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Inka Pakkala

Depressive Symptoms, Sense of Coherence, Physical Activity and Genetic Factors among Older People

JYVÄSKYLÄN YLIOPISTO

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ABSTRACT

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The purpose of this study was to investigate factors in middle age associated with depressive symptoms in old age and the potential factors underlying physical activity and depressive symptoms in middle and old age. In addition, the effects of two separate physical activity interventions on depressive symptoms and sense of coherence among older persons were studied.

Four different datasets were utilized. The Finnish Twin Study on Aging comprised 103 monozygotic (MZ) and 114 dizygotic (DZ) 63- to 76-year-old female twin pairs. The Finnish Twin Cohort study comprised 1327 MZ and 2467 DZ twin pairs with a mean age of 43.7 years. The SCAMOB study was a 2-year physical activity counseling randomized controlled trial (RCT) among older adults (n=624). The Asymmetry study was a 12-week RCT on the effects of resistance training among older persons with hip fracture history (n=46).

Personality in middle age was associated with depressive symptoms 28 years later, with extraversion protecting from later depressive symptoms and neuroticism increasing the risk. No effect on later depressive symptoms of physical activity, lifestyle habits or diseases in middle age was found. The relationship between neuroticism and depressive symptoms was partly the result of common genetic factors for both traits. In twins in middle and old age increased leisure time physical activity was associated with decreased depressive symptoms, but was not a result of common genetic factors that would influence both traits. The physical activity counseling intervention decreased depressive symptoms among participants with minor depressive symptoms at baseline. No effect of the intervention was found among those with no depressive symptoms or more severe depression at baseline. In addition, the 12-week intensive strength-power training among older people with a hip fracture history had no effect on participants' sense of coherence.

This study stresses the important effect of personality in middle age on later depressive symptoms. The results also suggest that physical activity counseling for older adults may prevent depressive symptoms, but should be studied more closely in different target groups. With regards to strength-training interventions among frail older people, interventions including psychological elements also warrant further studies.

Keywords: Aging, depressive symptoms, sense of coherence, physical activity, twins, genetic factors

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LIST OF ORIGINAL PUBLICATIONS

The thesis is based on the following original publications, which will be referred to by their Roman numerals.

I Pakkala I, Read S, Kaprio J, Koskenvuo M, Kauppinen M, Rantanen T. 2010. Genetic contribution to the relationship between personality and depressive symptoms among older women. Psychological Medicine 40, 1357-66.

II Pakkala I, Rantanen T, Read S, Kauppinen M, Rose RJ, Koskenvuo M, Kaprio J. Leisure time physical activity and depressive symptoms. Submitted for publication.

III Pakkala I, Read S, Leinonen R, Hirvensalo M, Lintunen T, Rantanen T. 2008. The effects of physical activity counseling on mood among 75-to 81-year-old people: A randomized controlled trial. Preventive Medicine 46, 412-418.

IV Pakkala I, Read S, Sipilä S, Portegijs E, Kallinen M, Heinonen A, Alen M, Kiviranta I, Rantanen T. The effects of an intensive strength-power training on sense of coherence among 60-85-year old people with a hip fracture: A randomized controlled trial.
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ABBREVIATIONS

A	Additive Genetic Effect
AIC	Akaike's information criterion
ANOVA	Analysis of Variance
Asymmetry	The Effects of Strength Training on Muscle Strength, Asymmetry in Lower Limb Muscle Strength and Mobility in Older Men and Women with History of Hip Fracture
BDI	Beck Depression Inventory
C	Shared Environmental Effect
CES-D	Center for Epidemiologic Studies Depression Scale
CI	Confidence Interval
DZ	Dizygotic
D	Dominant Genetic Effect
E	Individual Environmental Effect
EPI	Eysenck Personality Inventory
FITSA	Finnish Twin Study on Ageing
GEE	Generalized Estimating Equation
ICC	Intra-class Correlation Coefficient
LTPA	Leisure Time Physical Activity
MET	Metabolic Equivalent
MMSE	Mini-Mental State Examination
MZ	Monozygotic
OR	Odds Ratio
RCT	Randomized Controlled Trial
SCAMOB	Screening and Counseling for Physical Activity and Mobility in Older People
SD	Standard Deviation
SEM	Standard Error of the Mean
SOC	Sense of Coherence
WHO	World Health Organization
ZDS	Zung Self-Rating Depression Scale

CONTENTS

1 INTRODUCTION

Depressive symptoms are one of the most frequently occurring mental health problems among the older population. Depressive symptoms are also a frequent cause of emotional and physical suffering, and decrease the quality of life and increase the risk for death among older adults (Blazer 2003). Although a large body of knowledge exists on the factors underlying depressive symptoms (Blazer 2003, Blazer & Hybels 2005), the etiological picture of depression and depressive symptoms in late life has remained unrevealed (Fiske et al. 2009). As the number of older adults is increasing rapidly, their specific health care problems demand greater attention.

In general, physical activity decreases the risk for all-cause mortality among the elderly (Sundquist et al. 2004), is associated with higher levels of physical functioning (Hillsdon et al. 2005), and has consistently been found to be one of the most robust behavioral determinants of healthy aging (Peel et al. 2005). With respect to depressive symptoms, associations between lack of physical activity and increased depressive symptoms in old age have been confirmed in several cross-sectional (Lindwall et al. 2006), longitudinal (Strawbridge et al. 2002) and interventional studies (Penninx et al. 2002, Singh et al. 2005). Although studied widely, only a few studies have been investigated the origins of this association taking into account the genetic variation among individuals (De Moor et al. 2008). Understanding the underlying mechanisms in the association between physical activity and depressive symptoms could be useful in physical activity counseling in seeking to prevent mood problems among sedentary people at increased risk for depressive symptoms.

Despite the significance of physical activity in the preservation of health and functioning, the proportion of adults engaging in moderate or vigorous levels of physical activity declines with age (Hirvensalo et al. 1998, Troiano et al. 2008). In particular among older people with decreased psychological well-being, the factors associated with physical activity are complex and low mood is often associated with poor participation in physical activity programs (Mather et al. 2002). Physical activity counseling is an example of a low-cost educational intervention aiming to promote physical activity among older adults. Tailoring

physical activity counseling individually with an emphasis on self-efficacy for more active behavior has proven useful and highly applicable in physical activity counseling interventions (Kerse et al. 2005, Pinto et al. 2005). So far, the beneficial effects of physical activity counseling interventions on increasing physical activity among community-dwelling older adults have been documented in a number of recent studies (Kerse et al. 1999, Stewart et al. 2001, Dubbert et al. 2002, Elley et al. 2003, Pinto et al. 2005, Kolt et al. 2007, Dubbert et al. 2008). In addition, some positive effects on general health (Dubbert et al. 2008) and a decrease in hospitalization (Kerse et al. 2005) have also been reported. With respect to psychological outcomes some studies have found physical activity counseling to improve quality of life (Dubbert et al. 2000, Elley et al. 2003,) whereas others have found interventions to have no effects (Kerse et al. 1999, Dubbert et al. 2002, Kolt et al. 2007). However, whether physical activity counseling, by increasing physical activity, alleviates depressive symptoms has been little studied (Salminen et al. 2005, Kerse et al. 2010).

Whereas the majority of scientific research has examined the impact of physical activity on negative psychological states such as depression and depressive symptoms, the effects of physical activity on positive affects have been rarely studied (Kanning & Schlicht 2010). Especially among older people with disabilities, improved well-being is associated with higher rates of recovery and increased motivation towards rehabilitation programs (Proctor et al. 2008). For instance, among older hip fracture patients psychological factors such as depressive symptoms, quality of life and sense of coherence are nowadays thought to be important in the recovery from hip fracture, but information on how various physical activity interventions impact on these factors remains limited (Crotty et al. 2010).

In old age, changes in health status can either happen gradually over a long time period due to damaging physical and social environmental exposures or develop suddenly due to events such as diseases or accidents. The present study, utilizing longitudinal twin cohort studies, was conducted to obtain knowledge about the factors in middle age associated with depressive symptoms in old age and the potential factors underlying physical activity and depressive symptoms among adults in middle and old age. Two experimental studies were conducted to investigate the effects of physical activity interventions on depressive symptoms and sense of coherence among older people.

2 REVIEW OF THE LITERATURE

2.1 Depressive symptoms

Depression and depressive symptoms are major health problems among the elderly population world-wide. Estimates of the prevalence of depression vary depending on whether the figure reflects the clinical condition or depressive symptomatology (Heikkinen & Kauppinen 2011). Depressive symptoms are associated with serious negative outcomes (Blazer 2003) and significantly decrease quality of life in older adults (Goldney et al 2004). In this thesis, the main focus is on depressive symptoms that do not meet the criteria for a diagnosis of major depressive disorder.

2.1.1 Depressive symptoms in old age

Definition and presentation of depressive symptoms

In the literature, the definition of the term depression is complicated because of the inherent ambiguity involved. The concept of depression may refer to depressive mood, depressive symptoms or major depression, also called clinical depression. There is an ongoing debate about whether depression is a continuum or if there is a qualitative difference between mild depressive symptoms and major depression (e.g. Clark & Beck 1999). Among older people major life changes, such as losing a partner, or friend or having to leave a home of many years often cause natural grief and sorrow, which are normal temporary reactions to the inevitable losses and hardships of life (Fiske et al. 2009). However, unlike normal sadness, depressive symptoms and clinical depression are more long-standing conditions which in many cases do not disappear by themselves and must be treated (Fiske et al. 2009).

In older adults depression and depressive symptoms may present somewhat differently than in younger adults. Sleep disturbances, loss of appetite, fatigue, psychomotor retardation, loss of interest in living, and hopelessness about the future may be more prevalent in late-life depression than in depres-

sion in younger or middle-age adults. Subjective complaints of poor memory and concentration are also common among depressed older adults. (Fiske et al. 2009.) Slower cognitive processing speed and executive dysfunction are frequent findings from objective testing (Butters et al. 2004). Variants of major depression specific to older age have also been proposed, where one important variant is the "depression-executive dysfunction syndrome". In this syndrome, impairment in cognitive performance is typically emphasized while vegetative symptoms are less common (Alexopoulos 2005).

Epidemiology of depressive symptoms

High levels of depressive symptoms are common among the elderly population and a large number of studies have investigated the prevalence of depressive symptoms in later life. Among community-dwelling older adults reports of the prevalence of depressive symptoms have ranged from approximately 8% to 20% (Blazer 2003, Copeland et al. 2004, Goldney et al. 2004, Djernes 2006, Hidaka et al. 2011) and even higher prevalence rates have been reported in Southern European samples (Zunzunegui et al. 1998, Minicuci et al. 2002). A large part of the variation in the prevalence rates might be explained by differences in study measures and study populations, but cultural differences may also influence the reporting and perception of depressive symptoms (Blazer 2003). Whether the prevalence rates of depressive symptoms increase among the oldest old age groups has also been studied, but the results have shown contradictory results, some studies showing higher rates among the oldest old (Heikkinen & Kauppinen 2004) and some not (Haynie et al. 2001). With regard to gender differences among older people a large number of studies have reported higher prevalence of depressive symptoms in women than in men (Zunzunegui et al. 1998, Djernes 2006, Zunzunegui 2007), although contradictory results also exists (Fuhrer et al. 1999, Haynie et al. 2001). High rates of depressive symptoms are also common in particular subsets of older people including residents of long-term care facilities (Blazer 2003, Jongenelis et al. 2004, Djernes 2006) and older adults with other medical conditions (e.g. Blazer 2003).

Although the prevalence of depressive symptoms among older people shows higher rates compared to middle-age population, the prevalence of major depression is considerably lower (e.g. Blazer 2003). In community samples of adults aged 65 and older, the prevalence of major depression ranges from 1-5% in most large-scale epidemiological investigations internationally, with the majority of studies reporting prevalences at the lower end of the range (Djernes 2006, Fiske et al. 2009).

Consequences of depressive symptoms

Among older people depressive symptoms are associated with many negative outcomes. Multiple studies have demonstrated that older people with depressive symptoms are more likely to be and become disabled (Penninx et al. 1998, Schillerstrom et al. 2008, Carbonare et al. 2009, Covinsky et al. 2010). The associations have been confirmed among both men and women, using both self-

reported and performance-based measures and with shorter and longer follow-up times (Penninx et al. 1999, Carbonare et al. 2009, Covinsky et al. 2010). According to several studies depressive symptoms have also been frequently associated with increased risk for coronary heart disease (Ariyo et al. 2000, Marzari et al. 2005) stroke (Arbelaez et al. 2007) and cardiovascular disease mortality (Gump et al. 2005). Depressive symptoms have also been reported to increase the risk for mild cognitive impairment (Barnes et al. 2006), dementia and Alzheimer disease (Saczynski et al. 2010). In addition, depressive symptoms decrease the quality of life of older people (Webb et al. 2011) and are associated with negative attitudes towards aging (Chachamovich et al. 2008) and poorer self-rated health (Han 2002). Late-life depressive symptoms are also associated with increased use of hospital and outpatient medical services and increased risk for suicide (e.g. Blazer 2003).

2.1.2 Assessing depressive symptoms

There is no universal agreement among clinicians and clinical investigators as to what exactly constitutes clinically significant depression or depressive symptoms and what its components are. However, there are several commonly used scales for both clinical diagnoses and population screening.

When assessing major depression for clinical purposes, a diagnostic convention, based on the Diagnostic and Statistical Manual for Mental Disorders (4th edition; DSM-IV, American Psychiatric Association 1994) and International Classification of Diseases (ICD-10, WHO 1992) criteria, can be used. According to DSM-IV criteria, major depression is diagnosed, when one or both of the two core symptoms, depressed mood and lack of interest, are present together with four or more of the following symptoms for at least two weeks: feelings of worthlessness or inappropriate guilt; diminished ability to concentrate or make decisions; fatigue; psychomotor agitation or retardation; insomnia or hypersomnia; significant increase or decrease in weight or appetite; and recurrent thoughts of death or suicidal ideation (APA 2000). The ICD-10 avoids the term major depression and has three degrees of depression severity: mild, moderate and severe, where the symptoms are comparable with DSM-IV symptom criteria.

A common technique for assessing depressive symptoms that do not meet the criteria for major depression, is the use of different depressive symptoms scales, most of which are designed for self-ratings. The Center for Epidemiologic Studies Depression Scale (CES-D; Radloff 1977), the Beck Depression Inventory (BDI; Beck et al. 1961) and the Zung Self-Rating Depression Scale (ZSDS; Zung 1965) are among the most frequently used self-rating scales measuring depressive symptoms among older people. The CES-D scale has been used as a screening instrument for depressive symptoms in a large number of community-based studies of elderly people (Beekman et al. 2002) and its sensitivity and specificity for depression have been found to be very good in this population (Beekman et al. 1997, Lyness et al. 1997). The CES-D scale consists of 20 items primarily measuring affective and somatic aspects of depression. The total score of the CES-D scale ranges between 0 and 60 points. To identify those with clini-

cally relevant depressive symptoms in the general population, the cutoff score of 16 is normally used (Radloff 1986).

The BDI scale, although initially developed to measure the intensity or depth of the depressive symptomatology in patients with psychiatric disorders, is now widely used as a screening instrument to detect depressive symptoms in clinical practice and research projects (Beck et al. 1988). The BDI scale comprises 21 items covering emotional, behavioral and somatic symptoms of depression, which are rated on a four-point scale of severity from zero to three with a total score ranging from 0 to 63 (Beck et al. 1961). The Zung Self-Rating Depression Scale is a self-report test developed to assess depression among patients admitted to a psychiatric hospital, but also for non-institutionalized elderly (Zung et al. 1965). Although in clinical research the primary use of the ZSDS has been to monitor treatment effectiveness, it has also been used as a screening test in general medical practice and for research purposes (Zung 1990). In the ZSDS, depressive symptoms are classified into four categories of symptoms: affective, somatic, psychomotor and psychological. The ZSDS scale consists of 20 items, which are rated on a four-point severity scale with the total score ranging from 20 to 80. In addition to these scales, other less frequently used scales also exist and shortened versions of the older rating scales have also been developed.

2.1.3 Factors underlying depressive symptoms in old age

Although depressive symptoms and disorders are frequent causes of emotional and physical suffering, the origins of late-life depressive symptoms present a paradox to investigators and clinicians. The etiological factors underlying depressive symptoms in old age are multiple and range across different domains (e.g. Blazer & Hybels 2005). Therefore, a biopsychosocial model of etiology is especially applicable to the elderly because the model provides a dynamic framework for building scientific hypotheses about the etiology of depressive symptoms. In the biopsychosocial model, the multiple biological, psychological and social causes of depressive symptoms are not competing but complementary and almost always transactional (Lindau et al. 2003). Although depressive symptoms and major depression in older adults are often distinguished in the literature, there seem to be no systematic underlying differences in etiologies between these two conditions (Blazer & Hybels 2005. Therefore factors underlying major depression are also discussed below.

Biological factors underlying depressive symptoms

Biological risk factors for depressive symptoms are particularly important in old age, largely because of age-related changes that make them more common in older adults (e.g. Fiske et al. 2009). *Serotonin activity* decreases dramatically in a variety of brain regions through midlife, but there is less decrease from midlife to old age (Blazer 2003). However, this underactivity of serotonergic neurotransmission has been hypothesized to be one of the risk factors for old age depressive symptoms (Blazer & Hybels 2005). *Endocrine changes* such as hypersecretion of corticoptropin-releasing factor (CRF) have also been reported

to be associated with late-life depressive symptoms (Arborelius et al. 1999). In older men with depressive symptoms lower testosterone levels have been detected compared to men without these symptoms (Seidman et al. 2001). In women hormone replacement has been associated with some improvement in mood (Sherwin & Gelfand 1985). However, as regards to the association between depressive symptoms, low testosterone levels and hormone replacement therapy, the scientific evidence remains weak and more research is needed.

Late life depressive symptoms and depression frequently occur in the context of medical illness. Although any serious or chronic condition can produce a depressive reaction, the conditions believed to be most strongly associated with depressive symptoms include *cardiac and cerebrovascular diseases* and *neurological conditions* (Fiske et al. 2009). Depression and depressive symptoms are common in patients with coronary heart disease and other cardiac diseases. It has been estimated that approximately one fifth of patients have major depression or depressive symptoms following acute myocardial infarction. (e.g. Krishnan 2002.) With regard to stroke, clinical and epidemiological studies have found major depression to be a frequent outcome of stroke, occurring in nearly one-third of all ischemic stroke survivors (Tiemeier 2003, Blazer & Hybels 2005). There is also substantial co-morbidity of major depression, depressive symptoms and dementia, and differential diagnosis is often challenging. Individuals with late onset major depression with cognitive impairment are especially at risk for developing Alzheimer's disease, with as many as 40% developing dementia within three to five years (Alexopoulos 2005). Depressive symptoms and disorders in late life often co-occur with other psychiatric disorders as well (Blazer & Hybels 2005). For example *anxiety* commonly co-exists with depressive symptoms and has also been suggested to be a risk factor for late life depressive symptoms (Hettema et al. 2006). In addition to various illnesses, depression or depressive symptoms in older adults may also be caused by certain medications e.g. beta blockers, corticosteroids or certain cancer medications (Alexopoulos 2005).

Female gender is one of the most important risk factors for depression and depressive symptoms (e.g. Takkinen et al. 2004, Inaba et al. 2005, Heun & Hein 2005, Djernes 2006, Hölzel et al. 2011). Many factors have been suggested to explain these differences, such as selective survival as men often die earlier and mortality may be affected by genetic factors (Blazer & Hybels 2005). More frequent exposure to stressful life events due to selective survival have also been reported to explain the gender differences in depressive symptoms (Kendler et al. 2001). Older women have also found to be more sensitive to the depressogenic effects of low social support compared to older men, suggesting important gender differences in the pathways of depression risks (Kendler et al. 2005). However, despite strong scientific evidence, other studies have not confirmed these findings (Haynie et al. 2001) and it has been suggested that the increased risk among women might be an artifact depending on depressive symptoms measures that do not catch symptoms typical for older men (Bogner & Gallo 2004).

Psychological factors underlying depressive symptoms

Whereas many biological factors underlying older adults' depressive symptoms are specific to old age, psychological factors increasing the risk for depressive symptoms in late life include many of the same characteristics that are related to depression earlier in the lifespan.

There is accumulating evidence that people with certain types of *personality* are at higher risk for developing depressive symptoms. The most commonly studied traits in relation to depressive symptoms include *neuroticism and extraversion* (e.g. Kendler et al. 1993, Fanous et al. 2002). Several studies have suggested that the personality trait most closely related to depression and depressive symptoms is neuroticism (Roberts & Kendler 1999, Kendler et al. 2006, Steunenberg et al. 2006). Neuroticism and depressive symptoms have been associated in clinical (Duberstein & Heisel 2007), family (Duggan et al. 1995), twin (Kendler et al. 2006, Fanous et al. 2007) and general population-based (Romanov et al. 2003, Jylhä & Isometsä 2006) studies. The association between extraversion and depression has instead been controversial as some studies have found extraversion to protect from later depressive symptoms (Jylhä et al. 2006), while other studies have found no associations (Kendler et al. 1993).

Perhaps the most dominant psychological model of depression is the *model of cognitive distortions* (Beck 1987). According to this theory, depressed individuals may overreact to life events or misinterpret these events and exaggerate their adverse outcome. Devanand and colleagues (2002) found in their study that older adults with major depression reported more recent life events with negative impact and particularly interpersonal conflicts compared to elders' with dysthymia and healthy controls. Also ineffective coping styles e.g. rumination and avoidance are associated with increased depression and depressive symptoms risk (Kraaij et al. 2002, Garnefski & Kraaij 2006).

Social factors underlying depressive symptoms

A number of social stressors have been proposed as contributing to late-life depressive symptoms and depression including e.g. stressful life events, bereavement, chronic stress and impaired social support. These factors are not unique to older adults, although their importance may increase in very old age, when greater losses are faced in the context of fewer resources (Blazer & Hybels 2005, Fiske et al. 2009).

The association between *stressful life events* and depressive symptoms is complicated, and in some cases, e.g., long-standing vulnerabilities might modify the effects of stressful events on depression (Moos et al. 2005, Fiske et al. 2009). For example, in a study by Lenze and colleagues (2005), the serotonin transporter gene promoter region was associated with increased risk for depression following hip fracture in older adults. Also, cognitive styles influence individuals' responses to stressful life events, which responses might vary according to the interaction between cognitive style and type of event (Mazure et al. 2002). Also, the number of simultaneous stressful life events increases the risk for depressive symptoms (Kraaij et al. 2002).

A stressful event that occurs with greater frequency to older people and is associated with increased risk for depressive symptoms is *bereavement.* According to a large meta-analysis in adults aged 50 and older, bereavement more than tripled the risk for depression (Cole & Dendukuri, 2003). However, there is also evidence that older adults cope better with such loss and use more effective adaptation mechanisms compared to younger adults, as the loss of the spouse is more probable life event in old age (Torges et al. 2008).

Impaired social support increases the risk for depressive symptoms in older adults (e.g. Blazer 2003, Blazer & Hybels 2005). Instead, satisfaction with social support can mediate between risk factors and the onset of depressive symptoms, as in a study by Taylor & Lynch (2004) who found social support to mediate the relationship between disability and depressive symptoms over time. In general, it appears that it is the quality, not quantity, of social support that is important in the development of depressive symptoms, and that the effects of these variables may vary based on factors associated with both the person and the context (Fiske et al. 2009).

2.1.4 Genetic effects on depressive symptoms in old age

Previous twin studies have indicated that genetic factors are involved in the etiology of depressive symptoms and depression among older people (Gatz et al. 1992, McGue & Christensen 1997, Carmelli et al. 2000, Sullivan et al. 2000, Jansson et al. 2004, Kendler et al. 2006). However, there is a wide heterogeneity in the genetic and environmental contributions to depressive symptoms depending on the study populations and depressive symptoms measures used, suggesting that not all depressive symptoms appear to be equally influenced by genetic factors. In their twin study, Gatz and colleagues (1992) utilized the factor structure of the CES-D scale and found that genetic influences accounted for 16% of the variance in total depression score and 19% of psychosomatic and somatic complaints. In contrast, genetics contributed a minimal amount to the variance in reports of depressed mood and psychological well-being. The variability of the genetic effects on different dimensions of depressive symptoms was also confirmed in a study by Jang and colleagues (2004). In their study, a general population-based sample of twins completed three separate depressive symptoms scales, from which 14 factors representing a wide range of depressive symptomatology were identified. The heritability estimates across different factors ranged between 0% and 35%, with the highest heritability estimates found in the symptoms describing endogenous or physiological functions and lowest in negative affect and tearfulness. With respect to major depression, in a meta-analysis of twin studies with participants' average age ranging from 34 to 53, the overall heritability estimate was 37%, with almost no effect of shared environment, but a substantial effect of the unique environment (Sullivan et al. 2000).

There are also studies that have addressed the issue of gender differences in depression and depressive symptoms using a twin study design. Kendler and colleagues (2001) found higher heritability for clinical depression in women

compared to men as well as an indication of separate genes acting on the liability to clinical depression. Also, in a twin study by Jansson and colleagues (2004), the heritability was moderate in elderly women both for depressive symptoms (29%) and depressed state (49%) but limited in elderly men (14% and 7%, respectively).

The effects of ageing on the heritability of depressive symptoms have been rarely studied, and longitudinal studies investigating changes in the contribution of genetic influences are few. Carmelli and colleagues (2000) found in their longitudinal study that the heritability of depressive symptoms increased during a 10-year follow-up from 25% to 55% among older male twins. In addition, they found that the stability of symptoms over the follow-up period was primarily due to the continuity of genetic influences.

As depressive symptoms may not be a homogenous phenomenon but rather a representation of a multivariate factor with varied genetic and environmental sources underlying its different dimensions, the studies on specific genetic markers for late life depression have not yielded unambiguous results (e.g. Blazer & Hybels 2005). In addition to the multifactorial background of depressive symptoms, there is often considerable comorbidity between depressive symptoms and other diseases, which might make the finding for specific genetic markers for depressive symptoms even more difficult.

2.2 Sense of coherence

2.2.1 Theory of sense of coherence

Sense of coherence (SOC), according to Antonovsky's theory, is a way of seeing the world that facilitates successful coping with stressors in all cultures. Contrary to the traditional pathogenic models, where the interest is in the origins of sickness, Antonovsky formulated a salutogenic model where instead, the interest is in the factors promoting movement toward the healthy end of the continuum. According to Antonovsky, SOC does not represent a fixed way of behaving in a certain way in a given situation, but rather reflects a flexible orientation to life that promotes successful coping (Antonovsky 1979, Antonovsky 1987).

According to Antonovsky's definition (Antonovsky 1987) SOC is:

> "a global orientation that expresses the extent to which one has a pervasive, enduring though dynamic feeling of confidence that 1) the stimuli, deriving from one's internal and external environment in the course of living are structured, predictable and explicable; 2) the resources are available for one to meet the demands posed by these stimuli; 3) these demands are challenges, worthy of investment and engagement".

SOC thus has three main components, which are: comprehensibility, manageability and meaningfulness (Antonovsky, 1979, Antonovsky 1987).

According to Antonovsky (1979), the attainment of full strength SOC is dependent on the presence of generalized resistance resources, at least during

the developmental process. Generalized resistance resources refer to such factors as sufficient income, high education, intelligence, preventive health orientation and social support, which are effective in dealing with the demands of everyday life and can be applied in many situations, not just to solve certain kinds of problems. The more resistance resources an individual has, the better are her or his chances developing a strong SOC (Antonovsky 1979, Antonovsky 1987).

In the theory, SOC development begins in early childhood and ends at around the age of 30 (Antonovsky 1987). SOC is assumed to be stable thereafter, although this supposition has attracted much criticism and scientific evidence against the stability of SOC has been increasingly reported (e.g. Volanen et al. 2007, Nilsson et al. 2010).

SOC has been mostly studied among adolescents and the working age population, whereas studies that include elderly people are scarce. As in old age a decrease in individuals' generalized resistance resources and an increase in the probability of negative life events and disability risk might occur, more precise knowledge of how to increase SOC in older adults is needed.

2.2.2 Assessing sense of coherence

For the purposes of empirical exploration, Antonovsky put his theory into practice and developed a 29-item SOC questionnaire (SOC-29) from which a shorter version comprising 13 questions (SOC-13) was later derived. The SOC questionnaire is a summated Likert-type scale with seven response categories ranging from 1-7. Fourteen items are negatively stated and must be reversed before the total score is computed. The total score range is thus between 29 and 203, with higher scores indicating a higher sense of coherence. According to Antonovsky 11 items in the scale reflect comprehensibility, ten items manageability and eight items meaningfulness. In the 13-question version the corresponding numbers are five, four and four, respectively. (Antonovsky 1987.) Originally Antonovky's intention was to use the SOC questionnaire as a global measure, and not examine the three subscales separately. Despite this, many studies report mean values for the three subscales, while no general pattern has emerged regarding the relative importance of the three dimensions (Erikson & Lindström 2005).

The sense of coherence questionnaire is a widely used self-report measure the reliability and validity of which have been demonstrated in heterogeneous samples cross-culturally. The instrument has been examined in healthy populations from children to older adults, in different groups of patients and professionals and many areas of practice from health services to research settings (Eriksson & Lindström 2006, Naaldenberg et al. 2011). According to a systematic review by Erikson & Lindström (2005), Cronbach's alpha for SOC-29 version range between 0.70 and 0.95 and for SOC-13 between 0.70 and 0.92.

2.2.3 Sense of coherence in association with health and aging

The beneficial effects of strong SOC on several health outcomes have been well documented in earlier studies (e.g. Eriksson & Lindström 2006). According to longitudinal studies a strong SOC has been reported to predict better health (Suominen et al. 2001) and decrease the risk for chronic conditions e.g. diabetes (Kouvonen et al. 2008) and coronary heart diseases (Poppius et al. 1999) among population-based samples. Studies in which only older people have been included have also confirmed a positive association between a strong SOC and better health status (Lundman et al. 2010). There is also evidence of an association between high level of SOC and decreased mortality rates (Surtees et al. 2003, Lundman et al. 2010). Several studies have confirmed the predictive validity of high SOC for good quality of life among various study populations (e.g. Eriksson & Lindström 2007). SOC is also strongly and negatively related to depression and depressive symptoms, suggesting that the stronger SOC is, the fewer are the symptoms of depression (Luutonen et al. 2011). SOC has also been associated positively with self-esteem and self-efficacy (Eriksson & Lindström 2006) and negatively with neuroticism (Feldt et al. 2007) all of which are associated with health and well-being (Fiske et al. 2009).

Multiple pathways exist through which SOC has been suggested to improve individuals' health. First, a strong SOC is assumed to be a major coping resource for maintaining good health as it decreases the likelihood that the demands encountered by the individual will be perceived as stressful and threatening (Antonovsky 1987). This hypothesis was proven correct in a study by Richardson & Ratner (2005), who found that strong SOC buffered the impact of recent stressful life events on self reported health. Second, according to Antonovsky, people with strong SOC will engage in adaptive health behaviours more often than those with a weak SOC. This was confirmed in a study by Wainwright and colleagues (2007), where a strong SOC was associated with more health promoting behaviour choices, independently of social class and education. Finally, the third route between SOC and health has been hypothesized to go through the central nervous system, as an individual with a strong SOC also mobilizes neuroimmunological and neuroendocrinological resources to prevent damage to the organism (Antonovsky 1987).

Old age presents a high risk for both functional decline and several types of diseases; these factors in turn might have effects on individuals' level of SOC. In earlier research SOC has been reported to decrease after severe physical trauma, such as a severe accident (Schnyder et al. 2000, Snekkevik et al. 2003) and myocardial infarction among patients of different ages (Bergman et al. 2011). Although hip fractures are known to negatively influence many aspects of older adults' health (e.g. Lenze et al. 2007) the effects of hip fractures on older adults' sense of coherence have not been studied earlier .

While the association between SOC and various dimensions of health has been examined among heterogeneous study populations, studies with a specific focus on older people remain few. As increasing numbers of older persons are

living longer, and most have at least one chronic health problem, recognizing and enhancing the factors associated with better health and coping is important.

2.3 Depressive symptoms and physical activity

2.3.1 Physical activity in old age

Physical activity is defined as any bodily movement produced by the skeletal muscles that increase energy expenditure above the basal level. Exercise, a subcategory of physical activity, has been defined as physical activity that is planned, structured and repetitive for the purposes of conditioning any part of body. Physical fitness, in contrast with physical activity, is a set of attributes or characteristics that people have or achieve that relate to the ability to perform physical activity. The characteristics of physical fitness can further be separated into health-related, e.g. cardiovascular endurance, and skill-related, e.g. coordination, components (Caspersen 1989).

The physical activity recommendations for older adults by The American College of Sports Medicine and the American Heart Association emphasize the importance of moderate-intensity aerobic activity, muscle-strengthening activity, reduced sedentary behavior and risk management in the promotion of physical activity in older adults. According to the statement, physical activity should be one of the highest priorities for preventing and treating disease and disablement in older adults (Nelson et al. 2007).

Among older people, the most popular forms of physical activity include walking, home exercises and gardening (Rasinaho et al. 2006, Ashe et al. 2009). Physical activity among older people can also include home-based or centre-based activities of which the first may be more attractive to disabled older people, who have difficulties accessing sport facilities (King et al. 1992). The determinants of physical activity behavior consist of various physiological, psychosocial and environmental factors which become even more important in old age (DiPietro 2001, Trost et al. 2002). Among older people, the most frequently reported motives for physical activity include health maintenance and social relationships, whereas poor health, pain and lack of interest are among the most commonly reported obstacles to a more physically active lifestyle (Cohen-Mansfield et al. 2003, Rasinaho et al. 2006).

Despite the significance of physical activity in the preservation of health and functioning, the proportion of adults engaging in moderate and vigorous levels of physical activity declines with age (Hirvensalo et al. 1998, Troiano et al. 2008). In the light of these observations, effective evidence-based strategies to encourage older adults to be physically active are indisputably needed.

2.3.2 Associations between depressive symptoms and physical activity in old age

Associations according to observational studies

There is a general belief that physical activity and exercise have positive effects on depressive symptoms and depression. A great number of studies have reported an association between physical activity and psychological well-being among older adults (Barbour & Blumenthal 2005, Sjösten & Kivelä 2006, Teychenne et al. 2008, Ströhle 2009). Epidemiological studies have generally found that more frequent physical activity is associated with decreased risk for depression and depressive symptoms (e.g. Strawbridge et al. 2002, Wise et al. 2006). Several cross-sectional and longitudinal studies have confirmed the positive association between physical activity and depressive symptoms among population-based samples of people of different ages (Hassmen et al. 2000, De Moor et al. 2006), samples consisting only of older adults (Lee & Russell 2003, Lindwall et al. 2006) and of older adults with physical disabilities at baseline (Strawbridge et al. 2002). However, the results on gender differences in the association between physical activity and depressive symptoms are contradictory. Some studies have found physical activity to prevent depressive symptoms among both men and women (Brown et al. 2005, Lindwall et al. 2006), whereas others have found a positive association only among older men (Bhui & Fletcher 2000). Lack of a long-term protective effect of exercise against depressive mood have also been reported, as in a study by Kritz-Silverstein and colleagues (2001), where exercise was found to be cross-sectionally but not prospectively associated with less depressed mood among older persons.

With respect to the optimal effective dose of physical activity on depressive symptoms, some studies have found that vigorous physical activity is more strongly associated with decreased likelihood of depression than less intensive exercise (Lee & Russell 2003, Wise et al. 2006) whereas others have found no associations between physical activity of any intensity and depression (Bhui & Fletcher 2000). In a study by Lindvall and colleagues (2006), among older women, depression scores actually increased to some degree among the most active exercisers. In contrast, it has also been found that decreased physical activity intensity may predict increasing risk for depressive symptoms over time among older adults (Lampinen et al. 2000).

Associations according to experimental studies

Whereas observational studies do not enable conclusions to be drawn on causality between physical activity and depressive symptoms, intervention studies provide insights into the potential causal role of physical activity in reducing depressive symptoms among older adults. Several intervention studies have examined the effects of different forms of physical activity and exercise on depressive symptoms among older adults (Barbour & Blumenthal 2005, Netz et al. 2005, Sjösten & Kivelä 2006, Teychenne et al. 2008, Windle et al. 2010). Interventions specifically targeted at enhancing mood among elderly people have included, among others, resistance and strength training with varied intensities

(Singh et al. 1997, Singh et al. 2001), aerobic exercise such as walking programs (Penninx et al. 2001, Motl et al. 2005), and other forms of exercise such as Tai Chi (Wang et al. 2010). Positive effects of physical activity interventions have been reported among both healthy (Motl et al. 2005), and frail (Timonen et al. 2002) older populations and among elderly persons with clinical depression or depressive symptoms at baseline (Penninx et al. 2002, Singh et al. 2005) using various forms of exercise from resistance training to low intensity of walking programs (Netz et al. 2005, Teychenne et al. 2008).

As with the observational studies, there is no consensus in the experimental research about the optimal dose and format for exercise therapy that would be most beneficial for mood. Some studies have found high intensity resistance training to be most effective (Singh et al. 2005) whereas in other studies aerobic training has produced the best results (Penninx et al. 2002). With respect to other dose-response issues concerning exercise duration, frequency and length of session, the results to date are inconsistent and warrant further investigation (Netz et al. 2005).

Proposed mechanisms for the physical activity-depressive symptoms relationship

While the research on the relationship between exercise and depressive symptoms has yielded fairly consistent findings, the mechanisms underlying the antidepressant effects of exercise remain unclear, and several hypotheses have been suggested (Craft & Perna 2004). *Physiological mechanisms* include, for instance, the monoamine hypothesis, according to which exercise corrects the dysregulation of the central monoamines believed to lead to depression and depressive symptoms (Barbour & Blumenthal 2005). According to the endorphin hypothesis, exercise has positive effects on depression due to increased release of β-endorphins following exercise which in turn is related to positive mood and overall enhanced sense of well-being (Sjösten & Kivelä 2006). Rise in a core body temperature and of specific brain regions, such as the brain stem following exercise can lead to an overall feeling of relaxation and reduction in muscular tension through what the well-being is increased according to thermogenic hypothesis (Craft & Perna 2004). Increased level of physical fitness after exercise training might also be an important pathway to improved mood among older people (Teychenne et al. 2008).

Psychological mechanisms include, for example, the distraction hypothesis, which suggests that engaging in physical activity serves as a distraction from worries and depressing thoughts. Increased self-esteem and self-efficacy through positive experiences from exercise may also alleviate depressive symptoms and depression (Barbour & Blumenthal 2005).

Sosical mechanisms include the social interaction hypothesis, which posits that improvements in depressive symptoms following exercise might, at least partly, be related to the mutual support and social relationships that obtain when exercising in a group setting (Timonen et al. 2002). However, despite the multiple separate mechanisms hypothesized to explain the antidepressant effect of exercise on mood, it is highly likely that a combination of biological, psycho-

logical and sociological factors together influence the relationship between exercise and depression among older adults (Craft & Perna 2004).

2.3.3 Genetic effects on the association between depressive symptoms and physical activity

While most of the earlier studies address the effects of physical activity on depressive symptoms, only a few studies have investigated the origins of this association taking into account the genetic variation among individuals. Although prospective studies suggest causality between physical activity and depression, we cannot rule out the possibility that some underlying variable that influences physical activity behaviour at one time point also influences symptoms of depression at a later time point (De Moor et al. 2008). Experimental studies have indicated that it is possible that only subjects who are already attracted to exercise are likely to enrol and persist during interventions (De Geus & De Moor 2008). Also, treatment effects in clinical populations may not always be generalized to the population at large (Brosse et al. 2002).

A variety of population-based twin studies have shown that genetic factors contribute to individual differences in participation in leisure time physical activity (Frederiksen & Christiansen 2003) and risk for depressive symptoms (e.g. Kendler et al. 2006). In a large multinational collaborative study of seven Twin Registers, the heritability of exercise participation ranged from 27 to 70% among twins aged 19 to 40 years (Stubbe et al. 2006). In the second half of life, the influence of genetic factors on leisure time physical activity has been rarely studied. Among Danish twins aged 45-68 years, heritability was estimated to vary between 49 and 51% (Frederiksen & Christensen 2003). The heritability estimates of depressive symptoms also vary widely between studies as a result of both the definition of depressive symptoms used and the group in which it is measured; for example, in a large sample of twins aged 18-79 years, the heritability of depressive symptoms was found to be around 42% (Rijsdijk et al. 2003). Given the fairly high heritabilities of both engagement in leisure time physical activity and depressive symptoms, it is likely that some genetic factors influencing physical activity behaviour might overlap with genetic factors influencing depressive symptoms. It has been hypothesized that genes involved in dopaminergic, norepinephrenergic, opioidergic or serotonergic pathways of the brain are likely candidates for having a simultaneous effect on the regulation of physical activity and depressive symptoms (Chaouloff 1997; Goldfarb & Jamurtas 1997).

In our best knowledge only one earlier study has investigated the origins of the association between leisure time physical activity and depressive symptoms taking into account the genetic variation among individuals. In their study, De Moor and colleagues (2008) concluded that the cross-sectional and longitudinal associations found between regular exercise and depressive symptoms were best explained by common genetic factors, with inverse effects between exercise behavior and symptoms of depression among a Dutch cohort consisting a total of 8558 twins aged 18 to 50 years. The inverse of depressive symp-

toms, well-being, was studied by Stubbe and colleagues (2007) who found an association between exercise participation and levels of life satisfaction and happiness to be mediated by genetic factors that influence both the exercise behavior and well-being.

Although the number of studies supporting the evidence for common genetic background for physical activity and depressive symptoms is for the present time quite scarce, genetic pleiotropy, a phenomenon where low-level biological variation has effects on multiple complex traits at the organ and behavioral level, between physical activity and various other outcomes have been reported in earlier studies. In the case of physical health outcomes, there is evidence for genetic pleiotropy between exercise behavior and, e.g., heart rate (De Geus et al. 2003), blood pressure (Hernelahti et al. 2005), BMI, waist circumference (Mustelin et al. 2009), and self-rated health (De Moor et al. 2007). However, in the case of mental health outcomes, more research evidence is needed.

2.4 Effects of physical activity interventions on depressive symptoms and sense of coherence in old age

Studies with different types of physical activity interventions among older people with health differences at baseline have shown interventions to have modest (e.g. Mather et al. 2002) to strong beneficial effects on depressive symptoms (e.g. Singh et al. 2005), although no effects on depressive mood have also been presented (Chin A Paw et al. 2004). Most of these prior studies on promoting psychological health in older adults through physical activity have included organized exercise programs, such as resistance training and aerobic exercise, and have thus been able to increase psychological well-being (Penninx et al. 2002, Singh et al. 2005). Instead research-based evidence on the effects of physical activity counseling interventions on mood among older people is scarce (Eaton & Menard 1998, Eakin 2001, van der Bij et al. 2002) and new knowledge concerning the effects of educational physical activity interventions on psychological health in older adults is needed.

Whereas most studies have examined the impact of physical activity on negative psychological states such as depression and depressive symptoms, the effects of physical activity on positive affects have been rarely studied (Kanning & Schlicht 2010). Convincing evidence exists in the literature to support the practical importance of psychological well-being, suggesting that people with higher levels of well-being are healthier and function more effectively in many aspects of human life (Reed & Ones 2006). However, more research on the effects of physical activity interventions on positive affect especially among older people, is needed.

With respect to various forms of physical activity interventions, the main focus in this thesis is on the physical activity counseling interventions in preventing depressive symptoms among community-dwelling older adults and on

the strength-training interventions in enhancing psychological well-being in terms of sense of coherence among older people with disabilities. These issues are discussed in more detail in the following sub-sections.

2.4.1 Physical activity counseling interventions

The efficacy of specific interventions can be evaluated in optimal and highly controlled conditions in randomized trials. Specific exercise trials, such as controlled and supervised strength training interventions are examples of efficacy (explanatory) trials that are able to reveal the upper limit of the intervention effect. Effectiveness (pragmatic) studies, on the other hand, measure the beneficial effects of interventions in real-world clinical settings as opposed to optimal conditions (Gartlehner et al. 2006). Although explanatory studies have yielded important results on the efficacy of exercise training, they do not offer an insight into the feasibility and effectiveness of programs which aim to promote physical activity in general among older people (Jette et al. 1999). Physical activity counseling is an example of a low-cost educational intervention seeking to promote physical activity among older people through encouragement and the provision of advice about possibilities for exercise (Leinonen et al. 2007).

Factors associated with physical activity adherence are complex involving both individual and environmental factors (Satariano & McAuley 2003). Especially among older people with decreased psychological well-being these issues are of great importance. In considering older people with depressive symptoms, low mood is associated with poor participation in physical activity programs, increased drop-out rate and decreased exercise compliance among the most depressed study participants, all of which might complicate interpretation of the study results (e.g. Mather et al. 2002). It is also possible that among depressed older adults compared to healthy older populations, the motives for physical activity will differ. The study by Rosqvist and colleagues (2009) found the most often reported motivation for physical activity, i.e., health maintenance and positive experiences, to be less common among people with depressed symptoms than among those without these symptoms.

It has been argued that for regular exercise to be widely adopted and maintained by large numbers of older persons, it must be enjoyable and achievable with minimal levels of professional supervision (Jette et al. 1999). To reach this challenging goal in health promotion, the use of behavioral strategies such as the Social Cognitive Theory (Bandura 1998, Bandura 2004), the Transtheoretical Model (Prochaska et al. 2008) and motivational interviewing technique (Rollnick et al. 1999) have proven useful and highly applicable in physical activity counseling interventions (Kerse et al. 2005, Pinto et al. 2005). In the Social Cognitive Theory the emphasis is on the importance of control over one's own behavior, and belief in one's efficacy to exercise control is a common pathway through which psychosocial influences affect health behavior functioning (Bandura 1998, Bandura 2004). The Transtheoretical model (Prochaska et al. 2008) describes the individual's motivational readiness to change his or her health behavior and posits that behavior change involves progress through

six stages of change: precontemplation, contemplation, preparation, action, maintenance, and termination. The main idea of the model is that interventions targeting health behavior change should be tailored according to each person's level of readiness to change.

The beneficial effects of physical activity counseling interventions on increasing physical activity among community-dwelling older adults have been well documented in recent studies (Kerse et al. 1999, Stewart et al. 2001, Dubbert et al. 2002, Elley et al. 2003, Pinto et al. 2005, Kolt et al. 2007, Dubbert et al. 2008). In addition to observed increments in physical activity levels, some positive effects on general health (Dubbert et al. 2008) and also a decrease in hospitalization (Kerse et al. 2005) have been reported. In contrast, the few studies that have included psychological outcomes have yielded mixed results. For the effects on quality of life, the results are inconsistent, some studies finding physical activity counseling to improve quality of life (Dubbert et al. 2000, Elley et al. 2003) and others finding no such effects (Kerse et al. 1999, Dubbert et al. 2002, Kolt et al. 2007). For the effects of physical activity counseling on depressive symptoms, the research-based evidence is scarce and only a few studies exist. In a study by Salminen and collegues (2005), improvements in depressive symptoms were found after a health advocacy, counseling and activation program among older male coronary heart patients. However, no similar effects were found among older women. As the literature in this area is limited and results to date rather contradictory, new knowledge on the effects of educational physical activity interventions on depressive symptoms in older adults is needed.

2.4.2 Strength-training interventions

In healthy older people, progressive strength-training improves various physical outcomes such as strength and power (Latham et al. 2004, Liu & Latham 2009). Also among clinical and frail older populations, strength-training is feasible and improves several functional outcomes (Halbert et al. 2007). However, psychological outcomes have not been consistently reported in most physical activity interventions among older people (Crotty et al. 2010).

Disability, defined as difficulty in or inability to perform everyday activities (Nagi 1976, Verbrugge & Jette 1994), can be chronic and develop gradually, or it can develop suddenly as a result of an accident or an illness such as stroke, leading to hospitalization and restricted activity (Ferrucci et al. 1996, Gill et al. 2004). In older people, hip fractures are common traumas associated with a high risk for death and disability (Lönnroos et al. 2006). Successful rehabilitation among older hip fracture patients is a key determinant of long-term recovery (e.g. Lenze et al. 2004). However, the high risk for psychological health problems such as depressive symptoms and diminished quality of life among hip fracture patients might have a negative impact on recovery and decrease motivation towards rehabilitation programs (Proctor et al. 2008). Although psychological factors such as depressive symptoms, quality of life and sense of coherence are nowadays thought to be important in recovery from hip fracture, in-

formation on how various physical activity interventions impact on these factors continues to be limited (Crotty et al. 2010).

The few strength training studies that have also included psychological outcomes have yielded inconsistent results among older hip fracture patients. For quality of life, a global measure of wellbeing, both positive results (Binder et al. 2004, Tsauo et al. 2005) and no effects (Crotty et al. 2002) of interventions have been reported. Very few studies have included specifically psychological outcomes. Lotus Shyu and colleagues (2005) found positive effects on depression whereas in another study, a strength training intervention had no effect on self-efficacy among hip fracture patients (Resnick et al. 2007).

In respect of sense of coherence (SOC), little is known about how to enhance individuals' SOC although the health benefits of strong SOC have been extensively confirmed. Among working age populations the most often reported interventions to promote SOC have been done among the unemployed and work-disabled individuals, and these interventions have mostly comprised multidisciplinary rehabilitation programs (Lillefjell & Jakobsen 2007, Vastamäki et al. 2009). In our best knowledge, we found only one earlier study where the effects of a physical activity intervention on SOC among older people had been investigated (Kohut et al. 2006). In their study, Kohut and colleagues (2006) found that a ten-month aerobic exercise or strength training intervention increased the SOC among participants aged over 64 years. Taking into account the many health benefits of a strong SOC (e.g. Eriksson & Lindström 2006), more research on the effects of physical activity interventions on older adults' sense of coherence is needed.

2.5 Summary of the literature

High levels of depressive symptoms are common among the elderly population with prevalence rates ranging from approximately 8% to 30% (Heikkinen & Kauppinen 2011). As depressive symptoms are often associated with many negative health outcomes, studies on the underlying factors as well as effective interventions to prevent depressive symptoms are needed. Despite the extensive research done on the factors underlying depressive symptoms (Blazer 2003, Blazer & Hybels 2005), the etiological picture of depression and depressive symptoms in late life has remained unrevealed (Fiske et al. 2009).

Associations between lack of physical activity and increased depressive symptoms in old age have been confirmed by several cross-sectional (Lindwall et al. 2006), longitudinal (Strawbridge et al. 2002) and interventional studies (Penninx et al. 2002, Singh et al. 2005). While the effects of physical activity on depressive symptoms have been widely studied, only a few studies investigating the origins of this association have taken into account the genetic variation among individuals (De Moor et al. 2008). As both leisure time participation in physical activity (Frederiksen & Christiansen 2003) and depressive symptoms (Rijsdijk et al. 2003) are moderately heritable, some of the genetic factors influ-

encing physical activity behaviour might overlap with genetic factors influencing depressive symptoms (De Geus & De Moor 2008, De Moor et al. 2008). To date, only one study has investigated the possibility of a common genetic background between voluntary leisure time physical activity and depressive symptoms (De Moor et al. 2008).

The positive effects of prescribed and/or externally monitored physical activity interventions on psychological well-being have been observed in many studies (Sjösten & Kivelä 2006, Teychenne et al. 2008). Physical activity counseling is an example of a low-cost educational intervention promoting physical activity among older people by encouraging physical activity and providing advice about possibilities for exercise (Leinonen et al. 2007). However, whether physical activity counseling, through increasing physical activity, decreases depressive symptoms has been little studied (Salminen et al. 2005).

With respect to the various forms of physical activity interventions, most of the research has examined the impact of physical activity on negative psychological states, while the effects of physical activity interventions on positive affects have been rarely studied (Kanning & Schlicht 2010). In particular among older people with disabilities improved well-being has been associated with higher rates of recovery and increased motivation towards rehabilitation programs. Although the health benefits of strong sense of coherence (SOC) have been widely studied, little evidence has been gathered on how to enhance individuals' SOC through physical activity. To date only one study has reported on the effects of a physical activity intervention on the participants' sense of coherence (Kohut et al. 2006).

3 PURPOSE OF THE STUDY

The general objective of this thesis was to investigate the associations between depressive symptoms, sense of coherence, physical activity and genetic factors among middle to old age adults. Specifically, the aim was to study the factors in middle age that are associated with depressive symptoms in old age and the potential factors underlying physical activity and depressive symptoms among adults from middle to old age. In addition, effects of two separate physical activity interventions on depressive symptoms and sense of coherence among older persons were studied. The specific aims of the study were:

1. To investigate factors in middle age associated with depressive symptoms in old age among women. In addition, possible common genetic and environmental effects between factors in middle age and old age depressive symptoms were estimated using quantitative trait modeling. (Study I)
2. To investigate whether common genetic effects exist between leisure time physical activity and depressive symptoms among adults from middle to old age. (Study II)
3. To study the effects of physical activity counseling on depressive symptoms among older community-dwelling men and women. (Study III)
4. To study the effects of intensive resistance training on sense of coherence among older men and women with a hip fracture history. (Study IV)

The associations examined in this study are presented in Figure 1.

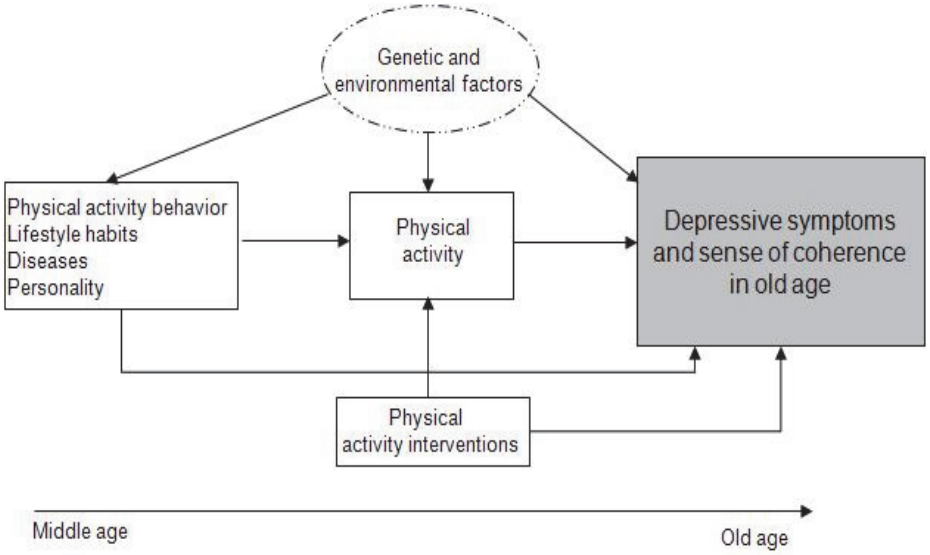

FIGURE 1 The associations examined in this study

4 MATERIAL AND METHODS

4.1 Study designs

4.1.1 Life course study on aging

Over the last few years there has been increasing interest in conceptualizing a life course framework. According to the life course approach experiences early in the life course may have long-term effects on the development of chronic diseases (Kuh 2007). The key idea in life course epidemiology is to study the long-term biological, behavioural and psychosocial processes that link adult health and disease risk to physical or social exposures acting during gestation, childhood, adolescence, earlier in adult life, or across generations (Ben-Shlomo & Kuh 2002). Chronic diseases in adulthood reflect cumulative lifetime exposures to damaging physical and social environments or influences of critical developmental periods (Sayer & Cooper 2004).

4.1.2 Quantitative genetic method

Quantitative genetic methods can be used to investigate the relative proportions of genetic and environmental effects on the differences between individuals in different traits. Quantitative genetics gives an estimation of the proportions of these effects, without specifying any single gene or environmental factor that affects the trait. The quantitative genetic method can be applied to twin, adoption and/or family data (Rijsdijk & Sham 2002).

The classical twin method is a commonly used design in quantitative genetics, in which two types of twin pairs, MZ and DZ, are used to disentangle genetic effects from environmental effects on a trait. In this method, variation in a trait is considered to arise from four sources: additive genetic effects (A), non-additive, dominant, genetic effects (D), shared environmental effects (C) and individual environmental effects (E). A represent the sum of the effects of individual alleles, whereas D refers to interactions between alleles of the same or

different genes. Shared environmental effects (C), include factors that are shared by both co-twins, such as those related to their childhood environment, whereas individual environmental effects (E) consist of exposures that are not shared by both co-twins, such as diseases and accidents that have affected only one sibling within a pair (Plomin et al. 2001, Boomsma et al. 2002, Rijsdijk & Sham 2002, Posthuma et al. 2003). Heritability describes the proportion of the variation which is accounted for by genetic effects, and is a estimate which is age-, gender- and population-specific. Heritability refers to the genetic contribution to individual differences at the population level, not to the phenotype of an individual (Plomin at al. 2001).

In the classical twin design, estimation of the variance components is based on both the different degrees of correlation for additive and dominance genetic effects and the same degrees of correlation for shared and unique environmental effects. As MZ co-twins have identical genes, the correlation for both A and D is 1, whereas the respective values for DZ pairs are 0.5 and 0.25. In both MZ and DZ co-twins the correlations of C and E are similar; 1 for C and 0 for E (Figure 2). E also contains measurement error.

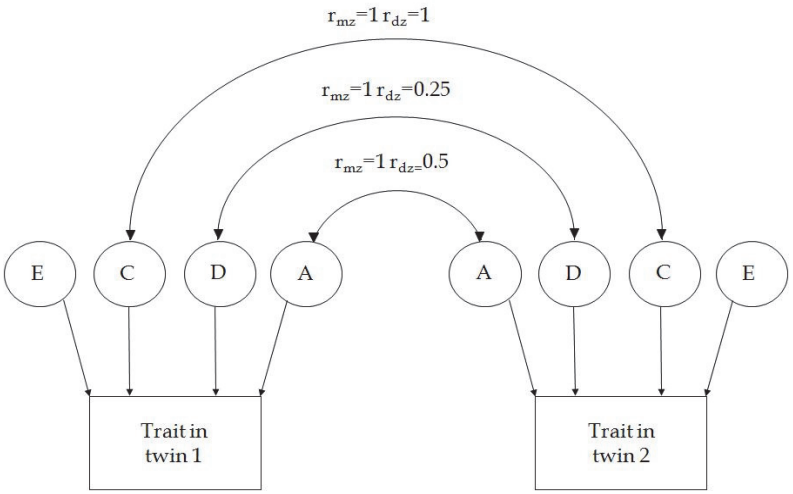

FIGURE 2 Correlations between monozygotic (r_{mz}) and dizygotic (r_{dz}) co-twins in quantitative genetic models. A, additive genetic effects; D, dominant genetic effects; C, shared environmental effects; E, individual environmental effects. Adapted from Rijsdijk & Sham (2002).

Using these correlations and the observed variance and co-variance between co-twins in a trait, structural equation modeling can be used to estimate the effects of latent factors A, D, C and E on a trait as regression coefficients (Rijsdijk & Sham 2002). Univariate quantitative genetic analysis decomposes the variation in a single trait into the variance components presented earlier whereas multivariate genetic models reveal to what extent the traits of interest are influenced

by the same and to what extent by different genetic and environmental factors (Boomsma et al. 2002, Rijsdijk & Sham 2002, Posthuma et al. 2003).

The twin method is based on several assumptions that should be met. First, MZ and DZ pairs are assumed to share their common environment to the same extent. Second, no major gene-environment correlations or gene-environment interactions for the studied trait should exist. In addition, pairing of mates is assumed to occur at random. Finally, with respect to generalizability, twins should not differ from the general population in the trait that is being studied. Violations of these assumptions may lead to incorrect estimates of genetic and environmental effects (Rijsdijk & Sham 2002).

4.1.3 Randomized controlled trial

Randomized controlled trials (RCTs), when appropriately designed, conducted, and reported, represent the gold standard in evaluating healthcare interventions. In addition, RCTs represent the most rigorous way of determining whether a cause-effect relation exists between treatment and outcome and for assessing the cost effectiveness of a treatment (Concato et al. 2000). In randomized controlled trials the key feature is that the study subjects, after assessment of eligibility, are randomly allocated to receive one of the alternative treatments under study. After randomization the two or more groups of the study participants are followed up in exactly the same way, the only differences between the care they receive being those intrinsic to the treatments being compared. The most important advantage of proper randomization is that allocation bias is minimized, balancing both known and unknown prognostic factors in the assignment of treatments (Cummings et al. 2001).

Despite the existence of strict methodological requirements and challenges, randomized controlled trials in the health sciences have been and are likely to remain a valuable tool for investigating the effects of new treatments and strategies on health outcomes (Bhargava 2008).

4.2 Participants

Data from four larger research projects were used in this study. The analyses included in this thesis were based on two separate twin studies and two randomized controlled trials. The Finnish Twin Study on Aging, FITSA, is a study on the genetic and environmental influences on the disablement process in older women. The Finnish Twin Cohort consists of all Finnish same-sex twin pairs born before 1958 with both members alive in 1975. The aim of the project is to investigate environmental, psychosocial and genetic factors affecting chronic diseases in adults and their risk factors. The data from the randomized controlled trials came from two separate projects. Screening and Counseling for Physical Activity and Mobility in Older People, SCAMOB (ISRCTN07330512), is a randomized controlled trial on the effects of physical activity counseling

among community-dwelling older adults. Asymmetry (ISRCTN34271567), is a randomized controlled trial on the effects of resistance training on muscle strength parameters, mobility and balance in older persons with a hip fracture history. The data used in the original publications are summarized in Table 1.

TABLE 1 Datasets, designs and numbers of participants in the different studies

Study	Dataset	Design	n	Age, years (mean ± SD)
I	FITSA	**Observational** Classical twin design	194 twin pairs 93 MZ 101 DZ	66-79 (71.5 ± 3.4)
II	FITSA	**Observational** Classical twin design	203 twin pairs 96 MZ 107 DZ	66-79 (71.5 ± 3.4)
	The Finnish Twin Cohort		3794 twin pairs 1327 MZ 2467 DZ	33-60 (43.7 ± 7.7)
III	SCAMOB	**Experimental** Randomized controlled trial 2-year intervention	624 individuals Intervention group n=314 Control group n= 310	75-81 (77.6 ± 1.9)
IV	Asymmetry	**Experimental** Randomized controlled trial 12-week intervention	46 individuals Intervention group n=24 Control group n=22	60-85 (74.0 ± 6.8)

MZ, monozygotic; DZ, dizygotic; SD, standard deviation
I Factors in middle age associated with depressive symptoms in old age
II Underlying factors between leisure time physical activity and depressive symptoms
III Effects of physical activity counseling on depressive symptoms
IV Effects of strength-power training on sense of coherence

4.2.1 Finnish Twin Study on Aging (FITSA; Studies I and II)

The first dataset, FITSA, was originally collected to investigate the genetic and environmental influences on the disablement process in older women (Rantanen et al. 2003, Tiainen et al. 2004). The participants were recruited from the nationwide Finnish Twin Cohort, which comprises all the same-sex twin pairs born before 1958 and with both co-twins alive in 1975 (Kaprio et al. 1978; Kaprio & Koskenvuo 2002). In August 2000, there were 1260 female twin pairs in the age group of 63-76 years who had participated in the Finnish Twin Cohort in 1975. From this group an invitation to participate in the FITSA study was sent on the basis of age and zygosity to a subsample of 414 twin pairs aged 63-76 years. To be included in the study, both individuals in a pair had to agree to participate and be sufficiently healthy to travel to the laboratory examina-

tions. Reasons for nonparticipation were refusal (106 pairs), poor health status (85 pairs), or death (6 pairs) of one or both twin sisters. The zygosity of the twin pairs was confirmed using a battery of 10 highly polymorphic gene markers in DNA extracted from a venous blood sample. The final baseline sample of the FITSA study was 103 monozygotic (MZ) and 114 dizygotic (DZ) twin pairs (434 individuals).

In 2003-2004, an invitation to take part in a 3-year follow-up examination was sent to all participants. Altogether 419 women participated in the follow-up study, of whom 313 participated in the laboratory measurements and filled in a questionnaire, while 106 women responded solely to the postal questionnaire. During the follow-up, 7 participants died and 8 participants dropped out for health reasons. For the purposes of the present study, the data used were drawn from the follow-up examinations (Studies I, II). The FITSA participants had responded to a questionnaire in 1975 as part of the Finnish Twin Cohort study and these data were also used in the analyses (Study I). In addition, in Study I, the analyses were limited to a subsample of participants who were healthy at baseline in the year 1975. To accomplish this, we excluded all participants who reported angina pectoris, myocardial infarction, stroke or diabetes at baseline. We also excluded those participants who had used a hypnotic/tranquilizer for more than 6 months during the preceding year or who, at baseline, were on a work disability pension due to any cause. Thus the final size of the study cohort in the Study I was 409 individuals of whom 391 (184 MZ and 207 DZ individuals) had valid measures of depressive symptoms.

4.2.2 Finnish Twin Cohort (Study II)

The second dataset, the Finnish Twin Cohort study consists of all Finnish twin pairs of the same gender born before 1958 with both co-twins alive in 1975. These twin pairs were selected from the Central Population Registry of Finland in 1974. The aim of the Finnish Twin Cohort is to investigate environmental, psychosocial and genetic factors that affect chronic diseases in adults and their risk factors. A baseline questionnaire including information on health, psychosocial and health-related factors was sent in 1975 to the twin candidates and follow-up questionnaires in 1981 and 1990 only to verified twins (Kaprio et al. 1978). In addition, the 1990 questionnaire was sent only to twin pairs with both co-twins alive, residing in Finland, and born 1930-1957. Twin zygosity was initially determined by a validated questionnaire methods in the entire cohort (Sarna et al. 1978). The overall response rates to the questionnaires were 89% in 1975, 84% in 1981 and 77% in 1990. In the analyses of the present study, data from the 1981 and 1990 questionnaires were used (Study II).

4.2.3 Screening and Counseling for Physical Activity and Mobility in Older People (SCAMOB; Study III)

The SCAMOB study (registered as ISRCTN07330512) was a 2-year single-blinded randomized controlled trial on the effects of customer-oriented physical

activity counseling in older people (Leinonen et al. 2007). The target population consisted of all the registered residents of the City of Jyväskylä aged 75 to 81 years and living in the city centre area in March 2003 (N=1310). It was considered that cognitively intact old people who were able to go outdoors independently but were physically sedentary would be the group most likely to benefit from physical activity counseling. At baseline, a four-phase screening and data collection process was conducted including a phone interview, an at-home face-to-face interview and a nurse's examination at the study center, supplemented with a physician's examination if needed. For individuals to be eligible for randomization, they had to be able to walk 500 meters without the help of another person, have a Mini-Mental State Examination (MMSE) (Folstein at al. 1975) score >21, be only moderately physically active or sedentary (at most 4 hours of walking or 2 hours of other exercise weekly), have no severe medical contraindications for physical activity (assessed by the study nurse and, when necessary, ascertained by a physician), and sign an informed consent to participate.

The final study group consisted of 632 persons, who were randomly assigned to the intervention group (n=318) or control group (n=314). Each week, after the completion of the baseline assessments, a trial administrator allocated participants to groups in blocks of 40-50 persons with a randomization ratio of 1:1 by drawing lots. Allocation concealment was achieved by drawing names from opaque envelopes for 40-50 persons at the same time. Study nurses and interviewers who collected and entered data were blinded to group allocation. After randomization, each participant in the intervention group received a two-year physical activity counseling intervention. For the purposes of the present study, the data used were drawn from self-reported depression (CES-D) questionnaires filled in before the study center examinations at baseline and at the end of the two-year intervention. In addition demographic, socioeconomic and health information were drawn from the face-to-face at-home interviews at baseline and follow-up. (Figure 3)

4.2.4 The effects of strength training on muscle strength, asymmetry in lower limb muscle strength and mobility in older men and women with a history of hip fracture (Asymmetry; Study IV)

Data for the second experimental trial were drawn from the Asymmetry study (registered as ISRCTN34271567), which was a 12-week randomized controlled trial on the effects of resistance training on muscle strength parameters, mobility and balance in older persons with hip fracture history (Portegijs et al. 2008).

To avoid confounding of acute recovery effects, community-living 60-85-year-old men and women with a femoral neck or trochanteric fracture within 6 months to 7 years prior to baseline were invited to participate in the study. In 2004 and 2005, all 452 surviving patients with hip fracture in the years 1998-2004 were identified using the patient records of the Central Hospital of Central Finland. First, a letter informing about the study was sent to all patients living independently in the Central Finland Health Care District (n=452). A total of 193 patients responded, of whom 132 expressed an initial interest and were in-

terviewed over the telephone. Patients with neurological and progressive severe illnesses, amputation or inability to walk outdoors without another person's assistance were excluded. Altogether, 79 patients participated in the baseline laboratory assessments after which those without physical (American College of Sports Medicine) or mental (Mini-Mental State Examination score<21; Folstein et al. 1975) contraindications for participation in the strength and power training were randomized into the training (8 men, 16 women) or control group (6 men, 16 women). The groups were randomized by sealed envelopes in blocks of gender and stratified by age. The training group participated in a 12-week individually tailored strength training program. For the purposes of this thesis, sense of coherence data drawn from self-report questionnaires at baseline and after the 12-week intervention were used. (Figure 4)

4.3 Ethics

The FITSA, SCAMOB and Asymmetry trials were all approved by the Ethics Committee of the Central Finland Health Care District. Before the laboratory examinations, the participants were informed about the study and a signed informed consent was obtained. The Finnish Twin Cohort study was set up with permission from the National Board of Health and the participants were given a complete description of the study before their informed consent was obtained.

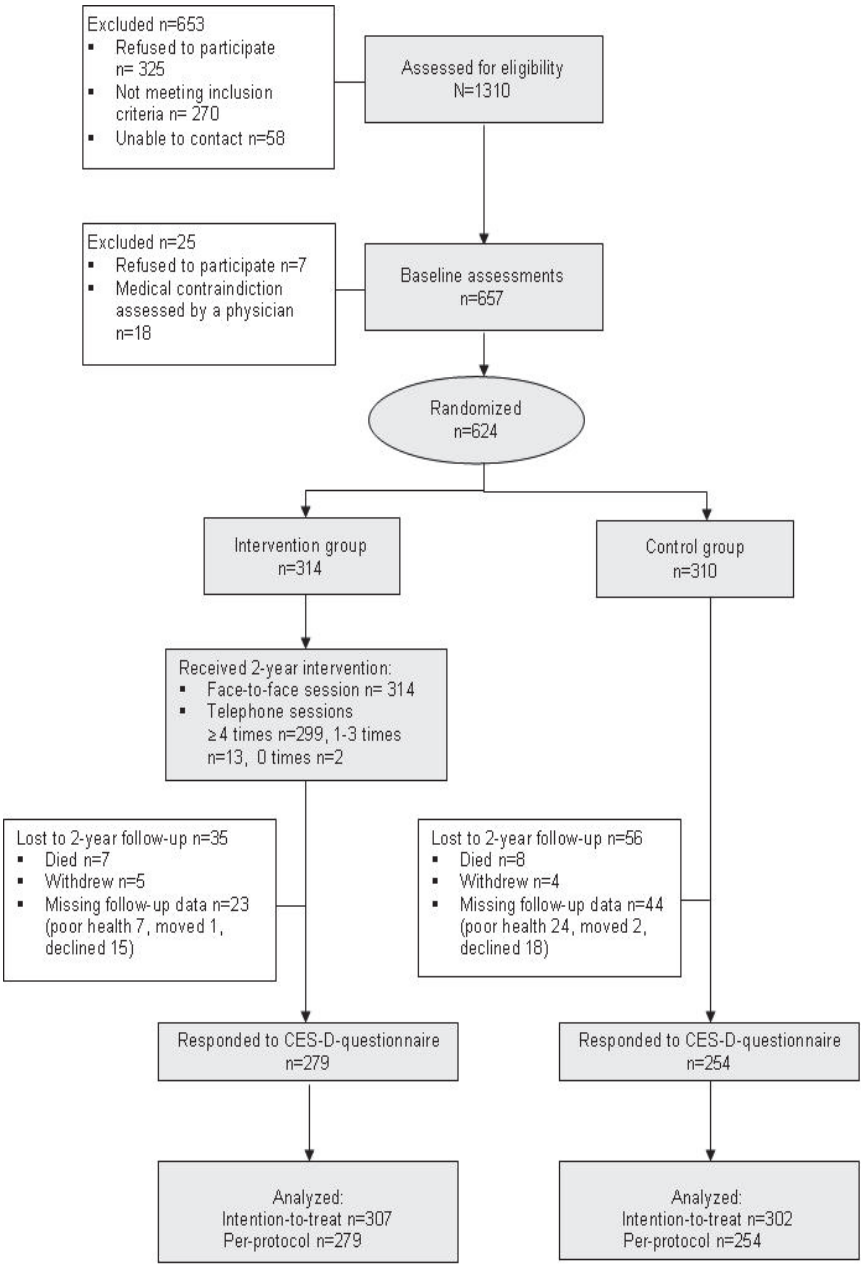

FIGURE 3 Flow chart of the SCAMOB trial according to depressive symptoms as outcome used in Study III.

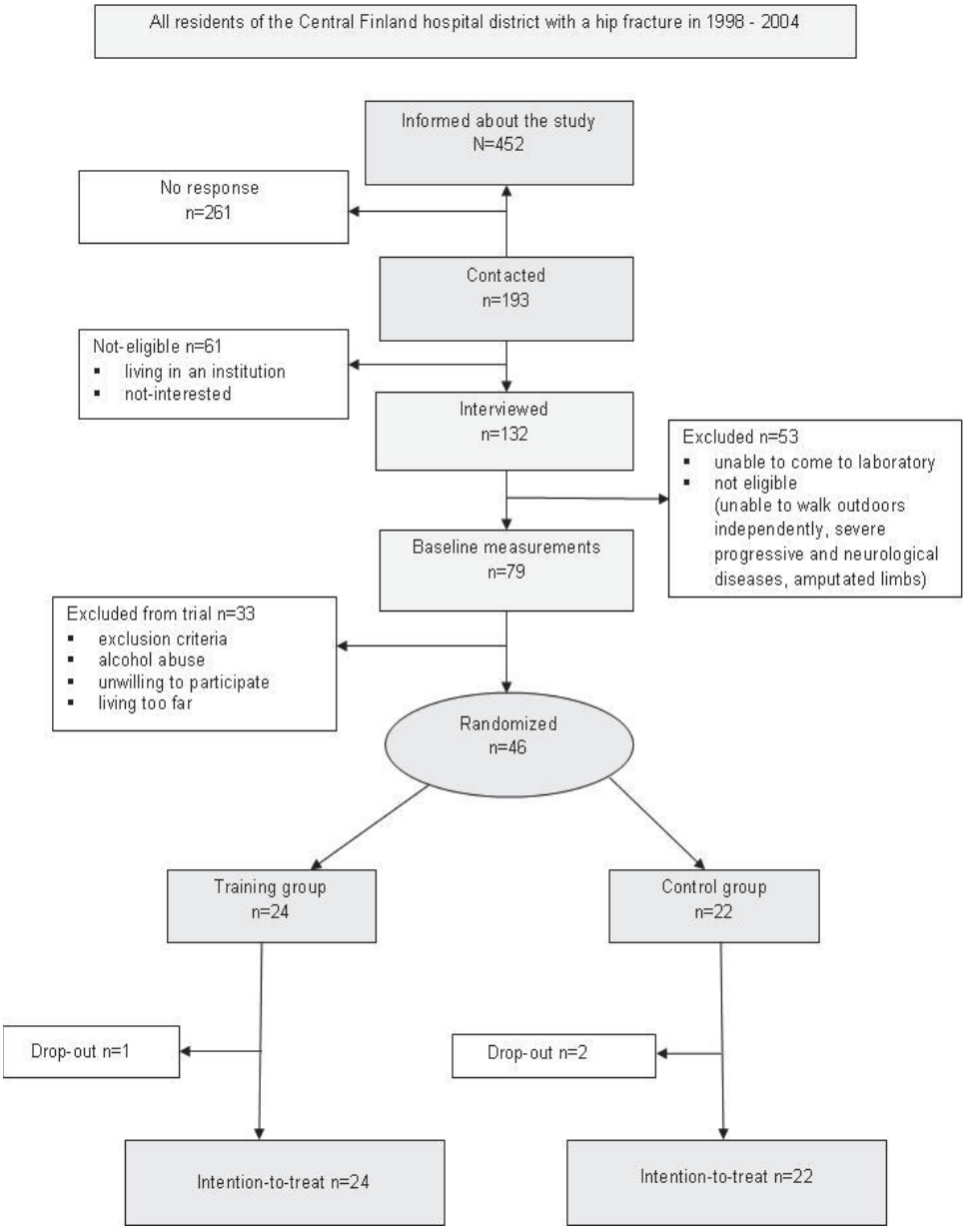

FIGURE 4 The flow chart of the Asymmetry trial according to sense of coherence as outcome used in Study IV.

4.4 Measurements

4.4.1 Depressive symptoms

Depressive symptoms were assessed as outcomes in the FITSA and SCAMOB projects using the Center for Epidemiologic Studies Depression Scale (CES-D; Radloff 1977). The CES-D scale is a widely used self-report measure in community samples the reliability and validity of which has been demonstrated in heterogeneous samples (e.g. Beekman et al. 1997). The total CES-D scale has 20 items and respondents rate the frequency with which they have experienced particular depressive symptoms during the past week. Each item is scored from 0 to 3, for a possible total range of 0 to 60. In the CES-D scale, the standard cut-off score indicating the presence of clinically important depressive symptoms in community populations is 16 or more of the possible 60 points (Radloff 1986).

In the follow-up measurements of the FITSA study (Studies I, II), the participants filled in the CES-D questionnaire which was later checked and, when necessary, incomplete or missing answers filled in during face-to-face interviews at the laboratory or over the telephone. The CES-D scale cut-off point of 16 was used to distinguish individuals considered to suffer from depressive symptoms from those classified as non-depressed (Study I). Also in the twin modeling, a continuous measure of depressive symptoms was used (Studies I, II). The internal consistency of the CES-D scale was adequate; Cronbach's alpha was 0.87 for the measurement in the year 2003.

In the SCAMOB project depressive symptoms were assessed at baseline before randomization and at the 2-year follow-up (Study III). On arrival at the study center, the participants were asked to fill in the CES-D questionnaire which later, during the examinations, was checked by a registered nurse practitioner who had received special training for the purpose. If necessary, missing responses were filled in by interviewing the subject. As the standard cut-off score indicating depressive symptoms is 16 of the possible 60 points, a cut-off score of 20 or more yields a higher accuracy for the diagnosis of major depression (Lyness et al. 1997, Haringsma et al. 2004). For the purposes of the present study, we classified persons scoring 16 or more, but below 21 points as suffering from minor depressive symptoms and those scoring 21 points or more as suffering from more severe depression. The internal consistency of the CES-D scale was adequate; Cronbach's alfa was 0.85 at the baseline and follow-up measurements in the SCAMOB study.

In the Finnish Twin Cohort depressive symptoms were assessed using the 21-item Beck Depression Inventory (BDI), which is a multiple-choice self-report questionnaire measuring the severity of depressive symptoms (Beck et al. 1961) (Study II). All the items are coded from 0 to 3 and summed to obtain a score ranging from 0 to 63, with the higher values indicating more severe depressive symptoms. The Beck Depression Inventory is a well recognized measure of depression and depressive symptoms with good properties for screening cases in

the population (Lasa et al. 2000). The BDI was included in the 1990 questionnaire, which was mailed to twins aged 33-60 years who had responded to one of the previous questionnaires. In this thesis, the BDI was used as a continuous measure. Cronbach's alpha for the Beck Depression Inventory was 0.85.

4.4.2 Sense of coherence

In the Asymmetry study, SOC was assessed at baseline and after the 12-week intervention using Antonovsky's short 13-item scale derived from the original 29-item scale (Antonovsky 1987) (Study IV). On arrival at the study center, the participants were asked to fill in the SOC-questionnaire which later, during the examinations, was checked by a registered nurse practitioner. In the questionnaire, the responses are made on a seven-point scale and the sum of the scores ranges from 13 (weak SOC) to 91 (strong SOC). The sense of coherence questionnaire is a widely used self-report measure the reliability and validity of which has been demonstrated in heterogenous samples cross culturally (Eriksson & Lindström 2005). The SOC scale has three interrelated subscales measuring different aspects of sense of coherence: comprehensibility, manageability and meaningfulness. For the purposes of the present study, we decided to use both the original scale with 13 items and the three separate subscales to measure the changes in the SOC scale after the intervention. The internal consistency of the SOC scale was adequate; Cronbach's alpha was 0.82 at baseline and 0.78 in the follow-up measurements.

4.4.3 Factors in middle age possibly associated with depressive symptoms in old age

To assess factors in middle age that are associated with depressive symptoms in old age from the FITSA dataset, the baseline data from available records in the Finnish Twin Cohort study was used (Study I). A baseline health questionnaire, including questions on demography, symptoms and diseases, health-related factors and health behaviour, was sent in the year 1975 to the study participants.

Personality (extraversion and neuroticism) was studied using a short form of the Eysenck Personality Inventory (EPI; Floderus 1974) questionnaire. The version has been widely used in Nordic twin studies, and has good reliability and validity (Floderus-Myrhed et al. 1980, Rose et al. 1988, Pedersen & Reynolds 1998, Read et al. 2006). The two subscales have nine items each, with dichotomous responses (1=no, 2=yes) for a possible total score of 9 to 18. The sociodemographic variables included were *age*, *marital status* and *education status*. Marital status was dichotomized as married or cohabitating or not married (single, divorced, widowed). Education status was dichotomised into lower (elementary school or less) and higher (more than elementary school) education. *Age* was used as a continuous measure.

The *number of chronic diseases* was assessed by asking participants if they had ever had any chronic diseases diagnosed by a physician (a list containing 16 diseases; chronic bronchitis, pulmonary emphysema, bronchial asthma, al-

lergic rhinitis, allergic eruption, urticaria, arterial hypertension, angina pectoris, myocardial infarction, stroke, gastric ulcer, cholelithiasis, diabetes, gout, operated varicose veins, some other chronic disease) and the number of diseases was calculated by summing up all the specific diseases reported to be present. *Smoking status* was classified from responses to a detailed smoking history questionnaire, including questions on quantity smoked and ages at initiation and cessation (Kaprio & Koskenvuo 1988), and was dichotomized as smokers (regular or occasional smokers) and non-smokers (former and never). A dichotomous index of *heavy use of alcohol* was obtained from a binge drinking item that asked whether "at least once a month and on a single occasion" the respondent consumed more than five beers, a bottle of wine, or a half-bottle of spirits (Kaprio et al. 1987). The frequency of *leisure time physical activity* was measured by a five-point scale with alternative response categories ranging from no physical activity to a high level of leisure time physical activity. Those who reported at least slight amount of leisure time physical activity were classified as physically active and those without any leisure time physical activity as physically inactive.

4.4.4 Leisure time physical activity

The assessment of leisure time physical activity in the Finnish Twin Cohort and FITSA studies were based on participants' self-reports in questionnaires (Study II). In the Finnish Twin Cohort study, data on participants' leisure time physical activity were drawn from the questionnaire in the year 1981 and was based on a series of structured questions on leisure physical activity (monthly frequency, mean duration and mean intensity of sessions) and physical activity during journeys to and from work. The index was calculated by assigning a multiple of resting metabolic rate (MET score) to each activity and by calculating the product of intensity x duration x frequency of activity (Kujala et al. 1998.). The MET index was expressed as the sum score of leisure MET hours/day.

In the FITSA study, calculating the MET index was impossible due to the different research questions. Instead, participation in leisure time physical activity was based on self-report questionnaire with the question "What alternative describes best your all-year leisure-time physical activity?". Participants could respond with No leisure-time physical activity at all, A little, Moderate, Quite a lot or Much/Extensive.

4.5 Physical activity counseling intervention

In the SCAMOB trial (Study III), approximately two weeks after randomization, each participant in the intervention group received one individual one-hour face-to-face physical activity counseling session at the study centre with a physiotherapist specifically trained for the task and who did not take part in the data collection process (Leinonen et al. 2007). The counseling session was followed up by regular phone contacts, by the same physiotherapist, to support

compliance and behaviour change over the 2-year intervention. Telephone contacts took place on average every 4 months during the intervention. In addition to personal counseling, the intervention group was invited to participate in two voluntary lectures with topics including e.g. aging and disability prevention. The control group received the usual services provided by the municipality.

The counseling approach was based on the social cognitive theory of health behaviour change (Bandura, 1998) and motivational interviewing technique (Rollnick et al. 1999). A central component of the motivational counseling was to promote self-efficacy for more active physical behaviour (Leinonen et al. 2007, Pelo-Arkko 2009). The physiotherapist reinforced the ideas for increasing physical activity presented by the participants themselves, e.g. doing home callisthenics, walking, and performing every-day activities such as shopping in a physically active way. Participants were also referred to inexpensive exercise classes organized by the municipality. A problem-solving method was used to address perceived obstacles to physical activity and to develop a plan for more active physical behaviour. After the face-to-face counseling, the physiotherapist and the participant together designed a personal physical activity plan that could be carried out by the person alone, for example, in an exercise center (Leinonen et al. 2007, Pelo-Arkko 2009).

Adverse outcomes in the SCAMOB trial were assessed by asking the participants whether they had sustained any injuries in the previous year, and if so, whether these injuries had required medical treatment.

4.6 Strength-power training intervention

In the Asymmetry trial (Study IV), the training group participated in a 12-week individually tailored strength training program that was organized twice a week (1-1.5h) in a senior gym and supervised by an experienced physiotherapist (Portegijs et al. 2008). Training was specifically focused on reducing asymmetric deficit and increasing the strength and power of the lower-limb muscles. Each training session included both strength and power exercises and started with a 10-minute warm-up sitting on a chair. The first two training sessions were used to familiarize the participants with the facility, equipment and staff. In the following sessions, exercises were performed with as large a range of motion (ROM) as possible with pain-free performance. Training intensity was adjusted individually and increased progressively throughout the training period when tolerated. The assessment was repeated in weeks 6-8 and the training resistance was adjusted accordingly. The power exercises, leg press and ankle plantarflexion, were performed at the beginning of the training sessions in sets of 12 repetitions. Relatively low resistance was used and the concentric phase of the contraction was performed as fast as possible. The strength exercises were performed at a slower pace, with fewer repetitions and at a higher resistance.

The control group did not receive any intervention. Participants were encouraged to continue their lives as usual and maintain their pre-study level of physical activity during the 12-week trial.

In the Asymmetry trial, a physician was consulted for all the pain and other medical symptoms that emerged during the training period. This was done to ascertain which of the symptoms were likely to be related to the training and whether they affected the training.

4.7 Statistical analyses

Twin and quantitative genetic analyses were used in Studies I and II, and in Studies III and IV, the intervention effects were assessed using ANOVA for repeated measures.

4.7.1 Twin analyses

In Study I (FITSA), the relationship between the factors in middle age that were suspected to be associated with depressive symptoms in old age was first studied with generalized estimating equation (GEE) models using the SAS procedure GENMOD (SAS, institute USA) to correct for co-twin dependence. All factors showing a significant association with late-life depressive symptoms in the GEE models were further analyzed by univariate and multivariate genetic analyses. Also in Study II (FITSA, Finnish Twin Cohort), univariate and multivariate genetic modeling was used to study the association between LTPA and depressive symptoms among different age groups of twins.

Preliminary twin analyses

In both studies, the preliminary twin analyses were started by examining the outcome variables for normality and distribution. The MET index obtained from the Finnish Twin Cohort study (Study II), was transformed by logarithmic transformation and depressive mood by the square root of the inverse. After the transformation, the absolute values of skewness and kurtosis for all the outcome measures were acceptable. The equalities of the means and distributions of the outcome variables between MZ and DZ twins were calculated and tested using an adjusted Wald test to take into account the within-pair dependence of twin individuals. The equality of the variances was tested using the variance ratio test (STATA 8.0; Stata Corp., USA). The with-in pair resemblances in the studied outcomes were estimated separately for MZ and DZ groups using age-adjusted ICCs (SPSS 14.0; SPSS Inc., USA).

In the quantitative genetic analyses, phenotypic variation is decomposed into four sources of variances: additive genetic (A), dominant genetic (D), shared environmental (C) and non-shared environmental effects (E) (Boomsma et al. 2002). The possible combinations of the different effects that can be tested in genetic models are the full models (ACE and ADE) and their submodels (AE,

DE, CE, E). The model with dominant genetic effects (D) but not additive genetic effects (A) is biologically implausible and hence not tested, while D and C cannot be estimated simultaneously when the data consists only of pairs of twins raised together (Rijsdijk & Sham 2002).

Univariate and multivariate genetic analyses

The genetic modeling was started by carrying out univariate models for old age depressive symptoms and the factors in middle age that had a statistically significant association with depressive symptoms in the GEE models (Study I). Also in Study II, univariate models for LTPA and depressive symptoms in both datasets were carried out. Multivariate genetic modeling was further used to study the association between the factors in middle age and depressive symptoms in old age (Study I) and between LTPA and depressive symptoms (Study II). Trivariate (Study I) and a bivariate Cholesky models (Study II) were utilized. The bivariate Cholesky model consists of genetic and environmental effects (A_1, C_1, E_1) that are common to both variables and of genetic and environmental effects (A_2, C_2, E_2) that are specific to the second variable (Figure 5). The more complicate trivariate Cholesky model consists of genetic effect A_1, which is shared by the first, second and third variables; genetic effect A_2, which is shared by the second and third variables; and genetic effect A_3, which loads only on to the third variable. The shared environmental (C_1, C_2, C_3) and non-shared environmental (E_1, E_2, E_3) effects have similar patterns of loadings (Figure 6).

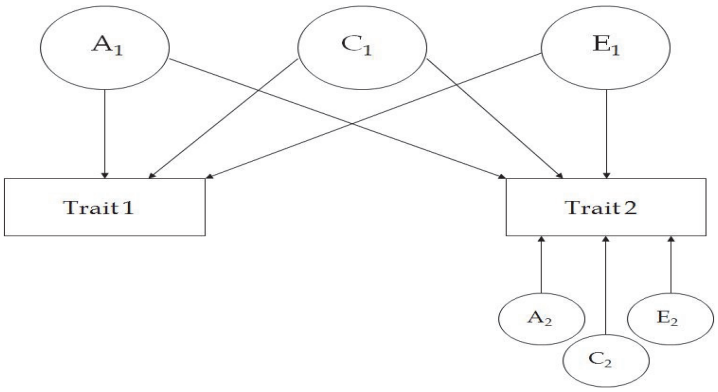

FIGURE 5 The full bivariate Cholesky decomposition ACE model including additive genetic effects (A) and shared (C) and non-shared (E) environmental effects.

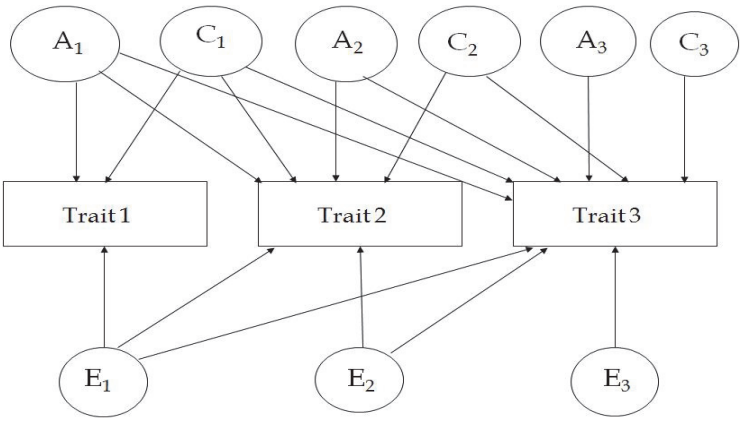

FIGURE 6 The full trivariate Cholesky decomposition ACE model including additive genetic effects (A) and shared (C) and non-shared (E) environmental effects.

Model fitting

The univariate and multivariate genetic analyses were performed with Mx software (Neale et al. 2003) using the full information maximum likelihood method with raw data input. In all the genetic analyses, age was used as a covariate. The aim of genetic modeling is to find a model which provides a theoretically meaningful interpretation, fits the data well and has as few explanatory parameters as possible (Rijsdijk & Sham 2002). The analyses were started with the hypothetical full ACE model. To obtain a more parsimonious model, the full model was modified by dropping the nonsignificant or very small parameters on by one. The obtained alternative univariate and multivariate model were compared against the full model by the χ^2 difference test and Akaike's information criterion (AIC = -2 times log-likelihood – 2 x degrees of freedom). A non-significant difference between the nested models and a smaller AIC indicates a better fitting model.

4.7.2 Intervention effects

In both the SCAMOB (Study III) and Asymmetry (Study IV) trials, the distribution of the outcome variables (CES-D for the SCAMOB trial and SOC for the Asymmetry trial) were acceptable. The baseline comparisons of the group characteristics were analyzed by unpaired t-tests for continuous variables and Chi-squared tests for categorical data in both trials.

In the SCAMOB trial, the effects of the physical activity counseling were assessed using ANOVA for repeated measures to analyze the effect of time and group x time interactions for change in the CES-D scale 2 years after the baseline. The analysis was performed according to the intention-to-treat principle, using the baseline CES-D value as a substitute for the missing 2-year follow-up value. We did not impute values for those who died during 2-year follow-up (n=15). To control for the possible confounding effect of the use of antidepressants, the data were adjusted for the use of antidepressants. Due to the small

number of users of antidepressants (n=48 at baseline and n=44 at follow-up), the most practical way to deal with the issue was to residualize the CES-D scores by the use of antidepressants prior to entry into the repeated measures ANOVA.

Also in the Asymmetry trial, the analyses were performed using ANOVA for repeated measures with the intention-to-treat principle. The baseline SOC value was used as a substitute for the missing 12-week follow-up value. In addition, per-protocol analyses were carried out by excluding the participants in the training group with poor training compliance (n=3).

In studies III and IV, the statistical analyses were done using SPSS software versions 12.0 and 15.0.

5 RESULTS

The results section includes the main findings of this study. More detailed information is given in original publications I-IV.

5.1 Characteristics of the participants

The total study population consisted of 11530 individuals aged 33 to 85 years. Table 2 shows the baseline characteristics of the participants in the SCAMOB and Asymmetry datasets and characteristics of the participants in the FITSA and Finnish Twin Cohort datasets from the follow-up measurements.

TABLE 2 Participant characteristics of the FITSA, Finnish Twin Cohort, SCAMOB and Asymmetry datasets.

	Study I&II **FITSA**	Study II **Finnish Twin Cohort**	Study III **SCAMOB**	Study IV **Asymmetry**
	n=419	n=10433	n=632	n=46
	Mean ±SD	Mean ±SD	Mean ±SD	Mean ±SD
Age (years)	71.5 ± 3.4	43.7 ± 7.7	77.6 ± 1.9	74.0 ± 6.1
Chronic diseases (number)	2.4 ± 2.9	-	3.0 ± 2.0	2.6 ± 1.4
Medication (number)	3.4 ± 2.9	-	4.0 ± 2.8	3.0 ± 2.0
MMSE score	27.1 ± 2.4	-	27.0 ± 2.3	26.3 ± 2.2
	%		%	%
Gender				
Male	-	45	25	30
Female	100	55	75	70
Marital status				
Married	46	77	43	50
Never married	12	-	12	7
Divorced	7	-	10	17
Widowed	31	-	35	26
Live alone	-	23	-	-
Working status				
Working	-	90	-	-
Unable to work	-	5	-	-
Unemployed	-	2	-	-

MMSE, Mini Mental State Examination

5.2 Factors in middle age associated with depressive symptoms in old age (Study I)

The mean (SD) ages of this sample in the years 1975 and 2003 were 43.6 (3.4) and 71.6 (3.4) years, respectively. Of the 391 individuals with valid data on depressive symptoms, 99 (25%) scored above the CES-D cut-off of 16 points and were considered to have depressive symptoms in year 2003. Associations between the factors in middle age and late-life depressive symptoms were first conducted by generalized estimating equations regression analysis (Table 3).

TABLE 3 Results of generalized estimating equations regression analysis for the effect of middle age factors on depressive symptoms experienced in later life in women followed for 28 years.

Predictor	OR	95% CI	*p*- value
Age	1.05	0.96-1.15	0.289
Marital status	1.10	0.55-2.17	0.800
Education	1.36	0.73-2.53	0.331
Diseases	1.21	0.95-1.54	0.123
Neuroticism	**1.34**	**1.16-1.56**	**0.001**
Extraversion	**0.84**	**0.73-0.97**	**0.014**
Physical activity	0.62	0.34-1.14	0.122
Alcohol use	1.51	0.07-3.87	0.513
Smoking	1.19	0.54-2.64	0.662

OR, Odds ratio; CI, confidence interval. The twin structure of the data was corrected by using an unstructured working correlation matrix.

The results of the regression analysis showed that personality in middle age, neuroticism and extraversion, were associated with later depressive symptoms such that extraversion protected from later depressive symptoms while neuroticism increased this risk. Physical activity, life style habits, diseases or demographic characteristics in middle age had no effect on later depressive symptoms. To understand further the nature of the association between personality in middle age and depressive symptoms later in life, the possible common genetic and environmental effects were estimated using quantitative genetic modeling.

The intra-class correlations for neuroticism, extraversion and depressive symptoms were higher among MZ than DZ twins suggesting the contribution of genetic effects. In neuroticism, the age-adjusted intra-class correlation for MZ twins was 0.51 (95% CI 0.34-0.66), for extraversion 0.53 (95% CI 0.36-0.67) and for depressive symptoms 0.61 (95% CI 0.46-0.72). The respective correlations for the DZ twins were 0.20 (95% CI 0.03-0.39), 0.06 (95% CI -0.14 to 0.26) and 0.14 (95% CI -0.06 to 0.33). Univariate genetic modeling confirmed the presence of genetic and non-shared environmental influences on both the personality variables and depressive symptoms. In the neuroticism, extraversion and depressive symptoms additive genetic effects accounted for 50%, 47% and 63% of the total variance, respectively. The remaining variance was due to non-shared environmental effects. The effect of age explained approximately 2% of the variance in extraversion, but had no effect on neuroticism or depressive symptoms in this sample from a relatively narrow birth cohort.

The cross-twin cross-trait and within-individual Pearson's correlation coefficients for MZ and DZ twins are presented in Table 4, and suggest the presence of genetic effects on the association between the traits.

TABLE 4 Intra-pair cross-twin and within individual Person's correlation coefficients (95% CI) for monozygotic and dizygotic twins

	Neuroticism twin 1	Extraversion twin 1	Depression twin 1	Neuroticism twin 2	Extraversion twin 2	Depression twin 2
Neuroticism twin 1		-0.22 (-0.42 to -0.01)	0.34 (0.15 to 0.57)	0.52 (0.36 to 0.80)	-0.14 (-0.35 to 0.08)	0.22 (0.01 to 0.44)
Extraversion twin 1	-0.26 (-0.45 to -0.07)		-0.17 (-0.38 to 0.04)	-0.15 (-0.37 to 0.07)	0.54 (0.38 to 0.82)	-0.22 (-0.44 to -0.01)
Depression twin 1	0.31 (0.13 to 0.51)	-0.15 (-0.34 to 0.04)		0.41 (0.21 to 0.65)	-0.14 (-0.36 to 0.07)	0.62 (0.52 to 0.95)
Neuroticism twin 2	0.20 (-0.01 to 0.40)	-0.07 (-0.27 to 0.14)	-0.06 (-0.26 to 0.15)		-0.25 (-0.47 to -0.05)	0.32 (0.11 to 0.55)
Extraversion twin 2	-0.01 (-0.21 to 0.19)	0.06 (-0.14 to 0.26)	-0.10 (-0.30 to 0.11)	-0.27 (-0.48 to -0.07)		-0.20 (-0.41 to 0.02)
Depression twin 2	0.04 (-0.17 to 0.24)	-0.03 (-0.23 to 0.18)	0.17 (-0.04 to 0.37)	0.29 (0.10 to 0.50)	-0.23 (-0.43 to -0.03)	

The correlations of the MZ pairs are shown above the diagonal and the correlations of the DZ pairs are shown below the diagonal.

We also fitted a series of trivariate twin models to data on neuroticism and extraversion in middle age and depressive symptoms in late life. This analysis began with the full ACE model (AIC=3844.4). The final model is presented in Figure 7 with the proportions of the variance explained by each factor and their confidence intervals. In the final model (AIC=3838.1, p-value of the χ^2 difference compared to the full model >0.05) neuroticism in middle age and depressive symptoms in old age shared an additive genetic component in common (A_1), explaining 55% (95% CI 40-67) of the total variance in neuroticism and 24% (95% CI 12-38) in depressive symptoms. The rest of the variance in neuroticism in middle age was due to trait-specific individual environmental factors (E_1), which accounted for 45% (95% CI 33-60) of the variance. Depressive symptoms in old age also had a trait-specific additive genetic component (A_3), accounting for 42% (95% CI 26-56) of the variance, and an individual environmental (E_3) component, accounting for 34% (95% CI 24-48), which explained the remaining variance. For extraversion in middle age, only trait-specific additive genetic (A_2) and individual environmental (E_2) factors explained the phenotypic variation. The relative contribution of a trait-specific additive genetic factor to extraversion was 50% (95% CI 34-63) and for individual environmental factors 50% (95% CI 37-66).

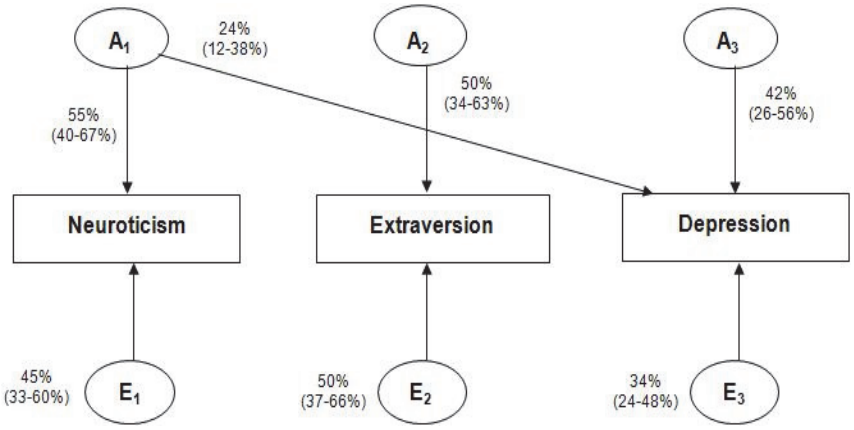

FIGURE 7 The most parsimonious Cholesky decomposition model for neuroticism, extraversion and depressive symptoms. The percentages (95% confidence intervals) are the proportions of genetic and environmental effects of the total variance.

Finally, to control for the possible confounding effect of the use of antidepressants in the year 2003, we repeated both the individual-based and twin analyses with data from which we had excluded the participants (n= 19) who reported using antidepressant medication in the year 2003. Controlling for the use of antidepressant medication had no effect on the study results.

5.3 Leisure time physical activity and depressive symptoms (Study II)

In order to investigate whether leisure time physical activity (LTPA) and depressive symptoms share genetic effects in common among adults in middle and old age, two separate twin datasets, Finnish Twin Cohort and FITSA, were used. Using data consisting of twins allowed us to take into account the genetic variation among individuals when investigating the origins of this association.

Among both the Finnish Twin Cohort and FITSA datasets, the within-individual Pearson's correlations between LTPA and depressive symptoms were small but statistically significant, demonstrating a phenotypic correlation between increased LTPA and decreased depressive symptoms. In the Finnish Twin Cohort, the correlation was -0.08 (95% CI -0.10 to -0.06) among the whole study population and among men and women separately -0.08 (95% CI -0.10 to -0.05) and -0.07 (95% CI -0.10 to -0.04), respectively. In the FITSA study the phenotypic correlation between these traits was -0.15 (95% CI -0.25 to -0.05). With regard to the genetic factors underlying LTPA and depressive symptoms, the within-pair intraclass correlations for both LTPA and depressive symptoms were higher for MZ twins than DZ twins in both datasets, indicating the probable effect of genetic factors on both traits (Table 5).

TABLE 5 Within-pair intra-class correlations (95% CI) of leisure time physical activity and depressive symptoms

	Finnish Twin Cohort		Finnish Twin Study on Aging	
	Within-pair intra-class correlations for LTPA			
	No. of pairs	ICC (95% CI)	No. of pairs	ICC (95% CI)
MZM	540	0.40 (0.32-0.47)	-	
DZM	1063	0.14 (0.08-0.20)	-	
MZF	787	0.34 (0.28-0.40)	95	0.47 (0.30-0.62)
DZF	1404	0.12 (0.07-0.17)	107	0.18 (-0.01 to 0.34)
	Within-pair intra-class correlations for depressive symptoms			
	No. of pairs	ICC (95% CI)	No. of pairs	ICC (95% CI)
MZM	601	0.31 (0.32-0.38)	-	
DZM	1213	0.13 (0.08-0.19)	-	
MZF	869	0.42 (0.36-0.47)	93	0.55 (0.39-0.68)
DZF	1582	0.16 (0.11-0.21)	104	0.23 (0.04-0.41)

MZM, monozygotic male twin pairs; DZM, dizygotic male twin pairs; MZF, monozygotic female twin pairs; DZF, dizygotic female twin pairs.

Genetic modeling was started by estimating the best univariate models for LTPA and depressive symptoms separately for men and women. In each dataset, the additive genetic/specific environment (AE) model offered the best fit for both LTPA and depressive symptoms. Table 6 summarizes the proportions of the phenotypic variance of LTPA and depressive symptoms explained by additive genetic and unique environmental factors in the best fitting AE-models by gender.

TABLE 6 Standardized variance components of additive genetic and unique environmental factors with 95% confidence intervals for leisure time physical activity and depressive symptoms by gender.

	Additive genetic factors		Unique environmental factors	
	Females	Males	Females	Males
Finnish Twin Cohort				
LTPA	0.32 (0.27-0.38)	0.38 (0.31-0.44)	0.68 (0.62-0.73)	0.62 (0.56-0.69)
Depressive symptoms	0.39 (0.34-0.43)	0.30 (0.30-0.37)	0.61 (0.57-0.66)	0.70 (0.63-0.76)
Finnish Twin Study on Aging				
LTPA	0.40 (0.22-0.55)	-	0.60 (0.45-0.77)	-
Depressive symptoms	0.56 (0.42-0.68)	-	0.44 (0.32-0.58)	-

Because the intra-class correlations and univariate models for each dataset indicated that a shared environmental component was not significant and could be dropped from the models, the bivariate analyses were carried out using AE

models with age and gender as covariates, except in the FITSA study, where all the participants were females.

In the Finnish Twin Cohort, about 8% of the genetic and 5% of the environmental effects were shared between the two variables (-2LL=42975.28, n of parameters=12, AIC=5137). According to the chi-square difference test between the nested models ($\Delta\chi^2$=3.419 (df=1), p > 0.05) and a lower AIC value of the reduced model (AIC=5135) the genetic correlation between LTPA and depressive symptoms could be set to zero. The non-shared environmental correlation between LTPA and depressive symptoms could also be set to zero ($\Delta\chi^2$=3.585 (df=1), p > 0.05, AIC of the reduced model=5135).

In the FITSA data, LTPA and depression shared about 6% of the genetic and 5% of the environmental effects (-2LL=2169.21, n of parameters=10, AIC=4358). The chi-square difference test and the comparison of AIC values indicated that the genetic correlation between the variables could be set to zero ($\Delta\chi^2$=0.409 (df=1), p > 0.05; AIC=4357). The non-shared environmental correlation between LTPA and depressive symptoms could also be set to zero ($\Delta\chi^2$ =874 (df=1), p > 0.05, AIC of the reduced model=4357). In sum, the results from the bivariate models suggested that only a small proportion of the genetic and environmental components of LTPA and depressive symptoms overlapped and statistically the overlap was non-significant in both the Finnish Twin Cohort and FITSA studies.

5.4 The effects of physical activity counseling on depressive symptoms (Study III)

In the SCAMOB randomized controlled trial, the baseline characteristics of the intervention and control groups were comparable. At baseline, a total of 61 (19%) participants in the intervention group and 62 (20%) in the control group scored above the CES-D cut-off of 16 points and were considered to have depressive symptoms. Of these, 32 participants (10%) in the intervention group and 32 (10%) in the control group scored 16-20 points on the CES-D scale, and among the participants with a CES-D score of ≥21 these numbers were 29 (9%) and 30 (10%), respectively.

Altogether, 85% (n=533) of the participants completed the baseline and follow-up measurements on depressive symptoms. Of the 314 persons randomized to the physical activity counseling intervention group, 279 (89%) completed the intervention and 35 (11%) dropped out of the intervention. These numbers were 254 (82%) and 56 (18%), respectively, for the control group. Those who failed to take part in the follow up were more likely in the control group (p=0.014), had a higher baseline CES-D value (12.0 vs. 9.7, p=0.020), poorer self-rated health (p<0.001) and were less active physically (p=0.001) at baseline. The dropout rate for both the intervention group and control group was higher among persons with CES-D ≥ 21 at baseline (17% and 33%, respec-

tively) than among those with a CES-D score of 16-20 (13% and 28%, respectively), although the difference was statistically significant only in the control group (p=0.014).

In the analysis carried out for all the study subjects there was a modest increase in the CES-D sum points over the two years in both groups (p<0.001), but no group x time interaction effect between the intervention and control group were found (group x time p-value 0.498). In the intervention group, the mean increase in the CES-D score was 1.41 points (standard error of the mean, SEM 0.44) and in the control group 1.05 points (SEM 0.43). In the analysis carried out separately for men and women, the results were similar and no group x time interaction was detected.

Subgroup analyses for the total CES-D scale were carried out for those with no depressive symptoms at baseline (CES-D score <16), for those with minor depressive symptoms (16-20) and for those with more severe depression (≥21). Among those with CES-D <16 at baseline (Figure 8A), depression scores increased over time in both groups (p<0.001), with a slightly higher increase in the intervention group (group x time p-value 0.044). On average, the score in the intervention group increased by 2.74 points (SEM 0.39) and in the control group it increased by 1.67 points (SEM 0.36). Among participants with a CES-D score of 16-20 at baseline (Figure 8B), a significant treatment effect was observed (group x time p-value 0.039). The average reduction in the depression score was 3.26 points (SEM 1.12) in the intervention group, whereas in the control group the depression score increased on average by 0.56 points (SEM 1.42). Among those with CES-D ≥ 21 at baseline (Figure 8C), depression scores decreased over time in both groups (p<0.001). The average reduction in depression score was 5.44 points (SEM 1.55) in the intervention group and 4.12 points (SEM 1.48) in the control group with non-significant group x time interaction. When the analysis were done on a per protocol basis, similar results were obtained. Adjustment for antidepressant use had also no effect on the results.

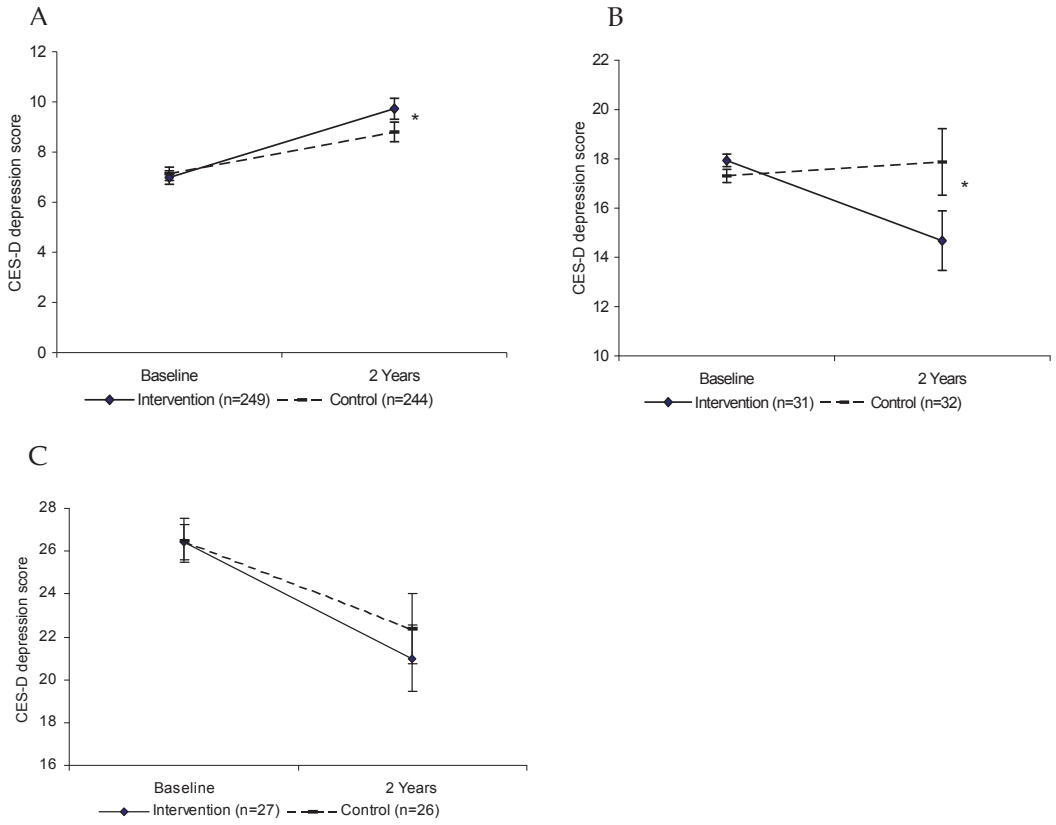

FIGURE 8 CES-D depression scores for the intervention and control groups during follow-up, (A) among subjects with no depressive symptoms at baseline (CES-D score 0-15), (B) among subjects with minor depressive symptoms (CES-D score 16-20) (C) and among subjects with more severe depression (CES-D score ≥21). Data are expressed as mean ± SEM. The p-values are based on repeated measures ANOVA: *$p<0.05$

At baseline, about 30% of the intervention group and 28% of the control group reported some form of injury in the previous year. At the 2-year follow-up, 25% of the intervention group and 24% of the control group reported some form of injury in the previous year. Accordingly, there were no statistical differences between the groups among those who needed medical treatment as a result of the injuries. This result indicates that the intervention did not cause excessive adverse events.

5.5 The effects of strength-power training on sense of coherence among older people with a hip fracture history (Study IV)

Forty-six participants of the Asymmetry study without contraindications for the strength-power training intervention participated in the RCT. There were no significant differences between the intervention and control groups at baseline for physical or psychosocial characteristics. The mean age of the study sample was 74 years and the majority were women (70%). In both groups the participants had an average three chronic conditions and three prescribed medications in use. The average time from the hip fracture was 3.5 years.

The mean score of the total SOC scale at baseline was 73.4 (SD 10.6) in the training group and 75.6 (9.6) in the control group (p=0.474). Table 7 shows the effect of the 12-week intervention on the level of the total SOC scale and its three subscales. The intervention had no statistically significant effect on the score for the total SOC scale (p=0.735) or its subscales (p=0.191-0.854). The sense of coherence scores decreased over time in both groups, although the change was statistically non-significant (p=0.292). The average decrease in the sense of coherence scale was 2.37 (2.63) points in the training group and 1.22 (2.03) points in the control group.

Training compliance was excellent being on average 95 ± 15%. During the training period, short-term adjustments for load or training frequency were made for 6 participants. In 2 cases musculoskeletal problems and in 1 case chest pain were likely to be related to the training. Additionally, 1 participant developed prolonged radicular pain in the lower limb after the training period. In 2 participants poor compliance with training was caused by health-related problems that were present also before the start of the trial, and in 1 participant this was due to an unrelated wrist fracture.

TABLE 7 The effects of intensive strength power training on the total Sense of Coherence scale (SOC) and its subscales among men and women in the training and control groups.

	Intervention (n= 24)	Control (n= 22)	Group p-value	Time p-value	Group x time p-value
SOC					
Baseline	73.4 (10.6)	75.6 (9.6)	0.474	0.292	0.735
Follow-up	71.1 (9.1)	74.3 (9.8)			
Meaningfulness subscale					
Baseline	24.9 (2.7)	23.7 (3.9)	0.232	0.051	0.191
Follow-up	23.3 (3.2)	23.3 (3.5)			
Manageability subscale					
Baseline	20.9 (4.7)	22.4 (3.5)	0.230	0.693	0.841
Follow-up	20.5 (3.8)	22.3 (4.3)			
Comprehensibility subscale					
Baseline	27.5 (5.0)	29.5 (4.9)	0.208	0.592	0.854
Follow-up	27.3 (4.4)	28.8 (4.4)			

Data are expressed as mean ± (SD)

6 DISCUSSION

This study investigated the factors in middle age that were considered possibly to be associated with depressive symptoms in old age and the potential factors underlying physical activity and depressive symptoms among middle to old age adults. In addition, the effects of two separate physical activity interventions on depressive symptoms and sense of coherence among older persons were studied. Four datasets were used in this study. The present findings suggest that personality in middle age, especially neuroticism, is strongly associated with later depressive symptoms. Leisure time physical activity in middle age, however, has no effect on later depressive symptoms and no common genetic vulnerability factors appear to exist between these traits. Further, the results showed that the 2-year physical activity counseling intervention had no effect on depressive symptoms among community dwelling older men and women. However, among the subgroup with minor depressive symptoms at baseline, a significant treatment effect was observed, where depressive symptoms decreased in the intervention group and increased in the control group. Finally, the 12-week intensive strength-power training among older people with a hip fracture history had no effect on the participants' sense of coherence.

6.1 Factors underlying depressive symptoms in old age

Factors in middle age associated with depressive symptoms in old age

Among older adults, depressive symptoms not meeting the diagnostic criteria for depression are highly prevalent, while their consequences for disability risk and decrease in well-being are similar to those of clinical depression (Blazer, 2003). Understanding what characteristics in middle age increase the risk for depression in old age could provide an insight into the aetiology of depression and therefore a more rational basis for targeted preventive interventions. Knowledge about these factors in early middle age would also offer opportunities for identifying younger persons who are at risk for developing depressive

symptoms later in life. Despite the fact, that many common risk factors for depressive symptoms have been partially identified, longitudinal studies comparable to our follow-up time of almost 30 years, are rare.

The results of this study indicate that in middle age the personality dimensions of neuroticism and extraversion were strongly associated with depressive symptoms in old age. In contrast to the relationship between neuroticism and depressive symptoms, extraversion in middle age had a protective effect on depressive symptoms experienced in old age. The best-fitting twin model contained a genetic component that was common to both neuroticism in middle age and depressive symptoms in old age, individual-specific environmental factors unique to both neuroticism and depressive symptoms, and a trait-specific genetic component unique to old age depression. Extraversion in middle age had only trait-specific additive genetic and individual environmental factors explaining the phenotypic variation.

With respect to personality, our results confirm previous findings from prospective and twin studies which have found neuroticism to be a strong predictor for later depression, and that this association is partly due to common genetic vulnerability to both neuroticism and depression (Kendler et al. 1993, Roberst et al. 1999, Steunenberg et al. 2006). We found neuroticism in middle age and depressive symptoms in old age to share only part of their genetic background, but Fanous and colleagues (2007) found neuroticism to predict the onset of depression and that all of the covariation between neuroticism and depression was due to additive genetic and individual-specific environmental factors shared by both traits.

With regard to extraversion the results were more controversial. In accordance with previous findings extraversion was found to protect from later depressive symptoms (Jylhä & Isometsä 2006, Fanous et al. 2007), but no genetic relationship between these two traits was detected. Some possible interpretations for these results can be offered. First, in the trivariate genetic modeling in which both personality traits were included, the effect of low extraversion, in other words introversion, was possibly mediated through the inverse correlation between neuroticism and extraversion. Second, to detect a significant genetic association between extraversion and depressive symptoms, we should probably have needed a substantially larger study population. The possibility of non-additive genetic effects in extraversion may also make the detection of common genes between depression and personality difficult.

In our study, physical activity, life style habits, diseases or demographic characteristics in middle age had no effect on depressive symptoms in old age. Although many studies reporting positive associations between physical activity and decreased depressive symptoms have been published, some previous studies have reported no effect of physical activity on later mood problems (e.g. Kritz-Silverstein et al. 2001). Compared to earlier longitudinal studies, our notably long follow-up time of 28 years may, at least in part, explain the lack of association. Very long follow-up times highlight only those variables that have the strongest associations with outcomes, since over the years many intervening

events may happen, which mask the initial associations. In addition, our data did not allow us to identify extreme groups in terms of high and low physical activity. Thus, it is possible that in a study population with greater range of midlife physical activities, such an association is present.

The results of this study together with those of the previous research confirm the importance of personality in middle age on depressive symptoms in old age and also extend earlier findings to older populations. These findings also have implications for identifying early risk factors for depressive symptoms in old age as well as planning individually targeted interventions to ameliorate depression in old age. Further research is required on exploring the mechanisms underlying the association of neuroticism and extraversion with depressive symptoms in old age.

Genetic and environmental influences on leisure time physical activity and depressive symptoms among middle to old age adults

Leisure time physical activity and depressive symptoms were found to be modestly heritable. However, despite the cross-sectional correlation between these traits we did not find evidence for common genetic vulnerability for low leisure time physical activity and depressive symptoms among twins from middle to old age.

Positive associations between physical activity and decreased depressive symptoms have been documented in several earlier studies using heterogeneous study populations as well as various measures of physical activity and depressive symptoms (e.g. Sjösten & Kivelä 2006, Teychenne et al. 2008), but only one study has investigated this association by taking into account the genetic variation among individuals. In their study, De Moor and colleagues (2008) found a modest genetic correlation between physical activity and depressive symptoms among a Dutch cohort, consisting of 8558 twins, additional siblings and parents, aged 18 to 50 years. However, as heritability estimates are always population-specific, there is a need for replication studies (Plomin et al. 2001).

Our results supported the previous research findings confirming the moderate importance of genetic factors in explaining individual differences both in leisure time physical activity and depressive symptoms among individuals from middle to old age. Our study also adds knowledge concerning the heritability of leisure time physical activity among older people, as little research has been conducted on the effects of genes on older adults' participation in physical activity. With respect to the heritability of depressive symptoms, the moderate effects, with increasing importance of genes during old age were also in accordance with earlier findings (Carmelli et al. 2000).

Our datasets consisted of relatively healthy twins of different ages. The association between physical activity and depressive symptoms may be more readily observed in clinical samples with more depressive symptomatology. Among experimental studies that have also included healthy, non-depressed people, the beneficial effects of exercise have been more controversial (Brosse et al. 2002, Teychenne et al. 2008). Also, the possibility of non-linear associations

between leisure time physical activity and depressive symptoms on the one hand and individuality in affective responses to physical activity on the other might complicate the association between physical activity and depressive symptoms (Ekkekakis et al. 2005). It has also been suggested that other factors such as personality might modify or account for these relationship by affecting both leisure time physical activity and depressive symptoms (De Moor et al. 2006).

Our study, aiming to confirm the earlier findings by De Moor and colleagues (2008) did not find evidence for common genetic vulnerability for low LTPA and depressive symptoms among adults from middle to old age. Differences between these two studies may result from several reasons. The use of different measures for both LTPA and depressive symptoms might explain some differences between these studies. The use of different measures may also have led to distinct heritability estimates for LTPA and depressive symptoms and therefore dissimilar results. Also the age range of the twins in our study was wider, including also older female twins with mean age of seventy-two years, which is likely to have affected the results. However, both studies found a notably small phenotypic correlation between LTPA and depressive symptoms in population-based samples, despite the importance of genetic factors for both LTPA and depressive symptoms among men and women of various ages. This for one's part argues in favour of a third underlying variable having an effect on both LTPA and depressive symptoms.

Although the study by De Moor and colleagues (2008) suggests that at the population level there is a common genetic vulnerability to lack of regular leisure time physical activity and risk for depression, this does not imply that manipulation of exercise cannot be used to change depressive symptoms. As also found in our study, only voluntary leisure time physical activity is influenced by genetic factors. In exercise interventions, the type of physical activity is more environmentally driven e.g. prescribed and externally monitored. However, individuals can strongly differ in their responsiveness to exercise. In the future, more studies aimed at increasing understanding of individual differences in genetic sensitivity to the mental health benefits of exercise is needed. In addition, understanding the underlying mechanisms in the association between leisure time physical activity and depressive symptoms would be useful in seeking to prevent mood problems among sedentary people at increased risk for depressive symptoms.

6.2 Effects of physical activity interventions on depressive symptoms and sense of coherence among older people

Effects of physical activity counseling on depressive symptoms among community-dwelling older adults

To date, empirical evidence on the effects of physical activity counseling on psychological health outcomes among older people is scarce and the few existing studies have yielded mixed results. With respect to quality of life, both positive effects (Elley et al. 2003, Kerse et al. 2005, Dubbert et al. 2008) and non-significant effects (Kerse et al. 1999, Dubbert et al. 2002, Kolt et al. 2007) have been reported. However, physical activity counseling interventions investigating specifically depressive symptoms are rare. In a study by Kerse and colleagues (2010), participants aged 75 years or older received an individualized home-based physical activity program supported by eight home visits during the 6-month intervention, which improved mood and quality of life among older men and women. Also Salminen and colleagues (2005) found improvements in depressive symptoms among older male coronary heart disease patients after a health advocacy, counseling and activation programme.

Our results extend the limited literature in this field by showing that a single individualized physical activity counseling session with a supportive phone contact every 4 months for 2 years decreased depressive symptoms among a subgroup with minor depressive symptoms at baseline. However, no effect of intervention was observed among those with no depressive symptoms or with more severe depression. Among all the study subjects depressive symptoms increased slightly over the two-year follow-up. In addition, the physical activity counseling intervention decreased mobility limitations (Mänty et al. 2009), reduced incident disability (von Bonsdorff et al. 2008) and need for home care (von Bonsdorff et al. 2009).

Our results are in agreement with Salminen and colleagues (2005) who found improvements in depressive symptoms among older male patients with coronary heart disease having a moderate or high level of depressive symptoms at baseline, but no change in depression scores among non-depressive population after a health advocacy, counseling and activation programme. This finding has also confirmed in other experimental studies which have shown that including non-depressed participants in the study population may produce a "ceiling effect", as there is less room for improvement in depression in such samples (e.g. Brosse et al. 2002, Teychenne et al. 2008).

The average depression scores to the whole study population and to the subgroup with no depressive symptoms at baseline increased over the two-year intervention, remaining nevertheless below the standard CES-D score of 16. Increasing depression scores have been reported earlier in older people with decreased health status and negative life events, which are more frequent in later life (Fiske et al., 2003). Part of the increasing depression scores may also be due to regression to the mean, as persons with low depression scores are likely

to obtain higher scores over time and vice versa. With respect to participants with more severe depression at baseline, also no effect of the intervention was found. This finding might instead be explained by the fact, that among control group participants depressive symptoms, and especially more severe depression at baseline increased the risk to drop out of the study, leaving the treatment effects among those with severe depression at baseline underestimated. In this subgroup the depression scores decreased among the intervention group participants, and it is thus possible, that in some way our intervention may have alleviated depression also among those with more severe symptoms. However, the reduction in depression scores may also be partly explained by the fact that depressive symptoms in older adults may fluctuate, with remissions and recurrences following each other sometimes even without any form of treatment (e.g. Geerlings et al. 2000).

In our study, several mechanisms may explain the improvements in mood among those with minor depressive symptoms at baseline. First, our physical activity counseling was motivational, individually tailored for each participant and was followed-up by personal phone contacts over the two-year intervention. So, it is thus possible that the counseling itself might have had some direct psychological stimulating effects on participants' mood level. Second, it was expected that the physical activity counseling, by increasing physical activity would also alleviate depressive symptoms and prevent deterioration of mood. As the physical activity level in the intervention group increased in this study (Rasinaho et al. 2011), we believe that the fitness benefits, together with increased social participation, may explain the positive effect of the intervention. We were not able to pinpoint the particular mechanism underlying the association between physical activity counseling and improved mood. Nevertheless, when aiming to alleviate depressive symptoms through physical activity it is likely that the presence of both the social and physical aspects of the intervention will probably give further benefits over having just the one or the other.

Overall, our study found that a physical activity counseling targeting initially sedentary older people was effective in reducing depressive symptoms among older men and women suffering from minor depressive symptoms. These results together with earlier findings of a decrease in mobility limitations (Mänty et al. 2009) and reduced incident disability (von Bonsdorff et al. 2008) and need for home care (von Bonsdorff et al. 2009) after the intervention suggest that physical activity counseling may offer an effective means to promote health and well-being among community-dwelling sedentary older adults. However, as the present study was based on secondary analyses of randomized controlled data, these results should be considered as hypothesis building. In addition, the subgroup analyses remove the effect of randomization, which makes it problematic to draw strong conclusions based on these analyses. Further research is required to clarify the optimal type, duration and intensity of educational physical activity counseling which will most benefit the growing older population.

Effects of strength-power training on sense of coherence among older people with a hip fracture history

The present randomized controlled trial among 60-85-year old people with a hip fracture history found no effect of twelve weeks of intensive strength-power training on the participants' sense of coherence. During the intervention a slight, but non-significant, decrease in sense of coherence score was observed in both the intervention group and control group. As research-based evidence on the effects of physical exercise training on sense of coherence and psychological well-being in general among older people with a hip fracture is scarce, our study provided new evidence in this area of research.

To date, the few physical activity intervention studies including also psychological outcomes among older hip fracture patients have showed inconsistent results. For quality of life, both positive results (Binder et al. 2004, Tsauo et al. 2005) and no effects (Crotty et al. 2002) of interventions have been reported. Lotus Shyu and colleagues (2005) found positive effects on depression after an interdisciplinary intervention program consisting of geriatric consultation, continuous rehabilitation, and discharge planning for older hip fracture patients. In another study, a physical activity intervention had no effect on self-efficacy of hip fracture patients (Resnick et al. 2007). We found only one earlier study where the effects of a physical activity intervention on sense of coherence had been investigated. In their study, Kohut and colleagues (2006) found that a ten-month physical activity intervention consisting either of aerobic exercise or strength training increased sense of coherence among healthy people aged 64 years or over. However, the participants in their study were healthier and the intervention was longer, which limits its comparability with our study.

In our study, there was a slight non-significant decrease in the total SOC scale in both groups. In the intervention group, the changes in the total SOC scale and its subscales varied between one and five percent and in the control group between one and two percent. However, the smallest meaningful change in SOC is 10%, and consequently the present minor decline in SOC found here may be considered insignificant (Karlsson et al. 2000). It is also worth noticing that the SOC scores both before and after the intervention were at a high level. Our study population consisted of rather well functioning people despite their hip fracture history. Those not living independently or unable to walk outdoors independently were excluded, which might, at least in part, explain the high level of SOC in our study.

There are some possible explanations why we were unable to detect changes in the participants' level of sense of coherence. First, our participants had a higher sense of coherence than found in earlier studies among younger and older adults with chronic illnesses (Lillefjell & Jakobsen 2007, Lundman et al. 2010, Nilsson et al. 2010). This may have produced a "ceiling effect", as there was less room for improvement. Second, our study, with a follow-up period of three months, may have been too short to detect differences in SOC levels. Although the participants' muscle strength, power and self-reported outdoor mobility improved (Portegijs et al. 2008), psychological changes might need more

time. Third, the earlier intervention studies that have been successful in enhancing participants' sense of coherence have often included also psychological interventions combined with other forms of rehabilitation (e.g. Lillefjell & Jakobsen 2007). As older adults with a hip fracture history often suffer from multiple medical and psychological problems, multidisciplinary intervention combining both physical and psychological aspects might lead to more beneficial results.

Among older hip fracture patients, psychological health is of great importance as, e.g., depression may further increase the risk for physical disability (Penninx et al. 1998), whereas a high level of psychological well-being may help to sustain motivation during the rehabilitation processes (Proctor et al. 2008). Therefore studies on ways to increase older adults' psychological health are urgently needed. It is possible that a longer intervention among hip fracture patients who have lower sense of coherence, may be beneficial and should be studied. To obtain psychological health improvements, physical rehabilitation interventions should also have specific psychological elements, such as motivational discussions. In the future, this should be taken into consideration when rehabilitation programs are being planned for hip fracture patients.

6.3 Methodological considerations

This study is based on four research projects, two twin studies (FITSA and Finnish Twin Cohort) and two randomized controlled trials (SCAMOB and Asymmetry), each consisting of community-dwelling older people. In addition, the Finnish Twin Cohort study also included middle-aged men and women.

The FITSA study comprised a population-based sample of older well-functioning community-dwelling women. To be recruited for the study, both sisters of the twin pair had to participate and be able to travel to the research laboratory for the baseline measurements. Therefore, the inclusion criteria may have lead to the exclusion of persons with poor health, and it is thus possible that some people with severe mental health problems dropped out of the study. Furthermore, the requirement that both individuals of the pair had to participate might have resulted in overestimation of twin similarity. The second twin study, the Finnish Twin Cohort, consisted of virtually all twin pairs of the same sex (13 888 twin pairs) born in Finland before 1958 and with both co-twins alive in 1967. The members of the twin cohort provided detailed data on several outcomes in the health questionnaires of 1975, 1981 and 1990 with overall high response rates of 89%, 84% and 77%, respectively.

The classical twin method used in the present genetic analyses is considered a valid way to estimate the total influence of genetic and environmental factors on a trait. In twin studies a basic assumption is that MZ and DZ pairs are assumed to share their common environment to the same extent. If MZ twins are treated more similarly than DZ twins, this may lead to an overestimation of genetic factors. Similarity can however be tested by comparing the

means and variances of a trait between the two zygosity groups (Rijsdijk & Sham 2002). In this study, the means and variances of the MZ and DZ groups did not differ from each other in any of the studied variables (Studies I, II).

The FITSA study with a follow-up time of 28 years offered an excellent possibility to investigate factors in middle age thought to be associated with depressive symptoms in old age as it enabled both longitudinal and genetic study designs. However, because the participants' baseline level of depressive symptoms was not assessed in the 1975 questionnaire we were not able to fully utilize the longitudinal study design. Thus, to avoid potential confounding effects of prevalent depressive symptoms, the analyses were limited to a subsample of participants who were healthy at baseline. Also our second twin dataset, the Finnish Twin Cohort, offered high quality genetic data on the participants' leisure time physical activity and depressive symptoms across a wide age range from middle to old age. However, as the measurements of leisure time physical activity and depressive symptoms were performed nine years apart, this may have caused selection bias, as attrition typically takes place among the less healthy participants, leading to possible underestimation of the relationship between leisure time physical activity and depressive symptoms (Brosse et al. 2002). It should also be noted that in both the twin datasets, only self-reported data were used, and therefore the likelihood of reporting bias needs to be considered.

With regard to the generalizability of our results, the question arises of whether twins in general and these twin cohorts in particular are representative of the general population. As to the general characteristics of the subjects, previous research within the Finnish Twin Cohort has shown that the cohort members are representative of the adult Finnish population (Kaprio et al. 1979). Research within other populations has also indicated that twins do not differ from other people with respect to their personalities, psychopathology or life-style characteristics (Andrew et al. 2001, Johnson et al. 2002).

In Studies III and IV, the randomized controlled designs allowed the true effects of physical activity counseling on depressive symptoms and intensive strength-power training on sense of coherence to be studied. In both studies, the randomization process was successful and the baseline characteristics of the intervention and control groups were comparable. With regard to the SCAMOB trial, both the intervention and follow-up times were considerably longer than those in previous physical activity counseling programs targeted at older populations. In addition, adherence to the physical activity counseling program was high. In the SCAMOB trial, the intervention group was encouraged to utilize already existing physical activity possibilities, e.g. exercise groups organized by the City of Jyväskylä. In the City of Jyväskylä, where the trial was conducted, the opportunities for supervised as well as independent exercise for older people are very well organized, which should be noted when generalizing the results of the trial. As the inclusion criteria for participation in the SCAMOB trial was either only moderately physically active or sedentary, generalizing the results to physically active older adults needs to be considered. Furthermore, the

results of the subgroup analyses in the SCAMOB trial need to be considered with caution, since the effect of randomization is uncertain. Also the statistical power of the subgroup analyses might not have been sufficient. In addition, subgroup analyses should be considered as hypothesis building, and no recommendation for practice may be based on them.

In the Asymmetry trial, the data allowed us to study the effects of the physical activity intervention on positive aspects of mental health, sense of coherence, among older people with a hip fracture history. Although older hip fracture patients are known to be especially vulnerable to mental health decline (e.g. Fiatarone Singh et al. 2009), studies on improving mental health among this frail population are rare. However, despite their hip fracture, the men and women in the Asymmetry study were relatively healthy and well-functioning due to the inclusion criteria for participation in the Asymmetry study (maximum age 85, community-dwelling and able to walk outdoors independently) which must be taken into consideration when generalizing these results to other hip fracture populations. Also the sample size in the Asymmetry study was relatively small, although everyone in the target population who met the inclusion criteria had the opportunity to join the study. The limited number of study participants also restricted the possibility to analyze changes in sense of coherence according to gender and age, which might have influenced our results.

The strengths of this study include the strong and high quality datasets, consisting of two population-based twin studies and two randomized controlled trials. The use of several datasets and different analytical methods yields versatile information on the association between physical activity, mental health and genetic factors among older people.

6.4 Implications and future directions

Depression and depressive symptoms are major health problems among the elderly population world-wide and are associated with multiple negative outcomes. The etiological picture of depression and depressive symptoms in late life have remained unrevealed. Studying the factors in middle age that could be associated with increased risk for depressive symptoms in old age could provide a insight into the etiology of depressive symptoms and hence a more rational basis for targeted preventive interventions. As the number of people living to very old ages is increasing, there is a need for new multidimensional methods through which well-being in old age can be maintained and increased.

The existing scientific evidence on the effect of personality on later depressive symptoms is convincing. Neuroticism increases the risk for later depressive symptoms, and extraversion protects from later decline in mental health. Our study, together with earlier findings, supports the modest genetic overlap between the genetic risk factors for middle age neuroticism and old age depressive symptoms. Given the stability of the mean levels of personality and its genetic basis in adulthood, investigating personality earlier in life is important.

More research is required to find the mechanisms that link neuroticism and extraversion to depressive symptoms in old age. In addition, more research on life-course influences on depressive symptoms in old age is urgently needed.

Physical activity and exercise are widely promoted as effective means to enhance health, physical functioning and psychological well-being in older persons. In the future, more studies targeted at increasing understanding of individual differences in genetic sensitivity to the mental health benefits of exercise are needed.

Physical activity counseling is an example of a low-cost educational intervention to promote physical activity among older adults. The present study showed that individually tailored physical activity counseling with an emphasis on self-efficacy for more active behavior was effective in reducing depressive symptoms among the older participants with minor depressive symptoms at baseline. However, further research is required before firm conclusions can be drawn. Given the heterogeneity of the elderly population in general, further research is required to clarify the optimal timing, type, duration and intensity of physical activity counseling which will most benefit the growing older population. Furthermore, the mechanisms through which physical activity counseling effects depressive symptoms should also be investigated.

Especially among older people with disabilities, psychological health is of great importance as it has positive effects on both recovery rates and motivation towards rehabilitation. The results of this study demonstrated, that although older hip fracture patients were able to participate in the intensive progressive resistance training intervention with a high rate of compliance, their sense of coherence was not affected after the intervention. More studies, also including specific psychological elements, such as motivational discussions, are needed.

7 MAIN FINDINGS AND CONCLUSIONS

The main findings of the present study can be summarized as follows:

1. Among older women, personality in middle age was associated with depressive symptoms 28-years later, such that extraversion protected from later depressive symptoms while neuroticism increased this risk. The relationship between neuroticism and depressive symptoms was partly the result of genetic factors that predispose to both neuroticism and depressive symptoms. Extraversion in middle age had no genetic relationship with depressive symptoms in old age.

2. Among men and women in middle and old age, increased leisure time physical activity was phenotypically associated with decreased depressive symptoms. However, common genetic factors influencing both traits were not found.

3. A physical activity counseling intervention comprising one face-to-face counseling session followed up by supportive phone contact every 4 months for 2 years had no effect on depressive symptoms among older community-dwelling men and women. However, subgroup analyses showed that among those with minor depressive symptoms at baseline depressive symptoms decreased in the intervention group compared to the control group.

4. An intensive 12-week strength-power training intervention among older men and women with a hip fracture history had no effect on the participants' sense of coherence.

In conclusion, this study stresses the important effect of personality in middle age on later depressive symptoms. The results also indicate that although genetic factors are important for both leisure time physical activity and depressive symptoms among adults in middle and old age, the small, but robust cross-

sectional association is not explained by common genetic factors for both traits. In addition, the results suggest that physical activity counseling for older adults may provide an effective means to prevent depressive symptoms among community-dwelling older adults but should be studied more closely among different target groups. With respect to strength-training interventions among frail older people, interventions including also psychological elements warrant further research.

YHTEENVETO (FINNISH SUMMARY)

Masentuneisuus, koherenssi, fyysinen aktiivisuus ja geneettiset tekijät ikääntyneillä ihmisillä

Masentuneisuus on ikääntyneiden ihmisten yleisimpiä mielenterveyden häiriötä lievän masentuneisuuden ollessa yleisempää kuin varsinainen masennussairaus. Iäkkäillä henkilöillä masentuneisuus on usein yhteydessä heikentyneeseen toimintakykyyn ja selviytymiseen päivittäisistä toiminnoista sekä lisääntyneeseen terveyspalvelujen käyttöön. Masentuneisuus voi myös heikentää sairauksista kuntoutumisen prosessia sekä lisätä kuolleisuusriskiä. Liikunnalla puolestaan on havaittu olevan positiivisia vaikutuksia iäkkäiden henkilöiden mielialaan. Fyysisen aktiivisuuden on havaittu vaikuttavan mm. positiivisesti itsetuntoon ja esimerkiksi sosiaalisten kontaktien määrä voi lisääntyä liikuntaharrastuksen kautta. Liikunnan on todettu myös vaikuttavan positiivisesti yksilön käsityksiin omasta vanhenemisestaan. Liikunnan fyysistä kuntoa parantava vaikutus voi myös olla kohentuneen mielialan taustalla.

Liikuntainterventioita on pääasiassa toteutettu hyvin kontrolloiduissa oloissa, joissa harjoitteiden sisältö on tarkkaan määritelty. Liikuntainterventiot voivat myös sisältää terveydenhuoltohenkilöstön antamaa liikuntaneuvontaa, lääkärin määräämiä ”liikuntareseptejä”, koteihin postitettavia informaatiokirjeitä tai puhelimitse tapahtuvaa fyysisen aktiivisuuden tukemista. Liikuntaneuvontainterventioiden pitkäaikaisvaikutuksia tai vaikutuksia esim. henkiseen hyvinvointiin ei ole tutkittu riittävästi. Myöskään liikunnan vaikutuksia koherenssin tunteeseen ei ole tutkittu aikaisemmin. Vahvan koherenssin tunteen on aikuisväestöllä todettu olevan yhteydessä parempaan fyysiseen ja psyykkiseen terveydentilaan sekä alhaisempaan kuolleisuusriskiin. Vaikka koherenssin tunteen on raportoitu olevan suhteellisen pysyvä tunnetila, uusimmat tutkimukset ovat osoittaneet erityisesti negatiivisten elämäntapahtumien olevan yhteydessä heikentyneeseen koherenssin tunteen kokemiseen. Ikääntyneellä väestöllä erityisesti terveydentilan muutokset voivat heikentää koherenssin tunnetta.

Tässä tutkimuksessa selvitettiin ikääntyneiden henkilöiden masentuneisuuden taustalla vaikuttavia tekijöitä. Sitä, miten erilaiset tekijät keski-iästä, kuten liikunta-aktiivisuus, elintavat ja sairaudet ennustavat vanhuuden masentuneisuusoireita ei ole juurikaan raportoitu. Lisäksi selvitettiin onko ikääntyneiden henkilöiden masentuneisuuden ja liikunnan harrastamisen taustalla yhteisiä geneettisiä tekijöitä. Ainoassa tätä kysymystä käsitelleessä aikaisemmassa tutkimuksessa havaittiin vapaa-ajan liikunta-aktiivisuuden ja masentuneisuuden välisen yhteyden selittyvän osittain yhteisillä geneettisillä tekijöillä. Tässä tutkimuksessa selvitettiin myös liikuntaneuvontaintervention vaikutuksia iäkkäiden henkilöiden mielialaan. Liikuntaneuvonnan avulla pystytään tehokkaasti tavoittamaan suuri joukko ikääntyneitä henkilöitä, mutta neuvonnan toteuttamisesta ja tuloksellisuudesta iäkkäillä liikkumisvaikeuksista kärsivillä henkilöillä ei ole tietoa. Näyttöön perustuva tutkimus on siis tarpeellinen. Lisäksi

tutkittiin myös intensiivisen voimaharjoittelun vaikutusta lonkkamurtuman sairastaneiden ikääntyneiden henkilöiden koherenssin tunteeseen.

Tässä tutkimuksessa käytettiin neljää eri aineistoa, kahta kaksosaineistoa sekä kahta satunnaistetun kontrolloidun kokeen aineistoa. Finnish Twin Study on Aging (FITSA) tutkimukseen osallistui 103 identtistä ja 114 epäidenttistä 63-76-vuotiasta naiskaksosparia, jotka ovat osallistuneet Suomen kaksoskohorttitutkimukseen vuodesta 1975. FITSA tutkimuksen ensimmäiset mittaukset toteutettiin vuosina 2000-2001 ja seurantamittaukset vuosina 2003-2004. Toisena kaksosaineistona käytettiin Suomen kaksoskohorttitutkimuksen aineistoa (Finnish Twin Cohort), johon on osallistunut 13888 kaksosparia, jotka ovat syntyneet ennen vuotta 1958 ja joista molemmat sisarukset ovat olleet elossa vuonna 1967. Kaksosia on tutkittu kattavien kyselylomakkeiden avulla vuosina 1975, 1981 ja 1990. Tässä väitöskirjatyössä hyödynnettiin vuosien 1981 ja 1990 kyselylomakkeiden tietoja. Kolmantena aineistona käytettiin Screening and counseling for physical activity and mobility (SCAMOB) tutkimusta, jonka kohdejoukkona olivat jyväskyläläiset 75-81-vuotiaat itsenäisesti asuvat henkilöt, joista satunnaistettiin koeryhmään 318 ja kontrolliryhmään 314 henkilöä. Koeryhmä osallistui fysioterapeutin yksilölliseen liikuntaneuvontaan ja lisäksi fysioterapeutti seurasi sekä tuki heitä fyysisen aktiivisuuden ylläpidossa säännöllisin puhelinkontaktein (4 krt/vuosi) kahden vuoden ajan. Neljäs aineisto, Asymmetry tutkimus, koostui ikääntyneistä miehistä ja naisista, jotka olivat kokeneet lonkkamurtuman puoli - seitsemän vuotta aiemmin. Tutkittavista ne, joilla ei ollut kontraindikaatioita voimaharjoittelulle rekrytoitiin 3 kuukautta kestävään kuntoutusohjelmaan. Koeryhmään osallistui 24 ja kontrolliryhmään 22 henkilöä. Koeryhmä osallistui 3 kuukautta kestävään intensiiviseen voima-nopeusharjoitteluun kahdesti viikossa.

Tutkimuksen tulokset osoittivat keski-iän persoonallisuuden olevan keskeisin ikääntyneiden masennuksella altistava tekijä. Keski-iän neuroottisuuden havaittiin lisäävän merkittävästi riskiä sairastua masennusoireisiin 28 vuotta myöhemmin kun taas ekstraversion havaittiin puolestaan ”suojaavan” vanhuusiän masentuneisuudelta. Keski-iän fyysisellä aktiivisuudella, elintavoilla tai sairauksilla ei ollut yhteyttä myöhemmin koettuihin masentuneisuus oireisiin. Geneettisen mallinnuksen tulokset osoittivat keski-iän neuroottisuuden ja vanhuuden masennusoireiden olevan ainakin osittain yhteisten geneettisten riskitekijöiden seurausta. Tämän tutkimuksen mukaan keski-iän ekstraversiolla ei ollut geneettistä yhteyttä myöhempiin koettuihin masentuneisuusoireisiin. Vaikka keski-iän fyysisen aktiivisuuden ei havaittu vähentävän riskiä vanhuusiän masentuneisuudelle, vapaa-ajan liikunta-aktiivisuus ja masentuneisuus olivat tilastollisesti merkitsevästi yhteydessä toisiinsa keski-ikäisten ja ikääntyneiden henkilöiden joukossa. Molemmat piirteet olivat kohtalaisen perinnöllisiä ominaisuuksia, mutta tässä aineistossa liikunta-aktiivisuuden ja mielialan välillä ei havaittu yhteisiä geneettisiä tekijöitä.

Lisäksi tässä tutkimuksessa havaittiin, että liikuntaneuvonta interventiolla voitiin vaikuttaa positiivisesti niiden henkilöiden mielialaan, jotka tutkimuksen alussa kärsivät lievistä masentuneisuusoireista. Vakavasti masentuneiden ja ei-

masentuneiden ryhmissä liikuntaneuvontaintervention vaikutusta ei havaittu. Intensiivisellä 12-viikon voimaharjoittelujaksolla ei puolestaan havaittu vaikutusta ikääntyneiden lonkkamurtuman kokeneiden henkilöiden koherenssin tunteeseen.

Yhteenvetona voidaan todeta keski-iän persoonallisuuden olevan merkittävä ikääntyneiden masentuneisuudelle altistava tekijä. Keski-iän neuroottisuuden ja vanhuudessa koettujen masentuneisuusoireiden välinen yhteys on voimakas ja osittain samojen geenien seurausta, jotka altistavat yksilön sekä neuroottisuudelle että masennusoireille. Vapaa-ajan liikunta-aktiivisuuden ja masentuneisuuden havaittiin myös olevan kohtalaisen perinnöllisiä ominaisuuksia, mutta viitteitä yhteisistä geneettisistä tekijöistä liikunta-aktiivisuuden ja masentuneisuuden välillä ei löydetty. Liikuntaneuvonnan avulla voidaan puolestaan edistää lievistä masentuneisuusoireista kärsivien mielialaa, kun taas koherenssin tunteeseen ei voimaharjoitteluinterventiolla pystytty vaikuttamaan. Tulevaisuudessa lisää tutkimuksia liikunnan ja mielialan välisistä yhteyksistä sekä erilaisten liikuntainterventioiden vaikuttavuudesta ikääntyneiden henkilöiden mielialaan tarvitaan.

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ORIGINAL PAPERS

I

GENETIC CONTRIBUTION TO THE RELATIONSHIP BETWEEN PERSONALITY AND DEPRESSIVE SYMPTOMS AMONG OLDER WOMEN

by

Inka Pakkala, Sanna Read, Jaakko Kaprio, Markku Koskenvuo,
Markku Kauppinen, Taina Rantanen 2010

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ORIGINAL ARTICLE

Genetic contribution to the relationship between personality and depressive symptoms among older women

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Background. Prior studies suggest that certain types of personality are at higher risk for developing depressive disorders. This study examined the relationship between old age depressive symptoms and two middle-age personality dimensions, neuroticism and extraversion.

Method. The present study is part of the Finnish Twin Study on Aging, where altogether 409 female twins who had completed the Eysenck Personality Inventory at the age of 38–51 years were studied for depressive symptoms 28 years later using Center for the Epidemiologic Studies Depression Scale. Logistic regression analysis suitable for dependent data and univariate and Cholesky models for decomposing the genetic and environmental factor were used.

Results. Middle age extraversion protected from later depressive symptoms while neuroticism increased the risk. Twin modeling indicated that the association between neuroticism and depressive symptoms resulted from shared genetic risk factors common to both traits. However, a substantial proportion of the genetic vulnerability was specific to old age depressive symptoms and was not shared with neuroticism. Middle age extraversion had no genetic relationship with old age depressive symptoms.

Conclusions. The relationship between middle age neuroticism and old age depressive symptoms is strong but only partly the result of genetic factors that predispose to both neuroticism and depressive symptoms. Extraversion, by contrast, has no genetic relationship with depressive symptoms experienced in old age.

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Key words: Aging, depressive symptoms, personality, twins.

Introduction

There is accumulating evidence that certain types of personality are at higher risk for developing depressive disorders (e.g. Kendler *et al*. 1993; Fanous *et al*. 2002). Several studies have suggested that the personality trait most closely related to depressive disorder is neuroticism (Roberts & Kendler, 1999; Kendler *et al*. 2006*a*; Steunenberg *et al*. 2006). Neuroticism and depression have been associated in clinical (Duberstein & Heisel, 2007), family (Duggan *et al*. 1995), twin (Kendler *et al*. 2006*a*; Fanous *et al*. 2007) and general population-based (Romanov *et al*. 2003; Jylhä & Isometsä, 2006) studies. Earlier twin studies (e.g. Kendler *et al*. 2006*a*) have also found a genetic correlation between these two traits, which indicates that genes having an impact on neuroticism are also likely to affect depression. The association between extraversion and depression has instead been controversial as some studies have found that extraversion protects from later depressive symptoms (Jylhä & Isometsä, 2006), while other studies have found no associations (Kendler *et al*. 1993). Also, twin studies investigating a genetic correlation between extraversion and depression have found contradictory results, where some studies have detected a modest genetic correlation between these traits (Kendler *et al*. 2006*a*), whereas others have not (Kendler *et al*. 1993).

The mean levels and test–retest correlations of personality traits are mostly consistent in adulthood and old age (Caspi *et al*. 2005). Extraversion and neuroticism are also moderately heritable and the greatest sources of individual differences during adulthood are

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non-shared environmental influences (for a review, see Bouchard & Loehlin, 2001). The genetic and environmental influences on personality are relatively stable over time in adulthood and old age (Viken *et al*. 1994; Pedersen & Reynolds, 1998; Johnson *et al*. 2005; Read *et al*. 2006). Depressive symptoms are also genetically influenced, although several studies have generally shown rather low genetic effects and considerable unique environmental effects explaining individual differences in adulthood and old age (Gatz *et al*. 1992; Carmelli *et al*. 2000; Jansson *et al*. 2004).

The relationship between depression and personality is complex. Personality characteristics may predispose to, result from or modify the expression of depressive illness (Kendler *et al*. 1993). A powerful natural experiment with which to evaluate such risk factors would include both longitudinal and genetic designs. We report here the results of a study where we have followed initially middle-aged female twin pairs for 28 years and assessed their personality at baseline and depressive symptoms at follow-up. Among older adults, depressive symptoms not meeting the diagnostic criteria for depression are highly prevalent, while their consequences for disability risk and decrease in well-being are similar to those of clinical depression (Blazer, 2003). Understanding what characteristics of personality increase the risk for depression in old age could provide a window to the etiology of depression and therefore provide a more rational basis for targeted preventive interventions. Investigating early personality factors would also offer opportunities for identifying those younger persons who are at risk for developing depressive symptoms later in life. Studying depressive symptoms among older women is also well-grounded as depressive symptoms in later life are more prevalent among women than men (Piccinelli & Wilkinson, 2000).

Our objective in the present study was to investigate if middle age personality traits of neuroticism and extraversion are associated with depressive symptoms experienced in old age. Using quantitative trait modeling, we also wanted to investigate to what extent the correlation between neuroticism, extraversion and depressive symptoms is due to shared genetic and/or shared environmental factors.

Method

Subjects

The present study is a part of the Finnish Twin Study on Aging (FITSA), which is a study on the genetic and environmental influences on the disablement process in older women. The participants were recruited from the Finnish Twin Cohort, which comprises all the same-sex twin pairs born before 1958 and with both co-twins alive in 1975 (Kaprio *et al*. 1978; Kaprio & Koskenvuo, 2002). In August 2000, there were 1260 female twin pairs in the age group of 63–76 years who had participated in the Finnish Twin Cohort in 1975. In this group an invitation to participate in the FITSA study was sent on the basis of age and zygosity to a subsample of 414 twin pairs aged 63–76 years. To be included in the study, both individuals in a pair had to agree to participate and be sufficiently healthy to travel to the laboratory exam. Reasons for non-participation were refusal (106 pairs), poor health status (85 pairs), or death (six pairs) of one or both twin sisters. The zygosity of the twin pairs was confirmed using a battery of 10 highly polymorphic gene markers in DNA extracted from a venous blood sample. The final sample of the FITSA study was 103 monozygotic (MZ) and 114 dizygotic (DZ) twin pairs (434 individuals). Follow-up measurements of the FITSA study were conducted after 3 years, in years 2003–2004, with 419 individuals from the original sample. The death of one twin sister had occurred in two MZ and five DZ twin pairs and eight participants dropped out for health reasons.

Measures

Assessment of depressive symptoms in the year 2003 questionnaire

Depressive symptoms were assessed at the follow-up measurements in year 2003 using the Center for the Epidemiologic Studies Depression Scale (CES-D; Radloff, 1977) questionnaire. The CES-D scale is a widely used self-report measure in community samples with reliability and validity demonstrated in heterogeneous samples (e.g. Beekman *et al*. 1997). The total CES-D scale has 20 items and respondents rate the frequency with which they have experienced particular depressive symptoms during the past week. Each item is scored from 0 to 3, for a possible total range of 0 to 60. In the CES-D scale, the standard cut-off score indicating the presence of clinically important depressive symptomatology in community populations is 16 or more of the possible 60 points (McDowell & Newell, 1996), which was also used here. In calculating intra-class correlation coefficients (ICC) and in the twin modeling a continuous measure of depressive symptoms was also used. The internal consistency of the CES-D scale was adequate in the present study; Cronbach's alpha was 0.87 in year 2003 measurements. Also, the distribution of the scale was acceptable.

Assessment of personality in the year 1975 questionnaire

Extraversion and neuroticism were studied in year 1975 using a short form of the Eysenck Personality

Inventory (Floderus, 1974) questionnaire. The version has been widely used in Nordic twin studies and has good reliability and validity (Floderus-Myrhed *et al*. 1980; Rose *et al*. 1988; Pedersen & Reynolds, 1998; Read *et al*. 2006). The two subscales have nine items each, with dichotomous responses (1 = no, 2 = yes) for a possible total range of 9–18. The Cronbach's alpha was 0.71 for extraversion and 0.72 for neuroticism. Both the personality scales were normally distributed.

Assessment of confounding variables in the year 1975 questionnaire

The following sociodemographic and health variables measured at baseline were examined as potential confounders when assessing current depressive symptoms during the 28-year study period. The sociodemographic variables included were age, marital status and education status. Marital status was dichotomized as married or cohabitating or not married (single, divorced, widowed). Education status was dichotomised into lower (elementary school or less) and higher (more than elementary school) education. The number of chronic diseases was assessed by asking participants if they had ever had any chronic diseases diagnosed by a physician (a list containing 16 diseases: chronic bronchitis; pulmonary emphysema; bronchial asthma; allergic rhinitis; allergic eruption; urticaria; arterial hypertension; angina pectoris; myocardial infarction; stroke; gastric ulcer; cholelithiasis; diabetes; gout; operated varicose vein; some other chronic disease) and the number of diseases was calculated by summing up all specific diseases reported to be present. Smoking status was classified from responses to a detailed smoking history questionnaire including questions on quantity smoked and ages at initiation and cessation (Kaprio & Koskenvuo, 1988) and was dichotomized as smokers (regular or occasional smokers) and non-smokers (former and never). Dichotomous index of heavy use of alcohol was obtained from a binge drinking item that asked whether 'at least once per month and on a single occasion' the respondent consumed more than five beers, a bottle of wine or a half-bottle of spirits (Kaprio *et al*. 1987). The frequency of leisure time physical activity was measured by a 5-point scale with alternative response categories ranging from no physical activity to a high level of leisure time physical activity. Those who reported at least a slight amount of leisure time physical activity were classified as physically active and those without any leisure time physical activity as physically inactive.

Statistical method

Analyses were limited to a subsample of participants who were healthy at baseline. To accomplish this, we excluded all participants who reported angina pectoris, myocardial infarction, stroke or diabetes at baseline. We also excluded those participants who had used a hypnotic/tranquilizer for more than 6 months in the preceding year or who were on a work disability pension due to any cause at baseline. Thus, the final size of the study cohort in the present study was 409 individuals, of whom 391 had valid measures of depressive symptoms and extraversion and 386 in neuroticism. If more than two items had missing answers in the CES-D scale, extraversion or neuroticism, the total score was not computed. In 180 pairs, we had complete information on depressive symptoms in both members, whereas the remaining pairs had varying degrees of partial information. The corresponding values for extraversion and neuroticism were 181 and 176, respectively.

The relationship between middle age personality and current late life depressive symptoms was first studied in generalized estimating equations models using the SAS procedure GENMOD (SAS Institute, USA) to correct for the co-twin dependence. Analyses were adjusted for age, marital status, number of chronic diseases, binge drinking, smoking status, level of leisure time physical activity and education status.

In the preliminary twin analyses the equality of means of personality and depressive symptom variables between MZ and DZ twins was analyzed with adjusted Wald test and the equality of variances was tested with variance ratio test (Stata 8.0; Stata Corp., USA). The dependence of observations of the co-twins was taken into account in these analyses. The within-individual correlations for the whole sample and cross-twin cross-trait correlations separately for the MZ and DZ groups were calculated using Pearson's correlation coefficient. The within-pair resemblances in personality and depression variables were estimated separately for MZ and DZ groups using age-adjusted ICC (SPSS 14.0; SPSS Inc., USA).

In quantitative genetic analyses, the phenotypic variation was decomposed to three sources of variances: additive genetic (A); shared environmental (C); non-shared environmental effects (E). The genetic analyses is based on the fact that MZ twins share 100% of their genes and DZ twins share on average 50% of their segregating genes. A further assumption is that MZ and DZ twins are equally susceptible to environmental influences that are productive of similarities between both twins (see Posthuma *et al*. 2003). It is also assumed that there is no effect of assortative mating or gene–environment interaction in the traits in question.

Genetic and environmental influences contributing to neuroticism, extraversion and depressive symptoms were estimated first with univariate quantitative trait models. To understand further the nature of the

Table 1. *Means and standard deviations (S.D.) for depressive symptoms, neuroticism and extraversion among monozygotic (MZ) and dizygotic (DZ) twin individuals*

	Assessed in year	Age Mean (S.D.)	MZ individuals		DZ individuals			
			n	Mean (S.D.)	*n*	Mean (S.D.)	p^a	p^b
Depression	2003	71.6 (3.4)	184	11.64 (7.58)	207	12.23 (7.76)	0.52	0.74
Neuroticism	1975	43.6 (3.4)	181	13.10 (2.33)	205	13.09 (2.28)	0.99	0.76
Extraversion	1975	43.6 (3.4)	183	12.83 (2.50)	208	12.72 (2.35)	0.69	0.37

[a] Adjusted Wald test.
[b] Variance ratio test.

association of personality and depressive symptoms, the trivariate Cholesky decomposition model was used to evaluate whether the genetic and environmental influences were common or specific to neuroticism, extraversion and depressive symptoms. The aim of the genetic modeling is to find a model that provides a theoretically meaningful interpretation, fits the data well and has as few explanatory parameters as possible. In the present study the obtained alternative univariate models (AE, CE, E) were compared against the full model (ACE) by χ^2 difference test and Akaike's information criterion (AIC = −2 times log-likelihood − 2 × degrees of freedom). A non-significant difference between the nested models and a smaller AIC indicates a better fitting model. The full Cholesky model consists of: genetic effect A_1, which is shared by neuroticism, extraversion and depressive symptoms; genetic effect A_2, which is shared by extraversion and depressive symptoms; genetic effect A_3, which loads only on to depressive symptoms. The shared environmental (C_1, C_2, C_3) and non-shared (E_1, E_2, E_3) environmental effects have similar patterns of loadings. The analysis was started with the hypothetic full Cholesky decomposition model. To get a more parsimonious model, the full model was modified by dropping the non-significant parameters one by one, until the model consisted only of significant parameters. The alternative multivariate models obtained were compared against the full model by using the χ^2 difference test and AIC. The univariate and multivariate genetic analyses were performed with Mx software using full information maximum likelihood method with raw data input (Neale *et al*. 2003). In all genetic analyses age was included as a covariate.

Results

Individual based analyses

The mean [standard deviation (S.D.)] ages of this sample in the year 1975 and year 2003 were 43.6 (3.4) and 71.6 (3.4) years, respectively. Among all the study subjects the mean (S.D.) scores of the CES-D scale, neuroticism and extraversion were 12.0 (7.7), 13.1 (2.3) and 12.3 (2.4) points, respectively. The means and variances of the MZ and DZ groups did not differ from each other in neuroticism, extraversion and depressive symptoms (Table 1). Of the 391 individuals with valid data on depressive symptoms in the sample, 99 (25.3%) scored above the CES-D cut-off 16 and were considered to have depressive symptomatology in year 2003. The within-individual Pearson's correlation between neuroticism and extraversion was –0.25 ($p < 0.01$), between neuroticism and depressive symptoms 0.32 ($p < 0.01$), and between extraversion and depressive symptoms –0.19 ($p < 0.01$). Associations between middle age personality and late life depressive symptoms were first conducted by generalized estimating equation regression analysis (Table 2). After adjusting for age, marital status, number of chronic diseases, binge drinking, smoking status, level of leisure time physical activity and education status, neuroticism in middle age was significantly associated with the risk for late life depressive symptoms. The same analyses with extraversion revealed a modest but significant inverse relationship on depressive symptoms. Because neuroticism and extraversion were negatively correlated, we also conducted the same analysis with both neuroticism and extraversion as predictors in the model. The association between depressive symptoms, neuroticism and extraversion remain the same although the statistical significance weakened compared with simple regression models.

Twin analyses

The intra-class correlations for neuroticism, extraversion and depressive symptoms were higher among MZ than DZ twins, which suggested the contribution of genetic effects. In neuroticism, the age-adjusted intra-class correlation for the MZ twins was 0.51 [95% confidence interval (CI) 0.34–0.66], for extraversion 0.53 (95% CI 0.36–0.67) and for depressive symptoms 0.61 (95% CI 0.46–0.72). The respective correlations

Table 2. *Results of generalized estimating equations regression analysis for the effect of middle age neuroticism and extraversion on depressive symptoms experienced in later life in women followed for 28 years*

	Simple regression model			Multiple regression model		
Predictor	OR	95% CI	*p* value	OR	95% CI	*p* value
Neuroticism	1.37	1.20–1.58	<0.0001	1.31	1.14–1.52	<0.001
Extraversion	0.78	0.69–0.88	<0.001	0.84	0.73–0.95	<0.01

OR, Odds ratio; CI, confidence interval.

Generalized estimating equations regression analysis adjusted for age, marital status, number of chronic diseases, binge drinking, smoking status, level of leisure time physical activity and education status. The twin structure of the data was corrected by using an unstructured working correlation matrix.

Simple regression model: the index variable is adjusted for confounders in the model.

Multiple regression model: both the index variables and confounders are included in the model.

Table 3. *Intra-pair cross-twin and within individual Pearson's correlation coefficients (95% CI) for monozygotic (MZ) and dizygotic (DZ) twins*

	Neuroticism twin 1	Extraversion twin 1	Depression twin 1	Neuroticism twin 2	Extraversion twin 2	Depression twin 2
Neuroticism twin 1		−0.22 (−0.42 to –0.01)	0.34 (0.15–0.57)	0.52 (0.3–0.80)	−0.14 (−0.35 to 0.08)	0.22 (0.0–0.44)
Extraversion twin 1	−0.26 (−0.45 to –0.07)		−0.17 (−0.38 to 0.04)	−0.15 (−0.37 to 0.07)	0.54 (0.3–0.82)	−0.22 (−0.44 to –0.01)
Depression twin 1	0.31 (0.1–0.51)	−0.15 (−0.34 to 0.04)		0.41 (0.2–0.65)	−0.14 (−0.36 to 0.07)	0.62 (0.5–0.95)
Neuroticism twin 2	0.20 (−0.01 to 0.40)	−0.07 (−0.27 to 0.14)	−0.06 (−0.26 to 0.15)		−0.25 (−0.47 to –0.05)	0.32 (0.1–0.55)
Extraversion twin 2	−0.01 (−0.21 to 0.19)	0.06 (−0.14 to 0.26)	−0.10 (−0.30 to 0.11)	−0.27 (−0.48 to –0.07)		−0.20 (−0.41 to 0.02)
Depression twin 2	0.04 (−0.17 to 0.24)	−0.03 (−0.23 to 0.18)	0.17 (−0.04 to 0.37)	0.29 (0.1–0.50)	−0.23 (−0.43 to –0.03)	

The correlations of the MZ pairs are above the diagonal and the correlations of the DZ pairs are below the diagonal.

for the DZ twins were 0.20 (95% CI 0.03–0.39), 0.06 (95% CI –0.14 to 0.26) and 0.14 (95% CI –0.06 to 0.33). Univariate genetic modeling confirmed the presence of genetic and non-shared environmental influences on both the personality variables and depressive symptoms. In the neuroticism, extraversion and depressive symptoms, additive genetic effects accounted for 50%, 47% and 63% of the total variance, respectively. The remaining variance was due to non-shared environmental effects. The effect of age explained approximately 2% of the variance in extraversion, but had no effect on neuroticism or depressive symptoms in this sample from a relatively narrow birth cohort (data not shown).

Given the evidence from the individual-based regression analyses that both the middle age neuroticism and extraversion were significantly associated with the risk for late life depressive symptoms, we wanted to test whether there are also shared genetic and environmental effects between the personality measures and depressive symptoms. It is important to note that high phenotypic correlation between the traits does not necessarily indicate genetic or environmental correlations or vice versa. The cross-twin cross-trait correlations (Table 3) suggest the presence of genetic effects on the associations between the traits when these correlations are greater for MZ than DZ pairs. We also fitted a series of trivariate twin models to data on neuroticism, extraversion and depressive symptoms. The analysis was started with the hypothetic full Cholesky decomposition model, including all plausible parameters (Table 4). Because several coefficients were statistically non-significant, the full model was modified by dropping the non-significant parameters one by one, until a more parsimonious and theoretically acceptable model was reached (Table 4). In the model, middle age neuroticism and old age depressive symptoms shared an additive genetic

Table 4. *Proportions of variances explained by the path coefficients in the Cholesky decomposition model for neuroticism, extraversion and depressive symptoms*

	ACE model (95% CI)			AE model (95% CI)		
Path	Neuroticism	Extraversion	Depression	Neuroticism	Extraversion	Depression
a11	0.74 (0.63–0.82)	–	–	0.74 (0.63–0.82)	–	–
a21	–	0.00 (0.00–0.03)	–	–	–	–
a22	–	0.70 (0.57–0.79)	–	–	0.71 (0.59–0.80)	–
a31	–	–	0.49 (0.34–0.62)	–	–	0.49 (0.34–0.61)
a32	–	–	0.00 (0.00–0.07)	–	–	–
a33	–	–	0.65 (0.31–0.75)	–	–	0.67 (0.51–0.75)
c11	0.06 (0.05–0.06)	–	–	–	–	–
c21	–	0.07 (0.07–0.08)	–	–	–	–
c22	–	0.04 (0.03–0.05)	–	–	–	–
c31	–	–	0.00 (0.00–0.28)	–	–	–
c32	–	–	0.00 (0.00–0.40)	–	–	–
c33	–	–	0.00 (0.00–0.49)	–	–	–
e11	0.68 (0.57–0.78)	–	–	0.67 (0.57–0.78)	–	–
e21	–	0.00 (0.00–0.04)	–	–	–	–
e22	–	0.71 (0.61–0.81)	–	–	0.71 (0.61–0.81)	–
e31	–	–	0.00 (0.00–0.11)	–	–	–
e32	–	–	0.00 (0.00–0.06)	–	–	–
e33	–	–	0.59 (0.49–0.69)	–	–	0.59 (0.49–0.69)
	Model fit					
−2LL	6146.368			6146.109		
df	1151			1154		
AIC	3844.368			3838.109		

A, Additive genetic effects; C, shared environmental effects; E, non-shared environmental effects; a11, a21, a22, a31, a32, a33, standardized path coefficient of phenotype on effect A; c11, c21, c22, c31, c32, c33, standardized path coefficient of phenotype on effect C; e11, e21, e22, e31, e32, e33, standardized path coefficient of phenotype on effect E; −2LL, −2 times log-likelihood; df, degrees of freedom; AIC, Akaike's Information Criterion.

component in common (A_1) explaining 55% (95% CI 40–67) of the total variance in neuroticism and 24% (95% CI 12–38) in depressive symptoms. The rest of the variance in middle age neuroticism was due to trait-specific individual environmental factors (E_1) accounting for 45% (95% CI 33–60) of the variance. Old age depressive symptoms also had their own trait-specific additive genetic component (A_3), accounting for 42% (95% CI 26–56) of the variance and individual environmental (E_3) factors of 34% (95% CI 24–48), which explained the remaining variance. As regards middle age extraversion, only trait-specific additive genetic (A_2) and individual environmental (E_2) factors explained the phenotypic variation. The relative contribution of a trait-specific additive genetic factor for extraversion was 50% (95% CI 34–63) and for individual environmental factors 50% (95% CI 37–66). In this most parsimonious model, none of the 95% CI for the parameter estimates included zero (Fig. 1).

As the patterns of intra-class correlations among MZ and DZ twins suggested the presence of non-additive (D) genetic effects for both the personality variables and depressive symptoms, the ADE model was also tested. However, in trivariate analysis the genetic modeling resulted to DE model, which is biologically implausible (as dominance effects in the absence of additive effects are rarely seen) and therefore the use of ADE model in our study was rejected (data not shown).

Finally, to control for the possible confounding effect of the use of antidepressants in year 2003, we repeated both the individual-based and twin analyses with data where we had excluded those participants ($n=19$) who reported using antidepressant medication in year 2003. Controlling for the use of antidepressant medication had no effect on study results (data not shown).

Discussion

The goal of our report was to examine, from both an epidemiologic and genetic perspective, the relationship between old age depressive symptoms and

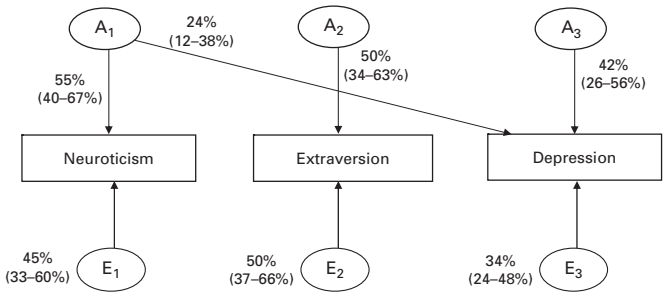

Fig. 1. The most parsimonious Cholesky decomposition model for neuroticism, extraversion and depressive symptoms. The percentages (95% confidence intervals) are the proportions of genetic and environmental effects of the total variance.

two important middle age personality dimensions, neuroticism and extraversion. Our epidemiologic analysis indicated that both of the middle age personality dimensions of neuroticism and extraversion were strongly associated with old age depressive symptoms. By contrast to the relationship between neuroticism and depression, middle age extraversion had a protective effect on depressive symptoms experienced in old age. The second research question aimed to clarify to what extent are the correlations between neuroticism, extraversion and depressive symptoms due to shared genetic and/or shared environmental factors. The best-fitting twin model contained a genetic component that was common to both middle age neuroticism and old age depressive symptoms, individual specific environmental factors unique to both neuroticism and depressive symptoms and a trait-specific genetic component unique to old age depression. Middle age extraversion had only trait-specific additive genetic and individual environmental factors explaining the phenotypic variation.

There were similarities and differences between our results and previous studies. Our results are in agreement with previous prospective and twin studies by Kendler *et al*. (1993), Roberts & Kendler (1999) and Steunenberg *et al*. (2006), who have found neuroticism to be a strong predictor for later depression and that this association is partly due to common genetic vulnerability for both neuroticism and depression. However, part of the genetic vulnerability to depression was not reflected in neuroticism. Fanous *et al*. (2007) found instead that neuroticism predicts the onset of depression and that all of the covariation between neuroticism and depression is due to additive genetic and individual specific environmental factors shared by both traits. As regards extraversion, the present study is in line with Jylhä and Isometsä (2006), who found extraversion to be associated with depression in the general population-based sample. Also, Fanous *et al*. (2007) found negative correlation between extraversion and 1-year prevalence of depression in a population-based sample of male twins. On the other hand, Kendler *et al*. (1993) found no longitudinal or genetic relationship between extraversion and depression among female twins. However, these previous studies are not entirely comparable to our study, because of the heterogeneity of the study populations, study designs, personality measures and psychological outcomes.

We found only one earlier twin study where the follow-up time was comparable to our study design. Kendler *et al*. (2006*a*) followed Swedish twins for 25 years and found that neuroticism reflects the liability to later depression and that this association arose partly from the same genetic factors influencing for both neuroticism and depression. However, also in this study, a significant proportion of the genetic vulnerability to depression was not common with neuroticism. Extraversion, by contrast, was only weakly related to risk for later depression and shared only a modest genetic relationship with later depression. The results we obtained in our epidemiological and genetic analyses of neuroticism and depressive symptoms were broadly similar to those from the study of Swedish twins. One major difference was the modest genetic relationship between extraversion and depression, which was not found in our study. However, differences between these two studies may result from having both sexes, a larger age range and a larger sample size used in the study by Kendler *et al*. (2006*a*).

According to our study, there is a modest genetic overlap between the genetic risk factors for middle age neuroticism and old age depressive symptoms. Given the stability of mean levels and test–retest correlations of personality and its genetic basis in adulthood, investigating personality risk factors earlier in adulthood to identify those people who might develop depressive symptoms in later adulthood is important. However, it is important to note that according to

our findings, old age depressive symptoms also had their own substantial genetic background and it would be unwise to assume that everybody with high middle age neuroticism would therefore be at risk for developing depressive symptoms in later life.

As regards extraversion, our study results are more controversial. We found extraversion in middle age to protect from later depressive symptoms, but no genetic relationship between these two traits. There are some possible interpretations for these results. First, in trivariate genetic modeling where both personality traits were included, the effect of low extraversion, in other words introversion, was possibly mediated through the inverse correlation between neuroticism and extraversion. Second, as Kendler *et al*. (2006*a*) found in their study, compared with the present study, there was only a weak genetic relationship between extraversion and depression with a larger sample size. It is possible that to detect such differences we should have had a substantially larger study population. It is also important to keep in mind that estimates of heritability may vary from population to population and from one type of environment to another (Bouchard & Loehlin, 2001). The possible non-additive genetic effects in extraversion may also make the detection of common genes between depression and personality difficult.

With regard to depressive symptoms, the somewhat high heritability estimate warrants further explanation. Our estimate of 63% for the heritability of CES-D is higher compared with estimates reported in many earlier studies. For example, the review study by Sullivan *et al*. (2000) revealed that the heritability of major depression was likely to be in the range of 32–42% according to different twin studies. However, Jansson *et al*. (2004) reported the heritability estimate of 49% for depressive state among female twins aged 50 years or older. Also, Carmelli *et al*. (2000) found higher heritability estimates in their longitudinal study, where the follow-up heritability estimate of CES-D was 55% among older male twins. Our somewhat high heritability estimate is nonetheless in accordance with the findings from earlier studies, that heritability is usually higher for females than males (e.g. Jansson *et al*. 2004; Kendler *et al*. 2006*b*) and for an older than younger population (Gatz *et al*. 1992). Also, changes in gene expression over the life cycle, in which genetic systems switch off and on, have been invoked as explanations for fluctuations in heritability estimates across adult life (Carmelli *et al*. 2000).

Some limitations of the present study should be taken into consideration. First, the inclusion of only female twins means that care should be taken in generalizing these findings to males. Second, a psychiatric assessment of clinical depression was not included and the measurement of depression was limited to the assessment of symptoms. Third, participants' baseline depression level was not assessed in the year 1975 questionnaire and, therefore, to avoid potential confounding effects of prevalent depressive symptoms, analyses were limited to a subsample of participants who were healthy at baseline. Fourth, extraversion and neuroticism were not tested for stability. Fifth, in the most parsimonious Cholesky decomposition model the confidence intervals were still quite large, indicating that care should be taken when interpreting these estimates. In addition, although our sample was population-based, the inclusion criteria may have led to the exclusion of pairs with at least one sister with poor health. This may have reduced the variance in the personality and depressive symptom phenotypes, increased the similarity within the pairs and thus influenced the heritability estimates. Sixth, although intra-class correlations suggested the presence of non-additive genetic effects, we had inadequate power to discriminate non-additive from additive genetic effects. Larger sample sizes and additional kinship groups (e.g. twins reared apart) would enable us to evaluate better the relative importance of non-additive genetic variance for personality dimensions of neuroticism and extraversion and depressive symptoms. Finally, these genetic analyses cannot differentiate the effects of possible gene–environment interactions, which may have an influence on personality and depression. The strengths of this study include its exceptionally long follow-up time and the use of both longitudinal and genetic analyses.

In summary, our results suggest that the middle age personality dimension of neuroticism is strongly associated with old age depressive symptoms and that this association arises partly because neuroticism and depressive symptoms share some genetic effects in common. However, substantial proportions of the genetic vulnerability to old age depressive symptoms are not reflected in middle age neuroticism. On the contrary, middle age extraversion has a protective effect on depressive symptoms experienced in old age, but no genetic relationship with old age depression. In the future, the number of people living up to very old age will increase, emphasizing the need for new multidimensional methods to maintain and increase well-being in old age. These findings have implications for identifying early risk factors for old age depressive symptoms as well as planning for more individually targeted interventions for old age depression. Further research is required to find the kind of mechanisms that strongly relate neuroticism and extraversion to depressive symptoms in old age.

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Declaration of Interest

None.

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II

LEISURE TIME PHYSICAL ACTIVITY AND DEPRESSIVE SYMPTOMS

by

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LEISURE TIME PHYSICAL ACTIVITY AND DEPRESSIVE SYMPTOMS

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Abstract

The positive association of exercise and depressive symptoms has been documented in several earlier studies. However, only a few studies have investigated this association taking into account genetic variation among individuals. Shared genetic factors may predispose to a sedentary lifestyle as well as mood problems. Using data from three different Finnish twin studies, the present study aimed to investigate whether the association between leisure time physical activity (LTPA) and depressive symptoms could be explained at least partly by genetic factors in common to both traits. The three datasets consisted of FinnTwin16 (n= 4623 twin individuals), the older Finnish Twin Cohort (n=10433 individuals) and the Finnish Twin Study on Aging (n=419 individuals) studies. Both LTPA and depressive symptoms were assessed by self-reports in each of our twin studies. Consistent with previous research, we found that among different age groups of twins, increased LTPA was phenotypically associated with decreased depressive symptoms. Both LTPA and depressive symptoms were modestly heritable, with higher heritability estimates for LTPA among younger twins and for depressive symptoms among older female twins. However, due in part to modest phenotypic correlations between LTPA and depressive symptoms, the bivariate genetic model did not find common genetic factors that would influence both traits in any of our three different twin datasets. As heritability estimates may vary from population to population and from one type of environment to another, more studies are needed about the possible genetic background underlying LTPA and depressive symptoms.

Keywords: leisure time physical activity, depressive symptoms, heritability, twin study

According to several epidemiological and experimental studies, regular exercise is associated with fewer depressive symptoms (Teychenne et al., 2008). Positive associations have been confirmed among both healthy (Motl et al., 2005) and clinical (Singh et al., 2005) populations, among different age groups (Singh et al., 2001; Tomson et al., 2003) as well as using various measures of physical activity and depressive symptoms (Penninx et al., 2002). Although prospective studies suggest causality between physical activity and depression, we cannot rule out that some underlying variables that influence physical activity behaviour at one time point also influence symptoms of depression at a later time point. In regard to experimental studies, there might be a tendency such that only subjects attracted to exercise or otherwise self-selected may enroll and comply during interventions. In addition, treatment effects in clinical populations may not always be generalized to the population at large (Brosse et al., 2002). To better understand the origins of the association between physical activity and depressiveness, we investigated the genetic and environmental correlation between physical activity and depressive symptoms.

Population-based twin studies have shown that leisure time physical activity (LTPA) and depressive symptoms are both influenced by genetic factors. In adolescence environmental factors shared by family members determine LTPA participation, whereas in young adulthood, genetic influences start to appear, and the role of common environmental effects decrease (Stubbe et al., 2005; Vink et al., 2011). Among twins aged 19 to 40 years, the heritability of exercise participation ranged from 27 to 70% in a large pooled sample from seven countries (Stubbe et al., 2006). In the second half of life, the influence of genetic factors on LTPA has been studied rarely, but among Danish twins aged 45-68 years, heritability was estimated to vary between 49 and 51% (Frederiksen & Christensen, 2003). Also, the heritability estimates of depressive symptoms vary widely between studies as a result of both the definition of depressive symptoms used and the group in which it is measured. In a large sample of twins aged 18-79 years, the heritability of depressive symptoms was around 42% (Rijsdijk et al., 2003) whereas in the study including only elderly participants, the heritability estimates vary between 29 to 49% among women and between 7 to 14% among men (Jansson et al., 2004). Given the fairly high heritability of both the LTPA and depressive symptoms one may hypothesize that some genetic factors influencing physical activity behaviour might overlap with genetic factors influencing depressive symptoms. It has been hypothesized as well, that genes involved in central pathways such as the dopaminergic, norepinephrenergic, opioidergic or serotonergic pathways of the brain could be likely candidates to simultaneously affect the regulation of physical activity and depressive symptoms (Chaouloff, 1997; Goldfarb & Jamurtas, 1997).

While most earlier studies address the consequences of physical activity on depressive symptoms and depression, we found only one study that investigated the origins of this association taking into account the genetic variation among individuals. De Moor and colleagues (2008) found a modest genetic correlation between physical activity and depressive symptoms among a Dutch cohort consisting of 8558 twins, additional siblings and parents aged 18 to 50 years. As heritability estimates are always population specific, there is a need for replication studies (Plomin et al., 2001). Understanding the underlying mechanisms in the association between LTPA and depressive symptoms can be useful in physical activity counselling when preventing mood problems among sedentary people at increased risk for depressive symptoms. Also, the use of twin

cohorts of varying ages would expand earlier findings as age differences might have some effects on study results. Based on earlier study by De Moor and colleagues (2008), two study hypotheses were defined. First, it was hypothesized, that among different age groups of Finnish twins, a negative relationship between LTPA and depressive symptoms would exist. Second, the relationship between LTPA and depressive symptoms would at least partly be explained by genetic factors in common.

MATERIAL AND METHODS

Participants

Three existing datasets on twin pairs were used in this study. The first study, FinnTwin16, is a broad population-based study of the health and health habits of five consecutive birth cohorts of Finnish twins born in the years 1975-79. The birth cohorts were identified from the Central Population Registry of Finland. The baseline assessments were collected sequentially during the years 1991-95 within 2 months of the twin's 16th birthdays. All respondent twins (n= 5563) were sent 4th-wave follow-up questionnaires as young adults at ages 22-27. (Kaprio et al., 2002.) For the present analysis, information from that fourth measurement wave was used. Although the data from FinnTwin16 project consisted also of opposite-sex twin pairs, only same-sex twin pairs were used in the present study.

The second dataset comes from the Finnish Twin Cohort study, which is compiled from the Central Population Registry of Finland and consists of virtually all twin pairs of the same sex (13 888 pairs) born in Finland before 1958 and with both co-twins alive in 1967 (Kaprio & Koskenvuo, 2002). The twins answered psychosocial-medical questionnaires in 1975, 1981 and 1990. For the present analysis, leisure time physical activity information from the year 1981 questionnaire was used (response rate 84%) while depressive symptom data were available from the 1990 questionnaire (response rate 77%).

The third dataset comes from the Finnish Twin Study on Aging (FITSA), which is a study of genetic and environmental effects on the disablement process in older women with extensive data collected among 103 monozygotic (MZ) and 114 dizygotic (DZ) female twin pairs aged 63 to 76 years who had participated in the Finnish Twin Cohort study in 1975 (Kaprio et al., 1978; Kaprio & Koskenvuo, 2002). In this study, we are using data from the follow-up measurements of FITSA-study, which were conducted after 3 years, in years 2003-2004, with 419 individuals from the original sample. In Table1, the numbers of participants from each dataset are illustrated.

"Table 1 about here".

Measures

Depressive symptoms

In the FinnTwin16 study, the General Health Questionnaire (GHQ) was used to assess depressive mood among study participants. The GHQ-scale is a self-report questionnaire that was designed to be used as a screening instrument to identify psychological distress and short-term changes in mental health in community and primary care settings (Goldberg, 1978; Goldberg & Williams, 1988). In the FinnTwin16

study the 20-item scaled version (GHQ-20) derived from the original 60-item scale was used. As the focus on our study was especially in depressive mood, we utilized the factor structure of the GHQ- scale confirmed by Penninkilampi-Kerola and colleagues (2006) who validated earlier findings showing that in the GHQ-scale there are four factors measuring different aspects of psychological distress. In our analyses we used the factor measuring especially depressive mood (item numbers 14, 39, 40, 43, 47, 49, 55 and 58 in the original 60-item GHQ-questionnaire). Responses were scored using a Likert scale (1-4) and the items were summed to get a total score. In the Finnish Twin Cohort, depressive symptoms were assessed using the 21-item Beck Depression Inventory (BDI), which is a multiple-choice self-report questionnaire measuring the severity of depressive symptoms. All the items are coded from 0 to 3 and summed to get a score range from 0 to 63, with the higher values indicating more severe depressive symptoms (Beck, et al., 1961; Varjonen et al., 1997). In the Finnish Twin Study on Aging depressive symptoms were assessed using the Center for the Epidemiologic Studies Depression Scale (CES-D; Radloff, 1977) questionnaire. CES-D scale is a widely used self-report measure in community samples with reliability and validity demonstrated in heterogeneous samples (e.g. Beekman et al. 1997). The total CES-D scale has 20 items and respondents rate the frequency with which they have experienced particular depressive symptoms during the past week. Each item is scored from 0 to 3, for a possible total range of 0 to 60. The internal consistencies of each of these scales were adequate in the present study; Cronbach's alpha was 0.88 for the depressive mood factor of the GHQ-scale (for the whole GHQ-scale $\alpha = 0.91$) for the Beck Depression Inventory 0.85 and for the CES-D scale 0.87.

Leisure time physical activity

In the FinnTwin16 study leisure time physical activity index was calculated from the product of self-reported exercise intensity, duration (hours) and yearly frequency (days). Intensity was expressed as estimated metabolic equivalent (MET) values (work metabolic rate divided by resting metabolic rate) (Wilson et al., 1986; Mustelin et al., 2009). The MET-index was described as the sum score of leisure MET hours/day. In the Finnish Twin Cohort the assessment of LTPA was nearly identical as in the FinnTwin16 study, but also the physical activity during journeys to and from work was included in the MET-index (Kujala et al., 1998). In the FITSA-study, calculating MET-index was impossible due to different study questions. Instead the participation in leisure time physical activity was based on self-report questionnaire with question "What alternative describes best your all-year leisure-time physical activity?". Participants could respond with five alternatives: No at all leisure-time physical activity, A little, Moderate, Quite a lot or A great deal of leisure time physical activity.

Ethics

Data collection and analysis of the FinnTwin16 study were approved by the ethics committee of the Department of Public Health of the University of Helsinki, and the IRB of Indiana University. The Finnish Twin Cohort study was set up with permission from the National Board of Health. The FITSA study was approved by the Ethics Committee of the Central Finland Hospital.

Statistical methods

The data were analyzed using quantitative genetic modelling of twin and family data (Neale & Cardon, 2003). In the twin modelling continuous measures of all outcome data

were used. Although the leisure time physical activity variable in the FITSA-study was categorical (with five alternatives), we decided to use it as a continuous measure to prevent the loss of valuable distributional information. All outcome variables were also examined for normality and distribution. From the Finnish Twin Cohort study, we transformed the MET-index by logarithmical transformation and depressive mood by square root of the inverse. After the transformation, the absolute values of skewness and kurtosis for all outcome measures were acceptable. The equalities of the means and distributions of the outcome variables were calculated and tested using an adjusted Wald test to take into account the within-pair dependence of twin individuals. The equality of the variances was tested using the variance ratio test (STATA 8.0; Stata Corp., USA). The phenotypic correlation between LTPA and depressive symptoms in our three datasets were calculated using Pearson's correlation coefficient. The within-pair resemblances in LTPA and depressive symptoms were estimated separately for MZ and DZ groups using age-adjusted intraclass correlations (ICCs) (SPSS 14.0; SPSS Inc., USA).

For each dataset, the genetic modelling was started by constructing univariate models for LTPA and depressive symptoms to estimate genetic and environmental influences and find the best model for each trait used in further modelling. The fit of alternative models was tested comparing the nested models (AE, CE, E) against the full model (ACE) by χ^2- difference test and Akaike's information criterion (AIC = -2 times log-likelihood – 2 x degrees of freedom). A non-significant difference between the nested models and a smaller AIC indicates a better fitting model. A bivariate Cholesky model was used to evaluate whether the potential association between LTPA and depressive symptoms could be explained by an overlap in latent genetic factors that influence both of these traits. This structural equation model consisted of the genetic and environmental effects that are common to both variables (LTPA and depressive symptoms) and of the genetic and environmental effects that are specific to each variable. To obtain a more parsimonious model, the models were modified by dropping the non-significant or small parameters one by one in line with χ^2- difference test and comparison of AIC values as prescribed above. The univariate and multivariate genetic analyses were performed with Mx software using full information maximum likelihood method with raw data input. In all genetic analyses in the FinnTwin16 and Finnish Twin Cohort, age and sex were included as covariates. In FITSA (where all were women), only age was included as a covariate. In a number of twin pairs, data from the co-twin was missing, but data from the participant twin in these broken pairs was included in the models as a separate group. These singletons contributed to the means and variances in the variables, but did not affect covariance in the models.

RESULTS

There were no systematic differences in means and variances of LTPA and depressive symptoms between the MZ and DZ twins in any of our datasets (Table 2.). In the pooled data of MZ and DZ twins in FinnTwin16 and Finnish Twin Cohort studies, males had higher LTPA levels ($p<0.001$ for both datasets) and lower depressive symptoms levels compared to female twins ($p<0.001$ for both datasets).

"Table 2 about here".

The within-individual Pearson's correlations between LTPA and depressive symptoms were small, but statistically significant ranging from -0.06 to -0.15, demonstrating a phenotypic correlation between increased LTPA and decreased depressive symptoms in each datasets (Table 3.). The associations were somewhat stronger among older female twins of the Finnish Twin Study on Aging. The within-pair intraclass correlations for both the LTPA and depressive symptoms were higher for MZ twins than DZ twins in all three dataset indicating the probable effect of genetic factors on both traits. (Table 3.).

"Table 3 about here".

Genetic modelling started by estimating the best univariate models for LTPA and depressive symptoms separately for men and women. For each dataset the additive genetic/specific environment (AE) model offered the best fit for both the LTPA and depressive symptoms (model fit statistics available from the authors). Table 4 summarizes the proportions of the phenotypic variance of LTPA and depressive symptoms explained by additive genetic and unique environmental factors in the best fitting AE-models by sex. The heritability estimates for LTPA were at highest level in the FinnTwin16 study whereas the heritability for depressive symptoms was highest among older female twins of the Finnish Twin Study on Aging.

"Table 4 about here".

Because the intra-class correlations and univariate models for each dataset indicated that shared environmental component was not significant and could be dropped from the models, the bivariate analyses were carried out using AE models as the stating point. In the FinnTwin16, Cholesky decomposition found low genetic and non-shared environmental correlation between LTPA and depressive symptoms: about 4% of genetic and 0% of environmental effects were shared between the two variables (-2LL=13441.70, n of parameters =12, AIC=26907). The chi-square difference test between the nested models ($\Delta\chi^2$ =0.001 (df=1), $p > 0.05$) and a lower AIC value of the reduced model (AIC =26905) indicated that the genetic correlation between LTPA and depressive symptoms could be set to zero. Similarly, the non-shared environmental correlation between LTPA and depressive symptoms could also be set to zero ($\Delta\chi^2$ =0.001 (df=1), $p > 0.05$, AIC of the reduced model = 26905).

In the Finnish Twin Cohort, about 8% of genetic and 5% of environmental effects were shared between the two variables (-2LL=42975.28, n of parameters =12, AIC=5137). According to the chi-square difference test between the nested models ($\Delta\chi^2$ =3.419 (df=1), $p > 0.05$) and a lower AIC value of the reduced model (AIC =5135) the genetic correlation between LTPA and depressive symptoms could be set to zero. Non-shared environmental correlation between LTPA and depressive symptoms could also be set to zero ($\Delta\chi^2$ =3.585 (df=1), $p > 0.05$, AIC of the reduced model = 5135).

In the FITSA data, LTPA and depression shared about 6% of genetic and 5% of environmental effects (-2LL=2169.21, n of parameters =10, AIC=4358). Chi-square difference test and the comparison of AIC values indicated that the genetic correlation between the variables could be set to zero ($\Delta\chi^2$ =0.409 (df=1), $p > 0.05$; AIC =4357). Non-shared environmental correlation between LTPA and depressive symptoms could also be set to zero ($\Delta\chi^2$ =874 (df=1), $p > 0.05$, AIC of the reduced model = 4357). In

summary, the results of the bivariate models suggested that only a small proportion of the genetic and environmental components of LTPA and depressive symptoms overlapped and statistically the overlap was non-significant in all samples.

DISCUSSION

Our study, aiming to replicate an earlier twin study by De Moor and colleagues (2008) corroborates earlier findings, that increased leisure time physical activity and decreased depressive symptoms rates are phenotypically associated. However, we did not find evidence for common genetic vulnerability for low LTPA and depressive symptoms in any of our three datasets unlike this earlier study.

There were some similarities and differences between our results and previous studies. Although earlier epidemiological and experimental studies have indicated a positive association between physical activity and reduced depressive symptoms, in our three datasets consisting of twins with different ages, the association between these two traits was weak. This might suggest that the positive effects of physical activity trials on depressive symptoms may be more readily observed in clinical samples where patients initially report more depressive symptomatology. Among experimental studies including healthy, non-depressed samples the beneficial effects of exercise have been more controversial. (Brosse et al., 2002; Teychenne et al., 2008.) Also the possible non-linear associations between LTPA and depressive symptoms and individuality in affective responses to physical activity of varying intensities might confound the complicate association between physical activity and depressive symptoms (Ekkekakis et al., 2005).

In our study also the overall heritability estimates of both the LTPA and depressive symptoms were in accordance with earlier studies reporting the importance of genetic factors explaining differences in LTPA in young adulthood and a decrease in genetic influences towards middle age (Aaltonen et al., 2011; Stubbe et al., 2005; Stubbe et al., 2006). Among older people the heritability of LTPA has been rarely studied. The few existing studies show similar results as our study in terms that genetic factors explain a moderate proportion of physical activity (Fredriksen & Christensen, 2003). As regards depressive symptoms, our results confirm earlier findings that about 30% to 50% of the variation is explained by genetic factors with increasing importance of genes during old age (Carmelli et al., 2000; De Moor et al., 2008).

Although we did not find evidence for common genetic background for LTPA and depressive symptoms in our study, genetic pleiotropy between LTPA and various other outcomes have been reported in earlier studies. As regards physical health outcomes there is evidence for genetic pleiotropy between exercise behavior and heart rate (De Geus et al., 2003), blood pressure (Hernelahti et al., 2005), BMI, waist circumference (Mustelin et al., 2009), and self-rated health (De Moor ym., 2007). While the pleiotropic effects of LTPA on physical health outcomes have been studied to some extent, the possible effects on mental health have been rarely investigated. Few studies have detected possible genetic pleiotropy between LTPA and well-being (Stubbe et al., 2007), and in one study between LTPA and depressive symptoms (De Moor et al., 2008).

Despite our large twin samples of different ages, we failed to find common genetic vulnerability factors for LTPA and depressive symptoms. Differences between our study and the only earlier study (De Moor et al., 2008) on this topic may result from several reasons. The use of different measures on both the LTPA and depressive symptoms might explain some differences between these studies. The use of different measures may also have led to distinct heritability estimates (for LTPA and depressive symptoms) and therefore dissimilar results. Also the age range of twins in our study was wider including also older female twins with mean age of seventy-two years which is likely to have affected the results. However, both studies found a remarkably small phenotypic correlation between LTPA and depressive symptoms among population-based samples, despite the importance of genetic factors for both the LTPA and depressive symptoms among various age of men and women. This for one's part argues in favour of third underlying variable having an effect on both LTPA and depressive symptoms.

Some limitations of the present study should be taken into consideration. First, our three datasets consisted of Finnish twins with different ages which might limit the generalizability of the findings to the population at large. However, several studies have reported very few differences in socio-demographic or life-style characteristics between twins and non-twins and confirmed the comparability of the twin samples to the general population (Andrew et al., 2001). Second, in the Finnish Twin Cohort study we include also physical activity during the work journey to our LTPA measure as very little research has investigated the association of likelihood of depression with other domains of activity such as work-related or transport-related physical activity (Teychenne et al., 2008). However, we did our analyses also by excluding work-related physical activity from our definition of LTPA, but these changes had no effect on study results (data not shown). Third, in the Finnish Twin Cohort Study, the LTPA data and depressive symptoms measurements were performed nine years apart which may have caused some selection bias, as attrition typically takes place among less healthy participants and may have lead to underestimation of the relationship between LTPA and depressive symptoms particularly in this dataset (Brosse, Sheets, Lett, & Blumenthal, 2002; Vink et al., 2004). Fourth, the use of different measures of LTPA and depressive symptoms in our three datasets might limit the comparison between datasets. However, all the three twin studies are separate projects and study measures are carefully constructed in focus of participant's characteristics at each project's. The three substudies are also very consistent in their lack of finding a common genetic correlation indicating that is independents of the actual measures. Fifth, in this analysis we examined the relationship between LTPA, genetic factors and depressive symptoms. It is possible that other factors such as personality modify or account for these relationship by affecting both the LTPA and depressive symptoms.

To conclude, despite the genetically informative large twin samples among healthy young to old age participants, our study aiming to replicate earlier findings by De Moor and colleagues (2008) found only small, but robust correlation between LTPA and depressive symptoms, which however was not explained by common genetic vulnerability factors. As heritability estimates may vary from population to population and from one type of environment to another, more studies are needed about the possible genetic background underlying LTPA and depressive symptoms.

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Table 1. Number of twins in different studies

	FinnTwin16	Finnish Twin Cohort	Finnish Twin Study on Aging
N	2950	10433	419
Complete pairs	1317	3794	203
Mean age	24.4	43.7	71.6
MZM	274	540	-
DZM	302	1063	-
MZF	401	787	96
DZF	340	1404	107

Note: MZM, monozygotic male twin pairs; DZM, dizygotic male twin pairs; MZF, monozygotic female twin pairs; DZF, dizygotic female twin pairs. No data on male twins were available in the Finnish Twin Study on Aging.

Table 2. Means and standard deviations of leisure time physical activity (LTPA) and depressive symptoms by sex and zygosity. In the Finnish Twin Study on Aging the LTPA is expressed by physical activity frequency.

	Female MZ	Male MZ	Female DZ	Male DZ
FinnTwin16				
LTPA (MET h/d)	4.35 (4.9)	5.38 (5.7)	4.14 (4.4)	5.13 (5.7)
Depressive symptoms (GHQ)	6.68 (5.0)	4.95 (4.3)	7.22 (5.1)	5.12 (4.5)
Finnish Twin Cohort				
LTPA (MET h/d)	2.68 (2.5)	3.24 (3.9)	2.69 (2.6)	3.22 (3.7)
Depressive symptoms (BDI)	5.43 (5.6)	4.33 (5.1)	5.80 (5.9)	4.42 (5.0)
Finnish Twin Study on Aging				
LTPA (frequency %)				
Not at all	2	-	6	-
A little	16	-	15	-
Moderately	55	-	58	-
Quite a lot	22	-	18	-
Much	5	-	3	-
Depressive symptoms (CES-D)	12.05 (7.6)	-	12.35 (7.8)	-

Note: GHQ = General Health Questionnaire, in this study the subscale measuring depressive symptoms was used (range 0-24); BDI = Beck Depression Inventory (range 0-63); CES-D= Center for Epidemiologic Studies Depression Scale (range 0-60). No data on male twins were available in the Finnish Twin Study on Aging.

Table 3. Within-person cross-trait and within-pair intra-class correlations (95% CI) of leisure time physical activity (LTPA) and depressive symptoms

	FinnTwin16		Finnish Twin Cohort		Finnish Twin Study on Aging	
Correlations between LTPA and depressive symptoms						
	No of. individuals	Pearson r (95% CI)	No of. individuals	Pearson r (95% CI)	No of. individuals	Pearson r (95% CI)
Total	2912	-0.07 (-0.11 to -0.03)	10433	-0.08 (-0.10 to -0.06)	411	-0.15 (-0.25 to -0.05)
Men	1292	-0.07(-0.12 to -0.02)	4707	-0.08 (-0.10 to -0.05)	-	-
Women	1620	-0.06 (-0.11 to -0.01)	5726	-0.07 (-0.10 to -0.04)	411	-0.15 (-0.25 to -0.05)
Within-pair intra-class correlations of LTPA						
	No. of pairs	ICC (95% CI)	No. of pairs	ICC (95% CI)	No. of pairs	ICC (95% CI)
MZM	264	0.53 (0.43-0.61)	540	0.40 (0.32-0.47)	-	-
DZM	292	0.39 (0.29-0.48)	1063	0.14 (0.08-0.20)	-	-
MZF	400	0.56 (0.49-0.63)	787	0.34 (0.28-0.40)	95	0.47 (0.30-0.62)
DZF	332	0.24 (0.14-0.34)	1404	0.12 (0.07-0.17)	107	0.18 (-0.01 to 0.34)
Within-pair intra-class correlations of depressive symptoms						
	No. of pairs	ICC (95% CI)	No. of pairs	ICC (95% CI)	No. of pairs	ICC (95% CI)
MZM	263	0.35 (0.24-0.45)	601	0.31 (0.23-0.38)	-	-
DZM	285	0.14 (0.03-0.25)	1213	0.13 (0.08-0.19)	-	-
MZF	384	0.33 (0.24-0.42)	869	0.42 (0.36-0.47)	93	0.55 (0.39-0.68)
DZF	327	0.17 (0.06-0.27)	1582	0.16 (0.11-0.21)	104	0.23 (0.04-0.41)

Note: MZM, monozygotic male twin pairs; DZM, dizygotic male twin pairs; MZF, monozygotic female twin pairs; DZF, dizygotic female twin pairs. No data on male twins were available in the Finnish Twin Study on Aging

Table 4. Standardized variance components of additive genetic and unique environmental factors with 95% confidence intervals for leisure time physical activity (LTPA) and depressive symptoms by sex

	Additive genetic factors		Unique environmental factors	
	Females	Males	Females	Males
FinnTwin16				
LTPA	0.52 (0.46-0.58)	0.56 (0.47-0.63)	0.48 (0.42-0.54)	0.44 (0.37-0.51)
Depressive symptoms	0.34 (0.26-0.42)	0.33 (0.24-0.43)	0.66 (0.58-0.74)	0.67 (0.57-0.76)
Finnish Twin Cohort				
LTPA	0.32 (0.27-0.38)	0.38 (0.31-0.44)	0.68 (0.62-0.73)	0.62 (0.56-0.69)
Depressive symptoms	0.39 (0.34-0.43)	0.30 (0.30-0.37)	0.61 (0.57-0.66)	0.70 (0.63-0.76)
Finnish Twin Study on Aging				
LTPA	0.40 (0.22-0.55)	-	0.60 (0.45-0.77)	-
Depressive symptoms	0.56 (0.42-0.68)	-	0.44 (0.32-0.58)	-

Note: No data on male twins were available in the Finnish Twin Study on Aging

III

THE EFFECTS OF PHYSICAL ACTIVITY COUNSELING ON MOOD AMONG 75-TO 81-YEAR-OLD PEOPLE: A RANDOMIZED CONTROLLED TRIAL

by

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The effects of physical activity counseling on mood among 75- to 81-year-old people: A randomized controlled trial

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Abstract

Objectives. To examine the effects of physical activity counseling on mood among older people unselected for their depressive symptomatology.

Methods. Data are from "Screening and Counseling for Physical Activity and Mobility in Older People" project (SCAMOB), conducted in Finland during 2003–2005. SCAMOB was a 2-year single-blinded randomized controlled trial among 624 participants 75 years and older randomized into physical activity counseling group and control group. Depressive symptoms were assessed at baseline and after 24 months using Center for the Epidemiologic Studies Depression Scale.

Results. Among all the study participants, no effect of intervention was observed. However, among subgroup with minor depressive symptoms at baseline, a significant treatment effect was observed, where depressive symptoms decreased in the intervention group and increased in the control group.

Conclusions. These findings suggest that physical activity counseling may reduce depression among those with minor depressive symptoms, which warrants for future studies.

Keywords: Physical activity; Counseling; Mood; Depressive symptoms; Older people

Introduction

The beneficial effects of physical activity on psychological health outcomes among older people have been well documented in earlier studies (McNeil et al., 1991; Penninx et al., 2002; Singh et al., 1997a, 2001, 2005). Multiple mechanisms, such as physiological (Singh et al., 1997a), biological (Singh et al., 1997b) and psychological (McNeil et al., 1991; Penninx et al., 2002), have been suggested to explain the antidepressive effect of physical activity. Most of the prior studies on promoting psychological health in older adults through physical activity have themselves included organized exercise programs such as resistance training and aerobic exercise and have thus been able to increase psychological well-being (Penninx et al., 2002; Sinhg et al., 2005). Instead research-based evidence on the effects of physical activity counseling on mood among older people is scarce (van der Bij et al., 2002; Eakin, 2001; Eaton and Menard, 1998) as most of the educational physical activity interventions have only examined physical activity outcomes (Aittasalo et al., 2006; Bull and Jamrozik, 1998; Smith et al., 2000; Stewart et al., 2001).

The beneficial effects of physical activity counseling interventions on increasing physical activity among older adults have been well documented in recent studies (Elley et al., 2003; Stewart et al., 2001; Pinto et al., 2005). The few studies including also psychological outcomes have instead yielded mixed results. A study by Elley et al. (2003) found improvements in quality of life outcomes such as self-rated "general health", "role physical", "vitality" and "bodily pain" in older patients after an educational physical activity intervention. Also Salminen et al.

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(2005) found improvements in depressive symptoms among older male coronary heart disease patients after a health advocacy, counseling and activation program. However, other studies (Dubbert et al., 2002; Kerse et al., 1999; Leveille et al., 1998) failed to detect any effects of physical activity counseling interventions on psychological health outcomes in older people. Because the literature in this area is limited and the results to date quite contradictory, new knowledge concerning the effects of educational physical activity interventions on psychological health in older adults is needed.

The present study is based on preplanned secondary analyses of a 2-year randomized controlled trial "Screening and Counseling for Physical Activity and Mobility in Older People" (SCAMOB, ISRCTN 07330512). The primary outcomes of SCAMOB project include disability prevention and increasing physical activity. The purpose of this report is to describe the effects of physical activity counseling on mood among home-dwelling 75- to 81-year-old people, who at baseline were cognitively intact, physically sedentary and able to move outdoors at least minimally. The analyses were carried out for the entire

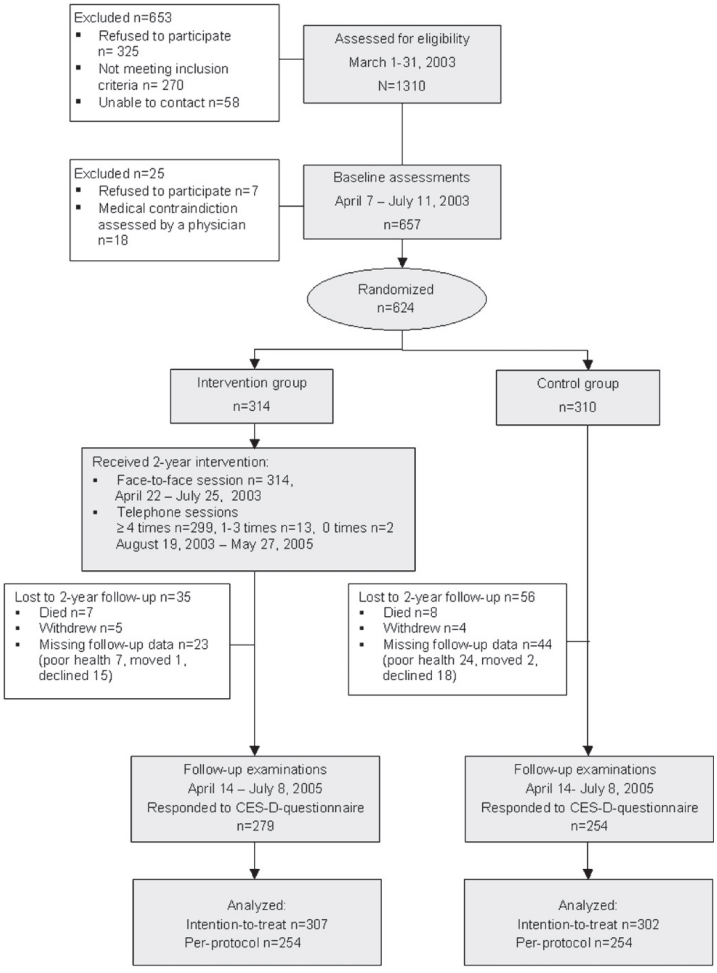

Fig. 1. Flow chart of the present study conducted in Finland in 2003–2005.

population as well as subgroups based on their level of depressive symptoms. We hypothesized that in older people physical activity counseling will increase physical activity participation and thereby alleviate depressive symptoms and prevent deterioration of mood.

Methods

Design

The design and methods for SCAMOB project have been published previously (Leinonen et al., 2007) and are briefly summarized here. SCAMOB was a 2-year single-blinded randomized controlled trial on the effects of customer-oriented physical activity counseling among older people. The Ethical committee of the Central Finland Health Care District approved this project and all participants signed an informed consent.

Participants

The target population consisted of all the registered residents of the City of Jyväskylä aged 75 to 81 years and living in the city center area in March 2003 (N=1310). The inclusion criteria to the study included the ability to walk at least 0.5 km without assistance, only moderately physically active or sedentary, no memory impairment, no medical contraindications for physical activity and consent to participate. After a four-phased screening and data collection process, the final study group included 632 persons who were randomized into physical activity counseling intervention group (n=318) and control group (n=314). Baseline depression data were missing for eight persons, leaving 624 persons for the present study (314 and 310 persons in the intervention and control group, respectively). Each week on Fridays after the completion of baseline assessments a trial administrator allocated participants to groups in blocks of 40–50 persons with a randomization ratio of 1:1 by drawing lots. Allocation concealment was achieved by drawing names from opaque envelopes for 40–50 persons at the same time. Study nurses and interviewers who collected and entered data were blinded to group allocation. Study subjects could not be blinded to the group assignment, but they were unaware of the exact study hypothesis and primary outcome measures. The flow chart of the present study is presented in Fig. 1.

Instruments

Depressive symptoms were assessed at baseline before randomization and in 2-year follow-up using the Center for the Epidemiologic Studies Depression Scale (CES-D; Radloff, 1977). At arrival to the study center, participants were advised to fill in the CES-D questionnaire which was later, during the examinations checked by a registered nurse practitioner who received special training for the purpose. If necessary, missing responses were filled in by interviewing the subject. CES-D scale is a widely used self-report measure in community samples with reliability and validity demonstrated in heterogeneous samples (e.g. Beekman et al., 1997). The total CES-D scale has 20 items and respondents rate the frequency with which they have experienced particular depressive symptoms during the past week. Each item is scored from 0 to 3, for a possible total range of 0 to 60.

In the CES-D scale, the standard cut-off score indicating depressive symptoms is 16 or more of the possible 60 points (McDowell and Newell, 1996) whereas a cut-off score of 20 or more is yielding a higher accuracy for the diagnosis of major depression (Beekman et al., 1997; Haringsma et al., 2004; Himmelfarb and Murrell, 1983; Lyness et al., 1997). In this study, we classified those persons scoring 16 or more, but below 21 points as suffering from minor depressive symptoms and those scoring 21 points or more as suffering from more severe depression. The internal consistency of the CES-D scale was adequate in the present study; Cronbach's alpha was .85 at baseline and in follow-up measurements.

The assessment of physical activity level at baseline and in follow-up was based on a standardized question of physical activity among elderly people presented by Grimby (1986). The question included seven alternative physical activity categories: mainly resting or only minimal physical activity, most activities performed sitting down, light physical activity, moderate physical activity about 3 h a week, moderate physical activity at least 4 h a week or heavy physical activity ≤ 4 h a week, physical exercise several times a week or heavy leisure time working at least 3 h a week and competitive sports several times a week. Self-reported information was collected in home interviews by university students who received special training for the purpose before the study started. When comparing changes in the physical activity level between intervention and control groups the following categories were used: those who moved two categories upwards in the seven-scale from baseline to follow-up were considered to have increased their physical activity level substantially, those who moved one category upwards to increase their physical activity level moderately, those whose score did not change were considered to have no change in their

Table 1
Baseline characteristics of the intervention and control group

Variable	Intervention group (n=318)		Control group (n=314)		t-test p-value
	Mean	(SD)[a]	Mean	(SD)	
Age	77.6	(1.9)	77.6	(1.9)	.80
CES-D score[b]	9.8	(7.6)	10.0	(7.6)	.71
MMSE score[c] (0–30)	27.1	(2.0)	27.0	(2.2)	.81
Number of chronic conditions	3.0	(2.0)	3.0	(2.0)	.63
Education (years)	9.05	(4.0)	9.25	(4.4)	.74
	%		%		χ^2 p-value
Gender					.85
Male	25.5		24.8		
Female	74.5		75.2		
Marital status					.27
Married	39.6		45.5		
Never married	14.2		10.5		
Divorced	9.4		10.8		
Widowed	36.8		33.1		
CES-D score					.98
< 16	80.6		80.0		
16–20	10.2		10.3		
≥ 21	9.2		9.7		
Proportion of participants using antidepressant medication	7.3		8.0		.59
Physical activity[d]					.76
Light	24.2		25.2		
Moderate	51.6		48.7		
Heavy	24.2		26.1		
Self-rated health					.08
Excellent	1.9		1.3		
Good	47.0		37.4		
Not so good	48.3		58.1		
Poor	2.8		3.2		
Feeling lonely					.35
Very seldom/never	70.1		75.2		
Seldom	21.7		17.5		
Often/almost always	8.2		7.3		

Notes: numbers vary: n=624 for CES-D, 630 for MMSE, 631 for number of chronic diseases and 627 for self-rated health.
The study was conducted in Finland in 2003–2005.
[a] Standard deviation.
[b] Center for the Epidemiologic Studies Depression Scale.
[c] Mini-Mental State Examination.
[d] The Grimby seven-point scale was categorized into three: (1) light physical activity at the most, (2) moderate physical activity about 3 h a week, (3) moderate physical activity at least 3 h a week.

Table 2
The effects of physical activity counseling intervention on CES-D scale scores among all the study subjects

Variable	Intervention (n=307)	Control (n=302)	Group p-value	Time p-value	Group × Time p-value
	mean (SEM)[a]	mean (SEM)			
CES-D					
Baseline	9.80 (0.42)	9.88 (0.43)	.709	< .001	.498
Follow-up	11.21 (0.43)	10.93 (0.45)			
Average change (%)	+14	+11			

Notes: CES-D=Center for the Epidemiologic Studies Depression Scale.
The study was conducted in Finland in 2003–2005.
[a] Standard error of the mean.

physical activity level, those who moved one category downwards were considered to have decreased their physical activity level moderately and finally those who moved two categories downwards to decrease their physical activity level substantially.

In addition to outcome data demographic, socioeconomic and health information was collected at baseline and in follow-up home interviews and study center examinations. At the study center examination, study nurses checked the questions of chronic diseases and prescription medications filled in by the interviewers at home interviews. In addition, adverse outcomes were assessed by asking the participants whether they had had injuries in the previous year and had the injuries required medical treatment.

Intervention

Approximately 2 weeks after randomization, each participant in the intervention group received one individual 1-hour face-to-face physical activity counseling session at the study center with a physiotherapist specifically trained for the task (Leinonen et al., 2007). The counseling approach was based on the social cognitive theory of health behavior change (Bandura, 1997) and motivational interviewing technique. Persons were encouraged to exercise on their own, e.g. by doing home callisthenics, walking and performing every day activities such as shopping in a physically active way and they were referred to inexpensive exercise classes organized by the municipality. Problem-solving method was also used to address the perceived obstacles to physical activity and to access to the exercise facilities offered by the municipality. The counseling session was followed up by regular phone contacts to support compliance and behavior change over 2 years. Originally follow-up contacts were planned to take place every 3 months, but due to practical reasons such as not reaching the participants, phone contacts took place on average every 4 months.

In addition to personal counseling, the intervention group was invited to participate in two voluntary lectures with topics including, e.g. aging and disability prevention. The control group received usual services provided by the municipality.

Statistical analyses

Baseline differences in group characteristics were analyzed by unpaired t-tests for continuous variables and chi-squared tests for categorical data. The intervention effects were assessed using ANOVA for repeated measures to analyze the effect of time and Group × Time interactions for CES-D scale change 2 years after the baseline. Analysis was performed according to the intention-to-treat principle using the baseline CES-D value as a substitute for the missing 2-year follow-up value. We did not impute values for those who died during 2-year follow-up (n=15). To control for the possible confounding effect of the use of antidepressants, the data were adjusted for the use of antidepressants. Due to the small number of the users of antidepressants, the most practical way to deal with the issue was to residualize CES-D scores by the use of antidepressants prior to entry into the repeated measures ANOVA. Ancillary analyses included comparisons of changes in physical activity level from baseline to follow-up in the intervention group and control group. Changes in the physical activity level were compared using chi-squared test. Statistical calculations were performed using the SPSS for Windows 12.0 version.

Results

The baseline characteristics of the intervention and control groups were comparable (Table 1). At baseline, a total of 61

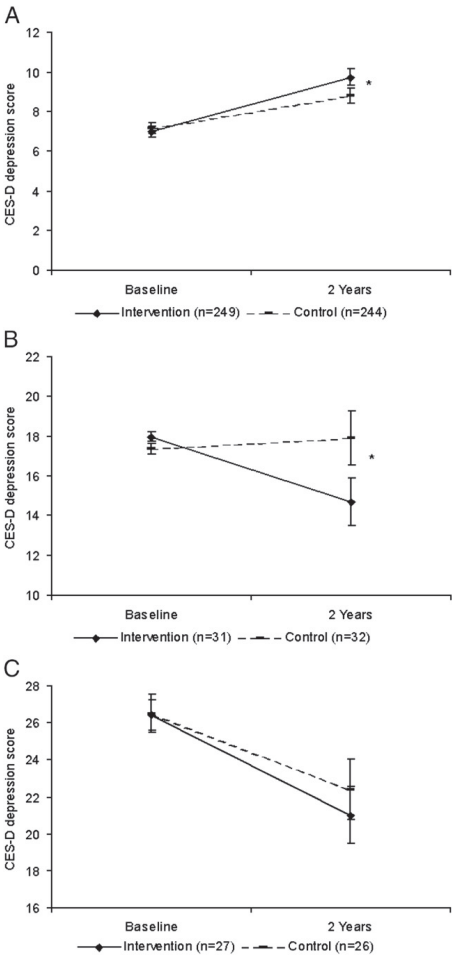

Fig. 2. CES-D depression scores for the intervention and control groups during follow-up, (A) among subjects with no depressive symptoms at baseline (CES-D score 0–15), (B) among subjects with minor depressive symptoms (CES-D score 16–20) (C) and among subjects with more severe depression (CES-D score ≥ 21). Data are expressed as mean±SEM. The p-values are based on repeated measures ANOVA: *p<.05. The study was conducted in Finland in 2003–2005.

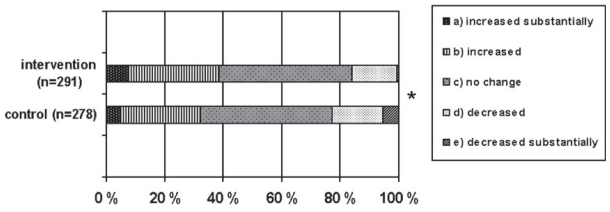

Fig. 3. Changes in physical activity level in the intervention and control group during intervention. The p-value is based on chi-squared test: *$p<.01$. The study was conducted in Finland in 2003–2005.

(19.4%) subjects participating in intervention group and 62 (20%) in control group scored above the CES-D cut-off 16 and were considered to have depressive symptomatology. Of these, 32 subjects (10.2%) in intervention group and 32 (10.3%) in control group scored 16–20 points in the CES-D scale and among subjects with CES-D score ≥21 these numbers were 29 (9.2%) and 30 (9.7%), respectively.

Follow-up depression data were available for 533 (85.4%) of the 624 enrolled participants. Of the 314 persons randomized to the physical activity counseling intervention group, 279 (88.9%) completed the intervention and 35 (11.1%) dropped out of the intervention. These numbers were 254 (81.9%) and 56 (18.1%), respectively, for the control group. Those who failed to take part in the follow up were more likely in the control group ($p=.014$), had a higher baseline CES-D value (12.0 vs. 9.7, $p=.020$), poorer self-rated health ($p<.001$) and were less active physically ($p=.001$) at baseline. The dropout rate for both the intervention group and control group was higher among persons with CES-D ≥21 at baseline (17.2% and 33.3 %, respectively) than among those with CES-D score 16–20 (12.5% and 28.1%, respectively) but the difference was statistically significant only in the control group ($p=.014$).

In analysis carried out for all the study subjects there was a modest increase in CES-D sum points over the two years in both groups, but no Group × Time interaction effect between intervention and control group was found (Table 2). In analysis carried out separately for men and women, the results were similar and no Group × Time interaction was detected (data not shown).

Subgroup analyses for the total CES-D scale were carried out for those with no depressive symptoms at baseline (CES-D score <16), for those with minor depressive symptoms (16–20) and for those with more severe depression (≥21). Among those with CES-D <16 at baseline (Fig. 2A), depression scores increased over time in both groups ($p<.001$) and the increase was slightly higher in the intervention group (Group × Time p-value .044). On average, the intervention group increased their depression score by 2.74 points (standard error of the mean, SEM 0.39) and control group by 1.67 points (SEM 0.36). Among participants with CES-D score 16–20 at baseline (Fig. 2B), a significant treatment effect was observed (Group × Time p-value .039). The average reduction in depression score was 3.26 points (SEM 1.12) in the intervention group whereas in the control group depression score increased on average 0.56 points (SEM 1.42). Among those with CES-D ≥21 at baseline (Fig. 2C), depression scores decreased over time in both groups ($p<.001$). The average reduction in depression score was 5.44 points (SEM 1.55) in the intervention group and 4.12 points (SEM 1.48) in the control group with non-significant Group × Time interaction. When analyses were done per-protocol basis, similar results were obtained (data not shown). Adjustment for antidepressant use had also no effect on the results (data not shown).

To study whether the improvement in mood level among those participants with CES-D score 16–20 was mediated through increased physical activity, the changes in the physical activity level were added to the analysis of repeated measures ANOVA. After adjusting for the change of physical activity level, the statistically significant difference between intervention and control groups in mood changes disappeared ($p=.769$). This gives indirect evidence to support that the increased physical activity level had an influence on mood. The changes in physical activity level among intervention and control group participants are seen in Fig. 3.

At baseline, about 30% of the intervention group and 28% of the control group reported some form of injury in the previous year. At 2-year follow-up, 25% of the intervention group and 24% of the control group reported some form of injury in the previous year. Accordingly, there were no statistical differences between the groups among those who needed medical treatment as a result of the injuries. This result indicates that the intervention did not cause excessive adverse events.

Discussion

This randomized controlled trial suggests that a customer-oriented counseling intervention for physical activity may improve the mood of old men and women with minor depressive symptoms. However, no effect of intervention was observed among those with no depressive symptoms or with more severe depression. Among all the study subjects depressive symptoms increased slightly over the 2 years follow-up. Our study provided novel evidence about the benefits of a relatively low intensity counseling approach in improving mood among those suffering from minor depressive symptoms. As even minor depressive symptoms increase the risk of clinical depression, functional decline, hospitalization and death (Blazer, 2003), our study is of clinical importance. Our findings give us a reason to recommend that in the future physical activity counseling

interventions studies should be implemented with the main focus on depressive symptomatology.

Our results are in agreement with Salminen and colleagues (2005) who found improvements in depressive symptoms among older male patients with coronary heart disease having moderate or high level of depressive symptoms at baseline, but no change of depression scores among non-depressive population after a health advocacy, counseling and activation program. On the other hand, Kerse and colleagues (1999) and Leveille and colleagues (1998) did not detect any effects of an education program intervention on psychological well-being in older adults and the few other studies examining the effects of exercise counseling on quality of life in older people have yielded mixed results (Dubbert et al., 2002; Elley et al., 2003). However, these previous studies are not entirely comparable to our study because of the heterogeneity of the study populations, interventions and psychological outcomes. In our opinion, it is also important to note that these previous studies have not included subgroup analysis of those with minor depressive symptoms at baseline and it is thus possible that some associations between educational counseling interventions and depressive symptoms have been unintentionally missed.

This kind of physical activity counseling intervention may have positive effects on depressive symptoms as far as older people with minor depressive symptoms are concerned. On the other hand, no significant effect of the intervention on more severe depression was found. This finding may partly be explained by the fact that among control group participants depressive symptoms and especially more severe depression at baseline increased the risk to drop out of the study, leaving the treatment effects among those with severe depression at baseline underestimated. In this subgroup depression scores decreased among the intervention group participants and it is thus possible that in some way our intervention may have alleviated depression also among those with more severe symptoms. However, reduction in depression scores may also be partly explained by the fact that depressive symptoms in older adults may fluctuate with remissions and recurrences following each other sometimes even without any form of treatment (e.g. Geerlings et al., 2000).

Overall, the average depression scores in the whole study population and in the subgroup with no depressive symptoms at baseline increased over the two-year intervention, remaining nevertheless below the standard CES-D =16. Increasing depression scores have been reported earlier in older people with decreased health status and negative life events, which are more frequent in later life (Fiske et al., 2003). Part of the increasing depression scores may also be due to regression to the mean as persons with low depression scores are likely to obtain higher scores over time and vice versa.

In our study, several mechanisms may explain the mood improvements among those with minor depressive symptoms. Firstly, our physical activity counseling was motivational, individually tailored for each participant and was followed up by personal phone contacts over the two-year intervention. So, it is thus possible that counseling itself might have had some direct psychological stimulating effects on participant mood level. Secondly, the physical activity level in the intervention group was increased in this study (Rasinaho et al., 2006) and we believe that fitness benefits together with increased social participation may explain the positive effect of intervention. We were not able to pin point, which was the actual underlying mechanism between physical activity counseling and improved mood. Nevertheless, when aiming to alleviate depressive symptoms through physical activity the presence of both social and physical aspects will probably give further benefits over to having just one or the other.

Some limitations of the present study should be taken into consideration. Firstly, our study participants were not selected based on the presence of depressive symptoms and a psychiatric assessment of clinical depression was not included. Secondly, the study sample consisted of 75- to 81-year-old urban residents and it is thus possible that the results obtained may not be transferable to other populations with differences in age and social and cultural context. Thirdly, subgroup analyses remove the effect of randomization, which makes it problematic to draw strong conclusions based on these analyses. Fourthly, the subgroup with minor depressive symptoms was quite a small group and multiple comparisons were done and the results obtained should therefore consider carefully. The strengths of this study include its size, the randomized controlled design and the fact that subjects were not recruited on volunteer basis. Many studies have shown that recruitment of volunteers results in a healthier and more physically active population than average (van Heuvelen et al., 2005).

As a conclusion, the number of people living to very old ages is increasing, emphasizing the need for new multidimensional methods to maintain and increase well-being in old age. Increasing physical activity among older people is expected to slow down the disablement process and thus positively influence psychological well-being and autonomy. The present study found that a physical activity counseling targeting initially sedentary older people was effective in reducing depressive symptoms among older men and women suffering from minor depressive symptoms. These findings extend the limited literature in this field, but further research is required to clarify the optimal type, duration and intensity of educational physical activity counseling which will most benefit the growing older population.

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IV

THE EFFECTS OF AN INTENSIVE STRENGTH-POWER TRAINING ON SENSE OF COHERENCE AMONG 60-85-YEAR OLD PEOPLE WITH A HIP FRACTURE: A RANDOMIZED CONTROLLED TRIAL

by

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The effects of an intensive strength-power training on sense of coherence among 60-85-year old people with a hip fracture: A randomized controlled trial

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ABSTRACT

Background and aims: Older people with disabilities are at an increased risk for psychological health decline. There are no earlier studies on the effects of resistance training on sense of coherence among older people with a hip fracture history. The aim of this study is to test the effects of intensive twelve-week strength-power training on sense of coherence among older adults with a hip fracture history.
Methods: A clinical sample of 60-85-year old community-dwelling men and women 0.5. to 7.0 years after hip fracture. Forty-six people had no contraindications for participation and were randomized into the training (n=24) and control groups (n=22). The training group participated in a 12-week individually tailored strength-power training program twice a week in a senior gym and supervised by an experienced physiotherapist. Sense of coherence (SOC) was assessed using Antonovsky´s short 13-item scale. Data were collected at baseline and after the intervention.
Results: Intensive twelve-week strength-power training had no effect on participants' sense of coherence level.
Conclusions: Results indicated no change in sense of coherence after twelve-week physical exercise training among participants with a hip fracture history. Further studies on sense of coherence among older people with disabilities and potential ways to increase it are needed.

INTRODUCTION

Hip fractures among older people are a major public health problem worldwide. As regards to psychological outcomes, earlier studies have found hip fractures to be associated with impaired quality of life (1) and increased clinical depression and depressive symptoms rates (2). However, the consequences of hip fractures and its interventions on older adults' sense of coherence have been rarely studied. In the present study, we investigated the effects of intensive twelve-week strength-power training on sense of coherence among older adults with a hip fracture history.

Sense of coherence (SOC), according to Antonovsky's salutogenic theory, is a way of seeing the world that facilitates successful coping with stressors in all cultures. Antonovsky (3) described three dimensions that constitute SOC: comprehensibility (the extent to which the world is perceived as making sense and being understandable), manageability (the extent to which individual perceive their resources to be sufficient to meet internal and external demands), and meaningfulness (the extent to which individuals see their life as having some purpose and their life tasks as being worthy investments). Though not a coping strategy in itself, SOC is an estimate of the ability individuals have in coping with different life situations. (3,4.) Sense of coherence has been described as a rather stable personality characteristic (5) but empirical evidence supporting stability is weak (6). Indeed, according to recent research SOC changes have been observed to happen as a result of drastic life events such as accidents and serious illnesses (7), negative employment trajectories (8) and other negative life events (9).

The beneficial effects of strong SOC on several health outcomes have been well documented in earlier studies (10). Higher SOC has been reported to be associated with better quality of life and psychological well-being (11, 12) and to predict better self-rated health and lowered mortality rates (6, 13). A strong SOC buffers the impact of stressful life events (14) and correlates with healthier lifestyle choices independently of social class and education, while lower SOC correlates with mental and physical diseases and may also weaken coping mechanisms (10). A strong SOC might therefore be a useful psychological resource for older people coping with the consequences of hip fracture (15).

Although the health benefits of strong SOC have been extensively confirmed, little is known about how to enhance individuals' SOC. Among working age population the most often reported interventions to promote SOC have been done among the unemployed and work-disabled individuals and the interventions have mostly comprised multidisciplinary rehabilitation programs (16, 17). Among healthy and frail older people, physical exercise is considered effective in enhancing psychological well-being in terms of reducing depressive symptoms (18) and increasing quality of life (19, 20, 21). Exercise may enhance psychological well-being through a variety of mechanisms including physiological, biological and psychological mechanisms (20). Improved physical fitness, alterations in central monoamine activity, reduced activity of the hypothalamo-pituitary-adrenocortical axis and distraction from negative thoughts are believed to explain the positive effects of exercise (20). Exercise training in a group-setting may also provide social interaction and thus promote psychological well-being (21).

However, research-based evidence on the effects of physical exercise training on sense of coherence among older people with disabilities is scarce. We found only one earlier study where the effects of physical activity intervention on SOC had been investigated (22). Kohut and colleagues (22) found that a ten-month intervention of an aerobic exercise or strength training increased the SOC among participants aged over 64 years. Because the literature in this area is limited, research on the effects of physical activity interventions on older adults' sense of coherence is needed.

The present study is based on secondary analyses of a randomized controlled trial concerning the effects of resistance training on muscle strength parameters, mobility and balance in older persons with hip fracture history (registered as ISRCTN 34271567). The purpose of this report is to describe the effects of intensive resistance training on sense of coherence among 60-85-year old people with a hip fracture history. We hypothesized that in frail older people the intensive strength-power training will result in better physical functioning, positive experiences related to improved fitness which together with encouragement provided by the instructor during intervention classes increase participants' sense of coherence.

METHODS

Design

The design and methods for this randomized controlled trial have been published previously in detail (23) and are briefly summarized here. A clinical sample of 60-85-year-old patients operated on a hip fracture at the Jyväskylä Central Hospital ½-7 years earlier were informed about the study (n=452). A total of 193 patients responded, of which 132 expressed an initial interest. Those with neurological or progressive severe illnesses and inability to walk outdoors independently were excluded. After clinical examination (N=79), persons without contraindications for participation strength training were randomly assigned into the training (8 men, 16 women) and control group (6 men, 16 women). The groups were randomized by sealed envelopes in blocks of gender and stratified by age. The training group participated in a 12-week individually tailored strength training program that was organized twice a week (1-1.5h) in a senior gym and supervised by an experienced physiotherapist. Training was specifically focused to reduce asymmetric deficit and to increase strength and power of the lower-limb muscles. The first two training sessions were used to familiarize the participants with the facility, equipment and staff. In the following sessions, the 1RM (1-repetition maximum, i.e. the maximum amount of weight one can lift in a single repetition for a given exercise) was estimated. Training intensity was adjusted individually and increased progressively throughout the training period when tolerated. The assessment was repeated in weeks 6-8 and the training resistance was adjusted accordingly. The control group was encouraged to continue their lives as usual and maintain their pre-study level of physical activity during the 12-week trial. In the control group, one participant dropped out for personal reasons and one participant because of dissatisfaction with the randomization outcome. In the training group, one participant dropped out for personal reasons. The study was approved by the Ethics Committee of Central Finland Health Care District and an informed consent form was signed before the baseline examinations.

Instruments

Sense of coherence (SOC) was assessed at baseline and after 12-week intervention using Antonovsky's short 13-item scale derived from the original 29-item scale (4). At arrival in the study center, participants were advised to fill in the SOC-questionnaire which was later, during the examinations, checked by registered nurse practitioner. In the questionnaire the responses are made on the seven-point scale and the sum of the scores ranges from 13 (weak SOC) to 91 (strong SOC). The sense of coherence questionnaire is a widely used self-report measure with reliability and validity demonstrated in heterogeneous samples cross culturally (24). In the present study, the internal consistency of the SOC-scale was adequate; Cronbach's alpha was .82 at baseline and .78 in follow-up measurements. The scale was also normally distributed (skewness -0.94, kurtosis 1.12 at baseline and -0.21 and -0.48 at follow-up, respectively). In addition to outcome data, physical and psychosocial information of the participants were collected at baseline and follow-up by a physician and a research nurse. The presence of chronic conditions was confirmed according to a pre structured questionnaire, clinical examination, and medical records. Physical activity was assessed by interview using the Yale Physical Activity Survey (YPAS) developed specifically to assess physical activity in the older population (25). Time since fracture was defined as the number of days between the date of hip fracture and the date of the measurements. Severe pain in the lower back, hip or knee region on both sides of the body during the last week was assessed with the Visual Analog Scale (VAS, a line of 100 mm long without numbers). The participants were classified as having severe pain if she or he rated the pain as 66 mm or over in at least one of the listed body regions. Pain below 66 mm was rated as little or no pain. (26.) Participants' marital status, self-rated health, sleeping problems and feeling of fatigue and loneliness were assessed by a structured questionnaire. All the measurers were blinded to the participants' group assignment.

Statistical analyses

Baseline differences in group characteristics were analyzed by unpaired t-tests for continuous variables and chi-squared tests for categorical data. The intervention effects were assessed using ANOVA for repeated measures to analyze the effect of time and Group x Time interactions for SOC-scale change after the 12-week intervention. Analysis was performed according to the intention-to-treat principle using the baseline SOC value as a substitute for the missing 12-week follow-up value. Statistical calculations were performed using the SPSS for Windows 15.0 version.

RESULTS

The characteristics of the study groups are shown in Table 1. There were no significant differences between the groups at baseline for physical and psychosocial characteristics. The mean score of the SOC-scale at baseline was 73.4 (SD 10.6) in the training group and 75.6 (9.6) in the control group (p=.474). Table 2. shows the effect of the 12-week intervention on the level of the SOC-scale and its three subscales. The intervention had no statistically significant effect on the total SOC-scale score (p=.735) or its subscale scores (p=.191- .854). The sense of coherence scores decreased over time in both groups, although the change was statistically non-significant (p=.292). The average decrease in the sense of coherence scale was 2.37 (2.63) points in the training group and 1.22 (2.03) points in the control group. In the per-protocol analysis, i.e., excluding

participants in the training group with poor training compliance (n=3), did not change the results (data not shown).

CONCLUSIONS

Our randomized controlled trial among 60-85-year old people with a hip fracture history found no effect of twelve-week intensive strength-power training on participants' sense of coherence. During intervention a slight, but non-significant decrease in sense of coherence scale was observed among both the intervention group and control group. As research-based evidence of the effects of physical exercise training on sense of coherence and psychological wellbeing in general is scarce in this populations, our study provides new evidence in this area of research.

Psychological outcomes have not been consistently reported in most physical activity interventions among older hip fracture patients and the few existing studies show inconsistent results. For quality of life, the most often included measure of global wellbeing in physical exercise interventions both positive results (27, 28) and no effects (29) of interventions have been reported. As regards to specifically psychological outcomes very few studies exists. Lotus Shyu and colleagues (30) found positive effects on depression. In another study, physical activity intervention had no effect on self-efficacy of hip fracture patients (31). The only earlier study investigating the effects of ten months exercise training on older adults' SOC found positive effects of intervention (22). However, participants were healthier and the intervention was longer and, consequently, comparability to our study is limited.

Overall, in our study, there was a slight non-significant decrease in the SOC-scale in both groups. In the intervention group, the changes in the whole SOC-scale and its subscales varied between one and five percent and in the control group between one and two percent. However, the smallest meaningful change in SOC is 10 % and consequently the current minor decline in SOC may be considered insignificant (32). It is also worth of noticing that the SOC scores before and after the intervention were at a high level. Our study population consisted of rather well functioning people despite their hip fracture history. Those not living independently or unable to walk outdoors independently were excluded which might, at least partly, explain the high level of SOC in our study (23).

There are some possible explanations why we were unable to detect changes in participants' sense of coherence level. First, our participants' had remarkably high sense of coherence level compared to earlier studies among younger and older adults with chronic illnesses (6, 11, 17). This may have produced a "ceiling effect" as there was less room for improvements. Second, our study with follow-up period of three months may have been too short to detect differences in SOC levels. Although participants' muscle strength, power and self-reported outdoor mobility improved (23), psychological changes might need longer follow-up time. Third, earlier intervention studies managing to enhance participants' sense of coherence level have often included also psychological aspects combined with other forms of rehabilitation in their interventions (e.g. 17). As older adults with hip fracture history often suffer from many medical and psychological problems, the multidisciplinary intervention combining both physical and psychological

aspects might lead to more beneficial results. Fourth, despite the very strict design, this study was slightly underpowered according to primary outcomes of the project, although everyone in the target population who met the inclusion criteria had the opportunity to join the study. The limited number of study participants also restricted the possibility to analyze changes according to gender and age, which might have influenced the results. A novel finding of our study was the unexpectedly high sense of coherence level among our hip fracture patients. Psychological health is of great importance for older hip fracture patients as e.g. depression may further increase the risk for physical disability (33). A high level of psychological well-being may also help to sustain exercise motivation during the rehabilitation processes (15).

In conclusion, these secondary analyses of a randomized controlled trial on effects of high intensity strength and power training showed no effect on sense of coherence. Nevertheless, it is possible, that a longer intervention among hip fracture patients who have lower sense of coherence may be beneficial and should be studied. To obtain psychological health improvement, the physical rehabilitation interventions should also have specific psychological elements, such as motivational discussions. In the future, this should be taken into consideration when rehabilitation programs are being planned for hip fracture patients.

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Table 1. Baseline characteristics of the men and women in the training and control groups.

Variable	Training group (n= 24) Mean	(SD)[a]	Control group (n= 22) Mean	(SD)	t-test p-value
Age	73.8	(6.6)	74.1	(7.2)	.88
No. of chronic diseases	2.8	(1.4)	2.3	(1.4)	.18
YPAQ[b] sum index	41.1	(20.1)	44.0	(20.2)	.63
Years from fracture	3.6	(2.0)	3.3	(2.4)	.59
	%		%		χ^2 p-value
Marital Status					
Married	54		45		.68
Never married	4		9		
Divorced	21		14		
Widowed	21		32		
Self-rated health					
Excellent/good	65		73		.58
Not so good	31		27		
Poor	4		0		
Severe pain					
Severe pain	33		46		.30
Little or no pain	67		54		
Sleeping problems					
Not at all	13		23		.33
Slight	29		45		
Some	46		23		
Very much	12		9		
Feelings of fatigue					
Very often	4		0		.82
Quite often	17		18		
Some times	75		77		
Never	4		5		
Feeling lonely					
Very seldom/never	62		50		.28
Seldom	38		41		
Often/almost always	0		9		

[a] Standard deviation

[b] Yale Physical Activity Questionnaire

Table 2. The effects of an intensive strength power training on Sense of Coherence scale (SOC) and its subscales among men and women in the training and control groups.

Variable	Intervention (n= 24)	Control (n= 22)	Group p-value	Time p-value	Group x Time p-value
SOC					
Baseline	73.4 (10.6)[a]	75.6 (9.6)	.474	.292	.735
Follow-up	71.1 (9.1)	74.3 (9.8)			
Meaningfulness subscale					
Baseline	24.9 (2.7)	23.7 (3.9)	.232	.051	.191
Follow-up	23.3 (3.2)	23.3 (3.5)			
Manageability subscale					
Baseline	20.9 (4.7)	22.4 (3.5)	.230	.693	.841
Follow-up	20.5 (3.8)	22.3 (4.3)			
Comprehensibility subscale					
Baseline	27.5 (5.0)	29.5 (4.9)	.208	.592	.854
Follow-up	27.3 (4.4)	28.8 (4.4)			

[a]Means and (SD)

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