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PERSONALITY AND DEPRESSION

by

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ABSTRACT

The aim of this study was to illustrate the associations of personality variables and depression.

The first study population consisted of 50 patients with DSM-IV defined major depressive disorder. Subjects were randomized to receive either fluoxetine medication or short-term psychodynamic psychotherapy. The Hamilton Depression Rating Scale was completed at the baseline and in the follow-up at four months.

Baseline mature defense style measured with the Defense Style Questionnaire predicted favorable outcome in the fluoxetine treatment group, whereas no associations were found in psychotherapy group.

The Psychological Mindedness Scale scores were not predictive for recovery in patients receiving psychotherapy or medication. The Psychological Mindedness Scale seems not to be useful in selecting optimal treatment in major depressive disorder.

Harm Avoidance measured with the Temperament and Character Inventory associated with the baseline severity of the depressive state. In the fluoxetine treatment group high Reward Dependence, high Self-Directedness and high Cooperativeness were predictive for more severe depression in the four months follow-up, whereas no associations were found in the psychotherapy treatment group. It is possible that the result reflects the differences in the placebo response.

The second data were derived from the Finnish Public Sector Study. These prospective studies with four years follow-up focused on the predictive value of optimism and pessimism, first, to work disability with a diagnosis of depression lasting at least 90 days and returning to work (N= 38214) , and second, to the likelihood of initiating antidepressant medication treatment lasting at least 100 days and ending the treatment (N= 29930). Results show that low optimism associates with the elevated risk of work disability and higher likelihood of antidepressant use. High pessimism associated with higher likelihood starting at least 100 days antidepressant medication and not stopping medication during the follow up. High pessimism did not seem to predict the entering to depression related work disability, but in the case of disability period it associated with the lower likelihood of returning to work.

The thesis shows that personality features play a role as a vulnerability factor, and influence the onset and course of depression. Taking these factors into account more than is currently done may increase the possibilities to enhance the treatment results in depression.

Keywords: Depression; Personality; Antidepressant; Psychotherapy

Kim Kronström

Persoonallisuus ja masennus

Lääketieteellinen tiedekunta, kliininen laitos, psykiatria
Turun Yliopisto

TIIVISTELMÄ

Tämän väitöskirjatyön tavoitteena oli selvittää persoonallisuuspiirteiden yhteyksiä masennuksen syntyyn, sekä masennuksesta toipumiseen.

Ensimmäinen väitöskirjassa käytetty aineisto koostui 50 masennusta sairastavasta potilaasta. Potilaat satunnaistettiin kahteen hoitoryhmään, jossa toisessa hoitona oli masennuslääke fluoksetiini ja toisessa psykodynaaminen lyhytpsykoterapia. Masennusoireiden voimakkuutta arvioitiin Hamiltonin depressioasteikolla tutkimuksen alussa, sekä neljän kuukauden hoidon jälkeen.

Puolustusmekanismeja arvioitiin Defense Style Questionary-kyselylomakkeella. Kypsät puolustusmekanismit ennustivat hyvää toipumista lääkehoitoryhmässä, kun taas psykoterapiaryhmässä puolustusmekanismien ja toipumisen välillä ei havaittu yhteyttä.

Psykologista orientaatiota kartoitettiin Psychological Mindedness Scale-kyselyllä. Psykologisen orientaation ja toipumisen välillä ei ollut yhteyttä kummassakaan hoitoryhmässä. Tulos viittaa siihen että käytetty kysely ei ole käyttökelpoinen masennuksen ennusteen arvioinnissa tai hoitomuodon valinnassa.

Persoonallisuuspiirteitä kartoitettiin Temperament and Character Inventory- kyselyllä. Lähtötilanteessa havaittiin yhteys korkeiden Harm Avoidance -pisteiden ("turvallisuushakuisuus") sekä masennuksen voimakkuuden välillä. Korkeat pistemäärät persoonallisuuspiirteisä Reward Dependence ("hyväksynnän hakeminen"), Self-Directedness ("itseohjautuvuus") ja Cooperativeness ("yhteistoiminnallisuus") olivat yhteydessä vakavampaan masentuneisuuteen neljän kuukauden seurannassa potilailla, jotka olivat saaneet masennuslääkehoitoa. Psykoterapiaryhmässä persoonallisuuspiirteet eivät olleet yhteydessä masennusoireiden voimakkuuteen seurannannassa. Erot lääkityksen luvemasteessa saattavat osaltaan selittää tulosta.

Toinen väitöskirjatyössä käytetty aineisto perustui Kunta-10 tutkimukseen. Tutkimuksissa tarkasteltiin optimismin ja pessimismin yhteyksiä neljän vuoden seurannan aikana 1. masennukseen liittyvään vähintään 90 päivää kestävään työkyvyttömyyteen ja myöhempään paluuseen työelämään (N= 38214) ja 2. vähintään 100 päivää kestävään masennuslääkkeen käyttöön ja käytön lopetukseen (N= 29930). Tutkimuksissa matala optimismi ennusti masennuksesta aiheutuvaa työkyvyttömyyttä sekä masennuslääkkeiden käyttöä. Korkea pessimismi oli yhteydessä masennuslääkkeiden käytön todennäköisyyteen sekä masennukseen liittyvän työkyvyttömyyden pitkittymiseen.

Tämän väitöskirjatyön tulokset viittaavat siihen, että persoonallisuuspiirteillä on vaikutusta sekä masennusalttiuteen että masennuksen kulkuun. Persoonallisuuspiirteiden arviointi ja huomioon ottaminen saattavat auttaa parantamaan masennuksen hoitotuloksia.

Avainsanat: Masennus; Persoonallisuus; Masennuslääke; Psykoterapia

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ABBREVIATIONS

| | |
|--------|--|
| ANCOVA | Analysis of Covariance |
| C | Cooperativeness |
| CI | Confidence Interval |
| FFM | Five-Factor Model of Personality |
| FLX | Fluoxetine |
| HR | Hazard Ratio |
| DDD | Defined Daily Dose |
| DMRS | Defense Mechanism Rating Scale |
| DSM-IV | Diagnostic and Statistical Manual of Mental Disorders, 4 th version |
| DSQ | Defense Style Questionnaire |
| HA | Harm Avoidance |
| HDRS | Hamilton Depression Rating Scale |
| ICD-10 | International Classification of Diseases, 10 th version |
| LOT | Life Orientation Test |
| LOT-R | Life Orientation Test-Revised |
| MD | Major Depression |
| MDD | Major Depressive Disorder |
| MDE | Major Depressive Episode |
| NS | Novelty Seeking |
| P | Persistence |
| PM | Psychological Mindedness |
| PMAP | Psychological Mindedness Assessment Procedure |
| PMS | Psychological Mindedness Scale |
| RC | Regression Coefficient |
| RD | Reward Dependence |
| SD | Self-Directedness |
| SD | Standard Deviation |
| SCID-1 | Structured Clinical Interview of DSM-IV Axis 1 Disorders |
| SES | Socio-Economic Status |
| ST | Self-Transcendence |
| STPP | Short-Term Psychodynamic Psychotherapy |
| SPSP | Short-Term Psychodynamic Supportive Psychotherapy |
| TCI | Temperament and Character Inventory |
| TPQ | Tridimensional Personality Questionnaire |
| WHO | World Health Organization |

LIST OF ORIGINAL PUBLICATIONS

- I Kronström K, Salminen JK, Hietala J, Kajander J, Vahlberg T, Markkula J, Rasi-Hakala H, Karlsson H. Does defense style or psychological mindedness predict treatment response in major depression? *Depression and Anxiety* 2009;26:689-695
- II Kronström K, Salminen JK, Hietala J, Kajander J, Vahlberg T, Markkula J, Rasi-Hakala H, Karlsson H. Personality traits and recovery from major depressive disorder. *Nordic Journal of Psychiatry* 2011;65:52-57
- III Kronström K, Karlsson H, Nabi H, Oksanen T, Salo P, Sjösten N, Virtanen M, Pentti J, Kivimäki M, Vahtera J. Optimism and pessimism as predictors of work disability with a diagnosis of depression: A prospective cohort study of onset and recovery. *Journal of Affective Disorders* 2010 Nov 3 (Epub ahead of print)
- IV Kronström K, Karlsson H, Nabi H, Oksanen T, Salo P, Sjösten N, Virtanen M, Pentti J, Kivimäki M, Vahtera J. Optimism and pessimism as predictors of initiating and ending an antidepressant medication treatment. Submitted.

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1 INTRODUCTION

Depression is among the leading causes of disability worldwide and its global burden seems to further increase in the future (Mathers 2006). The extensive human and economic costs stress the importance of studying various aspects of depression. Depression can be considered as a syndrome with variable background, possibly diverse psychological and neurobiological mechanism causing the symptoms, and with significant differences in phenotype, progress and recovery. The vulnerability, onset and course of depression is affected by several variables, among those the personality of the patient (Bagby 2008). Personality interplays with other psychological, biological and social components which affect individual reaction and adaptation to the situations of life. The personality may act as a buffering or predisposing factor for depression and its effect may vary in relation to different stressors.

There are a great number of different treatments which have some effect on the recovery in depression (Hollon and Ponniah 2010, Arroll et al. 2009). It has shown to be difficult to find significant and reliable differences in average effectiveness between the treatments (Simon and Perlis 2010). Length, recurrence and severity of the depressive state, comorbidity and socioeconomic state, i.e. factors that are not directly related to the treatment intervention seem to have a larger effect on the average outcome than the specific form of antidepressant or psychotherapy used (Sinyor et al. 2010). Despite the on average similar efficiency of the treatments, different people may benefit from different treatments. Personality is likely one of the factors which has an impact on individual treatment response in depression (Klein et al. 2010). The average treatment response could substantially increase, if we could predict which personality characteristics and depression treatments are likely to cohere to produce better outcome.

There are several major theories on personality, which differ largely regarding to the general approach to an individual. Each major theory seems to be further divided into various parallel modifications, often with different evaluating methods and terminology. This heterogeneity and abundance in theories and viewpoints may reflect the nature of human personality. The diversity of personality psychology can be considered as richness, but it is also problematic, since the results of the studies arising from different theories are not commensurable. Different theories do not interact with each other and the accumulation of the information is often insufficient. This reality is very much reflected in the field of this thesis. Despite the years of intensive studies there are a lot of open questions regarding the association between personality variables and depression. In this thesis I have aimed to illustrate and study the complicated relationships between personality and the depression from a few different viewpoints.

2 REVIEW OF THE LITERATURE

2.1 Personality

The term “personality” refers to the distinctive patterns of behavior, thoughts and emotions that characterize each individual's adaptations to the situations of his or her life. Personality characteristics are qualities that are considered at least somewhat consistent across time and different situations of individual's life. The concept of personality is used in addressing the universal properties of individuals, the differences between them, and the uniqueness of one subject. Theories differ greatly in their view of characterizing the main elements, nature and content of personality. Due to this, different theories highlight distinct aspects of personality, which respects the complex and multidimensional nature of human characteristics, but makes theories and the studies based on them difficult to reconcile. I will now review the measurements and concepts used in this study and their underlying personality theories.

2.1.1 The psychodynamic view

Psychodynamic theories of personality can be divided into the structural theory, the object relations theory, self-psychology and the attachment theory (Cervone and Pervin 2008). The concept of defense mechanism originates from the structural theory.

Structural theory of the mind

According to the structural theory, personality has three structures: the id, the ego and the superego, which are distinguished by their different functions. The id houses biological instincts, is unconscious, and operates according to the pleasure principle. The ego is the executive organ of the psyche and it controls logical and abstract thinking, verbal expressions, motility, perception, and contact with reality, and, through the mechanisms of defense, the delay and modulation of drive expression. The third component of the structural model is the superego, which is the moral branch of personality. The conflicting demands of the personality structures produce anxiety. In response to the anxiety, the ego uses defense mechanisms as protective methods resolving conflicts and reducing the anxiety (Fenichel 1946, Meissner 2004).

Freud's scheme of personality development emphasizes events in the first five years of life. It proposed that crucial stages of development of the libido must be passed through successfully if personality development is to proceed normally. The scheme allows some modification of the personality at the later stages of development thorough identification with other than parents, but this influence is thought to be less important than earlier ones. The scheme is comprehensive and flexible so that it is possible to explain many features of personality in terms of earlier experience. However, the same features of the theory make it difficult to test it scientifically (Fenichel 1946, Meissner 2004).

2.1.1.1 Defense mechanisms

In the DSM-IV-TR (APA 2000) defense mechanisms (or coping styles) are defined as “automatic psychological processes that protect the individual against anxiety and from the awareness of internal or external dangers or stressors. Individuals are often unaware of these processes as they operate”. Within classical psychoanalytical theory, which sees conflict as a central mental function,

defenses are considered as mainly unconscious attempts to adapt to intrapsychic conflicts. Defenses are assumed to vary in the degree in which they manage to successfully cope with the conflict of the warding-off process (Fenichel 1946). There has been evolution in the theory and increasing number of individual defense mechanism has been described by several theoreticians (Klein 1932, Freud A 1936, Kernberg 1967). In his pioneer work Vaillant (1971, 1976, 1986) used the hierarchy of defenses derived from psychodynamic theory, managed to measure them with good reliability and found correlation between defense maturity and life success.

2.1.1.1.1 Defense Style Questionnaire (DSQ)

As defense mechanisms are considered mainly unconscious phenomena, it is obvious that their measurement is problematic. When using self-reports, we must presume that subject becomes at least occasionally aware of their unacceptable impulses and their usual styles of defending against them. Bond et al. (1983) developed a self-report Defense Style Questionnaire (DSQ) to assess possible conscious derivatives of 24 defenses. DSQ consist of 88 statements and the agreement is rated on a nine-point Likert scale. DSQ has been widely used and it has been validated in several studies, also in a Finnish sample (Bond et al. 1983, Andrews et al. 1989, Bond et al 1994, Sammallahti et al. 1994) Based on the factor analysis, several models of grouping individual defenses into larger clusters have been used. Andrews and co-workers (1989) ended up with three defense styles, namely mature (adaptive), neurotic and immature (maladaptive) defences. Defenses defined in DSM-IV-TR (APA 2000) and clustered according to Andrews et al. are presented below:

Mature:

sublimation The individual deals with emotional conflict or external stressors by channelling potentially maladaptive feelings or impulses into more acceptable behavior.

humour The individual deals with emotional conflict or external stressors sizing the amusing or ironic aspects of the conflict or stressor.

anticipation The individual deals with emotional conflict or internal or external stressors by experiencing emotional reactions in advance of, or anticipating consequences of, possible future events and considering realistic, alternative responses or solutions.

suppression The individual intentionally avoids thinking about disturbing problems, wishes, feelings or experiences.

Neurotic:

undoing The individual deals with emotional conflict or internal or external stressors by words or behavioural designed to negate or to make amends symbolically unacceptable thoughts, feelings, or actions.

altruism The individual deals with emotional conflict or internal or external stressors by dedication to meeting the needs of others. Unlike the self-sacrifice characteristic

of reaction formation, the individual receives gratification either vicariously or from the response of others.

idealization The individual deals with emotional conflict or internal or external stressors by attributing exaggerated positive qualities to others.

reaction formation The individual deals with emotional conflict or internal or external stressors by substituting behaviour, thoughts, or feelings that are diametrically opposed to his or her own unacceptable thoughts or feelings (this usually occurs in conjunction with their repression).

Immature:

projection The individual deals with emotional conflict or internal or external stressors by falsely attributing to another his or her own unacceptable feelings, impulses, or thoughts.

passive aggression The individual deals with emotional conflict or internal or external stressors by indirectly and unassertively expressing aggression towards others. There is facade of overt compliance masking covert resistance, resentment, or hostility. Passive aggression often occurs in response to demands for independent action or performance or the lack of gratification of dependent wishes but may be adaptive for individual in subordinate positions who have no other way to express assertiveness more overtly.

acting out The individual deals with emotional conflict or internal or external stressors by actions rather than reflections or feelings. This definition is broader than the concept of acting out of transference feelings or wishes during psychotherapy and is intended to include behaviour arising both within and outside transference relationship. Defensive acting out is not synonymous with "bad behaviour", because it requires evidence that the behaviour is related to emotional conflicts.

isolation The individual deals with emotional conflict or internal or external stressors by separation of ideas from feelings originally associated with them. The individual loses touch with the feelings associated with a given idea (e.g. traumatic event) while remaining aware of the cognitive elements of it (e.g. descriptive details).

devaluation The individual deals with emotional conflict or internal or external stressors by attributing exaggerated negative qualities to self or others.

autistic fantasy The individual deals with emotional conflict or internal or external stressors by expressive daydreaming as a substitute for human relations, more effective action, or problem solving.

denial The individual deals with emotional conflict or internal or external stressors by refusing to acknowledge some painful aspects of external reality or subjective experience that would be apparent to others. The term psychotic denial is used when there is impairment in reality testing.

displacement The individual deals with emotional conflict or internal or external stressors by transferring a feeling about, or a response to, one object or (usually less threatening) substitute object.

dissociation The individual deals with emotional conflict or internal or external stressors with a breakdown in the usually integrated functions of consciousness, memory, perception of self or the environment, or sensory/motor behavior.

splitting The individual deals with emotional conflict or internal or external stressors by compartmentalizing opposite affect states and failing to integrate the positive and negative qualities of the self or others into cohesive images. Because ambivalent affects cannot be experienced simultaneously, more balanced views and expectations of others are excluded from emotional awareness. Self and object images alternate between polar opposites: exclusively loving, powerful, worthy, nurturing and kind– or exclusively bad, hateful, angry, destructive, rejecting, or worthless.

rationalization The individual deals with emotional conflict or internal or external stressors by concealing the true motivations for his or her own thoughts, actions, or feelings through the elaboration of reassuring or self-serving but incorrect explanations.

somatisation The defensive conversion of psychic derivatives into bodily symptoms; tendency to react with somatic rather than psychic manifestations.

source: DSM-IV-TR (APA 2000), Meissner (2004)

2.1.1.2 Psychological mindedness

The concept of psychological mindedness (PM) originates from the psychoanalytical literature. There are several varying definitions of PM. Appelbaum (1973) defined PM as the ability to see relationship among thoughts, feelings and actions, with the goal of learning the meaning and causes of his experiences and behavior. Hall (1992) did clarify the definition of PM by sorting out interest versus ability and intellect versus affect dimensions of the concept. She ended up with a conceptual model defining accurate PM as reflectivity about psychological processes, relationships and meanings, which includes both interest and ability for such reflectivity, and is displayed in both affective and intellectual dimension.

PM could be seen also as a cognitively toned personality variable, which includes flexibility, a sense of personal agency and a propensity for realistic thinking (Beitel et al. 2004). It has been proposed that since PM bespeaks a capacity to tolerate psychological conflict and stress intrapsychically, it has a major role in the genesis of psychosomatic illness (Shill and Lumley 2002). Theoretically PM is essentially opposite concept to alexithymia, although studies about this are inconsistent (Shill and Lumley 2002, McCallum et al. 2003). PM can be seen also as a moderating effect, which makes one's personality and "inter-personality" or attachment style to correlate (Beitel et al. 2004).

The PM has been assumed to be an essential attribute contributing patients' ability to engage and benefit especially from insight oriented psychotherapy (Conte et al. 1990, Andrews et al. 1989) and clinicians have made specific therapeutic recommendations based on a potential client's perceived PM (Hall 1992, Valbak 2004). However, empirical data on PM is limited and inconsistent.

Studies on the subject have been complicated by the lack of precise and common definition, and the varying assessment procedures of the PM.

2.1.1.2.1 Psychological Mindedness Scale (PMS)

Psychological Mindedness Scale is 45-item self-report measure (Conte et al. 1990), which conceptualizes the definition of PM as the ability to access one's own and other's feelings and utilize these for changing behavior. The scale represents a shortened version of Lotterman's 65-item scale (1979). The items are scored on a four-point scale ranging from "strongly agree" to "strongly disagree" and weighted 4,3,2 and 1 respectively. Twenty one of the items are reversely-scored and the total score is derived by summing up the weights across the items. There are reasonable results concerning the validity and reliability of the PMS (Conte et al. 1990, Shill and Lumley 2002, Conte et al. 1995, Conte et al. 1996).

2.1.2 Trait theories

Personality traits are tendencies to show the consistent patterns of thoughts, actions and feelings. Although in concrete instances many factors, including social contexts, aroused needs and learned habits affect the response of an individual, it is assumed that there are personality factors which predispose subjects to certain individual reaction manners. Due to the other affecting variables and potentially conflicting traits, the influence of specific trait on any particular response may be limited. Despite the restricted influence on response to individual occasion, traits are required to show some cross-situational consistency. Traits are considered as relatively enduring patterns that characterize the individual. In this respect, they differ from the moods or other transient mental states. In addition, different trait theories share the view that traits are continuously distributed, usually approximating the normal curve. Many trait theorists use the statistical technique of factor analysis to develop a classification of traits. Through this technique individual items or responses are grouped into larger clusters in relation to the degree they interconnect with other items.

There are several trait theories, which differ in the specific traits that they have conceptualized and measured. The methods of choosing a manageable set of potential traits among large number of possible constructs have varied between the researchers, thus producing various parallel trait theories. Two main comprehensive trait models up-to-date are the psychobiological model of personality developed by Cloninger et al. (1993) and the Five-Factor Model of Personality (McCrae and Costa 1985).

2.1.2.1 Temperament and Character Inventory (TCI)

Temperament and Character Inventory (TCI) is a battery of tests developed by Cloninger and coworkers (1993) based on his psychobiological theory of personality. TCI is designed to assess differences between people in seven basic dimensions of temperament and character. The four measured temperament dimensions are Harm Avoidance (HA), Novelty Seeking (NS), Reward Dependence (RD) and Persistence (P). The three measured character dimensions are Self-Directedness (SD), Cooperativeness (C) and Self-Transcendence (ST) (Cloninger et al.1994).

Temperament refers individual differences in mood or quality of emotional responses that appear early in life. These differences are viewed as primary inherited, biologically based and stable throughout life (Cervone and Pervin 2008). Individuals high in temperament trait of Harm Avoidance are described as worried, fearful and withdrawn (Cloninger 1986). Harm avoidance, and the trait of Neuroticism from the Five-Factor Model of Personality (McCrae and Costa 1985) are

conceptually similar and highly correlated (Fruyt et al. 2000). Both traits are subsumed within a general propensity to experience negative emotions known as negative emotionality (Markon et al. 2005). Novelty Seeking refers to exploratory activity and intense excitement in response to novel stimuli, thus subjects high in this trait are tend acting excitable, curious, impulsively. Subjects high in Reward Dependence are supposed to be sensitive to social cues and tend to maintain rewarded behavior. Persistence refers to tendency to be hard-working and stable despite frustration and fatigue (Cloninger 1986, Cloninger et al. 1994).

In contrast, character refers to self-concepts and individual differences in goals and values, which influence voluntary choices, intentions, and the significance or meaning of what is experienced in life. Differences in character are moderately influenced by socio-cultural learning and mature in progressive steps throughout life. Subjects high in the character trait of Self-Directedness are described as mature, self-sufficient and reliable. Cooperativeness has been formulated to account for individual differences in identification with and acceptance of other people. Highly cooperative persons are described as empathetic, tolerant, supportive and fair. Self-Transcendent individuals are described as fulfilled, patient, selfless and spiritual (Cloninger et al. 1994).

TCI consists of 240 items, which are scored by adding one point for each item answered appropriately. Items are grouped to produce 25 facet scales (i.e. subscales), which form four temperament and three character dimensions. In the work of Sato et al. (2001) the factor structure of the TCI was found valid also in patients with major depression.

2.1.3 Optimism and pessimism

Optimism and pessimism are individual difference variables that reflect the extent in which people hold favorable or unfavorable expectations for their future. Optimism and pessimism can be understood as broad, generalized versions of confidence and doubt, which affect attitudes to the possibility to achieve personal goals as well as to survive through difficulties. Optimism and pessimism may also refer to differences in explanatory styles. Individuals who perceive that good things happen to them because of internal (something about the individual), stable (happens all the time), and global (happens in all situations) factors are considered to have an optimistic explanatory style. Conversely, individuals who perceive that bad things (i.e. negative events) happen to them due to internal, stable, and global factors are considered to have a pessimistic explanatory style (Gillham et al. 2000). Positive and negative outcome expectancies seem to have major influence on how we perceive and interpret situations, motivate to actions and adapt to the challenges of our lives. (Scheier and Carver 1985, Scheier et al. 1994, Steptoe et al. 2008, Brydon et al. 2009, Prati and Pietrantonio 2009, Carver et al. 2010).

2.1.3.1 Life Orientation Test (LOT)

One of the most widespread measures used to assess optimism and pessimism is the Life Orientation Test (LOT) (Scheier and Carver 1985) and its briefer version, the revised Life orientation Test (LOT-R, Scheier et al. 1994). Both LOT-scales reflect generalized positive and negative outcome expectancies. LOT-R issues six statements, of which three are worded positively for optimism (e.g. "In uncertain times, I usually expect the best") and three negatively to indicate pessimism (e.g. "If something can go wrong for me, it will"). In the earlier work using LOT and LOT-R optimism and pessimism were considered to represent the polar opposites of a single continuum. In this unidimensional model concept of optimism is used in the meaning of both (high) optimism and (low) pessimism. This view of unidimensionality has been challenged by

several studies suggesting that optimism and pessimism may act more like two separate constructs. For example, low level of pessimism (but not high optimism) has been predictive for lower level of psychological distress (Chang and Bridewell 1998), negative affectivity, perceived stress and anxiety (Robinson-Whelen et al 1997) and the incidence of stroke (Nabi et al. 2009). In contrast, high optimism (but not low pessimism) has associated with smaller increase in sick days after death of onset of severe illness in family (Kivimäki 2005). The internal structure of LOT-R has been studied in a sample of 46,133 participants (Herzberger et al 2006). Confirmatory factor analysis showed that dispositional optimism, as measured by the LOT-R, is bidimensional, consisting of optimism and pessimism factor. The correlation between optimism and pessimism was $-.13$ in the whole data (mean age 53,9 years, $SD = 17.3$). The association between optimism and pessimism was strongest in age groups 24-31 years ($-.39$) and continuously decreased with age.

2.2 Depression

2.2.1 Definition of depression

Depression is a syndrome or disorder consisting of a cluster of signs and symptoms in mood, psychomotor activity, cognitive and vegetative spheres. Diagnostic classifications outline the criteria for depression diagnosis on the basis of symptoms, but do not try to define the possible underlying factors of causes for the emergence of the symptoms. Depression may be considered a heterogeneous concept with most likely variable background, possibly diverse psychological and neurobiological mechanisms causing the symptoms and with significant differences in phenotype and course.

In both DSM-IV-TR (APA 2000) defining the *major depressive episode* and ICD-10 (WHO 1992) defining the *depressive episode* the core symptoms are specified as depressed mood or loss of interest or pleasure. In addition, both classifications require other symptoms to be present, in DSM-IV-TR at least five and in the ICD-10 at least four out of nine symptoms altogether. The common supplemental symptoms include disturbances in sleep and appetite, agitation or retardation, fatigue and difficulties to concentrate. Patients' self-esteem and self-confidence are almost always reduced and they commonly present ideas of guilt, worthlessness or even death. In both current diagnostic classifications the minimum duration of the symptoms is defined to be at least 2-weeks. In ICD-10 depending upon the number and severity of the symptoms, a depressive episode may be specified as mild, moderate or severe. In DSM-IV-TR the diagnosis of *major depressive disorder (MDD)* requires the presence of *major depressive episode* when this episode is not better accounted for by other psychiatric states, for example schizoaffective or bipolar disorder. In this context *major depressive episode or MDD* can be specified as chronic, as with catatonic, melancholic or atypical features, or as having postpartum onset. Furthermore, *major depressive episode* may be defined as being mild, moderate, or severe with- or without psychotic symptoms. When the full criteria for *major depressive episode* are not currently met, *MDD* can be defined as being in partial or full remission.

As with several other psychiatric diagnoses, the diagnosis of depression is far from explicit. Each of the symptoms presented in diagnostic criteria are likely to be dimensionally distributed in the patient populations and the cut-off point for the symptoms to be or not to be present may be in many cases open to interpretations. The selection of individual symptoms to the criteria of

depression has been a matter of discussion, as well as the number of the symptoms required for diagnosis. The nature of depression may not be commensurate with different patients, since several symptomatic profiles have the possibility to fulfill the diagnostic criteria (Empelkamp 2004).

In addition it has been suggested that *the DSM-IV-TR* diagnostic criteria for depression provide no more than a general guide, and only after in-depth phenomenological approach can a clinician ascertain the diagnosis of depression. Furthermore, those disturbances in all four spheres (mood, psychomotor activity, cognitive, and vegetative) should be ordinary present for a definite diagnosis of MDD although that is not specified in *DSM-IV-TR* (Akiskal 2005).

2.2.2 Epidemiology of depression

The 12-month and lifetime prevalence of major depressive disorder have varied in studies between 4-11 and 7-17 percent, respectively (Kessler et al. 1994, Lindeman et al. 2004, Waraich et al. 2004, Pirkola et al. 2005, Kessler et al. 2003, Eaton et al. 2008). It is possible that studies have underestimated the lifetime prevalence due to recall bias and even higher proportion of the population may suffer MDD during their lifetime. This interpretation is supported by recent longitudinal study that followed a community sample of 7457 subjects. In the follow-ups completed every two years the annual prevalence of MDD ranged between 4-5 percent. However, after seven follow-up intervals the cumulative prevalence of MDD had reached 19.7 percent, including 24.2 percent of women and 14.2 percent of men (Patten 2009).

2.2.3 Aetiology of depression

Individual's probability of developing depression associates with several risk- and protective factors, which seem to interact with each other, and the genetic liability (Lee et al 2010). Since the associations with depression can be found on greatly different levels, from molecular to society and life events, the interaction of different factors in the causative process leading to depression is the subject of great complexity. There are several major theories on biological and psychological mechanisms which may contribute to the emergence on depression and affect the outcome in depressive state.

Multiple factors that have shown to elevate the risk for depression include female sex (Lindeman et al. 2000, Patten 2009), socioeconomic difficulties (Lindeman et al. 2000, Pirkola et al. 2005), child abuse or neglect (Widom et al. 2007), whereas among others the social support and well-developed intrapersonal skills seem to protect against the onset of depression (Donald and Dower 2002). Stress sensitivity has been shown to predict the emergence of depression particularly in subjects with genetic liability (Wichers et al. 2009). Stressful life events increase the risk of depression onset, but the influence of live events on depression seems to decrease with multiple past episodes of depression (Kendler et al. 2000).

2.2.3.1 Heritability

Studies comparing concordance rates for major depression between monozygotic and dizygotic twins suggest heritability of about 37 percent, with a minimal contribution of environmental effect common to siblings (Sullivan et al. 2000). Early-onset, severe, and recurrent depression may have higher heritability than other forms of depression (Kendler et al. 1999). Despite significant overall genetic influence, no single genetic variation has been identified to increase the risk of depression

substantially. Multiple genetic factors in conjunction with environmental factors are likely necessary for the development of MDD (Lohoff 2010).

2.2.3.2 Biologic mechanisms of depression

Monamine hypothesis

Monoamine hypothesis, which suggests a deficiency or imbalances in the monoamine neurotransmitters, such as serotonin, dopamine and norepinephrine, as the cause of depression has been the central topic of depression research for decades. This hypothesis was implicated by the observations that effective antidepressant drugs exerted their primary biochemical effect by regulating intrasynaptic concentrations serotonin and norepinephrine (Manji et al. 2001). Study partly sharing the study population of the first two publications of this thesis, reported that in MDD patients the binding potential of serotonin (5-HT_{1A}) is reduced in compared with healthy controls, which gives further support to the significance of monoamine system in depression (Hirvonen et al. 2008). However, the clinical effects of antidepressants that acutely modify monoamine system are significantly delayed, which indicates that cascades of downstream effects are responsible for their therapeutic effects. In addition, significant proportion of patients suffering from depression does not benefit from antidepressants (Fava and Kendler 2000). Consequently, there seems not to be a simple relationship between biogenic amines and depression postulated by classical monoamine hypothesis (Lee et al. 2010).

Serotonin transporter and stressful life events

Relating to the monoamine hypothesis and possible gene environmental interactions, there has been extensive study on interaction between the serotonin transporter linked polymorphic region (5-HTTLPR) and stressful life event on an increase risk of major depression. In the recent meta-analysis of published data, the number of stressful life events was significantly associated with depression. However, no association was found between 5-HTTLPR genotype and depression, and no interaction effect between genotype and stressful life events on depression was observed (Risch et al 2009).

Hypothalamic-pituitariness-adrenal- axis

Stress and the hypothalamic-pituitariness-adrenal (HPA) -axis has been a topic of interest in depression research. Corticosteroid hormones are important mediators of the response to stress, which is affected by both genetic predispositions and external, especially early life, factors. Traumatic life events in subjects with genetic disposition can produce enhanced emotional and neuroendocrine reactivity, which creates a vulnerable phenotype for depression. Stress and high concentrations of glucocorticoids are associated with neuronal atrophy, and reduced cellular resilience and plasticity, which may all predispose the emergence, and impair the prognosis, of MDD (Kloet et al. 2005, Manji et al. 2001).

Brain-derived neurotrophic factor

One hypothesis concerning the neurobiological basis of depression focuses on the role of brain-derived neurotrophic factor (BDNF). BDNF is known to enhance plasticity, and its levels are affected by stress and cortisol. Depression may be associated with the inability of neuronal systems to exhibit appropriate adaptive plasticity (Angelucci et al. 2005). According to the neurotrophic hypothesis of depression, the loss of BDNF may contribute to especially hippocampal alteration

that underlie the symptoms of depression, while antidepressant may mediate some of their therapeutic effects by increasing BDNF levels in this brain region (Monteggia et al. 2007).

Additional biologic theories

Additional approaches understanding the biologic mechanisms of depression include theories on altered glutamatergic or GABAergic neurotransmission, abnormal circadian rhythms, cytokines, impaired endogenous opioid function (Belmaker and Agam 2008). No single mechanism of disease seems to explain the emergence and course of depression. The complexity may be due to multiple factors, which is likely because depression is a group of disorders with several underlying pathologies (Lee et al. 2010).

2.2.3.3 Major psychological models of depression

There are several models rising from different theoretical perspectives trying to explain the psychological origin and process of depression.

Object loss – aggression turned inward

In the classic psychoanalytic understandings, depression has been related to object loss, in reality, or in fantasy. The tendency to react by developing depressive symptoms after object loss has been assumed to occur in part because the current loss invokes an earlier, childhood loss, also of a realistic or fantastical nature. Depression has been seen as a result of patients' attack toward themselves after the tie to object is shattered. This reaction has been associated especially with ambivalent or hostile object relations, along with object relations characterized by excessive dependency, symbiotic or narcissistic tie. The ambivalent object has been hypothesized to become internalized or incorporated into the patient's sense of self and hostility directed towards the object instead directed at the self. Thus, this model proposes that the aggressive instinct turns into the depressive affect (Abraham 1911, Freud 1917, Akiskal and McKinney 1975).

Object loss – grief

Another suggested mediating process between object loss and depression is grief. Early breaks in affectional bonds have been proposed to provide the behavioral predisposition to depression. In this model adult losses could revive the traumatic childhood loss, thus increasing the likelihood of grief process to turning into depression (Bowlby 1960, Akiskal and McKinney 1975).

Collapse of self-esteem

Depression has been associated with ego suffering a collapse of self-esteem due to its inability to give up unattainable goals and ideals. Not reaching the criteria of demanding superego or failing living up to the ego ideal may precipitate guilt or shame, which could produce narcissistic injury and decline in self-esteem. Because the construct of ego is rooted in cultural and social reality, loss of self-esteem may result of symbolic losses involving power, status, values, identity, and the purpose for existence (Bibring 1965, Akiskal and McKinney 1975).

Cognitive model – depressed cognitions

The cognitive model is based on the recognition that individual's idiosyncratic perception of events affects his or her emotions and behaviors. Depressed individuals perceive reality in subjective depressed ways. They also tend to have skewed and negative thoughts about themselves, their environment and the future. Some of the typical distortions are all-or-nothing

thinking, and tendency to make arbitrary (negative) inference about events, to over generalize and catastrophize. The automatic thoughts of typically self-deprecatory and hopeless nature pop involuntarily in patient's mind. Because these thoughts are mood congruent, depressed individuals find them believable. These depressed, distorted cognitions effect of maintaining and worsening the depressed state. Immediate and specific negative cognitions fit into larger, more basic and stable patterns of self-conception called schemas or core beliefs, which are of earlier background. The general cognitive explanation of depression could be that vulnerable subject, perhaps predisposed by biology or by negative schemas based on early childhood experiences a stressful situation that evokes negative automatic or distorted thoughts, which lead gradually to depressive mood and more pervasive negative thoughts (Beck 1967).

Interpersonal theory – depression as a psychosocial disease

Interpersonal theory emphasizes the psychosocial nature of depression. Current interpersonal relations –support, stress and burden related to them– play major role in protecting or predisposing subjects to depression. The main application of interpersonal theory, IPT psychotherapy focuses on mood and events in relation to interpersonal context. For all people, upsetting events evoke a sad or demoralize mood. Subjects who are biologically or environmentally predisposed, disturbing life events can trigger an episode of depression. Examples of such life events are the death of significant other, which could promote depression through complicated bereavement or problematic relationship burdening subject by role dispute or role change (Markowitz 2005).

Learned helplessness model

Learned helplessness model, based on experiments in dogs, proposes that the depressive posture is learned from previous experiences in which individual has been incapable to escape from undesirable situations. Cumulative past episodes of uncontrollable unpleasant situations have been hypothesized to produce a trait of learned helplessness, i.e. a belief that it is futile to initiate personal action to reverse aversive circumstances (Seligman 1975).

Hopelessness theory

According to the hopelessness theory, following interpretations can put one at risk for depression following a negative event. First, the event may be attributed to stable and global causes. Second, negative or catastrophic consequences of the event may be inferred. Third, negative characteristics about the self may be inferred. When these interpretations are made frequently, they lead to negative expectations about the occurrence of highly valued outcomes (negative outcome expectancy) and to negative expectations about one's ability to change the likelihood of these outcomes (helpless expectancy). According to the hopelessness theory, these negative expectations may lead to the onset of depression (Abrahamson et al. 1989, Gillham et al. 2000).

Lack of adequate rewards

According to the reinforcement model, depressive behavior is associated with lack of appropriate rewards. Some environments may deprive persons of rewarding opportunities, thereby causing the chronic state of boredom or eventually despair. On the other hand, overestimated rewards which the person considers undeserved may lead to the lowering of self-esteem. Inadequate social skills are hypothesized to decrease the changes of the subject to find rewarding contingencies in the environment (Lewinsohn et al. 1979).

2.2.4 Treatments and outcome of depression

Two main treatment options for depression are psychotherapy and medication, which both divide into several groups of more specific forms of treatment. A number of different psychological therapies (Hollon and Ponniah 2010) and pharmacological treatments (Duval et al. 2006) have been shown to be effective in the treatment of depression and the average efficiency of these treatments seems to be similar (Simon and Perlis 2010). In addition to psychotherapy and antidepressants, other treatment options for depression include electroconvulsive therapy (Popeo 2009) and transcranial magnetic stimulation (George 2010).

In the evidence-based guidelines for the treatment of moderate to severe MDD, the recommendations are very much congruent with each other: first-line treatment recommendations for moderate MDD include antidepressant monotherapy, psychotherapy, and the combination of both. Severe depression may require the combination of an antidepressant and antipsychotic, electroconvulsive therapy, or the combination of an antidepressant and psychotherapy (Davinson 2010).

Severity, length, recurrence and comorbidity of the depressive state seem to be main predictors of the outcome in the treatment of MDD (Blom et al. 2007, Fournier et al. 2009, Sinyor et al. 2010). Recent review of studies on differential response to alternative treatments (Simon and Perlis 2010) summarized that research does not identify any biologic or genetic predictors of sufficient clinical utility to inform the choice between medication and psychotherapy, the selection of specific medication, or the selection of a specific psychotherapy. Regarding initial choice between medication and psychotherapy, severity of depression does not appear to predict greater likelihood of response to medication or psychotherapy. Modest evidence suggests that personality disorder predicts more favorable response to pharmacotherapy and that negative life events (either recent stress or childhood trauma) predict better response to psychotherapy (Nemeroff et al. 2003). Clear preference for either medication or psychotherapy seems to predict greater success with the preferred treatment (Simon and Perlis 2010).

Two recent meta-analytical reviews suggest that severity of the depression moderates the effects of both psychotherapy and medication treatments in a very similar way (Fournier et al. 2010, Driessen et al. 2010). The magnitude of benefit of antidepressant medication compared with placebo increases with severity of depression symptoms and may be minimal or nonexistent, on average, in patients with mild or moderate symptoms. For patients with very severe depression, the benefit of medications over placebo is substantial (Fournier et al. 2010). Furthermore, psychological treatments seem to be more efficacious for high-severity than for low-severity patients when compared with a control condition in randomized controlled trials (Driessen et al. 2010).

2.2.5 Measures of depression; Hamilton Depression Rating Scale (HDRS)

Hamilton Depression Rating Scale (HDRS) (Hamilton 1960, 1967) has been for decades the most frequently used rating scale for depression (Bech 2006). It is a clinician rated measurement originally consisting of 17 items pertaining to the symptoms of depression experienced over the past week. Items are scored on a scale of 0-4 or 0-2 according to the severity of each symptom. Altogether, the possible score range for the 17-item HDRS is 0-50. The reliability and overall validity of the scale is considered adequate although criticism has been established due to that HDRS

does not capture all the diagnostic criteria in DSM-IV for MDD, for example anhedonia (Furukawa 2010). Furthermore, it has been proposed that the use of total HDRS scale may not be adequate to define the change in the depression, if the total score change is a reflection of items focusing items like sleep problems of anxiety (Bech 2006, Prien and Levine 1984), but the other items more specific for depression are intact.

2.3 Personality and depression

2.3.1 Models of personality–depression relationships

There are several ways in which the personality–depression relationship can be conceptualized. (Akiskal 1983, Klein and Miller 1993, Shea and Shirley 2005).

Independence: Assumes that personality and depression are distinct conditions with unrelated etiology. Associations found are considered to be caused by chance or help-seeking factors. For example having both personality disorder and depression could increase the likelihood of seeking treatment, which would increase co-occurrence in clinical samples.

Pathoplasty: Assumes that personality and depression are distinct conditions with unrelated etiology, but emphasize the influence of features of one on the presentation and course of the other. Personality may influence the manner depression is experienced and expressed, and depression may influence the expression of the personality style. For example personality might have an effect on the psychotherapy response in depression.

Common cause: Assumes that personality and depression are distinct conditions, but share common etiology. For example neurotic personality traits and depression could have the same genetic background.

Spectrum: This model is close to the common cause model in their assumption of shared etiology, but assumes that one disorder is the variant of the other, rather than distinct disorder. For example neurotic personality traits could be considered as subclinical manifestations of depression.

Vulnerability: Assumes that personality and depression are distinct conditions with unrelated etiology. In this model one condition acts as a risk factor for the second condition. For example avoidant personality traits may increase social stress in certain environments and this could predispose depression.

Complication: Is similar to the vulnerability model in assuming that personality and depression are distinct conditions, but one condition is predisposed by the other. However, complication model focuses on the residual or the recovery phase of the first condition and view the second condition as a complication or scar, resulting from the first. For example the neurotic personality traits might result from the recurrent episodes of depression.

2.3.2 State or trait?

The stability of personality characteristics is not complete. The relationship between measured personality variables and depression is somewhat reciprocal. As personality seems to have an

influence on the onset and course of depression, there is evidence that depression also affects personality variables in varying degree. Of the personality variables focused in this study prevailing depressive symptoms seem to have an effect at least on defense profiles (Bond 2004), TCI scores Harm Avoidance and Self-Directedness (de Winter et al. 2007) and optimism and pessimism (Robinson-Whelen et al. 1997). It is likely that at least the severity of depressive symptoms and the nature of the measured personality variable relate to the average change. One could assume that personality variables which are close to the diagnostic criteria or clinical picture of depression would be the most liable to transition caused by prevailing depression, but evidence on this is inconsistent. Whereas low optimism and high pessimism appear to be prevalent cognitive outlook in clinical depression, it is not clear that the changes in depression are reflected in the optimism or pessimism (Schou et al. 2005). Summing up the studies on the stability of the personality variables focused in this thesis, one could conclude that they act more like traits, but are not completely resistant to state effects.

2.3.3 Correlates of personality measures and depression

2.3.3.1 Defense Style Questionnaire and depression

According to previous studies (Luborsky 1962, Lovering 1976), adaptive defense style correlates with greater health whereas immature style shows the opposite. In a review of published studies (Bond 2004) it was summarized that in general intermediate defenses tend to be more stable (traitlike) over the time, whereas adaptive and maladaptive defense styles are affected by the prevailing symptoms. The studies (Kneepkens and Oakley 1996, Akkerman et al. 1999, Mullen et al 1999, Bond 2004) on depressed patients show increased use of adaptive defenses and decrease in the use of maladaptive defenses after recovery. In several studies there has been a correlation between the use of immature defenses and intensity of the depression (Bond 2004, Corruble et al. 2004, Spinhoven and Kooiman 1997)

There are only few small studies focusing on the predictive value of Defense Style Questionnaire in depression: DSQ has failed to predict the outcome in three studies with less than 20 depression patients in the final analysis in each study (Høglend and Perry 1998, Mullen et al. 1999, Hersoug et al. 2002). In the study with 39 depressive patients who received psychodynamic psychotherapy as their treatment, the baseline DSQ did neither predict the outcome (Bond and Perry 2004). Recent study of Sukul et al. (2009) with 85 depressive patients found that combination of immature defense functioning and trait anxiety had negative effect on the antidepressant treatment outcome. Another recent study with 81 depressive patients treated with psychodynamic psychotherapy found that DSQ mature defense profile predicted remission of the symptoms during the follow-up (Van et al. 2009). Consequently, the theoretical assumption that more mature defense profile would predict the favourable outcome in MDD (Bond 2004) has received some support, but due to the insufficient research so far no distinct conclusion can be made.

2.3.3.2 Psychological Mindedness Scale and depression

Based on the previous studies on non-psychiatric population, PM is positively related to health and mental well-being (Hall 1992, Beitel and Cecero 2003). There are several studies using varied patient groups in which Psychological Mindedness Scale has failed to predict the outcome in psychodynamical and other forms of psychotherapy (Conte et al. 1990, Conte et al. 1996, Kadish 1999, Boylan 2006). PMS has associated positively with the lower drop-out rate (Conte et al. 1990,

Conte et al. 1996) and several forms of therapy seem to have an effect of increasing PMS scores during the treatment (Boylan 2006).

Consequently, in the previous psychotherapy studies Psychological Mindedness Scale has not succeeded in predicting treatment outcomes, which is noteworthy considering that PMS was actually developed for assessing suitability for psychodynamically oriented individual psychotherapy (Conte et al. 1990).

2.3.3.3 Temperament and Character Inventory and depression

Several controlled studies have focused on the relation between depression and personality traits measured by the TPQ or its successor TCI. Most of the studies have been medication trials with HDRS as their outcome measure.

Several studies have reported cross-sectional correlation between the severity of depression and high Harm Avoidance and low Self-Directedness (Hansenne et al. 1999, Hirano et al. 2002, Richter et al. 2003, Marijnissen et al. 2002, Jylhä and Isometsä 2006) Also low Cooperativeness (Hirano et al. 2002, Hansenne et al. 1999) and high Self-Transcendence (Hansenne et al.1999) have significantly correlated with the severity of the depression.

In the study of Hansenne et al. (1999) the prevailing depressive symptoms seem to have affected the TCI scores, since the deviant trait scores changed toward normal values in treatment responders, but were stable in nonresponders. In the study de Winter et al. (2007) state-dependent changes of self-directedness and Harm Avoidance were found in all depressed patients, but compared with the healthy controls even fully remitted depression patients had high Harm Avoidance and in anxious-retarded subtype of depression, also low Self-Directedness. In the study of Marijnissen et al. (2002) post-treatment TCI scores did not differ significantly from pre-treatment values.

Two studies have focused on the predictive value of combination of temperament characteristics to the antidepressant response measured with the decline in HDRS scores. Joyce et al. (1994) reported that in their study of 84 MDD patients temperament predicted 35% variance in antidepressant response. Much lesser association was found in the large multi-site study by Nelson and Cloninger (1997) with over 1100 patients treated with nefazodone; Reward Dependence and Harm Avoidance and their interaction accounted statistically significant, but trivial 1.1% variance of the antidepressant response.

In a study of 40 patients with MDD treated with antidepressants Joffe and colleagues (1993) found negative association between Harm Avoidance and the outcome in depression. Tome et al. (1997) reported better outcome in depression for those high in Reward Dependence and low in Harm Avoidance. In a study of 86 MDD patients treated with antidepressant maprotiline Sato and colleagues (1999) found that Self-Directedness and Cooperativeness predicted the decline of HDRS scores at 8- and 16 weeks follow-ups, respectively.

In the report of Joyce et al. (2007) evaluating two therapies in the treatment of 167 patients with depression, low Harm Avoidance, high Reward Dependence and high Self-Directedness were the main determinants of the better outcome in patients treated with interpersonal therapy, whereas no correlation was found in cognitive-behavioral treatment group. In the study of 199 MDD patients treated with fluoxetine Newman et al. (2000) found no associations between baseline TPQ scores and the decline in HDRS scores during the 8-week follow-up. Another negative finding

was reported by Marijnissen and coworkers (2002) in their study of 35 depressive patients treated with antidepressants for 6 weeks.

In conclusion, previous studies have reported high Harm Avoidance and low Self-Directedness during the acute depressive episode most consistently. Studies on the predictive value of TCI scores measured during the depressive episode have inconsistent results: Two studies found negative association between high Harm Avoidance and depression outcome, one found connection between high Reward Dependence and the recovery; in one study only character measures Self-Directedness and Cooperativeness were associated with the better prognosis. Two studies reported no predictive value at all, one found it only in another therapy group, and the largest study made found only marginal effect.

The reason for inconsistent results in studies focusing on TCI and outcome in major depression may be the differences in patient populations, treatments used and designs between the studies. Due to the differences between previous studies, it is difficult to combine the results and to make firm conclusions. It is possible that the assumed moderating effect of the personality traits on the outcome varies between different treatments and patient groups.

2.3.3.4 Life Orientation Test and depression

Optimism has been repeatedly found to be negatively correlated with depression (Andersson 1996, Achat et al. 2000, Carter and Gayle 2006, Conway et al. 2008, Hart et al. 2008) in cross-sectional settings. Optimistic individuals have been reported to possess more flexible coping strategies (Scheier et al. 1994, Fry 1995, Brissette et al. 2002, Szalma 2009).

In the follow-up studies, optimism has been associated with the lower probability of developing depression after childbirth (Carver and Gaines 1987, Fontaine and Lindsay 1997) and in women approaching menopause (Bromberger and Matthews 1996). Three studies focused on students concordantly reported that greater optimism associates with lower likelihood to depressive symptoms during academic year (Steward et al. 1997, Segerstrom et al. 1998, Brissette et al. 2002). Two studies on elderly men reported that baseline high optimism associated positively with better mental health (Achat et al. 2000) and lower likelihood of developing depressive symptoms during the follow-up (Giltay et al. 2006). Consequently, even though using variously selective populations, the results of the previous prospective studies are very much congruent: optimism associates negatively with the development of depression.

However, none of the above-mentioned longitudinal studies have differentiated the effect of optimism and pessimism, but used the concept of optimism in the meaning of both (high) optimism and (low) pessimism. Since several studies have strongly suggested that optimism and pessimism are distinct constructs rather than bipolar opposites (Herzberg et al. 2006, Robinson-Whelen et al. 1997, Kivimäki et al. 2005, Conway et al. 2008, Szalma 2009, Kubzansky et al. 2004) they may also differ in their relation with depression.

Using two-dimensional model of optimism and pessimism, Herzberg et al. (2006) reported that in the sample of 46.133 subjects, (low) optimism was stronger associated to depression than (high) pessimism. Furthermore, depression was highest among participants with true pessimism (high pessimism and low optimism) and lowest among those with true optimism (high optimism and low pessimism).

There are so far two prospective studies published focusing on the differentiated optimism and pessimism and the development of depression: in the study of 224 older adults neither optimism nor pessimism were significantly associated with the depression in one year perspective (Robinson-Whelen et al. 1997). This study conflicts with the previous ones using unidimensional model of optimism and pessimism, where being in the optimism-end of the continuum has repeatedly associated negatively with the risk of developing depression. In another study with 215 students (Chang and Bridewell 1998) followed for six weeks, high pessimism, but not low optimism predicted depressive symptoms. The baseline depressive symptoms were not evaluated, which is the major limitation of this study. In a prospective study among 5007 employees high optimism predicted smaller increase in sickness absence days after major negative life events. Parallel changes were not observed in relation to pessimism, which further indicates the possibility that optimism and pessimism may differ in the way they contribute to the individual coping with psychological stress. (Kivimäki et al. 2005).

2.4 A conclusion of the literature and the motivation of the present study

Several previous studies have focused on the association between individual personality variables and the outcome in depression.

Of the studies focusing on the defense styles, four studies with less than 40 subject in each found no association between defense profiles and outcome (Høglend and Perry 1998, Mullen et al. 1999, Hersoug et al. 2002, Bond and Perry 2004), while two studies with 81-85 patients in each reported significant association: A negative correlation between immature defense functioning and outcome in antidepressant treatment (Sukul et al. 2009), and positive association between the mature defense profile and a remission in patients treated with psychodynamic psychotherapy (Van et al. 2009).

Of the eight studies reviewed in this thesis concerning the predictive value of Temperament and Character Inventory in depression, the results varied in such an extent that the similar results were reported no more than two of the studies: Joffe et al (1993) and Tome et al. (1997) reported that high Harm Avoidance associated negatively with the outcome and in another two studies no association between TCI scores and outcome were reported (Newman et al 2000, Marijnissen et al. 2002).

Due to significant differences in study design, study population, outcome measures and treatments used, it is difficult to make any definite conclusions of the previous studies focusing on both defense styles and Temperament and Character Inventory to the outcome in depression. It is possible that the moderating effects of personality features to the outcome vary in relation to differences in studies and this is reflected in the inconsistent results. In the studies of this thesis the predictive value of defense styles and TCI scores to recovery in MDD were studied in randomized comparative study design. This design makes it possible to study the potentially different moderating effect of personality variables on the effectiveness of both psychotherapy and antidepressant in the similar study population.

Psychological mindedness seems to associate with mental well-being (Hall 1992, Beitel and Cecero 2003). The Psychological Mindedness Scale is designated to assess psychological mindedness and especially the suitability for psychodynamic psychotherapy. However, positive results on its

predictive value in the psychotherapy of depression are very much lacking. There are no previous studies on the Psychological Mindedness Scale and antidepressants.

When optimism and pessimism are conceptualized as bipolar concept, being in the optimism-end of the continuum has congruently associated with the lower likelihood of development of depression (Steward et al. 1997, Brisette et al. 2002, Giltay et al. 2006). Much less is known about the possible diverse effect of separate optimism and pessimism to the development and course of depression. Since optimism and pessimism in the Life Orientation Scale seem to act like separate dimensions (Herzberg et al. 2006) and they have shown to differ in their predictive value on several health variables (Chang and Bridewell 2008, Nabi et al. 2009), it seemed very much possible that they could also have different effect on depression. There have been two prospective studies on the topic: in the study of Robinson-Whelen et al. (1997) neither optimism nor pessimism associated with the depression and in the study of Chang and Bridewelle (1998) only (high) pessimism but not (low) optimism. The result in former study conflicts with the result of studies using unidimensional model, whereas the in the latter study baseline depressive depression was not excluded which in addition the short follow-up time of six weeks limits the follow-up nature of the study. Thus, there have been few studies on the separate associations between optimism, pessimism and the development and the course of depression. Present studies on this topic were motivated by the idea, that individual generalized positive and negative outcome expectancies, i.e. optimism and pessimism may have significant effect on depression and studying this might help in the process of improving the prevention and treatment of depression.

3 AIMS OF THE STUDY

The aim of this thesis was to investigate the relations of personality factors and the prevalence and outcome of depression.

The specific aims were:

Studies 1. and 2.

To investigate defense style and psychological mindedness (study 1.) and personality traits measured with Temperament and Character Inventory (study 2.) as the predictors of treatment response in major depression in a randomized comparative study.

Studies 3. and 4.

To examine optimism and pessimism as predictors of depression related work disability (study 3.) and antidepressant medication use (study 4.) in a large prospective cohort study.

4 SUBJECTS AND METHODS

4.1.1 Study design (1,2)

The first two studies were part of larger project investigating the clinical, psychological and neurobiological aspect of major depressive disorder. The study was carried out at the Research Department of Social Insurance Institution (Turku, Finland) in 2000-2004 in collaboration with the psychiatric clinics of the Helsinki and Turku Universities, and the Turku PET Centre. The patients were recruited from five occupational health service units. At the Research Department, all subjects were interviewed by a psychiatrist, using the Structured Clinical Interview for DSM-IV Axis 1 Disorders (SCID-I; First et al. 1997). The severity of the depression was assessed by the psychiatrist using the 17-item Hamilton Depression Rating Scale (HDRS) (Hamilton 1967). Subjects were also asked to fill 88-item Defense Style Questionnaire (DSQ) (Bond et al. 1983, Andrews et al. 1989, Andrews et al. 1993), the 45-item Psychological Mindedness Scale (PMS) (Conte et al. 1990) and 240-item Temperament and Character Inventory (TCI) (Cloninger et al. 1993). All three questionnaires were versions translated into Finnish. DSQ scores were rated according to Andrews et al. (1989) to produce scores for immature, neurotic and mature defense style.

The inclusion criteria for the study were: (1) the mild or moderate episode of major depressive disorder assessed with the SCID-I, (2) HDRS scores of 15 or more, (3) age 20–60 years, (4) no psychotherapeutic or psychopharmacological treatment during the preceding 4 months, (5) no DSM-IV axis I or II comorbidity, (6) no severe somatic illnesses, and (7) no contraindication to fluoxetine treatment.

After the psychiatrist's interview, subjects meeting the inclusion criteria were randomly assigned to psychotherapy or a fluoxetine group according to a 1:1 schedule made beforehand.

Short-term psychodynamic psychotherapy (STPP) consisted of 16 weekly sessions with experienced psychiatrists or psychologists ($n=5$), who had specific training in short-term psychodynamic psychotherapy and a working experience of over ten years as a psychotherapist. For the purposes of the present study, no formal assessment of the therapies was made.

Pharmacotherapy with 20-40 mg of fluoxetine (FLX) also lasted 16 weeks. The medication was supervised by a general physician, who was a member of the research team and met the patients one to two times a month. Plasma fluoxetine and norfluoxetine levels were measured at the 4-month follow-up.

The psychiatric follow-up examination was made at the Research Centre when the active therapy ended, i.e., 4 months after the baseline evaluation. The follow-up examination included a diagnostic interview (SCID-I), carried out by the same psychiatrist as at the baseline and the assessments of the severity of depression (HDRS). The psychiatrist was aware of which therapy group each subject belonged to. After the active treatment ended in 4-months, the study proceeded as a naturalistic 12-month follow-up of the patients (study 1.).

Study by Salminen et al. (2008) focusing on the clinical outcome of the study population reported major improvement in both treatment groups at the 4-month follow-up with no statistically significant difference in the efficacy between the treatments as regards the alleviation of depressive symptoms, diagnostic distribution, or functional ability.

Additionally, articles focusing on the neuroreceptor system have been published from this study. Karlsson et al. (2010) reported that psychotherapy increased brain serotonin 5-HT_{1A} receptors in patients with MDD. Hirvonen et al. found that in MDD patients the binding potential of serotonin 5HT_{1A} receptors was reduced (2008, A), but no differences in striatal dopamine D₂ receptors (2008, B) was observed, when compared with healthy controls. Furthermore, neither fluoxetine nor psychodynamic psychotherapy was found to have effects on dopamine receptors in the striatum (Hirvonen et al. 2010).

4.1.2 Participants (1,2)

A total of 85 subjects (M=27; F= 58) were initially recruited and screened. Fifty of these subjects (59%) (M=16; F=34) met the inclusion criteria, and 35 (M=11; F= 24) did not. The mean age was 42.7 years for the subjects included, and 43.1 years for those excluded. Of the included 50 subjects, 25 were randomized into the short-term psychodynamic psychotherapy group (STPP) and 25 to the fluoxetine group (FLX). 37 of the patients had their first depressive episode and 13 suffered from the recurrent depression.

Two subjects in the FLX group failed to fill the DSQ and the TCI, however they completed the PMS and participated in the study. Three subjects in the STPP group and two in the FLX group refused to continue to the treatment phase of the study. During the treatment one subject in the STPP group deteriorated and the psychotherapy had to be stopped and another two did not participate in the follow-ups. In the FLX group, one patient deteriorated during the treatment and had to be hospitalized and 5 subjects did not participate in the follow-ups. One of the dropouts in the FLX-group was the same individual who had failed to complete the DSQ and TCI at the baseline. Consequently, 36 subjects (STPP n=19; FLX n=17) of those who had completed PMS scale at the baseline and 35 subjects (STPP n=19; FLX n=16) of those with completed DSQ and TCI at the baseline participated in the 4-month follow-up assessment.

4.1.3 Data analysis (1,2)

Categorical socio-demographic or clinical baseline characteristics were compared between groups using Chi-square test. Two-sample t-test was used in comparison of continuous clinical characteristic between groups.

Correlations were calculated using Pearson correlation coefficients. Association of defense profiles or PMS scores at the baseline with the change in the HDRS scores during the 4-month and 12-month follow-up was examined using linear regression analysis. (Study 1.)

The significance of change in HDRS scores during 4 months follow-up was tested using a paired t-test. Baseline HDRS and TCI variables were used as predictors for HDRS scores at 4 months follow-up in linear regression analysis. Analysis of covariance (ANCOVA) was used to test the interaction between group and baseline TCI score variables on the HDRS scores at the 4 months follow-up. Baseline HDRS did not correlate with HDRS at the 4 months follow-up, and thus it was not used as a covariate in ANCOVA models. (Study 2.)

Statistical analyses were done with SAS System for Windows, release 9.1 (SAS Institute Inc., Cary, NC).

4.2.1 Study design (3,4)

For the studies three and four, the data were derived from the on-going Finnish Public Sector Study, which includes a prospective follow-up of employees in the service of ten municipalities (Vahtera et al. 2010). The eligible population for the study of optimism and pessimism was all 63,460 full-time employees at work when the surveys were carried out (1997, 2000-2001 and 2004). In total, 46,352 employees (80% women) answered at least one survey (response rate 73%). For those who responded to several surveys, the first response was considered to represent the baseline. We used personal identification numbers to link the participants to their records in the national health registers. Of the participants, we excluded the respondents with missing data on depression, optimism or pessimism, and those who, at the beginning of the follow-up, were eligible to special imbursement for medication for severe mental disorders, were receiving psychotherapy due to depression, were retired, or had died. We also excluded participants with any previous indicator of depression prior to the survey, i.e. those who according to self-report had been diagnosed with depression by a physician or who according to health records had been on a long-term work disability period or hospitalized due to depression, or who had purchased antidepressant medication or received psychotherapy for depression in the survey year (n=6599 altogether). The final cohort for depression related work disability study (Study 3.) included 38,214 (76% women) employed persons with no indication of depression at the baseline. In the study focusing antidepressant medication use (Study 4.) we excluded additional 8284 employees from one town where the prescription data were not available in the national prescription register because the medication costs were paid by the employer. The studies were approved by the Ethics Committee of the Finnish Institute of Occupational Health.

4.2.1.1 Optimism and pessimism

Dispositional optimism and pessimism were measured with the revised Life Orientation Test (LOT-R; Scheier et al. 1994) in the baseline survey. The respondents were asked to indicate how well the statements described them in general, as expressed on a scale ranging from 1 (not at all) to 4 (very much so), a 4-point modification of the standard 5-point response format (Kivimäki et al. 2005). Mean of the positively worded items was calculated to yield optimism score and mean of the negatively worded items comprised pessimism score. High score in the scale referred to greater amount of the feature in question. Only responses with no more than one missing value per scale were included in the analysis. Using data derived from the Finnish Public Sector Study, Karlsson et al. (2011) have found that low optimism (but high pessimism) influences the initiation of psychotherapy as a treatment modality for depression.

4.2.1.2 Work disability

The work disability outcomes were the beginning of a new period of work disability (≥ 90 days), either a long-term sickness absence or disability pension (temporary or permanent, part- or full-time) or the end of such period because of returning to work. Data on sickness absences were obtained from the register kept by the Social Insurance Institution while information on disability pensions was obtained from the Finnish Centre for Pensions. Both registers require the physician assigned diagnoses of disability coded according to the ICD-10, and include the beginning and end dates of each work disability period. Work disability was considered as a continuum and thus we combined all consecutive or overlapping periods of work disability irrespective of the register. In the present study only periods of work disability with depression (ICD-10 codes F32-F34) as the main diagnosis were considered. The decision to include only those work disability periods which

lasted at least 90 days was motivated by the aim to focus on more severe incidences of depression.

4.2.1.3 Antidepressant medication

We determined antidepressant use using the nationwide Drug Prescription Register. The available data contain information on the day of purchase; the dose, stated as the international standard daily defined dose; and medication classified according to the WHO Anatomical Therapeutic Chemical (ATC) classification. We determined the consumption of antidepressants on the basis of defined daily doses for the purchases of any antidepressants (ATC code N06A).

We used a refill-sequence model of adherence to quantify the length of treatment (Caetano et al. 2006). Thus, we measured the total duration of the sequence of all refills during the follow-up, using 100 defined daily doses as a maximum for a refill (the maximum days supplied is 100 in the Finnish reimbursement legislation) and added 50 days to all refills to prospectively fill the gaps between subsequent purchases. This grace period for the gap in medication implies that the patients treated with half of the defined daily dosage are correctly assigned as having 100 days of treatment. We identified then the date of the beginning of the first treatment period that lasted more than 100 days during the follow-up as calculated with this model. To be able to examine the length of the treatment, we also identified the last day of this medication period.

The decision to include only medication treatments lasting at least 100 days was motivated by the aim to focus on those treatments that are likely effective. Guidelines suggest continuing with the same antidepressant after 6-8 weeks only if moderate or greater improvement has been reached (Anderson et al. 2008).

4.2.2 Baseline covariates (3,4)

All covariates were measured at baseline. The following variables were treated as potential confounders in the analyses: age, sex, and SES, use of anxiolytics or hypnotics, which were derived from the employers' records and marital status, smoking and physical inactivity, alcohol consumption, which were derived from the survey responses. SES was categorized according to the occupational-title classification of the Statistics Finland to upper-grade non-manual workers (e.g. physicians, teachers), lower-grade non-manual workers (e.g. technicians, registered nurses), and manual workers (e.g. cleaners, maintenance workers) (Statistic Finland 2001). Marital status was dichotomized to married or cohabiting vs. single.

Alcohol consumption was obtained from the survey responses in which the participants reported their average weekly consumption of beer, wine, and spirits in portions. The data were transformed into grams of pure alcohol and classified as low (0-210 g per week) or high (> 210 g per week) consumption. Other medication use, drawn from the Drug Prescription Register of the Social Insurance Institution of Finland, was indicated by the purchases of anxiolytics (ATC code N05B) and hypnotics or sedatives (ATC code N05C) (WHO 2004). Participants purchasing at least one Defined Daily Dose (DDD) during the year of the baseline survey were coded as being on anxiolytic or hypnotic treatment. Current smoking and low physical activity (<2 Metabolic Equivalent Task hours per day) were encoded yes/no (Vahtera et al. 2010).

Data on prevalent hypertension, cardiac failure, ischemic heart disease, diabetes, asthma or other chronic obstructive lung disease, and rheumatoid arthritis were obtained from the Drug

Reimbursement Register of the Social Insurance Institution of Finland. The national sickness insurance scheme covers all permanent residents and provides at least basic reimbursement (currently 42%) for all filled prescriptions. The Drug Reimbursement Register contains information about persons entitled to the special medication reimbursement of 72% or 100% for the costs of medications to treat many chronic and severe diseases. Patients who apply for special reimbursement must attach a detailed medical certificate prepared by the treating physician, who also provides data to confirm the diagnosis. The Finnish Cancer Register, which covers all diagnosed cancer cases in Finland, provided information about a history of malignant tumors diagnosed during the 5 preceding years of the study baseline.

4.2.3 Data analysis (3,4)

The associations of baseline covariates with the risk of work disability due to depression and the likelihood of return to work (study 3.) / antidepressant medication use and the length of the medication (study 4.) were studied with Cox proportional hazards models. Cox proportional hazards models were also used to study the associations between baseline optimism and pessimism and the outcome measures: In the study 3. the first long-term work disability period and the subsequent return to work after work disability, and in the study 4. the first antidepressant medication period (≥ 100 days) and the length of the period. The follow-up for the outcome measures started at the beginning of the year following the baseline survey and ended at the occurrence of the event, old age pension, death, or the end of the follow-up in 31 December, 2005, whichever came first. The follow-up ended at the day of returning to work (study 3.) / last day of the medication (study 4.) , death, or the end of the follow-up, whichever came first. Hazard ratios (HR) and their 95% confidence intervals (CI) were sequentially adjusted for (1) age and sex, (2) socioeconomic and marital status and (3) alcohol use, purchases of anxiolytics or hypnotics, smoking, physical activity and baseline health. In the study 4. we used also a model in which optimism and pessimism were adjusted for each other. Since optimism and pessimism were considered as continuous variables, HR reflected the change in the risk of work disability or probability of returning to work (study 3.) / risk of starting and stopping antidepressant medication (study 4.) per one point increase in the scale measuring optimism or pessimism (range 1-4). Optimism and pessimism scores were rounded to the nearest integer.

All statistical analyses were carried out using the SAS 9.1.3 program package (SAS Institute Inc., Cary, NC, USA).

5 RESULTS

5.1 Results (1,2)

In the first two studies, there were no statistically significant differences in the socio-demographic or clinical baseline characteristics between the two treatment groups. No significant differences were found either in the baseline HDRS scores, defense profiles, PMS or TCI scores between the treatment groups. When 35 subjects who participated in the DSQ analysis in the 4-month follow-up were compared with 13 dropouts, the only significant difference was found in working status: 85% of the dropouts were on sick leave compared with 49% of the others ($P=.024$)

During the 4-month intervention period, none of the completers in the FLX group had received psychotherapy and none in the STPP group had used antidepressant medication. At the 4-month follow-up, plasma fluoxetine and norfluoxetine concentrations in the FLX group were between reference values in all subjects. The mean fluoxetine dose was 25 mg/day. HDRS-scores decreased significantly in both groups during 4-months follow-up ($p<0.001$). *Table 1*.

Table 1. The mean (SD) HDRS scores at the baseline and follow-ups in FLX and STPP groups (Studies 1. and 2.)

| | BASELINE | AT 4-MONTH |
|-------------|--------------|-------------|
| HDRS, FLX* | 19.32 (3.25) | 7.59 (6.69) |
| HDRS, STPP‡ | 18.72 (2.19) | 8.00 (5.98) |

* n=25 at the baseline and n=17 at the follow-ups

‡ n=25 at the baseline and n=19 at the follow-ups

In the study 1. no association was found with the defense styles and baseline HDRS scores. In the FLX group recovery measured by the decrease in the HDRS during the 4-month follow-up correlated significantly with the baseline mature defense style ($r=-0.59$, $P=.015$). The same association was found even during the 12-month follow-up ($r=-0.46$, $P=.07$). No statistically significant correlations were found in STPP group between defense style and outcome measures. PMS scores did not associate with baseline HDRS, nor with recovery measure by the decrease in HDRS during the follow-up. *Table 2*,

Table 2. Regression coefficients for the change in the HDRS scores during the 4-month follow-up (Study 1.) (Kronström et al. 2009)

| Independent variable | FLX group | | | STPP group | | |
|------------------------|------------------------|-----------------------|--------------|------------------------|-----------------------|---------|
| | Regression coefficient | 95% confidence limits | P-value | Regression coefficient | 95% confidence limits | P-value |
| Mature defense style | -3.68 | -6.53 – -0.83 | 0.015 | -0.99 | -3.82 – 1.85 | 0.47 |
| Neurotic defense style | 1.91 | -0.91 – 4.74 | 0.17 | -0.23 | -3.41 – 2.96 | 0.88 |
| Immature defense style | 2.91 | -1.96 – 7.78 | 0.22 | -0.39 | -5.30 – 4.53 | 0.87 |
| PMS | -0.15 | -0.38 – 0.07 | 0.17 | 0.08 | -0.14 – 0.30 | 0.45 |

In the study 2. In the combined group (n=35) Harm Avoidance associated with the severity of the depression measured by the HDRS at the baseline (Regression Coefficient RC 0.14, Standard Error SE 0.05, P=0.01). In the combined group baseline high Self-Directedness associated with high HDRS at 4-months follow-up (P=0.03). In the FLX treatment group high Reward Dependence (P=0.03), high Self-Directedness (P=0.01) and high Cooperativeness (P=0.02) at the baseline associated with high HDRS at 4-months follow-up. None of the TCI dimensions associated with HDRS at 4-months follow-up in the PSY treatment group. The association of baseline Reward Dependence (P=0.03) and Cooperativeness (P=0.04) with the HDRS at 4-months follow-up was significantly different between the two treatment groups (group×TCI interaction, P=0.03 and P=0.04, respectively). Baseline HDRS did not predict HDRS scores at 4-months (RC -0.01, SE 0.42, p=0.98). *Table 3.*

Table 3. The association of baseline TCI dimensions with HRDS at 4 months in FLX and STPP groups and the interaction between group and TCI dimension. (Study 2.) (Kronström et al. 2010, A)

| TCI dimension | FLX group (n=16) | | | | STPP group (n=19) | | | | combined group (n=35) | |
|---------------|----------------------|---|----------------|-----------------|----------------------|---|----------------|-----------------|-----------------------|-----------------------|
| | T-value ¹ | regression coefficient (standard error) | R ² | P-value for TCI | T-value ¹ | regression coefficient (standard error) | R ² | p-value for TCI | F-value ² | P-value for TCI×group |
| NS | 0.79 | 0.31 (0.40) | 0.04 | 0.44 | -0.58 | -0.11 (0.19) | 0.02 | 0.57 | 1.00 | 0.33 |
| HA | -0.78 | -0.22 (0.28) | 0.04 | 0.45 | -0.38 | -0.07 (0.17) | 0.01 | 0.71 | 0.22 | 0.64 |
| RD | 2.44 | 0.94 (0.39) | 0.30 | 0.03 | -0.90 | -0.37 (0.41) | 0.05 | 0.38 | 5.40 | 0.03 |
| P | 1.07 | 0.81 (0.76) | 0.08 | 0.30 | -0.58 | -0.40 (0.69) | 0.02 | 0.57 | 1.41 | 0.24 |
| SD | 3.10 | 0.63 (0.20) | 0.41 | 0.01 | 0.27 | 0.07 (0.26) | 0.00 | 0.79 | 2.90 | 0.10 |
| Co | 2.64 | 0.62 (0.23) | 0.33 | 0.02 | -0.54 | -0.14 (0.26) | 0.02 | 0.60 | 4.77 | 0.04 |
| ST | -0.20 | -0.04 (0.22) | 0.00 | 0.84 | 0.63 | 0.12 (0.20) | 0.02 | 0.54 | 0.33 | 0.57 |

¹Degrees of freedom = 1, ²Degrees of freedom = 1, 31

5.2 Results (3,4)

In the studies three and four, baseline high optimism and low pessimism were associated with female sex, non-manual work, being married or cohabiting, physical activity, non-smoking and having no somatic disease. In addition, low pessimism (but not high optimism) was more common in younger subjects, and those with low alcohol consumption, and no purchases of prescribed anxiolytics or hypnotics.

Work disability with a diagnosis of depression and antidepressant medication were both associated with older age, female sex, high alcohol consumption, use of prescribed anxiolytics and hypnotics and having somatic disease. In addition, antidepressants associated with being single, smoking and physical inactivity. Higher probability of returning to work after sickness absence was related to younger age and non-manual work. High alcohol consumption was the only baseline characteristic showing significant association not interrupting the medication during the follow-up. *Table 4.*

Table 4. Associations of baseline characteristics with optimism, pessimism, and subsequent work disability and treatment with antidepressants (Studies 3. and 4.)

| | Work disability data (N 38214) | | | Antidepressan use data (N 29930) | | |
|---------------------|---------------------------------|---------------------|---------------------------|----------------------------------|--------------------------------|--------------------------------|
| | Optimism | Pessimism | Work disability | Returning to work N 164 | Starting | Stopping treatment |
| | N | mean | HR (95% CI) ¹⁾ | HR (95% CI) ¹⁾ | N 1681 | N 1288 |
| All | | 2.73 | 1.45 | | | |
| Sex | | | | | | |
| | | p<.001 | p<.001 | | | |
| Men | 9269 | 2.67 | 1.48 | 1.00 (ref.) | 1.00 (ref.) | 1.00 (ref.) |
| Women | 28945 | 2.75 | 1.44 | 1.56 (1.14-2.13) | 1.51 (1.32-1.72) | 0.99 (0.85-1.15) |
| Age | | | | | | |
| | | p=0.111 | p<.001 | | | |
| mean | 44.4 | 0.008 ²⁾ | 0.042 ²⁾ | 1.54 (1.34-1.77) ³⁾ | 1.02 (0.97-1.08) ³⁾ | 1.03 (0.96-1.09) ³⁾ |
| SES | | | | | | |
| | | p<.001 | p<.001 | | | |
| Manual | 8029 | 2.61 | 1.63 | 1.00 (ref.) | 1.00 (ref.) | 1.00 (ref.) |
| Lower non-manual | 16919 | 2.74 | 1.45 | 0.80 (0.59-1.09) | 1.05 (0.92-1.20) | 0.97 (0.83-1.13) |
| Upper non-manual | 13156 | 2.80 | 1.33 | 0.73 (0.53-1.01) | 0.95 (0.82-1.09) | 0.99 (0.84-1.16) |
| Marital status | | | | | | |
| | | p<.001 | p<.001 | | | |
| Married/cohabiting | 29155 | 2.74 | 1.43 | 1.00 (ref.) | 1.00 (ref.) | 1.00 (ref.) |
| Single | 8630 | 2.71 | 1.52 | 0.82 (0.61-1.11) | 1.13 (1.01-1.27) | 1.08 (0.95-1.23) |
| Alcohol consumption | | | | | | |
| | | p<.001 | p<.001 | | | |

| | | Work disability data (N 38214) | | | Antidepressant use data (N 29930) | | |
|----------------------------------|--|--------------------------------|-----------|---------------------------|-----------------------------------|---------------------------|------------------------------|
| | | Optimism | Pessimism | Work disability N 287 | Returning to work N 164 | Starting N 1681 | Stopping treatment N 1288 |
| | | mean | mean | HR (95% CI) ¹⁾ | HR (95% CI) ¹⁾ | HR (95% CI) ¹⁾ | HR (95% CI) ¹⁾ |
| 0-210g/wk | | 2.74 | 1.44 | 1.00 (ref.) | 1.00 (ref.) | 1.00 (ref.) | 1.00 (ref.) |
| >210g/wk | | 2.69 | 1.50 | 1.53 (1.06-2.21) | 1.01 (0.62-1.64) | 1.42 (1.21-1.67) | 1.21 (1.01-1.46) |
| Smoking | | | | | | | |
| | | p<.001 | p<.001 | | | | |
| No | | 2.74 | 1.43 | 1.00 (ref.) | 1.00 (ref.) | 1.00 (ref.) | 1.00 (ref.) |
| Yes | | 2.70 | 1.52 | 1.27 (0.95-1.69) | 0.86 (0.58-1.28) | 1.35 (1.20-1.52) | 0.98 (0.86-1.12) |
| Physical inactivity | | | | | | | |
| | | p<.001 | p<.001 | | | | |
| No | | 2.76 | 1.42 | 1.00 (ref.) | 1.00 (ref.) | 1.00 (ref.) | 1.00 (ref.) |
| Yes | | 2.63 | 1.52 | 1.21 (0.93-1.57) | 0.80 (0.55-1.16) | 1.21 (1.09-1.35) | 0.93 (0.82-1.06) |
| Use of anxiolytics/ hypnotics | | | | | | | |
| | | p=.003 | p<.001 | | | | |
| No | | 2.73 | 1.45 | 1.00 (ref.) | 1.00 (ref.) | 1.00 (ref.) | 1.00 (ref.) |
| Yes | | 2.67 | 1.52 | 4.12 (2.77-6.11) | 1.30 (0.79-2.14) | 3.77 (3.18-4.48) | 0.93 (0.77-1.13) |
| Somatic disease | | | | | | | |
| | | p<.001 | p<.001 | | | | |
| No | | 2.74 | 1.44 | 1.00 (ref.) | 1.00 (ref.) | 1.00 (ref.) | 1.00 (ref.) |
| Yes | | 2.70 | 1.51 | 1.41 (1.03-1.94) | 0.77 (0.48-1.23) | 1.47 (1.29-1.68) | 0.99 (0.85-1.16) |

¹⁾ Adjusted for age and sex

²⁾ Pearson correlation coefficient

³⁾ HR / 10 years

In the study 3. during a mean follow-up of 4.0 (SD 2.3) years, 287 employees encountered work disability with a diagnosis of depression . Of those employees, 164 (57%) returned to work during the follow-up of 2,5 (SD 1.8) years. After adjustment for age, sex, marital status, alcohol consumption, smoking, physical inactivity, use of anxiolytics/hypnotics and somatic disease one unit increase in the optimism score was associated with a 21% lower risk of work disability due to depression (HR 0.79, 95% CI 0.66-0.96) whereas the pessimism score was not associated with the occurrence of work disability period (HR 1.11, 95% CI 0.90-1.37)

Among the 287 participants who were disabled due to depression, one unit increase in optimism score was associated with a 30% higher probability of returning to work after long-term work disability in the fully adjusted model (HR 1.30, 95% CI 1.01-1.66). Participants with higher pessimism scores, in turn, were less likely to return to work, with one unit increase in pessimism being associated with a 34% lower probability (HR 0.65, 0.49-0.88). We found no sex interactions with optimism or pessimism on either the risk of work disability or the probability of returning to work. *Figure 1.*

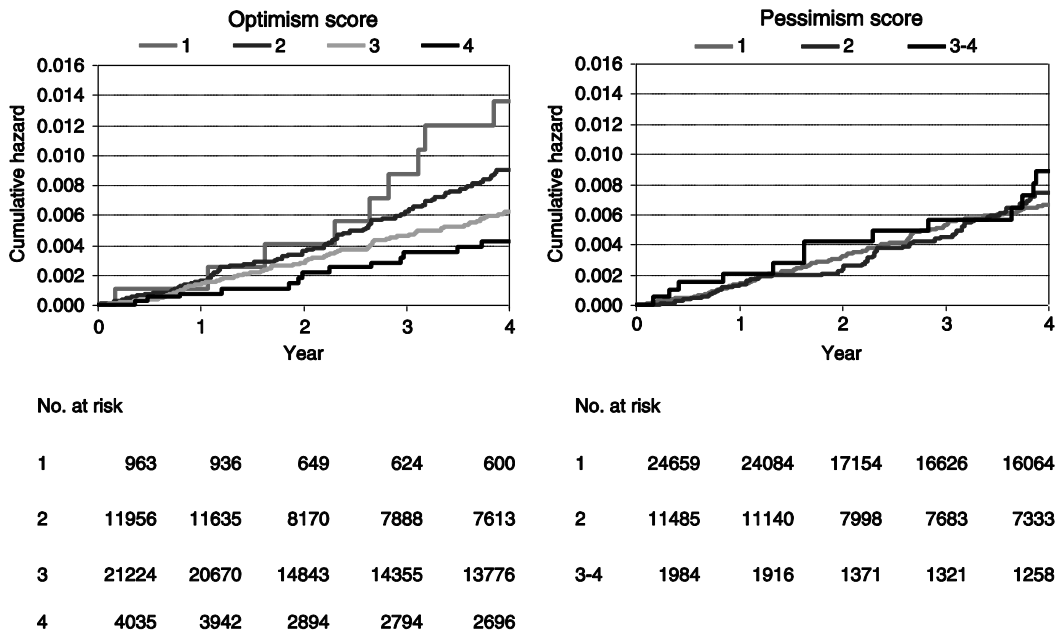


Figure 1. Cumulative hazard rates for work disability due to depression differed by optimism and pessimism scores (Study 3.) (Kronström et al. 2010, B)

In the study 4. during the mean follow-up of 4.4 years, 1681 employees purchased antidepressants for an uninterrupted period lasting at least 100 days. Of those employees, 1288 subjects interrupted the use of medication during the remaining mean follow-up of 2.8 years.

In a model adjusted for sex, age, socioeconomic and marital status, use of alcohol and anxiolytics/hypnotics and somatic disease, baseline high optimism associated with the lower likelihood of starting (HR 0.67, 95%CI 0.62-0.72) and higher likelihood to interrupting medication (HR 1.1, 95% CI 1.06-1.27) during the follow-up. Pessimism showed opposite associations:

employees with high pessimism had increased risk of starting antidepressant (HR 1.29, 95%CI 1.18-1.40) and lower risk of interrupting it (HR 0.90, 95%CI 0.81-0.99). *Table 4.*

Table 4. The association between optimism/pessimism and work disability and antidepressant use outcomes (Studies 3. and 4.)

| | Work disability (287 events) | Returning to work (164 events) | Initiating medication (1681 events) | Ending medication (1288 events) |
|-----------|---------------------------------|-----------------------------------|--|------------------------------------|
| Optimims | 0.79(0.66-0.96) | 1.30(1.01-1.66) | 0.67(0.62-0.72) | 1.16 (1.06-1.27) |
| Pessimims | 1.11(0.90-1.37) | 0.66(0.49-0.88) | 1.29(1.18-1.40) | 0.90 (0.81-0.99) |

Adjusted for sex, age, SES, marital status, alcohol consumption, smoking, physical inactivity, use of anxiolytics or hypnotics and somatic disease

6 DISCUSSION

6.1 Discussion (1,2)

The temperament trait of Harm Avoidance associated with the severity of depression at the baseline. In the fluoxetine treatment group mature defense style correlated with the decrease in HDRS during the follow-up. In the same group high baseline Reward Dependence, high Self-Directedness and high Cooperativeness associated with high HDRS at the follow-up. TCI measured at the baseline were not predictive for the outcome in patients treated with short-term psychodynamic psychotherapy. Psychological mindedness failed to predict the recovery in both treatment groups.

6.1.1 Defense profiles

Mature defense style associated with better recovery in the fluoxetine treatment group, but no associations between the defense profiles and outcome was found in the psychotherapy treatment group. Patients with a high level of mature defenses, i.e. sublimation, humor, anticipation and suppression, were more likely to improve in the fluoxetine treatment group compared with those with the lower levels of these defenses.

It is possible that association between mature defenses and the outcome in the fluoxetine treatment group could account for differences in neurobiology underlying the depression. If so, mature defenses would associate with neurobiological mechanisms that predispose the favourable response to fluoxetine treatment. However, there are no studies focusing on the neurobiology of defenses, and thus the mechanisms could account for possible differences in the treatment response are unclear.

The association between better outcome and the high level of mature defense in the fluoxetine treatment group could also be explained by differences in the placebo response. The response to placebo has been shown to be substantial accounting for on average 50 percent or more from the antidepressant response (Walsh et al. 2002), and it is possible personality affects on the level of placebo response (Geers et al. 2005).

One possible explanation could be that that mature defense profile would be connected to better prognosis in general and for some reason this trend did not come out in psychotherapy group. There is some support to the assumption that mature defense profile would increase the likelihood of favorable outcome in depression (Van et al. 2009, Sukul et al. 2009).

In a study with 81 depressed patients treated with short-term psychodynamic supportive psychotherapy (SPSP) (Van et al. 2009) mature defense profile in the baseline associated with the better outcome. This study differs from our psychotherapy group in our study mainly in relation to psychotherapy used; Van et al. used short-term psychodynamic *supportive* psychotherapy (SPSP), while in the present study short-term psychodynamic psychotherapy (STPP) was used. In general, psychodynamic psychotherapies can be placed on a supportive-expressive continuum. SPSP is situated within the supportive half of this continuum, whereas STPP is more expressive form of treatment. Psychodynamic therapies located on the expressive end emphasize the interpretation of transference and STPP interventions include early transference interpretations. SPSP recognizes the existence of transference but does not interpret it (Driessen et al. 2007).

Høglend and collages reported from their study with 100 patients randomly assigned to two different treatment groups, one receiving psychodynamic therapy with transference interpretations and the other without. The analysis of the data showed that patients with the poor quality of object relations profited significantly more from the therapy with transference interpretations, whereas transference interpretations were not associated with the recovery in subjects with the high quality of object relations (Høglend et al. 2006 and 2008). This result combined with several other studies (Hersoug et al. 2003, Høglend 1993, Piper et al. 1991, Høglend 1993) indicate that contrary to traditional assumption it is possible that patients with poor object relations and less mature defense profile benefit more from expressive psychotherapy with transference interpretations, whereas for patients with the higher quality of interpersonal relationships or more mature level of defenses, transference interpretations could be neutral or negative ingredient in the psychotherapy. If so, it seems possible that in our study patients with less mature defense profile would have benefitted relatively more from psychotherapy compared with those with more mature defenses and general assumed association between mature defense profile and favorable prognosis would have manifested only in the fluoxetine treatment group.

6.1.2 Psychological mindedness

Psychological mindedness refers to a set of skills that are thought to enhance the prospects of successful psychodynamic psychotherapy and it is still used in assessing the suitability of the patients for such psychotherapy. The major problem in empirical studies on this field is the lack of consensus on the exact meaning and definition for the concept of PM. This problem is reflected in the developed evaluating methods of the PM. We used Psychological Mindedness Scale, which conceptualizes the definition of PM as the ability to access one's own and other's feelings and utilize these for changing behavior. The negative result in our study, combined with the previous studies with similar results, strongly conflicts with the assumption that high PMS scores are associated with favorable outcome in psychodynamic psychotherapy neither in depression, nor in other patient groups. Furthermore, it seems that Psychological Mindedness Scale is not useful in assessing the prognosis or selecting optimal treatment for MDD patients.

The inability of the PMS to predict the outcome in psychodynamic psychotherapy may refer that theory need reconsideration in this sense, or that PMS scores would not reflect "the real psychological mindedness". Due to lack of the exact definition of PM, there is no solid ground to research this conceptual question. Judging the appropriateness of the definition or measurement of PM by its capability to predict treatment response in dynamic psychotherapy possess the risk of circular reasoning, thus making PM subordinate and pragmatic, rather than individual concept.

Several studies have used standardized video and interview format Psychological Mindedness Assessment Procedure (PMAP; McCallum and Piper 1997) to assess PM conceptualized as ability to identify others intrapsychic components and relate them to person's difficulties. In those studies PMAP has performed significantly better in comparison with PMS in predicting psychotherapy outcome (Piper et al. 1998, Piper et al. 1994 (A), Piper et al. 1994 (B)). Due to its nature, the implementation of the PMAP procedure to the clinical practice is much more demanding compared to simple self-report format of PMS. Consequently, other measurement of PM than PMS, especially PMAP procedure seems to work better in predicting the treatment outcome, but due to the conceptual confusion it is unclear how this should be interpreted.

6.1.3 Temperament and character

There was a significant correlation between baseline high Harm Avoidance and the severity of the depressive state in the whole data. In the fluoxetine group high Reward Dependence, high Self-Directedness and high Cooperativeness were associated with higher HDRS scores at 4 months follow-up. High Self-Directedness at the baseline was associated with the higher depression scores at 4 months also in the whole data combined.

The cross-sectional correlation between Harm Avoidance and the depression reported in this study is consistent with the previous findings (e.g. Hansenne et al.1999, Marjnissen et al. 2002, Jylhä and Isometsä 2006). Majority of the prospective studies have not found associations between Harm Avoidance and the outcome in MDD. Harm Avoidance refers to tendency to act worried, fearful, nervous, negativistic (Cloninger et al. 1994) and it has been associated with the general propensity to experience negative emotions (Markon et al. 2005). Conceptually, the essence of this personality traits and the cognitive and emotional changes typical for depressive disorder share some common aspects, which makes their co-occurrence impending. Previous studies suggested significant state effect of depression on Harm Avoidance (de Winter et al. 2007, Spittlehouse et al. 2010). There are some studies indicating that personality trait of Harm Avoidance might predispose subject to the depression (Cloninger et al. 2006), which also might increase their co-occurrence in clinical samples.

Previous studies on the predictive value of the TCI scores have reported inconsistent results. Nelson and Cloninger (1997) reported negative association between Reward Dependence and outcome in subjects treated with antidepressant medication nefazodone, which is in line with the result of present study. Joyce et al. (1997) reported reverse association; high Reward Dependence associated with better treatment response in patients treated with Inter Personal Therapy.

In the study of Sato et al. (1999) using antidepressant medication maprotiline for the treatment of depression, Cooperativeness and Self-Directedness were correlated positively with the outcome during the follow-up, which is an opposite result compared with ours. Even if it is possible that antidepressants may differ in personality configurations that predict optimal responses, it seems unlikely that this would fully account for the conflicting result between the study of Sato and the present one.

It is possible that associations of Reward Dependence, Self-Directedness and Cooperativeness with remaining the depressive symptoms after four months of fluoxetine treatment could cause potential differences in the proportion of placebo effect of the antidepressant. Subjects high in Reward Dependence can be described as being sensitive, dependent, sociable, and Cooperativeness refers to ability and willingness to social contacts and cooperation (Cloninger et al. 1994). Especially subject scoring high on these traits might benefit more from the active support and encouragement they receive from regular psychotherapy sessions, and ending up in the medication group with less regular interaction and personal support could diminish the placebo effect these subjects receive from the medication. The actual magnitude of the placebo response seems to be related with many variables, including the study population and design (Brunoni et al. 2009). The varying role of placebo effect may contribute to the inconsistent results of the studies.

Despite years of intensive research the predictive role of Temperament and Character traits are very much unclear. Due to greatly inconsistent result one could conclude that personality traits

measured with the TCI during the depressive episode do not possess the essence that could outweigh the confounders when comparing the outcome in different study settings. The aim of finding correlations between two variables, trait and recovery, is complicated by the reality that so many distinct aspects have an effect on the recovery. It seems that the complexity of the human personality, the process of individual recovery and their interaction do not to produce solid and consistent associations between the measured variables. The risk of coincidental findings between the outcome and TCI variables is increased by the multivariable nature of the TCI.

6.2 Discussion (3,4)

These large prospective studies focused on the predictive value of optimism and pessimism to first, work disability with a diagnosis of depression lasting at least 90 days and returning to work, and second, likelihood of initiating antidepressant medication treatment lasting at least 100 days and ending the treatment.

Results show that low optimism associates with the elevated risk of long-term sick leave with depression diagnosis and higher likelihood of antidepressant use. Subjects with low optimism were also more prone not to return to work or not to stop medication during the follow-up. High pessimism associated with higher likelihood starting at least 100 days antidepressant medication and not stopping medication during the follow up. High pessimism did not seem to predict the entering to depression related sick leaves, but in the case of such sick leave it associated with the lower likelihood of returning to work.

Both outcome measures are depression-related in the sense that they are likely to reflect the incidences of depressions in the study population, but are also vulnerable to other factors affecting the ability to work and antidepressant use.

Of the outcome measures the rate of work disability with a diagnosis of depression does not capture all the depressive patients in study population, but by definition should include only patients with depression. The outcome measure of antidepressant medication use does neither capture all depressive patients, but additionally includes subjects with other disorders, since about one-third of antidepressant use is for other indications than depression (Henriksson et al. 2003, Patten et al. 2007, Sihvo et al. 2008), especially for anxiety disorders, sleep problems, and pain (Gardasdottir et al. 2007, Patten et al. 2007).

Optimistic view on future may diminish the perceived need for sickness absence even in the face of great adversity or depressive symptoms (Carver et al. 2010). Pessimistic or hopeless view might have an oppositional affect on expectations concerning the ability to survive in the work after prolonged sick leave. Personality may impact treatment seeking process, either through modifying the subjective threshold of perceived need, or by affecting the actual steps needed for access to treatment (Mojtabai et al. 2002, Spendelov and Jose 2010, Kravitz et al. 2010). Patients' attitudes toward antidepressants have been shown to be a major factor affecting physician decision on prescriptions (Kravits et al. 2005), and it seems likely that patients views affect also the decisions on sick leaves. The effect of optimism on the medication adherence is not known, but it is possible that optimism may enhance placebo effect (Geers et al. 2005, Geers et al. 2007, Krell et al. 2004, Morton et al. 2009) of the medication received, which might lead to contentment and higher compliance to the medication. Higher placebo effect among those with high optimism or low pessimism could also contribute to the associations observed concerning the duration of the sick leaves and medication, if

the elevated likelihood of remission would account for the higher rates of returning to work and cessation of the medication during the follow-up. The accessibility and practises of the health care services evidently also affect the rates of sick leaves and medications use, but it seems unlikely that services would substantially vary in the relation to optimism or pessimism of the employees.

Several previous studies using the one-dimensional concept of optimism and pessimism have found that being in the pessimism-end of the continuum is associated with the elevated risk of developing depressive symptoms (Steward et al. 1997, Segersrom et al. 1997, Brissette et al. 2002, Giltay et al. 2006, Carver and Gaines 1987, Fontaine and Jones 1997, Bromberger and Matthews 1996). Studies examining optimism and pessimism as separate concepts, however, have yielded inconsistent results with regard to depression related outcome measures: significant associations have been reported with only high pessimism (Chang and Bridewell 1998) or neither optimism nor pessimism (Robinson-Whelen et al. 1997). The former study conflicts with the previous studies using unidimensional model for optimism and pessimism, where being in the optimism-end of continuum has repeatedly associated with a reduced likelihood of development or depression. A drawback in the latter study is that baseline depression symptoms were not evaluated, which in addition to short follow-up time (six weeks) limits the longitudinal nature of the study. In our studies only low optimism associated with the likelihood of entering long-term sick leave, whereas low optimism and high pessimism predicted both, but independently, the use of antidepressants. Based on existing evidence, it is still unclear whether, and to what extent, optimism and pessimism differ in their ability to predict the development of depression.

It is possible that lack of optimism predisposes subjects to the development of depression by weakening individual resources to cope with the burden of life and leads to longer periods of work disability. Previous studies have reported that lower optimism is associated with childhood adversities (Korkeila et al. 2004) lower education and discontinuous working history (Ellen et al. 2004). Furthermore, these same variables have been shown to predict the higher probability of developing depression (Danese et al 2009, Richie et al. 2009, Andersen et al. 2009). Thus it is possible that there is a common factor which affects by both lowering optimism, and increasing the risk of depression. This could account for the associations between low optimism and increased depression related work disability and antidepressant use. According to the study by Plomin et al. (1992) individuals with genetic propensity towards low optimism and high pessimism are also at genetic risk for depression and that genetic factors account about a third of the phenotypic associations between optimism, pessimism and depression. High optimism is associated with lower levels of stress and increased social support (Brissette et al. 2002, Hakanen and Lindbohm 2008, Bozo et al. 2009), which may protect against depression and its outcomes, such as work disability and antidepressant use.

Results showing that subjects with more pessimistic or less optimistic view have an elevated likelihood of both prolonged work disability due to depression and antidepressant use, may indicate that the incident disorder observed was, on average, more severe or more treatment resistant than among the subjects with more optimistic or less pessimistic view.

6.3 Methodological considerations

The strong point of the first two studies was the design. There are no earlier studies on these issues using a randomized comparative study design with medication and psychotherapy groups. Of the fifty patients who met the inclusion criteria, 35 remained in the study at 4-months follow-

up. The drop-out rate was modest and the dropouts did not differ in their personality profile from those who remained in the study. Despite that, it is not completely excluded that the loss to follow-up might have had some influence on the results. All the subjects who participated in the 4-moths follow-up had received the therapy which they were randomized into. The psychotherapy was not manualized, thus it is possible that there has been some variability in the procedure. The main limitation in the first two studies was the small size of the study population.

The subjects in the first two studies had a depressive episode when the personality variables were measured. It is possible that prevailing symptoms had an effect on measurements, for example by lowering scores in mature defense style and increasing the trait of Harm Avoidance. Since the idea of the studies was to try to find variables which could help in making treatment decisions, which are generally made during the depressive episode, the possibility of state effect can be considered irrelevant. However, it should be noted that the result of these first two studies may not be generalized to non-depressive populations.

In the third and fourth study the possibility of state effects is more problematic. Although we excluded baseline respondents with any indication of previous or coexisting depression, it is possible that some individual experienced subclinical depression at the baseline. These subjects might have reported lower optimism and higher pessimism scores due to the state effect of depression. In this case, the associations found between optimism, pessimism and the depression related outcomes could have partially accounted for merely worsening of the subclinical depression. If the state effect discussed above would have significantly contributed to the results, the appearance of work disability on those with low optimism or high pessimism should have accumulated in the first year or two of the follow-up, but this was not the case. Thus, the state effect of possibly subclinical depression or depressive symptoms to the results is likely very limited.

The outcome measure of antidepressants medication reveals only the medication purchases from the pharmacies, not the actual use. The compliance in antidepressant use might associate with the optimism or pessimism of the patient and this could have an effect on the recovery and the length of antidepressant treatment. However, the purchases of at least 100 days antidepressant medication suggests that physician (and the patient) has assessed that the patient suffers from such a severe condition, that the medication is needed. According to previous studies, this condition is in two out of three cases depression (Henriksson et al. 2003, Patten et al. 2007, Sihvo et al. 2008).

The third and fourth study benefitted from a large sample size, longitudinal study design and high response rate (73%). Due to the use reliable and comprehensive national registers to define the outcomes, there was practically no loss to follow-up.

Despite the use of extensive registers, the records on work disability may be susceptible to workplace-dependent source of errors, such as incomplete recording. However, it seems unlikely that such errors are related to employees' personality. The outcome measures on risk of and recovery from psychiatric work disability can be considered as clinically highly relevant and it provides complementary evidence for studies based on self-report depression scales.

Study population in both studies was relatively homogenous. All the subjects had been in the working life, they were majority female with the mean age of 43-45 years. In the first two studies subjects with DSM-IV comorbidity or severe somatic illness were excluded. In both studies subjects showed interest in participating the study or survey. Thus, the findings cannot be generalized to different populations or all patients suffering from depression.

7 CONCLUSIONS

Mature defense profile predicted better recovery in the fluoxetine treatment group, whereas no associations between recovery and defense profiles were found in patients treated with short-term psychodynamic psychotherapy.

The negative result in the study focusing on the predictive value of Psychological Mindedness Scale combined with the previous studies with similar results, strongly conflicts with the assumption that high PMS scores are associated with the favorable outcome in psychodynamic psychotherapy in depression. Furthermore, it seems that Psychological Mindedness Scale is not useful in assessing the prognosis or selecting optimal treatment for MDD patients.

The consistent result in previous studies concerning the association between high Harm Avoidance measured with Temperament and Character Inventory and the severity of the depressive state was replicated in this study. This association is likely largely explained by the state effect of depression to the Harm Avoidance. In the fluoxetine treatment group high Reward Dependence, high Self-Directedness and high Cooperativeness associated with higher HDRD scores at 4 months follow-up, whereas no association between personality traits and the depression was found in patients treated with psychotherapy.

In the studies focusing on the predictive value of optimism and pessimism to work disability and antidepressant treatment we found significant associations. Our results showed that subjects with more pessimistic or less optimistic view have an elevated likelihood of both prolonged work disability due to depression and antidepressant use. Thus, generalized favourable or unfavourable expectations seem to predict both the likelihood to develop depression and its course.

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