, T., Larsen, R. J., & Braver, T. S. (2005). Affective personality differences in neural processing efficiency confirmed using fMRI. *Cognitive Affective & Behavioral Neuroscience, 5,* 182-190.

Hamel, M., Gold, D. P., Andres, D., Reis, M., Dastoor, D., & Grauer, H. (1990). Predictors and consequences of aggressive behavior by community-based dementia patients. *Gerontologist, 30*, 206-211.

Hanninen, T., Reinikainen, K. J., Helkala, E. L., Koivisto, K., Mykkanen, L., & Laakso, M. (1994). Subjective memory complaints and personality traits in normal elderly subjects. *American Journal of Geriatric Psychology, 42*, 1-4.

Hardy, J., & Allsop, D. (1991). Amyloid deposition as the central event in the aetiology of Alzheimer's disease. *Trends in Pharmacological Science, 12*, 383-388.

Harris, S. E., Wright, A. F., Hayward, C., Starr, J. M., Whalley, L. J., & Deary, I. J. (2005). The functional COMT polymorphism, Val 158 Met, is associated with logical memory and the personality trait intellect/imagination in a cohort of healthy 79 year olds. *Neuroscience Letters, 385*, 1-6.

Harrison, R. W. S., & McKeith, I. G. (1995). Senile dementia of Lewy body type - a review of clinical and pathological features: implications for treatment. *International Journal of Geriatric Psychiatry, 10,* 919-926.

Heaven, P. L. C. (1996). Personality and self-reported delinquency: Analysis of the big five personality dimensions. *Personality and Individual Differences*, *20*, 47-54.

Heidrich, A. Thome, J., & Rosler, M. (1997). Apoliprotein E-e4 frequency in late-onest depression, *Biological Psychiatry, 41*, 912-914.

Heinik, J., Keren, P., & Vainer-Benaiah, Z. (1999). Agreement between spouses and children in descriptions of personality change in Alzheimer's disease. *Israel Journal of Psychiatry and Related Science, 36,* 88-94.

Helson, R., Jones, C., & Kwan, V. S. (2002). Personality change over 40 years of adulthood: hierarchical linear modeling analyses of two longitudinal samples. *Journal of Personality and Social Psychology, 83*, 752-766.

Heneka, M. T., O'Banion, M. K., Terwel, D., & Kummer, M.P. (2010). Neuroinflammatory processes in Alzheimer's disease. *Journal of Neural Transmission, 117*, 919-947.

Hindle, D., & Smith, M. V. (1999). Personality development: A psychoanalytic perspective. London, England: Routledge.

Hogan, R., DeSoto, C.B., & Solano, C. (1977). Traits, tests, and personality research. *American Psychologist*, *32*, 255-264.

Hohagen, F., Käppler, C., Schramm, E., Rink, K., Riemann, D., & Berger, M. (1994). Prevalence of insomnia in ealderly general practice attenders and the current treatment modalities. *Acta Psychiatrica Scandinavica, 90*, 102-108.

Holland, A. L., McBurney, D. H., Moossy, J., & Reinmuth, O. M. (1985). The dissolution of language in Pick's disease with neurofibrillary tangles: A case study. *Brain Lang*, *24*, 36-58.

Holmans, P., Zubenko, G. S., Crowe, R. R., DePaulo, J. R., Scheftner, W. A., & Weissman, M. M. (2004). Genome-wide significant linkage to recurrent, early-onset major depressive disorder on chromosome 15q. *American Journal of Medical Genetics*, *74*, 1154-1167.

Holmes, C., Arranz, M. J., Powell, J. F., Collier, D. A., & Lovestone, S. (1998). 5-HT 2A and 5-HT 2C receptor polymorphism and psychopathology in late onset Alzheimer's disease. *Human Molecular Genetics 7*, 1507-1509.

Holmes, C., Boche, D., Wilkinson, D., Yadegarfar, G., Hopkins, V., & Bullock, R. (2008). Long-term effects of Aβ42 immunisation in Alzheimer's disease: Follow-up of a randomised, placebo-controlled phase I trial. *The Lancet, 372,* 216-223.

Holst, G., Hallberg, I. R., & Gustafson, L. (1997). The relationship of vocally disruptive behaviour and previous personality in severely demented institutionalized patients. *Archives of Psychiatric Nursing, 11,* 147-154.

Hopwood, C. J., Thomas, K. M., Markon, K. E., Wright, A. G. C., & Krueger, R. F. (2012). DSM-5 personality traits and DSM-IV personality disorders. *Journal of Abnormal Psychology.*

Horn, J. L. (1985). Remodeling old models of intelligence. In B. B. Wolman (Ed.), *Handbook of intelligence: Theories, measurements, and applications* (pp. 267-300). New York, NY: Wiley.

Horney, K. (1942). *Self-analysis.* New York, NY: Norton.

Hoyle, R. H. (2006). Personality and self-regulation: Trait and information-processing perspectives. *Journal of Personality, 74, 1507-1526.*

Huang, C., Wahlund, L. O., Svensson, L., Winblad, B., & Julin, P. (2002). Cingulate cortex hypoperfusion predicts Alzheimer's disease in mild cognitive impairment. *Neurology, 12,* 2-9.

Itzhaki, R. F., & Wozniak, M. A. (2008). Herpes simplex virus type 1 and Alzheimer's disease: The autophagy connection. *Journal of Neurovirology, 14*, 1-4.

Jang, K. L., Livesley, W. J., & Vernon, P. A. (1996). Heritability of the big five personality dimensions and their facets: A twin study. *Journal of Personality*, *64*, 577-591.

Jelicic, M., Bonnebakker, A. E., & Bonke, B. (1995). Implicit memory performance of patients with Alzheimer's disease: A brief review. *International Psychogeriatrics, 73,* 385-392.

Jensen-Campbell, L. A., & Graziano, W. G. (2001). Agreeableness as a moderator of interpersonal conflict. *Journal of Personality*, *6,* 323-362.

Johnson, J. K., Head, E., Kim, R., Starr, A., & Cotman, C. W. (1999). Clinical and pathological evidence for a frontal variant of Alzheimer's disease. *Archives Neurology, 56*, 1233-1239.

Johnson, W., McGue, M., & Krueger, R.F. (2005). Personality stability in late adulthood: a behavioural genetic analysis. *Journal of Personality, 73*, 523-551.

Jonker, C., Launer, L. J., Hooijer, C., & Lindeboom, J. (1996). Memory complaints and memory impairment in older individuals. *American Journal of Geriatrics Sociology, 44*, 44-49.

Jorm, A. F., & Jacomb, P. A. (1989). The informant questionnaire on cognitive decline in the elderly (IQCODE): Socio-demographic correlates, reliability, validity, and some norms. *Psychological Medicine, 19*, 1015-1022.

Jorm, A. F., Mackinnon, A. J., Christensen, H., Henderson, S., Scott, R., & Korten, A. (1993). Cognitive functioning and neuroticism in an elderly community sample. *Personality and Individual Differences, 15,* 721-723.

Jung, C. G. (1981). *The structure and dynamics of the psyche* (5th Ed.). Princeton, NJ: Princeton University Press.

Karim, S., Minhas, H. M., Battacharya, S., Sein, K., Nayar, B., & Burns, A. (2010). The symptomatology of Alzheimer's disease: A cross-cultural study. *International Journal of Geriatric Psychiatry, 26,* 415-422.

Katz, I. (1998). Diagnosis and treatment of depression in patients with Alzheimer's disease and other dementias. *Journal of Clinical Psychiatry, 59*, 38-44.

Kazui, H., Matsuda, A., & Hirono, N. (2005). Everyday memory impairment of patients with mild cognitive impairment. *Dementia Geriatrics Cognitive Disorders*, *19*, 331-337.

Kawas, C., Gray, S., Brookmeyer, R., Fozard, J., & Zonderman, A. (2000). Age-specific incidence rates of Alzheimer's disease: The Baltimore longitudinal study of aging. *Neurology, 54*, 2072-2077.

Keightley, M. L., Seminowicz, D. A., Bagby, R. M., Costa, P. T., Fossati, P., & Mayberg, H. S. (2003). Personality influences limbic-cortical interactions during sad mood induction. *Neuroimage, 20,* 2031-2039.

Kelly, G. (1955). *The psychology of personal constructs.* New York, NY: Norton & Co.

Kendler, K. S., Kuhn, J. W., & Prescott, C. A. (2004). Childhood sexual abuse, stressful life events and risk for major depression. *Psychological Medicine, 34,* 1475-1482.

Kendler, K. S., Neale, M. C., Kessler, R. C., Heath, A. C., & Eaves, L. J. (1993). A longitudinal twin study of personality and major depression in women. *Archives of General Psychiatry*, *50*, 853-862.

Kenrick, D. T., & Funder, D. C. (1988). Profiting from controversy: Lessons from the person-situation debate. *American Psychologist, 43*, 23-34.

Kim-Cohen, J., Moffitt, T. E., Caspi, A., & Taylor, A. (2004). Genetic and environmental processes in young children's resiliance and vulnerability to socioeconomic deprivation. *Child Development, 75*, 651-668.

Knesevish, J. W., Martin, R. L., & Berg, L. (1983). Preliminary report on affective symptoms in early stages of senile dementia of the Alzheimer type. *American Journal of Psychiatry, 140*, 350-355.

Kitwood, T. (1993). Person and process in dementia: Editorial. *International Journal of Geriatric Psychiatry*, *1,* 541-545.

Ko, K. J., Berg, C. A., Uchino, B., & Smith, T. W. (2007). Profile of successful aging in middle-aged and older married couples. *Psychology and Aging, 22,* 705-718.

Kokmen, E., Beard, C. M., Chandra, V., Offord, K. P., Schoenberg, B. S., & Ballard, D. J. (1991). Clinical risk factors for Alzheimer's disease: A population based case-control study. *Neurology, 41*, 1393-1397.

Kolanowski, A. M., & Whall, A. L. (1996). Life-span perspective of personality in dementia. *Journal of Nursing Scholarship, 28*, 315-320.

Kolanowski, A. M., Strand, G., & Whall, A. L. (1997). A pilot study of the relation of premorbid characteristics to behavior in dementia. *Journal of Gerontological Nursing, 23*, 21-30.

Kolanowski, A., & Garr, M. (1999). The relation of premorbid factors to aggressive physical behavior in dementia. *Journal of Neuroscience Nursing*, *31*, 278-284.

Krahe, B. (1992). *Personality and social psychology: Toward a synthesis*. London, England: Sage.

Kral, V. A., & Emery, O. B. (1989). Long-term follow-up of depressive pseudodementia of the aged. *Canadian Journal of Psychiatry*, *34*, 445-446.

Kraus, C. A., Seignourel, P., Balasubramanyam, V., Snow, A. L., Wilson, N. L., Kunik, M. E., Schulz, P. E., & Stanley, M. A. (2008). Cognitive-behavioral treatment for anxiety in patients with dementia: two case studies. *Journal of Psychiatric Practice*, *14*, 186-192.

Krishnan, K. R. R., Tupler, L. A., Ritchie, J. C., McDonald, W. M., Knight, D. L., & Nemeroff, C. B. (1996). Apolipoprotein E-e4 frequency in geriatric depression. *Biological Psychiatry*, *40*, 69-71.

Kumar, R., Parslow, R. A., Jorm, A. F., Rosenman, S. J., Maller, J., & Meslin, C. (2006). Clinical and neuroimaging correlates of mild cognitive impairment in a middle-aged community sample: Personality and total health through life 60+ study. *Dementia Geriatric Cognitive Disorders*, *21*, 44-50.

Kurtz, J. E., Lee, P. A., & Sherker, J. L. (1999). Internal and temporal reliability estimates for informant ratings of personality using the NEO personality inventory and interpersonal adjective scales. *Assessment, 6,* 103-113.

Lacor, P. N., Buniel, M. C., Furlow, P. W., Clemente, A. S., Velasco, P. T., & Klein, W. L. (2007). A β oligomer-induced aberrations in synapse composition, shape, and density provide a molecular basis for loss of connectivity in Alzheimer's disease. *Journal of Neuroscience, 27,* 796-807.

Laifenfeld, D., Karry R., Klein E., & Ben-Shachar D. (2005). Alterations in cell adhesion molecules L1 and functionally related genes in major depression: A post-mortem study. *Biological Psychiatry, 57*, 716-725.

Lamb, M. E., Chuang, S. S., Wessels, H., Broberg, A. G. & Hwang C.P. (2002). Emergence and construct validation of the big five factors in early childhood: A longitudinal analysis of their ontogeny in Sweden. *Child Development*, *73*, 1517-1524.

Larsen, R. J., & Diener, E. (1992). Promises and problems with the circumplex model of emotion. In M. S. Clark (Ed.), *Emotion* (pp. 25-59). Thousand Oaks, CA: Sage Publications.

Laub, J. H., & Sampson, R. J., (2003). *Shared beginnings, divergent lives: Delinquent boys to age 70.* Cambridge, MA: Harvard University Press.

Lauren, J., Gimbel, D. A., Nygaard, H. B., Gilbert, J. W., & Strittmatter, S. M. (2009). Cellular prion protein mediates impairment of synaptic plasticity by amyloid-β oligomers. *Nature, 457,* 1128-1132.

Lautenschlager, N.T. & Förstl, H. (2007). Personality change in old age. *Current Opinion in Psychiatry, 20*, 62-66.

Lawton, M. P., & Brody, E. M. (1969). Assessment of older people: Self-maintaining and instrumental activities of daily living. *Gerontologist, 9*, 179-186.

Lebert, F., Pasquier, F., & Petit, H. (1995). Personality traits and frontal lobe dementia. *International Journal of Geriatric Psychiatry, 10,*1047-1049.

LeDoux, J. (1996). *The emotional brain: The mysterious underpinings of emotional life*. New York, NY: Touchstone Books.

Lesch, K. P., Bengel, D., Heils, A., Sabol, S. Z., Greenberg, B. D., & Petri, S. (1996). Association of anxiety related traits with a polymorphism in the serotonin transporter gene regulatory region. *Science, 274*, 1527-1531.

Levy, R. (1994). Aging-associated cognitive decline. *International Psychogeriatrics*, *6*, 63-68.

Levinson, D. F. (2006). The genetics of depression: A review. *Biological Psychiatry*, *15,* 84-92.

Ley, K., & Young, D. B., (1998). Self-regulation behaviors in underprepared (developmental) and regular admission college students. *Contemporary Educational Psychology 23*, 42-64.

Lim, Y. Y., Pietrzak, R. H., Snyder, P. J., Darby, D., & Maruff, P. (2012). Preliminary data on the effect of culture on the assessmen of Alzheimer's disease-related verbal memory impairment with the international shopping test. *Archives of clinical neuropsychology, 27,*136-147.

Linn, R. T., Wolf, P. A. & Bachman, D. L. (1995). The "preclinical phase" of probable Alzheimer's disease: A 13-year prospective study of the Framingham cohort. *Archives of Neurology, 52*, 485-490.

Loehlin, J. C. (1992). Genes and environement in personality development. *European Journal of Personality, 7,* 209-210.

Lopez, O. L., Jagust, W. J., Dulberg, C., Becker, J. T., DeKosky, S. T., Fitzpatrick, A. L. …. Kuller, L. H. (2003). Risk factor for mild cognitive impairment in the cardiovascular health study cognition study: Part 2. *Archives of Neurolology, 60,* 1394-1399.

Low, L. F., Brodaty, H., & Draper, B. (2002). A study of premorbid personality and behavioral and psychological symptoms of dementia in nursing home residents. *International Journal of Geriatric Psychiatry*, *17*, 779-783.

Lupien, S. J., Gaudreau, S., & Tchiteya, B. M. (1997). Stress-induced declarative memory impairment in healthy elderly subjects: Relationship to cortisol reactivity. *Journal of Clinical Endocrinology Metabolism, 82*, 2070-2075.

Lupien, S. J., Nair, N. P., & Briere, S. (1999). Increased cortisol levels and impaired cognition in human aging: implication for dementia and depression in later life. *Reviews in the Neuroscience*, *10*, 117-139.

Lyketsos, C. G., Lopez, O., Jones, B., Fitzpatrick, A. L., Breitner, J., & DeKosky, S. (2002). Prevalence of neuropsychiatric symptoms in dementia and mild cognitive impairment. *Journal of the American Medical Association, 288*, 1475-1483.

Mackenzie, T. B., Robiner, W. N., & Knopman, D. S. (1989). Differences between patient and family assessments of depression in Alzheimer's disease. *American Journal of Psychiatry, 146*, 1174-1178.

Maddi, S. R. (1984). Personology fort he 1980s. In R. A. Zucker, J. Aronoff, & A. I. Rabin (Ed.), *Personality and the prediction of behavior* (pp. 7-41). New York, NY: Academic Press.

Magai, C., Cohen, C. I., Culver, C., Gomberg, D., & Makatestsm, C. (1997). Relation between premorbid personality and patterns of emotion expression in mid to late-stage dementia. *International Journal of Geriatric Psychiatry, 12*, 1092-1099.

Malafosse, A. (2005). Genetics of suicidal behaviour. *American Journal of Medical Genetics, 133C*, 1-2.

Mann, J. J. (2003). Neurobiology of suicidal behaviour. *Nature Reviews Neuroscience*, *4,* 819-828.

Manuck, S. B., Flory, J. D., McCaffery, J. M., Matthews, K. A. Mann, J. J., & Muldoon, M. F. (1998). Aggression, impulsivity and central nervous system serotonergic responsivity in a nonpatiant sample. *Neuropsychopharmacology, 19*, 287-299.

Manuck, S. B., Flory, J. D., & Ferrell, R. E. (1999). Aggression and anger-related traits associated with a polymorphism of the tryptophan hydroxylase gene. *Biological Psychiatry, 45,* 603-614.

Marcia, J. E. (1966) Development and validation of ego identity statuses. *Journal of Personality and Social Psychology, 3,* 551-558.

Mardaga, S., & Hensenne, M. (2007). Relationships between Cloninger's biosocial model of personality and the behavioral inhibition/approach systems (BIS/BAS). *Personality and Individual Differences*, *42*, 715-722.

Marx, M. S., Cohen-Mansfield, J., & Werner, P. (1990). A profile of the aggressive nursing home resident. *Behavioural Health Aging, 1*, 65-73.

Maslow, A. H. (1968). *Toward a psychology of being*. New York, NY: D. Van Nostrand Company.

Matsumoto, D. (2007). Culture, context, and behavior. *Journal of Personality, 75,* 1285-1319.

Matthews, G., & Gilliand, K. (1999). The personality theories of H. J. Eysenck and J. A. Gray: A comparative review. *Personality and Individual Differences, 26,* 583-626.

Matthews, G., Zeidner, M., & Roberts, R. D. (2002). *Emotional intelligence: Science and Myth.* Cambridge, MA: MIT Press.

Matthews, G., & Zeidner, M. (2004). Traits, states and the trilogy of mind: An adaptative states perspective on intellectual functioning. In D. Y. Dai & R. J. Strenberg (Ed.), *Motivation, emotion and cognition: Integrative perspectives on intelectual functioning and development* (pp. 143-174). Mahwah, NJ: Lawrence Erlbaum.

McAdams, D.P. (2001). *The person: An integrated introduction to personality psychology* (3th Ed.). Fort Worth, TX: Harcourt College Publishers.

McCrae, R. R., & Costa, P. T., Jr. (1985). Comparison of EPI and psychoticism scales with measures of five-factor model of personality. *Personality and Individual Differences*, *6*, 587-597.

McCrae, R. R., & Costa, P. T. (1987). Validation of the five-factor model of personality across instruments and observers. *Journal of Personality and Social Psychology*, *52,* 81-90.

McCrae, R. R., & John, O. P. (1992). An introduction to the five-factor model and its applications. *Journal of Personality, 60,* 175-215.

McCrae, R. R. (1994). Openness to experience: Expanding the boundaries of Factor V. *European Journal of Personality, 8,* 251-272.

McCrae, R. R., & Costa, P. T., Jr. (1996). Toward a new generation of personality theories: Theoretical contexts for the five-factor model. In J. S. Wiggins (Ed.), *The five-factor model of personality: Theoretical perspectives* (pp. 21-50). New York, NY: Guilford

McCrae, R. R., & Costa, P. T., Jr. (1997). Personality trait structures as a human universal. *American Psychologist, 52,* 509-516.

McCrae, R. R., Costa, P. T., del Pilar, G. H., Rolland, J. P., & Parker, W. D. (1998). Cross-cultural assessment of the Five-Factor Model: The revised NEO-Personality Inventory. *Journal of Cross-Cultural Psychology*, *29*, 171-188.

McCrae, R. R., & Costa, P. T., Jr. (1999). A five-factor theory of personality. In L. A. Pervin & O. P. John (Ed.), *Handbook of personality: Theory and research* (2nd Ed., pp. 139-153). New York, NY: Guilford Press.

McCrae, R. R. (2000). Trait psychology and the revival of personality and culture studies. *The American Behavioral Scientist, 44*, 10-23.

McCrae, R. R., Costa, P. T., Ostendorf, F., Angleitner, A., Hrebickova, M., & Avia, M. D. (2000). Nature over nurture: Temperament, personality, and life span development. *Journal of Personality and Social Psychology, 78*, 173-186.

McCrae, R. Jang, K. L., Livesley, W. J., Riemann, R., & Angleitner, A. (2001). Sources of structure: Genetic, environmental, and artifactual influences on the covariation of personality traits. *Journal of Personality*, *69,* 511-535.

McCrae, R. R. (2002). The maturation of personality psychology: Adult personality development and psychological well-being. *Journal of Research in Personality, 36,* 307-317.

McCrae, R. R., & Costa, P. T., Jr. (2003). *Personality in adulthood: A five-factor theory perspective* (2nd ed.). New York, NY: Guilford Press.

McCrae, R. R., Costa, P. T. Jr., Hrebickova, M., Urbanek, T., & Martin, T.A. (2004). Age differences in personality traits across cultures: Self-report and observer perspectives. *European Journal of Personality, 18*, 143-157.

McCrae, R. R., Terracciano, A., & 78 members of the personality profiles of culture project. (2005). Universal features of personality traits from the observer's perspective: Data from 50 cultures. *Journal of Personality and Social Psychology*, *88,* 547-561.

McCrae, R. R., & Costa, P. T. (2006). Personality, coping, and coping effectiveness in an adult sample. *Journal of Personality*, *54*, 385-404

McDaniel, K. D., Edland, S. D., & Heyman, A. (1995). Relationship between level of insight and severity of dementia in Alzheimer's disease. CERAD clinical investigators. Consortium to establish a registry for Alzheimer's disease. *Alzheimer Disorders & Association Disorders*, *9,* 101-104.

McEwen, B. S. (1998). Protective and damaging effects of stress mediators. *New England Journal of Medicine, 338*, 171-179.

McEwen, B. S. (2000). Protective and damaging effects of stress mediators: Central role of the brain. *Progress in Brain Research, 122*, 25-34.

McGee, M. A., & Brayne, C. (1998). The impact on prevalence of dementia in the oldest age groups of differential mortality patterns: A deterministic approach. *International Journal of Epidemiology, 27,* 87-90.

McGhee, R. L., Ehrler, D. J., Buckhalt, J. A., & Phillips, C. (2012). The relation between five-factor personality traits and risk-taking behavior in preadolescents. *Psychology, 8*, 558-561.

McKhann, G., Drachman, D., Folstein, M., Katzman, R., Price, D., & Stadlan, E. M. (1984). Clinical diagnosis of Alzheimer's disease: Report of the NINCDS-ADRDA work group under the auspices of the department of health and human services task forces on Alzheimer's disease. *Neurology,* 34*,* 939-944.

McKeith, I. G., Galasko, D., & Kosaka, K. (1996). Consensus guidelines for the clinical and pathologic diagnosis of dementia with Lewy bodies (DLB): Report of the consortium on DLB international workshop. *Neurology, 47,* 1113–1124.

McPherson, S., La Rue, A., Fitz, A., Matsuyama, S., & Jarvik, L. F. (1995). Self-reports of memory problems in relatives of patients with probable Alzheimer's disease. *International Psychogeriatrics, 7*, 367-376.

Mega, M. S., Cummings, J. L., Fiorello, T., & Gornbein, J. (1996). The spectrum of bahvarioral changes in Alzheimer's disease. *Neurology, 46,* 130-135.

Meier, B., Perrig-Chiello, P., & Perrig, W. (2002). Personality and memory in old age. *Aging Neuropsychology and Cognition, 9,* 135-144.

Meins, W., Frey, A., & Thiesemann, R. (1998). Premorbid personality traits in Alzheimer's disease: Do they predispose to noncognitive behavioural symptoms? *International Psychogeriatrics, 10*, 369-378.

Meins, W. (2000). Impact of personality on behavioral and psychological symptoms of dementia. *International Psychogeriatrics, 12,* 107-109.

Mentis, M. H., Weinstein, E. A., Horwitz, B., McIntosh, A. R., Pietrini, P., Alexander, G. E., Furey, M., & Murphy, D. G. M. (1995). Abnormal brain glucose metabolism in the delusional misidentification syndromes: A positron emission tomography study in Alzheimer's disease. *Biological Psychiatry*, *38,* 438-449.

Merrian, A., Aaronson, M., & Gaston, P. (1988). The psychiatric symptoms of Alzheimer's disease. *Journal American Geriatric Sociology*, *26*, 7-12.

Migliorelli, R., Teson, A., Sabe, L., Petracchi, M., Leiguarda, R., & Starkstein, S. E. (1995). Prevalence and correlates of dysthymia and major depression among patients with Alzheimer's disease. *American Journal of Psychiatry, 152,* 37-44.

Million, T. (1969). *Modern psychopathology: A biosocial approach to maladaptative learning and functioning*. Philadelphia, PA: Saunders.

Million, T., & Davis, R. (2000). *Personality disorders in modern life*. New York, NY: John Wiley.

Mischel, W. (1968). *Personality and assessment*. New York, NY: John Wiley & Sons.

Mischel, W. (1973). Toward a cognitive social learning reconceptualization of personality. *Psychological Review*, *80*, 252-283.

Mischel, W. (1977). On the future of personality measurement. *American Psychologist*, *32*, 246-254.

Mischel, W. & Peake, P.K. (1982). Beyond déjà vu in the search for cross-situational consistency. *Psychological Review*, *89*, 730-755.

Mischel, W. & Shoda, Y. (1995). A cognitive-affective system theory of personality: Reconceptualising situations, dispositions, dynamics, and invariance in personality structure. *Psychological Review, 102*, 246-268.

Mitchell, P., Wilhelm, K., & Parker, G. (2004). Interaction between life events and 5-HTT genotype in determining the likelihood of depression and anxiety in a 25-year longitudinal study of Australian teachers. *American Journal of Medical Genetics, 130,* 36.

Moan, R. (2009). MRI software accurately TDS preclinical Alzheimer's disease. *Journal of Clinical Psychiatry, 64*, 7-10.

Monastero, R., Mariani, E., Camarda, C., Ingegni, T., Averna, M. R., & Senin, U. (2006). Association between apolipoprotein E4 allele and apythy in probable Alzheimer's disease. *Acta Psychiatrica Scandinavica, 113*, 59-63.

Moresco, F. M., Dieci, M., Vita, A., Messa, C., Gobbo, C., & Galli, L. (2002). In vivo serotonin 5HT receptor binding and personality traits in healthy subjects: A positron emission tomography study. *Neuroimage, 17*, 1470-1478.

Morris, J. C. (1993). The clinical dementia rating (CDR): Current version and scoring rules. *Neurology*, *43*, 2412-2414.

Morizot, J., & Le Blanc, M. (2003). Continuity and change in personality traits from adolescence to midlife: A 25-year longitudinal study comparing representative and adjudicated men. *Journal of Personality, 71*, 705-755.

Morizot, J., & Le Blanc, M. (2005). Searching for a developmental typology of personality and uts relations to antisocial behavior: A longitudinal study of a representative sample of men. *Journal of Personality*, *73*, 139-182.

Morizot, J., & Miranda, D. (2007). Développment des traits de personality au cours de la vie: Continuité ou changement? *Canadian Psychology, 48*, 156-173.

Moskowitz, D. S. (1990). Convergence of self-reports and independent observers: Dominance and friendliness. *Journal of Personality and Social Psychology*, *58*, 1096-1106.

Möttus, R., Johnson, W., & Deary, I. J. (2011). Personality traits in old age: Measurement and rank-order stability and some mean-level change. *Psychology and Aging*, *27*, 243-249.

Mudher, A., & Lovestone, S. (2002). Alzheimer's disease-do tauists and baptists finally shake hands? *Trends Neuroscience, 25*, 22-26.

Müller-Thomsen, T., Arlt, S., Ganzer, S., Mann, U., Mass, R., & Naber, D. (2002). Depression in Alzheimer's disease might be associated with apolipoprotein E4 allele frequency in women but not in men. *Dementia Geriatric of Cognitive Disorders, 14*, 59-63.

Mychack, P., Rosen, H., & Miller, N. L. (2001). Novel applications of social-personality measures to the study of dementia. *Neurocase*, *7*, 131-143.

Myers, I. B., & McCaulley, M. H. (1985). *Manual: A guide to the development and use of the Myers- Briggs Type Indicator.* Palo Alto, CA: Consulting Psychologists Press.

Nacmias, B., Tedde, A., Forleo, P., Piacentini, S., Guarnieri, M., & Bartoli, A. (2001) Association between 5-HT 2A receptor polymorphism and psychotic symptoms in Alzheimer's disease. *Biological Psychiatry, 50*, 472-475.

Nash, M. W., Huezo-Diaz, P., Williamson, R. J., Sterne, A., Purcell, S., & Hoda, F. (2004). Genome-wide linkage analysis of a composite index of neuroticism and mood-related scales in extreme selected sibs hips. *Human Molecular Genetics, 13*, 2173-2182.

Neale, B. M., Sullivan, P. F., & Kendler, K. S. (2005). A genome scans of neuroticism in nicotine dependent smokers. *American Journal of Medicine Genetics, 132,* 65-69.

Neugarten, B. L. (1974). The future and the young-old. *Gerontologist, 15*, 4-9.

Neuman, G. A., & Wright, J. (1999). Team effectiveness: Beyond skills and cognitive ability. *Journal of Applied Psychology*, *84*, 376-389.

Nikolaev, A., McLaughlin, T., O'Leary, D. D., & Tessier-Lavigne, M. (2009) APP binds DR6 to trigger axon pruning and neuron death via distinct caspases. *Nature, 457*, 981-989.

Ohm, T. G., Kirca, M., Bohl, J., Scharnagl, H., Gross, W., & März, W. (1995). Apolipoprotein E polymorphism influences not only cerebral senile plaque load but also Alzheimer type neurofibrillary tangle formation. *Neuroscience, 66*, 583-587.

Ormel, J., & Wohlfarth, T. (1991). Haw neuroticism, long-term difficulties, and life situation change influence psychological distress: A longitudinal model. *Journal of Personality and Social Psychology, 60,* 744-755.

Orrell, M., & Bebbington, P. (1995). Life events and senile dementia. I. Admission, deterioration and social environment change. *Psychological Medicine, 25*, 373-386.

Ostwald, S. K., Duggleby, W., & Hepburn, K. W. (2002). The stress of dementia: View from the inside. *American Journal of Alzheimer's disease and Other Dementias, 17*, 9-10.

Ouwehand, C., de Ridder, D. T. D., & Bensing, J. M. (2006). A review of successful aging models: Proposing proactive coping as an important additional strategy. *Clinical Psychology Review, 27,* 873-884.

Palmer, A. M., Stratmann, G. C., Procter, A. W., & Bowen, D. M. (1988). Possible neurotransmitter basis of behavioral changes in Alzheimer's disease. *Annals of Neurology, 23,* 616-620.

Palmer, K., Bäckman, L., Small, B. J., & Fratiglioni, L. (2006). *Cognitive impairment in elderly persons without dementia: findings from the Kungsholmen project*. In H. A. Tuokko & D. F. Hultsch (Eds.), *Mild Cognitive Impairment. International perspectives* (pp. 57-75). New York, NY: Taylor & Francis.

Palsson, S., Johannsson, B., Berg S., & Skoog, I. (2000). A population study on the influence of depression on neuropsychological functioning in 85-year-olds. *Acta Psychiatrica Scandinavica*, *101*, 185-193.

Pavlov, I. P. (1952). Statements in response to the presentation by S. G. Vulfson of the function of salivary glands. In I. P. Pavlov (2nd ed.), *Polnoe Sobranie Sochinenii*. Moscow, Rusia: Leningrad.

Pearson, P. R. (1993). Cognitive functioning and neuroticism in elderly psychiatric patients. *Personality and Individual Differences*, *14,* 265–266.

Pearlson, G. D., Ross, C. A., & Lohr, W. D. (1990). Association between family history of affective disorder and the depressive syndrome of Alzheimer's disease. *American Journal of Psychiatry, 147*, 452-456.

Persson, G., Berg, S., Nilsson, L., & Svanborg, A. (1991). Subclinical dementia: relation to cognition, personality and psychopathology: A nine-year prospective study. *International Journal of Geriatric Psychiatry*, *6*, 239-247.

Petersen, R. C. (2003). Conceptual Overview. In R. C. Petersen (Ed.), *Mild Cognitive Impairment: Aging to Alzheimer's disease* (pp. 1–14). New York, NY: Oxford University Press, Inc.

Petersen, R. C. (2007). The current status of mild cognitive impairment-what do we tell our patients? *Natura Clinical Practice Neurol*ogy, *3*, 60-61.

Petry, S., Cummings, J. L., Hill, M. A., & Shapira J. (1988). Personality alterations in dementia of the Alzheimer type. *Archives of Neurology*, *45*, 1187-1190.

Philo, S. W., Richie, M. F., & Kaas, M. J. (1996). Inappropriate sexual behaviour. *Journal of Gerontological Nursing, 22*, 17-22.

Piaget, J. (1958). Les étapes du développement mental. *Bulletin de psychologie*, *11*, 217-219.

Pickering, A. D., & Gray, J. A. (1999). The neuroscience of person- ality. In L. Pervin & O. John (Eds.), *Handbook of personality* (2nd ed.). New York, NY: Guilford Press.

Plotkin, D. A., Mintz J., & Jarvik, L. F. (1985). Subjective memory complaints in geriatric depression. *American Journal of Psychiatry, 142,* 1103-1105.

Pocnet, C., Rossier, J., & von Gunten, A. (2009). *Preliminary validation of the Structured Interview for the five-factor model.* Poster presented at the 11th Congress of the Swiss Psychological Society, University of Neuchâtel, Switzerland.

Pocnet, C., Rossier, J., Antonietti, J.-Ph., & von Gunten, A. (2011). Personality changes in patients with beginning Alzheimer's disease. *The Canadian Journal of Psychiatry, 56*, 408-417.

Pocnet, C., Rossier, J., Antonietti, J.-Ph., & von Gunten, A. (2013). Personality traits and behavioral and psychological symptoms in patients at an early stage of Alzheimer's disease. *International Journal of Geriatric Psychiatry*, *28,* 276-283.

Pocnet, C., Rossier, J., Antonietti, J.-Ph., & von Gunten, A. (2013). Personality and cognitive level in patients at an early stage of Alzheimer's disease. *Personality and Individual Differences*, *54*, 174-179

Purandare, N., Bloom, C., Page, S., Morris, S., & Burns, A. (2002). The effect of anticholinesterases on personality changes in Alzheimer's disease. *Aging and Menthal Health, 6,* 350-354.

Quartier, V., & Rossier, J. (2008). A study of personality in children aged 8-12 years: Comparing self- and partents' ratings. *European Journal of Personality, 22*, 575-588.

Quilty, L. C., Meusel, L. A. C., & Bagby, R. M. (2008). Neuroticism as a mediator of treatment response to SSRIs in major depressive disorders. *Journal of Affectives disorders, 111,* 67-83.

Rabins, P. V., Merchant, A., & Nestadt, G. (1984). Criteria for diagnosing reversible dementia caused by depression: Validation by 2-year follow-up. *British Journal of Psychiatry*, *144*, 488-492.

Ramachandra, G., Marder, K., Tang, M., Schofield, P. W., Chun, M. R., & Devanand, D. P. (1996). A preliminary study of apolipoprotein E genotype and psychiatric manifestations of Alzheimer's disease. *Neurology, 47*, 256-259.

Ranganath, C., Cohen, M. X., & Brozinsky, C. J. (2005). Working memory maintenance contributes to long-term memory formation: Neural and behavioral evidence. *Journal of Cognitive Neuroscience, 15*, 994-1010.

Rankin, K. P., Kramer, J. H., Myhack, P. & Miller, B. (2003). Double dissociation of social functioning in frontotemporal demantia. *Neurology*, *60,* 266-271.

Rankin, K. P., Rosen, H. J., Kramer, J. H., Schauer, G. F., Weiner, M. W., & Schuff, N. (2004). Right and left medial orbitofrontal volumes show an opposite relationship to agreeableness in FTD. *Dementia of Geriatric and Cognitive Disorders*, *17*, 328-332.

Rankin, K. P., Baldwin, E., Pace-Savitsky, C., Kramer, J. H., & Miller, B. (2005). Self-awareness and personality change in dementia. *Journal of Neurology, Neurosurgery and Psychiatry*, *76*, 632-739.

Rasmusson, A. M., Shi, L., & Duman, R. (2002). Downregulation of BDNF mRNA in the hippocampal dentate gyrus after re-exposure to cues previously associated with footshock. *Neuropsychopharmacology*, *27*, 133-142.

Reifler, B. V., Larson, E., Teri, L., & Poulson, M. (1986). Dementia of the Alzheimer's type and depression. *Journal American of Geriatric Sociology, 34,* 855–859.

Reifler, V. R. (1996). Depression, anxiety, and sleep disturbances. *International Psychogeriatrics, 8*, 415-418.

Reisberg, B., Borstein, J., Franssen, E., Salob, S., Steinberg, G., & Chulman, E. (1987). BEHAVE-AD: A clinical rating scale for the assessment of pharmacologicaly remediable behavioural symptomatology in Alzheimer's disease. In H. J. Altman (Ed.), *Alzheimer's disease: Problems, prospects and perspectives*. New York, NY: Plenum Press.

Riemann, R., Angleitner, A., & Strelau, J. (1997). Genetic and environmental influences on reared together using the self-and peer report NEO-FFI scales. *Journal of Personality, 65*, 449-475.

Rigozzi, C., & Rossier, J. (2004). Validation d'une version abrégée du TCI (TCI-56) sur un échantillon de jeunes fumeurs et non-fumeurs. *Annales Médico-Psychologiques*, *162,* 541-548.

Rigozzi, C., Rossier, J., Verardi, S.**,** Dahourou, D., Ah-Kion U., Adjahouisso, M., … Sfayhi, N. (2009). A cross-cultural study of the higher-order structures underlying personality disorders in French-speaking Africa and Switzerland, *Journal of Personality disorders, 23,* 175-186.

Roberts, B. W., & DelVecchio, W. F. (2000). The rank-order consistency of personality traits from childhood to old age: A quantitative review of longitudinal studies. *Psychological Bulletin, 126*, 3-25.

Roberts, B. W., Caspi, A., & Moffitt, T. E. (2001). The kids are alright: Growth and stabilty in personality development from adolescence to adulthood. *Journal of Personality and Social Psychology, 81*, 670-683.

Roberts, B. W., Chernyshenko, O. S., Stark, S., & Goldberg, L. R. (2005). The structure of conscientiousness: An empirical investigation based on seven major personality questionnaires. *Personnel Psychology*, *58,* 103-139.

Roberts, B. W., Walton, K. E., & Viechtbauer, W. (2006). Patterns of mean-level change in personality traits across the life course: A meta-analysis of longitudinal studies. *Psychological Bulletin*, *132*, 1-25.

Robins Wahlin, T. B., & Byrne, G. J. (2011). Personality changes in Alzheimer's disease: A systematic review. *Geriatric Psychiatry,* 26, 1019-1029.

Rogers, C. R. (1961). *On becoming a person.* Boston, MA: Houghton Mifflin.

Rogers, C. R. (1980). *A way of being.* Boston, MA: Houghton Mifflin.

Rolland, J-P. (2004). *L'évaluation de la personnalité: Le modeèle en cinque facteurs.* Wavre, Belgium: Mardaga.

Rossier, J., Meyer de Stadelhofen, F., & Berthoud, S. (2004). Hierarchical structures of the NEO PI-R and of the 16PF5. *European Journal of Psychological Assessment, 20,* 27-38.

Rossier, J., Dahourou, D., & McCrae, R. R. (2005). Structural and mean level analyses of the five-factor model and locus of control: Further evidence from Africa. *Journal of Cross-Cultural Psychology, 36*, 227-246.

Rossier, J., Quartier V., Enescu, R., & Iselin, A. (2007). Validation of the French version of the Hierarchical Personality Inventory for Children (HiPIC): Influence of gender and age on personality traits from 8 to 12 years. *European Journal of Psychological Assessment 23,* 125-132.

Rossier, J., Rigozzi, C., & Personality across culture research group (16 members). (2008). Personality disorders and the five-factor model among French speakers in Africa and Europe. *Canadian Journal of Psychiatry, 53*, 534-544.

Rothbart, M. K., Derryberry, D. & Hershey, K. (2000). Stability of temperament in childhood: laboratory infant assessment to parent report at seven years. In V. J. Molfese & D. L. Molfese (Ed.). *Temperament and personality development across the life span* (pp. 85-119). Mahwaah, NJ: Erlbaum.

Rubin, E. H., Kinscherf, D. A., & Morris, J. C. (1989). Psychopathology of very mild dementia of the Alzheimer type. *American Journal of Psychiatry*, *146*, 1017-1021.

Rubin, E. H., Morris, C. M., Storandt, M., & Berg, L. (1987). Behavorial changes in patients with mild senile dementia of the Alzheimer's type. *Psychiatry Research*, *21*, 55-62.

Ruby, P., Collette, F., D'Argembeau, A., & Péters, F. (2009). Perspective taking to assess self-personality: What's modified in Alzheimer's disease. *Neurobiology of Aging, 30,* 1637-1651.

Rushton, J. P., Bons, T. A., Ando, J., & Hur, Y. M. (2008). The genetics and evolution of a general factor of personality. *Journal of Research in Personality*, *42*, 1173-1185.

Samuel, D. B., & Widiger, T. A. (2008). A meta-analytic review of the relationships between the five-factor model and DSM-IV-TR personality disorders: A facet level analysis. *Clinical Psychology Review, 28,* 1326 -1342.

Sandbrink, R., Hartmann, T., Masters, C. L., & Beyreuther, K. (1996*).* Genes contributing to Alzheimer's disease*. Molecular Psychiatry, 1,* 27-40.

Schacter, D. L., Gilbert, D. T., & Wegner, D. M. (2011). Explicit and implicit memory in Psychology (2nd Ed). New York, NY: Worth.

Schmidt, R., Fazekas, F., Reinhart, B., Kapeller, P., Fazekas, G., Offenbacher, H., Eber, B., Schumacher, M., & Freidl, W. (1996). Estrogen replacement therapy in older women: A neuropsychological and brain MRI study. *Journal American of Geriatric Sociology*, *44,* 1307-1313.

Scheier, M. F., & Carver, C. S. (1987). Dispositional optimism and physical well-being: The influence of generalized outcome expectancies. *Health Psychology*, *5*, 219-247.

Schenk, F., Leuba, G., & Büla, C. (2004). *Du vieillissement cérébral à la maladie d'Alzheimer: Autour de la notion de plasticité*. Bruxelles, Belgium: De Boeck.

Schmitz, C., Rutten, B. P., Pielen, A., Schafer, S., Wirths, O., & Bayer, T. A. (2004). Hippocampal neuron loss exceeds amyloid plaque load in a transgenic mouse model of Alzheimer's disease. *American Journal of Pathology*, *164,* 1495-1502.

Schroeder, M. L., Wormsworth, J., & Livesley, W. J. (1992). Dimensions of personality disorders and their relationships to the big five dimensions of personality. *Psychological Assessment*, *4,* 47-53.

Seibert, S. E., & Kraimer, M. L. (2001). The five-factor model of personality and career success. *Journal of Vocational Behavior*, *58*, 1-21.

Seidler, A., Bernhardt, T., Nienhaus, A., & Frölich, L. (2003). Association between the psychosocial network and dementia: A case-control study. *Journal of Psychiatric Research*, *37*, 89-98.

Seiffer, A., Clare, L., & Harvey, R. (2005). The role of personality and coping style in relation to awareness of current functioning in early-stage dementia. *Aging & Mental Health*, *9*, 535-541.

Sheline, Y. I., Wang, P. W., Gado, M. H., Csernansky, J. G., & Vannier, M. W. (1996). Hippocampal atrophy in recurrent major depression. *Proceedings of National Academy of Sciences USA, 93*, 3908-3913.

Shweder, R.A., & D'Andrade, R.G. (1979). Accurate reflection or systematic distortion? A replay to Block, Weiss, and Thorne. *Journal of Personality and Social Psychology*, *37*, 1075-1084.

Siegler, I. C., Dawson, D. V., & Welsh, K. A . (1994). Caregiver ratings of personality change in Alzheimer's disease patients: A replication. *Psychological Aging, 9*, 464-466.

Shiner, R. L. (1998). How shall we speak of children's personalities in middle childhood? A preliminary taxonomy. *Psychological Bulletin, 124,* 308-332.

Skinner, B. F. (1957). *Verbal Behavior*. Englewood Cliffs, NJ: Pretince Hall.

Skinner, B. F. (1971). *Beyond freedom and dignity.* New York, NY: Bantam.

Small, G. W., Okonek, A., Mandelkern, M. A., La Rue, A., Chang, L., & Khonsary, A. (1994). Age-associated memory loss: Initial neuropsychological and cerebral metabolic findings of a longitudinal study. *International Psychogeriatrics*, *6,* 23-44.

Smith, G. E., Petersen, R. C., Ivnik, R. J., Malec, J. F., & Tangalos, E. G. (1996). Subjective memory complaints, psychological distress, and longitudinal change in objective memory performance. *Psychological Aging, 11*, 272-279.

Smith, T. W., & Spiro, A. (2002). Personality, health, and aging: Prolegomenon for the next generation. *Journal of Research in Personality, 36,* 363-394.

Smith-Gamble, V., Baiyewu, O., Perkins, A. J., Gureje, O., Hall, K. S., & Ogunniyi, A. (2002). Informant reports of changes in personality predict dementia in a population-based study of elderly African Americans and Yoruba. *American Journal of Geriatric Psychiatry*, *10,* 724-732.

Snowden, J. S., Bathgate, D., & Varma, A. (2001). Distinct behavioural profiles in frontotemporal dementia and semantic dementia. *Journal of Neurology, Neurosurgery and Psychiatry*, *70*, 323 -332.

Snowdon, D. A., Kemper, S. J., Mortimer, J. A., Greiner, L. H., Wekstein, D. R., & Markesbery, W. R. (1996). Linguistic ability in early life and cognitive function and Alzheimer's disease in late life. *Journal of American Medical Association*, *275*, 528-532.

Song, J., & Algase, D. (2008). Premorbid characteristics and wandering behaviour in persons with dementia. *Archives of Psychiatric Nursing, 22*, 318-327.

Spaan, P. E., Raaijmakers, J. G., & Jonker, C. (2003). Alzheimer's disease versus normal ageing: A review of the efficiency of clinical and experimental memory measures. *Journal of Clinical Experimental Neuropsychology*, *25*, 216-233.

Srivastava, S., John, O. P., Gosling, G. D., & Potter, J. (2003). Development of personality in early and middle adulthood: set like plaster or persistent change? *Journal of Personality and Social Psychology, 84*, 1041-1053.

Starkstein, S. E., Sabe, L., Chemerinski, E., Jason, L., & Leiguarda, R. (1996). Two domains of anosognosia in Alzheimer's disease. *Journal Neurological, Neurosurging and Psychiatry, 61*, 485-490.

Starkstein, S. E., & Mizrahi, R. (2006). Depression in Alzheimer's disease. *Expert Review Neurother, 6*, 887-895.

Steele, C., Rovner, B., Chase, G. A., & Folstein, M. (1990). Psychiatric symptoms and nursing home placement of patients with Alzheimer's disease. *American Journal of Psychiatry*, *147*, 1049-1051.

Steffens, D. C., Plassman, B. L, Helms, M. J., Welsh-Bohmer, K. A., Saunders, A. M., & Breitner, J. C. (1997). A twin study of late-onset depression and apolipoprotein E epsilon 4 as risk factors for Alzheimer's disease. *Biological Psychiatry*, *41,* 851-856.

Stenberg, G., Risberg, J., Warkentin, S., & Rosen, I. (1990). Regional patterns of cortical blood flow distinguish extraverts from introverts. *Personality and Individual Differences*, *11*, 663-673.

Stepaniuk, J., Ritchie, L., & Tuokko, H. (2008). Neuropsychiatric impairments as predictors of mild cognitive impairment, dementia, and Alzheimer's disease. *American Journal of Alzheimer's Disease and Other Dementia, 23*, 326-333.

Stern, Y., Tang, M. X., Albert, M. S., Brandt, J., Jacobs, D. M., & Tsai, W. Y. (1997). Predicting time to nursing home care and death in individuals with Alzheimer's disease. *Journal of the American Medical Association, 277*, 806-812.

Stokes, G. (*2000*). *Challenging behaviour in dementia*. Bicester, England: Speechmark.

Strauss, M., Pasupathi, M., & Chatterjee, A. (1993). Concordance between observers in descriptions of personality change in Alzheimer's disease. *Psychological Aging, 8,* 475-480.

Strauss, M. E., & Pasupathi, M. (1994). Primary caregivers' descriptions of Alzheimer's disease personality traits: Temporal stability and sensitivity to change. *Alzheimer Disease and Association Disorders*, *8,* 166-176.

Strauss, M. E., Lee, M. M., & DiFilippo, J. M. (1997). Premorbid personality and behavioural symptoms in Alzheimer's disease: Some cautios. *Archives of Neurology, 54*, 257-259.

Strelau, J. (1983). *Temperament, personality, activity.* Academic: London.

Strelau, J. (2001). The role of temperament as a moderator of stress. In T. D. Wachs & G. A. Kohstamm (Ed.), *Temperament in context* (pp. 153-172). Mahwah, NJ: Lawrence Erlbaum.

Su, B., Wang, X., Nunomura, A., Moreira, P. I., Lee, H., G., Perry, M., Smith, A., & Zhu, X. (2008). Oxidative stress signaling in Alzheimer's disease. *Current Alzheimer Research, 5,* 525-532.

Suchy, Y. (2009). Executive functioning: Overview, assessment, and research issues for non-neuropsychologists. *Annals of Behavioral Medicine, 37,* 106-116.

Sugiura, M., Kawashima, R., Nakagawa, M., Okada, K., Sato, T., & Goto, R. (2000). Correlation between human personality and neural activity in cerebral cortex. *Neuroimage, 11,* 541-546.

Sujuan, G., Hugh, C. H., Kathleen, S. H., & Siu, H. (1998). The relationships between age, sex and incidence of dementia and Alzheimer's disease: A meta-analysis. *Archives Generales of Psychiatry, 55,* 808-815.

Sukonick, D. L., Pollock, B. G., Sweet, R. A., Mulsant, B. H., Rosen, J., & Klunk, W. E. (2001). The 5-HTTPR*S/*L polymorphism and aggressive behavior in Alzheimer's disease. *Archives of Neurology, 58*, 1425-1428.

Sultzer, D. L., Mahler, M. E., Mandelkern, M. A., Cummings, J. L., Van Corp, W. G., & Hinkin, C. H. (1995). The relationship between psychiatric symptoms and regional cortical metabolism in Alzheimer's disease. *Journal of Neuropsychiatry and Clinical Neurosciences, 7*, 476-484.

Sutin, A. R., Beason-Held, L. L., Resnick, S. M., & Costa, P. T. (2009). Sex differences in resting-state neural correlates of openness to experience among older adults. *Cerebral Cortex, 19,* 2797-2808.

Sutton, S.K., & Davidson, R.J. (1997). Prefrontal brain asymmetry: A biological substrate of the behavioural approach and behavioural inhibition systems. *Psychological Science*, *8*, 204-210.

Suzman, R. M., Willis, D. P., & Manton, K. G. (1992). *The oldest old*. New York: Oxford University Press.

Suzuki, W. (2007). The role of the hippocampus in new associative learning. *Imaging and the Aging Brain, 1097*, 1-11.

Swearer, J. M., Hoople, N. E., Kane, K. J., & Drachman, D. A. (1996). Predicting aberrant behaviour in Alzheimer's disease. *Neuropsychiatry, Neuropsychology and Behavioural Neurology, 9*, 162-170.

Talassi, E., Cipriani, G., & Bianchetti, A. (2007). Personality changes in Alzheimer's disease. *Aging Mental Health, 11*, 526-531.

Tarbuck, A. F., & Paykel, E. S. (1995). Effects of major depression on the cognitive function of younger and older subjects. *Psychological Medicine, 25*, 285-296

Terracciano, A., McCrae, R. R., Brant, L. J., & Costa, P. T., Jr. (2005). Hierarchical linear modelling analyses of the NEO-PI-R scales in the Baltimore longitudinal study of aging. *Psychological Aging*, *20*, 493-506.

Terracciano, A., Costa, P. T., & McCrae, R. R. (2006). Personality plasticity after age 30. *Personality and Social Psychology Bulletin, 32*, 999-1009.

Tian, J., Bucks, R. S., Haworth, J., & Wilcock, G. (2003). Neuropsychological prediction of conversion to dementia from questionable dementia: Statistically significant but not yet clinically useful. *Journal of Neurology, Neurosurging and Psychiatry, 74*, 433-438.

Tobiansky, R., Blizard, R., Livingston, G., & Mann, A. (1995). The Gospel Oak study stage IV: the clinical relevance of subjective memory impairment in older people. *Psychological Medicine*, *25*, 779-786.

Tow, P. M., & Whitty, C. W. (1953). Personality changes after operations on the cingulate gyrus in man. *Journal of Neurology, Neurosurging and Psychiatry*, *16*, 186-193.

Tronson, N. C., & Taylor, J. R. (2007). Molecular mechanisms of memory reconsolidation. *Nature Reviews Neuroscience, 8,* 262-275.

Trull, T. J., & Widiger, T. A. (1997). *Structured interview for the five-factor model*. Odessa, FL: Psychological Assessement Ressources.

Tsolaki, M., Fountoulakis, K., Chantzi, E., & Kazis, A. (1997). Risk factors for clinically diagnosed Alzheimer's disease: A case control study of a Greek population. *International Psychogeriatric*, *9,* 327-341.

Tulving, E. (1983). *Elements of episodic memory*. Oxford, England: Clarendon Press.

Van der Zee, K. I., Buunk, B. P., & Sanderman, R. (1998). Neuroticism and reactions to social comparison information among cancer patients. *Journal of Personality*, *66*, 175-194.

van Duijn, C. M. (2004). Prospects of genetic research of mild cognitive impairment. *Journal of Internal Medicine, 256*, 235-239.

Veit, R., Flor, H., Erb, M., Hermann, C., Lotze, M., Grodd, W., & Birbaumer, N. (2002). Brain circuits involved in emotional learning in antisocial behavior and social phobia in humans. *Neuroscience Letters, 16*, 233-236.

Victoroff, J., Zarow, C., Mack, W. J., Hsu, E., & Chui, H.C. (1996). Physical aggression is associated with preservation of substantia nigra pars compacta in Alzheimer's disease. *Archives Neurology, 53*, 428-434.

Volicer, L., Harper, D. G., Manning, B. C., Goldstein, R., & Satlin, A. (2001). Sundowning and circadian rhythms in Alzheimer's disease. *American Journal of Psychiatry*, *158*, 704-711.

Vollrath, M., Knoch, D., & Kassano, L. (1999). Personality, risky health behavior, and perceived susceptibility to health risks. *European Journal of Personality*, *13,* 39-50.

von Dras, D. D., & Siegler, I. C. (1997). Stability in extraversion and aspects of social support at midlife. *Journal of Personality and Social Psychology*, *72,* 233-241.

von Gunten, A., Fox, N., Cipolotti, L., & Ron, M. (2000). A volumetric study of hippocampus and amygdala in depressed patients with subjective memory problems. *Journal of Neuropsychiatry and Clinical Neurosciences, 12,* 493-498.

von Gunten, A., Giannakopoulos, P., & Duc, R. (2005). Cognitive and demographic determinants of dementia in depressed patients with subjective memory complaints. *European Neurology*, *54*, 154-158.

von Gunten, A., Alnawaqil, A., Abderhalden, C., Needham, I., & Schüpbach, B. (2008). Vocally disruptive behavior in the elderly: A systematic review. *International Psychogeriatrics, 20*, 653-672.

von Gunten, A., Pocnet, C., & Rossier, J. (2009). The impact of personality characteristics on the clinical expression in neurodegenerative disorders: A review. *Brain Research Bulletin, 80*, 179-191.

Waldemar, G., Dubois, B., & Emre, M. (2007). Recommendations for the diagnosis and management of Alzheimer's disease and other disorders associated with dementia: EFNS guideline. *European Journal of Neurology, 14,* 1-26.

Wang, H. X., Karp, A., Herlitz, A., Crowe, M., Kareholt, I., & Winblad, B. (2009). Personality and lifestyle in relation to dementia incidence. *Neurology, 72*, 253-259.

Ware, C. G., Fairburn, C. G., & Hope, R. A. (1990). A community-based study of aggressive behaviour in dementia. *International Journal of Geriatric Psychiatry, 5*, 337-342.

Watson, D., Clark, L. A., & Harkness, A. R. (1994). Structures of personality and their relevance to psychopathology. *Journal of Abnormal Psychology, 103,* 18-31.

Wechsler, D. (1950). Cognitive, conative, and non-intelective intelligence. *American Psychologist, 5,* 78-83.

Weiner, M. F., Svetlik, D., & Risser, R. C. (1997). What depressive symptoms are reported in Alzheimer's patients? *International Journal of Geriatric Psychiatry, 12*, 648-652.

Weinstein, E., Friendland, R., & Wagner, E. (1994). Denial/ unawareness of impairment and symbolic behaviour in Alzheimer's disease. *Neuropsychiatry, Neuropsychology and Behavioural Neurology*, *7,* 176-184.

Welleford, E. A., Harkins, S. W., & Taylor, J. R. (1995). Personality change in dementia of the Alzheimer's type: Relations to caregiver personality and burden. *Experimental Aging Research, 21*, 295-314.

Wells, A., & Matthews, G. (1994). *Attention and emotion: A clinical perspective.* Hove, England: Lawrence Erlbaum Associates.

Wenk, G. L. (2003). Neuropathologic changes in Alzheimer's disease. *Journal of Clinical Psychiatry, 64*, 7-10.

Westen, D., & Gabbard, G. O. (1999). Psychoanalitic approaches to personality. In L. A. Pervin & O. P. John (Ed.), *Handbook of personality: Theory and research* (2nd ed., pp. 57-101). New York, NY: Guilford.

Whitehouse, P. J., Patterson, M. B., Strauss, M. E., Geldmacher, D. S., Mack, J. L., & Gilmore, G. C. (1996). Hallucinations. *International Psychogeriatrics, 8*, 387-392.

Widiger, T. A., & Costa, P. T. (1994). Personality and personality disorders. *Journal of Abnormal Psychology, 103*, 78-91.

Widiger, T. A. (2002). Personality disorders. In M. M. Antony & D. H. Barlow (Ed.), *Handbook of assessment, treatment planning, and outcome for psychological disorders* (pp. 453-480). New York, NY: Guilford.

Widiger, T. A., & Simonsen, E. (2005). Alternative dimensional models of personality disorder: Finding a common ground. *Journal of Personality Disorders, 19,* 110-130.

Widiger, T. A., & Trull, T. J. (2007). Plate tectonics in the classification of personality disorder. *American Psychologist, 62,* 71-83.

Wiggins, J., & Pincus, A. (1989). Conceptions of personality disorders and dimensions of personality. *Psychological Assessment, 1,* 305-316.

Wiggins, J., & Pincus, A. (1992). Personality: Structure and assessment. *Annual Review of Psychology, 43*, 473-504.

Williams, K., & Kemper, S. (2010). Exploring intervention to reduce cognitive declin in aging. *Journal of Psychosocial Nursing and Mental Health Services, 48*, 42-52.

Wilson, R. S., Evans, D. A., Bienias, J. L., Mendes De Leon, C. F., & Schneider, J. A. (2003). Proneness to psychological distress is associated with risk of Alzheimer's disease. *Neurology, 61,* 1479-1485.

Wilson, R. S., Fleischman, D. A., & Myers, R. A. (2004). Premorbid proneness to distress and episodic memory impairment in Alzheimer's disease. *Journal Neurology Neurosurgery Psychiatry*, 75, 191-195.

Wilson, R. S., Bennett, D. A., Mendes De Leon, C. F., Bienias, J. L., Morris, M. C., & Evans, D. A. (2005). Distress proneness and cognitive decline in a population of older persons. *Psychoneuroendocrinology, 30*, 11-17.

Wilson, R. S., Arnold, S. E., Schneider, J. A., Kelly, J. F., Tang, Y., & Bennett, D. A. (2006). Chronic psychological distress and risk of Alzheimer's disease in old age. *Neuroepidemiology, 27,* 143-153.

Wilson, R. S., Scherr, P. A., Schneider, J. A., Li, Y., & Bennett, D. A. (2007) The relation of cognitive activity to risk of developing Alzheimer's disease. *Neurology, 69,* 1911-1920.

Wilson, R. S., Schneider, J. A., Arnold, S. E., Bienias, J. L., & Bennett, D. A. (2007). Conscientiousness and the incidence of Alzheimer's disease and mild cognitive impairment. *Archives of General Psychiatry, 64*, 1204-1212.

Wilson, R. S., Arnold, S., Beck, T., Bienias, J., & Bennett, D. (2008). Change in depressive symptoms during the prodromal phase of Alzheimer's disease. *Archives of General Psychiatry*, *65*, 439-445.

Windholz, G. (1987). Pavlov's conceptualization of unconditional reflexes, or instincts, within the framework of the theory of higher nervous activity. *Pavlovian Journal of Biological Science, 22*, 123-131.

Witkin, H. A. (1954). *Personality through perception: An experimental and clinical study*. Westport, CT: Greenwood Press.

Wright, A. G. C., Thomas, K. M., Hopwood, C. J., Markon, K. E., Pincus, A. L., & Krueger, R. F. (2012). The hierarchical structure of DSM-5 pathological personality traits. *Journal of Abnormal Psychology*.

Word Health Organization. (1993). *The ICD-10 classification of mental and behavioral disorders: Diagnostic criteria for research.* Geneva, Switzerland: Word Health Organization.

Yaffe, K., Blackwell, T., Gore, R., Sands, L., Reus, V., & Browner, W. S. (1999). Depressive symptoms and cognitive decline in nondemented elderly women. *Archives of General Psychiatry*, *56,* 425-430.

Zandi, T. (2004). Relationship between subjective memory complaints, objective memory performance, and depression among older adults. *American Journal of Alzheimer's Disease and Other Dementias, 19,* 11-12.

Zigmond, A. S., & Snaith, R. P. (1983). The Hospital Anxiety and Depression Scale. *Acta Psychiatrica Scandinavica, 67*, 361-370.

Zubenco, G. S., Moosy, J., Martinez, A. J., Rao, G., Claassen, D., & Rosen, J. (1991). Neuropathologic and neurochemical correlates of psychoses in primary dementia. *Archives of Neurology, 48,* 619-624.

Zubenko, G. S., Henderson, R., Stiffler, J. S., Stabler, S., Rosen, J., & Kaplan, B. (1996). Association of the ApoE4 allele with clinical subtypes of late life depression. *Biological Psychiatry, 40,* 1008-1016.

Zuckerman, M. (1984). Sensation seeking: A comparative approach to a human trait. *Behavioural and Brain Sciences*, *7,* 413-471.

Zuckerman, M. (1991). *Psychobiology of Personality*. New York, NY: Cambridge University Press.

Zuckerman, M., Kuhlman, D. M., Teta, P., Joireman, J., & Kraft, M. (1993). A comparison of three structural models of personality: The big three, the big five, and the alternative five. *Journal of Personality and Social Psychology, 65*, 757–768.

Zuckerman, M. (1994). Impulsive, unsocialized sensation seeking: the biological foundations of a basic dimension of personality. In J. E. Bates & T. D.Wachs (Ed.), *Temperament: Individual differences at the interface of biology and behaviour* (pp. 219-255). Washington, DC: American Psychological Association.

Zuckerman, M. & Cloninger, C. R. (1996). Relationships between Cloninger's, Zuckerman's, and Eysenck's dimensions of personality. *Personality and Individual Differences*, *21,* 283-285.

Zuckerman, M. (2002). Zuckerman-Kuhlman Personality Questionnaire (ZKPQ): An alternative five-factorial model. In B. de Raad & M. Perugini (Ed.), *Big Five Assessment* (pp. 377-396). Göttingen, Germany: Hogrefe & Huber.