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# SUBJECTIVE COMPLAINTS IN DIFFERENT NEUROLOGICAL DISEASES – CORRELATIONS TO THE NEUROPSYCHOLOGICAL PROBLEMS AND IMPLICATIONS FOR THE EVERYDAY LIFE

**Abstract**

TALLINN 2009

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**Abctract**

Institute of Psychology, Tallinn University, Estonia.

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# ERINEVATE NEUROLOOGILISTE HAIGUSTE KORRAL ESINEVAD SUBJEKTIIVSED KAEBUSED – SEOSED TEGELIKE PROBLEEMIDEGA JA MÕJU IGAPÄEVAELUGA TOIMETULEKULE


**Resümee**

Neuropsühholoogiline hindamine on muutunud pelgalt diagnostikast aja jooksul teaduseks, mis on võimeline mõõtma inimese mõtlemise tugevaid ja nõrku külgi. Käesolevas töös uuritakse *sclerosis multiplex*i, hereditaarse spastilise parapleegia ja epilepsiaga kaasneda võivaid psühholoogilisi ja neuropsühholoogilisi muutusi ning inimeste poolt esitatavate subjektiivsete kaebuste esinemise määra. Uurimistöö koosneb neljast artiklist.

Töö eesmärkideks on:

- uurida *sclerosis multiplex*i diagnoosiga inimeste grupis seoseid puhta enesekateteriseerimise õppimiseks kuluva aja ja kognitiivse düsfunktsiooni olemasolu vahel (**I**);
- hinnata üheküsimuselise intervjuu "Kuidas Teie meeleolu on?" tundlikkust depressiooni sõelumisel kahes erinevas kliinilises grupis (*sclerosis multiplex* ja hereditaarne spastiline parapleegia) (**II**, **IV**);
- uurida seoseid subjektiivsete kaebuste ja depressiooni esinemise vahel epilepsia diagnoosiga inimestel (**III**).

Esimese uuringu tulemused tõestasid, et *sclerosis multiplex*i diagnoosiga inimesed on võimelised omandama puhta enesekateteriseerimise protseduuri olenemata nende neuropsühholoogilise hindamise tulemustest ning said seeläbi parandada oluliselt oma igapäevaelu kvaliteeti. Õppimiseks kuluv aeg korreleerus füüsilise puude määraga, aga mitte kognitiivse düsfunktsiooni tasemega.

Teise ja neljanda uurimuse tulemused näitasid, et üheküsimuseline intervjuu "Kuidas Teie meeleolu on?" osutus väga efektiivseks depressiooni tuvastavaks sõelküsimuseks kahe erineva kroonilise neuroloogilise haigusega (*sclerosis multiplex* ja hereditaarne spastiline parapleegia) inimeste gruppides.

Kolmandast, epilepsia diagnoosiga inimeste hulgas läbi viidud uuringust selgus, et nende inimeste subjektiivsed kaebused on oluliselt seotud depressiooni esinemisega.

Töö tulemuste põhjal saab järeldada, et *sclerosis multiplex*i korral võib kognitiivne düsfunktsioon esineda sageli. Töö tulemused näitavad, et hoolimata neuropsühholoogiliste probleemide olemasolust saab inimene oluliselt parandada oma elukvaliteeti puhta enesekateteriseerimise omandamise läbi. Nii *sclerosis multiplex*i, hereditaarse spastilise parapleegia kui ka epilepsiaga kaasneb tihti depressioon. Seetõttu on äärmiselt oluline üheküsimuselise intervjuu ("Kuidas Teie meeleolu on?") vastuste märkamine ja arvesse võtmine raviplaani koostamisel või meeleoluhäirete edasisel uurimisel.

# LIST OF ORIGINAL PUBLICATIONS

## Original publications

I. L. Vahter, I. Zopp, M. Kreegipuu, P. Kool, T. Talvik, K. Gross-Paju. 2009. Clean intermittent self-catheterization in persons with multiple sclerosis: the influence of cognitive dysfunction. – *Multiple Sclerosis*, 15, 379–384.

II. L. Vahter, M. Braschinsky, S. Haldre, K. Gross-Paju. 2009. The prevalence of depression in hereditary spastic paraplegia. – *Clinical Rehabilitation*, in press.

III. M. Liik, L. Vahter, K. Gross-Paju, S. Haldre. 2009. Subjective complaints compared to the results of neuropsychological assessment in patients with epilepsy: the influence of the comorbid depression. – *Epilepsy Research*, 84, 194–200.

IV. L. Vahter, M. Kreegipuu, T. Talvik, K. Gross-Paju. 2007. One question as a screening instrument for depression in people with multiple sclerosis. – *Clinical Rehabilitation*, 21, 460–464.

V. M. Liik, L. Sema, S. Haldre. 2005. Neuropsühholoogilised muutused epilepsia korral. – *Eesti Arst*, 5, 322–326.

VI. L. Sema, A. Kolk. 2005. Neuropsühholoogia kui eriala ja selle areng Eestis. – *Eesti Arst*, 5, 327–330.

## Conference abstracts

VII. M. M. Uccelli, C. Specchia, M. Bohmker, M. R. Deleu, A. Donven, N. Haahr, T. Hesselberg, K. Hrkal, A. Kemppi, J. Kominkova, L. Lazar, L. Leutmezer, K. Muscat, A. O'Connor, B. Omerbasic, J. Sastre Garriga, D. Sutovic, L. Vahter, A. Vryenniou, D. M. Miller. 2007. Factors that influence employment status of people with multiple sclerosis: a multi-national study. – *Multiple Sclerosis*, 13, S261–S262, Suppl. 2.

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IX. M. Braschinsky, S. Haldre, L. Sema et al. 2004. Hereditary spastic paraplegia in Estonia – Preliminary epidemiological results of a study (ongoing clinical trial). – *European Journal of Neurology*, 11, 165–165, Suppl. 2.

X. L. Sema, K. Kompus, A. Toomela, M. Kreegipuu, K. Gross-Paju. 2004. Effect of depression on subjective evaluation and actual verbal abilities of patients with multiple sclerosis: preliminary results. – *Multiple Sclerosis*, 10 (Supplement 2), S126.

# CONTENTS

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# INTRODUCTION

Neuropsychology has developed from the purely diagnostic role it had after the Second World War to the science which is able to characterize an individual person's cognitive strengths and weaknesses. It is also able to investigate the connections between the subjective complaints and ability to cope with the problems in everyday life (Goldstein, McNeil 2004). Traditionally neurology is considered a strong speciality in Estonia. The need for neuropsychological evaluation is extremely important in different neurological disorders. However, compared to the rest of the world neuropsychology in Estonia is a relatively new science.

Neuropsychological changes and depression are very common in chronic neurological disorders. However, the question how a person with chronic neurological disorder is perceiving his/her cognitive abilities or mood disorders remains unclear.

Therefore three different neurological disorders have been chosen for this study: epilepsy, multiple sclerosis and hereditary spastic paraplegia. All these chronic neurological disorders quite often may result in depression and cognitive dysfunction but not in dementia.

# 1. REVIEW OF LITERATURE

## 1.1. MULTIPLE SCLEROSIS

Multiple sclerosis (MS) is one of the most prevalent non-traumatic chronic progressive neurological illnesses affecting the central nervous system (brain and spinal cord) (McDonald et al. 2001). Estonia is situated on the border of the so called Fennoscandian focus of multiple sclerosis with the high disease prevalence rates of 51 cases per 100 000 inhabitants (Gross, Kokk, Kaasik 1993). The disease process results in inflammation and damage to myelin (insulation of the nerve fibres) and other cells within the nervous system (Patti 2009). The myelin aids the conduction of nerve signals therefore the damage of myelin results in impaired nerve signalling and may impair normal sensation, movement, and cognition. Multiple sclerosis affects primarily young adults, with an age of onset typically between 20 and 50 years, and is more common in women than in men. The cause of this disorder is still not known, but environmental, viral, and genetic factors are thought to play a role (McDonald et al. 2001). Recently there are studies performed which are focusing on the clinical features of the childhood multiple sclerosis (Banwell et al. 2007).

Cognitive problems may be another obstacle when planning treatment in neurological disorders. Neuropsychological studies have indicated that cognitive dysfunction occurs in 40–65% of persons with MS (Patti 2009, Rao et al. 1991). Natural history studies suggest that once cognitive dysfunction develops it is not likely to remit (Patti 2009, Bagert, Camplair, Bourdette 2002). Persons with MS who had cognitive decline tend to have fewer social interactions, more sexual dysfunction, greater difficulties with household tasks and higher unemployment than those without cognitive dysfunction and these people need more assistance with personal care and household management (Patti 2009, Rao, Leo, Ellington 1991). These persons tend sometimes to have also greater physical disability than other patients (Wilken et al. 2003).

According to different studies certain areas of cognition in MS are more affected than others – most frequently memory and learning dysfunction are described with some memory processes demonstrating substantial deficits and others remaining intact (Patti 2009, Kujala, Portin, Revonsuo 1994, Fisher et al. 1994), also disorders of information processing speed and attention have been described (Patti 2009, Kujala, Portin, Revonsuo 1994, Rao, Aubin-Faubert, Leo 1989). Quite often persons with MS demonstrate the impairment on measures of executive functioning (Rao et al. 1991, Elpern et al. 1984, Heaton et al. 1985). Problems with verbal functions are described infrequently (Friend et al. 1999, Laakso, Brunnegård, Hartelius, Ahlsén 2000).

Until recently, impaired long-term memory in MS was primarily thought to be due to deficient information retrieval (Rao 1986, Rao, Leo, Aubin-Faubert 1989). A recent meta-analysis supports the notion that MS may be associated with deficits in acquisition rather than recall (Heath, Gaudino, DeLuca, Ricker 2000, Thornton, Raz 1997). This suggests that persons with MS may experience impaired information

acquisition and thus may encode stimuli in a less efficient form, leading to reduced behavioural performance when presented with retrieval paradigm (Heath et al. 2000). Chiaravalloti and colleagues have studied learning process in persons with MS. They demonstrated that persons with MS who required more trials to reach the perfect learning results performed significantly worse on the recall trials (Chiaravalloti et al. 2003). Recent study demonstrated that persons with MS retain insight into their cognitive dysfunction. Subjectively reported impairment reflects subtle decline in memory and information processing speed independent of mood, fatigue and physical impairment (Marrie, Chelune, Miller, Cohen 2005).

Bladder problems are very common in persons with MS – 80% of them experience these at some stage of their disease and in 60% these problems are persistent. Persons with MS often describe their bladder symptoms as the "worst part" of their disease – poor bladder control is difficult to live with and it adds heavy social and psychological burden (Petersen et al. 1997).

In an elegant algorithm suggested by Claire Fowler for bladder management for the persons with MS in 1996 (Fowler 1996), clean intermittent self catheterization (CISC), combined with anticholinergic medication is recommended for patients with urgency, frequency and incomplete bladder emptying. Bladder management according to the Fowler algorithm, including clean intermittent self catheterization to manage incomplete emptying, has been found to be effective in persons with MS (Fowler 1996, DasGupta, Fowler 2003, Gross-Paju, Sema, Zopp 2002). Adequate hand function is thought to be necessary for clean intermittent self catheterization performed by the patient him/herself (Petersen et al. 1997).

However, in practice the cognitive decline is frequently present in persons with MS with advanced disability. Also, progressive failure to void necessiting clean intermittent self- catheterization is more prevalent in persons with advanced disease. Therefore, the question how cognitive dysfunction influences contemporary management methods is important.

Emotional issues are some of the major problems having implications on everyday functioning in both healthy and medical populations (Ketterer, Knyz 2009). Therefore it is important to detect possible mood disorders as early as possible. Depression is a common problem in older adults and chronically ill patients. It is diagnosed more often when people have cardiac disease, cancer and central nervous system disorders (Ketterer, Knyz 2009, Arnett, Barwick, Beeney 2008, Siegert, Abernethy 2005, Petersen, Kokman 1989).

Depression is a common psychiatric condition associated with multiple sclerosis (Arnett, Barwick, Beeney 2008, Siegert, Abernethy 2005) with prevalence rates ranging form 42–62% (White, Nyenhuis, Sax 1992, Schiffer, Babigian 1984) and one quarter to one third of MS patients are thought to be depressed at any particular time (Joffe et al. 1987, Whitlock, Siskind 1980). The rates of depression are higher in persons with MS than in the general population and among the patients with general medical conditions (Arnett, Barwick, Beeney 2008, Rao et al. 1991). Also, the rate of depression in persons with MS is higher than in other neurological dis-

orders without brain involvement (White, Nyenhuis, Sax 1992, Joffe et al. 1987). Depression may appear before, during and after the acute neurological episode of the disease (Minden, Orav, Reich 1987). Berrios & Quemada asked whether depression is or is not associated with specific MS lesions in brain (Berrios, Quemada 1990). The presence of depression is an important concern for patients with MS who are candidates for disease-modifying treatment since depression may affect treatment adherence (Feinstein et al., 2004). Disability level but not therapy with beta-interferons may be a risk factor for depression in MS and regular screening for depression in this population is appropriate (Pandya, Metz, Patten 2005).

The presence of emotional problems in persons with different neurological problems can be diagnosed with different screening instruments (Ketterer, Knyz 2009, Nicholl, Lincoln, Francis, Stephen 2001). However, in everyday clinical practice few scales are used because they may be time consuming and clinicians often rely only on their clinical impression. In attempt to find a test that is reliable, easy and quick to use, many short screening questionnaires have been developed – for example by Leon and colleagues (Leon, Portera, Walkup 1999). Even a shorter version – a single-item interview "Are you depressed?" detected 85–90% of patients with depression in primary care and the second question about anhedonia increased the sensitivity to 95% (Williams et al. 1999, Whooley, Avins, Miranda, Browner 1997). In persons with multiple sclerosis (PwMS) the Yale Single Question has the sensitivity of 65.3% and could be recommended as a replacement for Beck Depression Inventory (Avasarala, Cross, Trinkaus 2003).

Depression often goes unrecognised by treating clinicians and therefore "case finding" may be preferable with routine screening (Baleazzi et al. 2005, Kroenke 2005). The "missed cases" in clinical practice are more likely to have less severe depression and be more reluctant to embrace diagnosis or treatment of their depression (Simon et al. 1999). Some factors, such as a multidrug regimen, lack of efficacy, and side effects of antidepressants may explain why depression is not adequately treated in patients with neurologic disorders (Fregni, Pasqual-Leone 2005).

Multiple sclerosis serves as an excellent example of a disease that causes many different problems like depression, cognitive dysfunction but also bladder and bowel dysfunction, spasticity, mobility problems, number and severity of relapses etc, that should be discussed during a clinical interview. It has been shown that one in four persons with MS had unrecognised and therefore untreated symptoms of depression. (McGuigan, Hutchinson 2005). There are problems with adequate diagnosing as professionals may not show interest in depression as persons with MS themselves often presume (Mohr, Goodkin 1999), and not enough self-report questionnaires are used in everyday clinical practice though it is often recommended (Ong et al. 1995).

## 1.2. HEREDITARY SPASTIC PARAPLEGIA

The hereditary spastic paraplegias (HSPs) are neurodegenerative disorders of the motor system characterized by slowly progressive lower limb spasticity. The hereditary spastic paraplegias are classified into "pure" when spastic paraplegia exists as an isolated syndrome and "complex" forms when other major clinical symptoms are present, e. g. ataxia, amyotrophy, mental retardation, eye symptoms, epilepsy, dystonia and peripheral neuropathy (Harding 1983). The most frequent form of autosomal dominant HSP is associated with the SPG4 locus, described originally as a pure form of the disease. Complex forms of the disease are rare and usually inherited in an autosomal recessive pattern (Tallaksen et al. 2003).

Neuropsychological features of persons with HSP are described only in small number of studies. Depression was considered to be part of the complex form of HSP (Nielsen et al. 2004). Nielsen and colleagues have described the family of four generations with autosomal dominant HSP with a complex phenotype with variable expression: co-existing ataxia, dysarthria, unipolar depression, epilepsy, migraine and cognitive impairment (Nielsen et al. 2004). In addition, one case of 35 years old male having hypomanic behaviour has been reported (Jansen, Kayser, Raes 1988).

## 1.3. EPILEPSY

Epilepsy may develop because of an abnormality in brain wiring, an imbalance of nerve signalling chemicals called neurotransmitters, or some combination of these factors. Having a seizure does not necessarily mean that a person has epilepsy (Meador 2002). Only when a person has had two seizures at least 24 h apart he or she is considered to have epilepsy (Fisher, Leppik 2008).

Epilepsy is a disorder with many possible causes. Anything that disturbs the normal pattern of neuron activity – from illness to brain damage to abnormal brain development – can lead to seizures (Fisher, Leppik 2009). A diagnosis of epilepsy has potentially serious consequences for health, psychosocial well-being and economics. Therefore it should be made with a high level of certainty (Fisher, Leppik 2008).

Epilepsy is a cause of different psychological and neuropsychological disturbances and patients with epilepsy are at increased risk of cognitive deficits (Meador 2002). The neuropsychological studies on frontal lobe epilepsy report deficits in motor coordination and planning, reduced attention span and difficulties in response inhibition in complex cognitive tasks (Patrikelis, Angelakis, Gatzonis 2009). Studies have shown that perceived memory status of epilepsy patients is significantly lower than that of controls and that the prevalence of subjective memory problems in the case of epilepsy can be as high as 50% (Hendriks et al. 2002). Paradoxically there are only moderate correlations between self-reported memory complaints and results of neuropsychological memory tests (Piazzini et al. 2001, Fargo et al. 2004, Vermeulen et al. 1993). There are different causes suggested to explain the dis-

crepancy between subjective and objective memory status. One of the reasons for this discrepancy could be concurrent depression (Marino et al. 2009, Piazzini et al. 2001, Fargo et al. 2004). There are evidence based management guidelines for the persons with epilepsy who have intellectual problems been developed lately (Kerr et al. 2009).

It may be concluded that in everyday clinical work it is extremely important to rely both on each person's subjective complaints and objective characteristics when diagnosing, planning treatment and rehabilitation or evaluating its effectiveness.

## 1.4. AIMS OF THE RESEARCH

This thesis is concentrated on the following issues:

- to study the relationship between learning clean intermittent self-catheterization and the cognitive dysfunction in persons with multiple sclerosis (**I**)
- to find the effectiveness of the single item interview "Are you depressed?" in two different patient populations – multiple sclerosis and hereditary spastic paraplegia (**II, IV**)
- to find the correlations between subjective complaints and depression in persons with epilepsy (**III**)

# 2. PATIENTS AND METHODS

## 2.1. PATIENTS

*The correlations between learning clean intermittent self-catheterization and the cognitive dysfunction in persons with multiple sclerosis (**I**).*

Study group (**I**) included consecutive 23 adult persons with multiple sclerosis (PwMS) (11 male and 12 female), drawn from 201 consequent persons with MS with bladder problems referred to the Estonian MS centre in 2001. Of these, 169 persons with MS had problems suggesting the applicability of Fowler's algorithm (Fowler, 1996, DasGupta & Fowler, 2003) and 25/169 had incomplete emptying of the bladder. Two of the 25 persons with MS refused to participate in the study. The mean (SD) age of the participants was 45.6 (11.4) years. The mean (SD) of education was 11.8 (3.1) years. The mean (SD) EDSS was 4.7 (1.8) and the mean (SD) duration of the disease was 12.7 (6.9). Sociodemographic data and the number of lessons required to learn clean intermittent self catheterization are shown in Table 2, study **I**.

*The effectiveness of the single item interview "Are you depressed?" in two different patient populations – multiple sclerosis and hereditary spastic paraplegia (**II, IV**).*

The study **IV** was conducted from October 2001 to April 2002 in Estonian Multiple Sclerosis Centre. The study group consisted 134 consecutive Estonian speaking in-patients with confirmed diagnosis of multiple sclerosis using McDonald criteria (McDonald, 2001), 99 females and 35 males with different courses of the disease. Mean (SD) age of the participants was 43.8 (12.4) years. The mean (SD) of education was 11.6 (3.4) years. The mean (SD) duration of the disease was 9.9 (8.5) years and mean (SD) EDSS score was 5.8 (2.5). 50% (72/134) had relapsing-remitting MS, 27% (36/134) had secondarily progressive MS, 13% (17/134) had benign course and 10% (9/134) had primary progressive course. The group was a representative sample of the clients of MS centre – including recently diagnosed persons with MS and /or persons with MS admitted for the "second opinion", for differential diagnosis, for symptom management and rehabilitation.

The study group (**II**) of patients with definite hereditary spastic paraplegia (HSP) consisted of 59 persons with clinically confirmed diagnosis (Braschinsky et al. 2009). All persons with HSP from epidemiological study performed by Braschinsky and colleagues (Braschinsky et al. 2009) were invited to participate in the psychological sub-study and 48/59 (81%) of them agreed (**II**). In the study group 81% (39/48) of patients had pure and 19 % (9/48) complex form of HSP. There were 30 men and 18 women, both Estonian and Russian speaking. The mean (SD) age of the participants was 49.9 (13.9). The mean (SD) years of education was 11.2 (2.7). The mean (SD) duration of the disease was 11.9 (10.3) years.

*The correlations between subjective complaints, cognitive dysfunction and depression in persons with epilepsy (**III**).*

Epilepsy study group (**III**, in cooperation with Maarika Liik and colleagues, 2009) was formed from 87 consecutive patients treated in the outpatient clinic of Department of Neurology and Neurosurgery of the University of Tartu. Inclusion criteria were: age between 18 and 65 years, no other neurological diseases and native Estonian speaking. 22% (19/87) refused to participate and 7 % (6/87) did not meet the inclusion criteria. 71% (62/87) patients with defined diagnosis of epilepsy agreed to participate in the study. There were 37 female and 25 male patients in the study group. Mean (SD) age of the patients was 34.6 (11.10) years. All patients had completed the first nine years of regular primary and secondary education and the mean (SD) years of education was 13.9 (4.0). The diagnosis of epilepsy was confirmed by clinical data, EEG study, and in majority of cases MRI study. Mean (SD) duration of the disease was 19.2 (10.5) years. Patients who were intellectually and cognitively challenged and incapable of completing the questionnaires and Beck Depression Inventory (BDI) were excluded from the study.

All persons gave their informed consent to participate in the studies.

## 2.2. METHODS

*The correlations between learning clean intermittent self catheterization and the cognitive dysfunction in persons with multiple sclerosis (**I**).*

In study **I** all participants passed a careful neurological examination and evaluation using the expanded disability status scale (EDSS). A screening battery of cognitive tests using the Brief Repeatable Battery of Neuropsychological Tests (BRB-N) (Rao 1990) was performed before patients were referred for learning clean intermittent self-catheterization. All patients were trained to perform clean intermittent self-catheterization by the same experienced nurse continence advisor using the same training methods. The nurse was blinded to the results of the neuropsychological tests. The goal was to train all participants to the stage of independent clean intermittent self catheterization performance. All patients were given the same standardized training in 45-minute sessions, without the use of written materials. The first session contains introduction when patients are provided with information about the reasons of bladder problems, advantages and techniques of clean intermittent self catheterization and “hands-on” training part in which the patient himself performs clean intermittent self catheterization. In the following sessions patient has to perform clean intermittent self catheterization himself until he is able to learn the procedure. The number of sessions allocated to train each patient was not limited. The ability to learn clean intermittent self catheterization was evaluated at the end of the rehabilitation period (1–2 weeks). None of the routine medications for bladder management were used before clean intermittent self catheterization instruction, and medication regimes were started as needed only after all clean intermittent self catheterization sessions were completed. After three months all patients were fol-

lowed up by a telephone interview in which the nurse continence advisor asked about performing clean intermittent self catheterization, any problems and possible causes for discontinuation. EDSS was used as a standard screening method to evaluate the physical disability of the persons with MS. In spite of its well known limitations, EDSS is the most widely used scale. Hand function was not evaluated separately (**I**).

BRB-N is often used as a screening battery for cognitive dysfunction in persons with MS and measures verbal and visuospatial memory, sustained attention and word generation with six subtests: the selective reminding test (SRT), the 10/36 spatial recall test, the symbol digit modalities test, the paced auditory serial addition test (2 subtests), delayed recall of SRT, delayed recall of 10/36 spatial recall test and word list generation. BRB-N has 71% sensitivity and 94% specificity in discriminating cognitively impaired from intact persons with MS (Rao, 1990). The degree of cognitive dysfunction was defined as no decline, mild decline (-1 SD), moderate decline (-2 SD) or severe dysfunction (-3 SD) (**I**).

*The effectiveness of the single item interview "Are you depressed?" in two different patient populations – multiple sclerosis and hereditary spastic paraplegia (**II, IV**).*

One item interview was modified in Estonian language as "*Kuidas Teie meeleolu on*?". In study **IV** one item interview "Are you depressed?*/Kuidas Teie meeleolu on*?" was asked as a part of the medical history taking by the neurologist. During 2 weeks of in-patient stay all patients filled Beck Depression Inventory (BDI, Beck, 1961), which is based on the 21 depressive symptoms and attitudes – 1. Mood, 2. Pessimism, 3. Sense of Failure, 4. Anhedonia, 5. Guilt, 6. Punishment, 7. Self-dislike, 8. Self-Accusations, 9. Suicidal ideas, 10. Crying, 11. Irritability, 12. Social Withdrawal, 13. Indecisiveness, 14. Body Image Change, 15. Work Difficulty, 16. Insomnia, 17. Fatigability, 18. Loss of Appetite, 19. Weight loss, 20. Somatic Preoccupation and 21. Loss of libido. In BDI respondent uses a 4-point scale (Beck et al., 1961). The clinical diagnosis of depression according to the ICD-10 was defined as score of > or = 10 and positive answers in the structured clinical interview performed by the clinical psychologist. Depression was diagnosed when the clinical opinion of clinical psychologist and treating neurologist confirmed the diagnosis. Sociodemographical data, disease history and neurological disability using EDSS scale (Kurtzke 1983) were evaluated and documented by the treating neurologist.

In study **II** the single item interview as a screening question "Are you depressed?/*Kuidas Teie meeleolu on*?" was conducted with the same method in patients with hereditary spastic paraplegia (HSP) as described in study **IV**. Following the screening question all participants filled Beck Depression Inventory (BDI). Depression was defined as a score of 10 or more points. Mild depression was defined as a score between 10 and 18, moderate depression as a score between 19 and 29 and severe depression as a score between 30 and 63 points on BDI (**II**).

*The correlations between subjective complaints and depression in persons with epilepsy (**III**).*

In study of persons with epilepsy (**III**) subjective complaints of the patients were assessed using a simple modified subjective complaints questionnaire by Toomela and colleagues (Toomela et al., 2004) which was modified for this particular study adding epilepsy specific items. Items for the questionnaire were selected with the purpose to describe the general and cognitive subjective complaint rate. The questionnaire consisted of thirteen items where patients had to assess the presence and the degree of different complaints on a four-point scale, where higher scores indicated higher degree of subjective complaints – from 1 (never) to 4 (constantly). The questionnaire included questions about possible problems with forgetting, retrieving information from the memory, attention, speech, mood, dizziness, coordination, vision, fatigue, headache, and pain. Scores for the items were analysed separately and total score of the questionnaire was calculated. Depressive symptoms were assessed with the Beck Depression Inventory (BDI). A cut-off score of >11 points was used (**III**).

# 3. RESULTS AND DISCUSSION – IMPLICATIONS FOR THE EVERYDAY PRACTICE

## 3.1. THE INFLUENCE OF COGNITIVE FUNCTIONING TO MANAGEMENT DECISIONS IN PERSONS WITH MULTIPLE SCLEROSIS – THE CORRELATIONS BETWEEN LEARNING CLEAN INTERMITTENT SELF CATHETERIZATION AND THE COGNITIVE DYSFUNCTION

Severe cognitive dysfunction is a contraindication to teach clean intermittent self catheterization (CISC) to the persons with multiple sclerosis (PwMS) in some clinical practices. This may lead to the placement of a suprapubic catheter, which may cause additional problems for persons with MS and caregivers (Petersen et al. 1997). It is clear that physical disability affects a person's ability to learn clean intermittent self catheterization but there is little information about the specific relationship between cognitive impairment and the ability to learn this in practice. Therefore study **I** evaluated the influence of cognitive dysfunction on the ability to learn clean intermittent self catheterization with a blinded methodology.

The most important result of this study (**I**) was that the majority (87%, 20/23) of the persons with multiple sclerosis were able to learn clean intermittent self catheterization. The role of an experienced, goal-oriented and highly motivated nurse in the training process cannot be overestimated. To avoid the influence of neuropsychological test results the nurse was blinded to the cognitive dysfunction of patients and the results of the neuropsychological test battery and planned clean intermittent self catheterization teaching sessions according to the needs of each patient. The results of our study indicate that the time needed to acquire the skills of clean intermittent self catheterization differed considerably depending on physical disability, but not on cognitive dysfunction. We have demonstrated the strong statistical evidence that an increase in disability (as measured by EDSS) is associated with an increase in the number of lessons needed to acquire clean intermittent self catheterization. This is an important factor in planning bladder management strategies. Again, cognitive dysfunction should not be a factor automatically influencing treatment decisions.

The profiles of the cognitive functions of persons with multiple sclerosis in our study group varied from cognitively intact to severe dysfunction. The most frequently affected functions were memory, information processing speed and executive functions, similar to those previously described in the literature (Patti 2009, Rao et al. 1991, Kujala et al. 1994, Fisher et al. 1994, Rao, Aubin-Faubert, Leo 1989, Elpern et al. 1984, Heaton et al. 1985). It is a challenge to describe clean intermittent self catheterization in neuropsychological terms and to accordingly compose a neuropsychological test battery. One interesting finding of our study – the statistically significant correlation between later recall in visuospatial memory and the number of lessons to learn it – is that it might be useful to improve the clean intermittent self catheterization training method by including handout materials

accordingly. Other components of the clean intermittent self catheterization training process also require further evaluation (**I**).

The most important factor determining our results was the time professionals could spend teaching the patient. This aspect needs further investigation with a larger group of persons with multiple sclerosis. Our results confirm that it is necessary to adapt the number of training sessions to the cognitive ability level of each individual. Persons with MS with more severe cognitive dysfunction need longer training periods to successfully learn clean intermittent self catheterization and to adhere to the procedure in everyday life (**I**).

Follow-up inquiry revealed that six persons with MS had ceased clean intermittent self catheterization. Two had no need to continue clean intermittent self catheterization because their bladder problems had been solved. The remaining four participants who quit had more severe cognitive dysfunction with significant impairment in executive functions. Effective bladder management after three months did not depend on cognitive abilities assessed at the baseline evaluation. There were no statistically significant correlations with any of the subscores of the cognitive test battery nor the EDSS score, course of the disease and the time required to learn clean intermittent self catheterization. Our study confirmed that persons with cognitive decline need more support during the follow-up than just a phone call, potentially including additional clinic visits or support at home by a specialized nurse (**I**).

Cognitive dysfunction of persons with MS may result in the need for longer training sessions and in worse compliance during follow-up. This is in contradiction to the study by Chiaravalloti and colleagues, who proposed that the retrieval of the cognitively impaired persons with MS was impaired after more repetitions (Chiaravalloti et al. 2003). Our study showed that the results of executive function tests might not be the most important factor determining learning effectiveness while planning medical treatment in a clinical setting. The time needed to teach clean intermittent self-catheterization to cognitively impaired persons with MS varies considerably and should be taken into account while planning treatment and rehabilitation (**I**).

According to our study we could conclude that all the persons with multiple sclerosis with different levels of cognitive dysfunction were able to learn clean intermittent self catheterization. Although persons with MS with cognitive dysfunction are able to perform the procedure independently by the end of the sufficient training sessions, it may also be useful to conduct more frequent follow-up meetings in an out-patient setting to guarantee adequate care (**I**).

## 3.2. THE EFFECTIVENESS OF ONE ITEM INTERVIEW IN PERSONS WITH CHRONIC NEUROLOGICAL DISORDERS

### 3.2.1. The effectiveness of one item interview "Are you depressed?" ("*Kuidas Teie meeleolu on*?") in persons with multiple sclerosis

Our study confirmed that one question "Are you depressed?" (in Estonian "*Kuidas Teie meeleolu on*?") is a very useful tool for screening for depression of persons with multiple sclerosis (**IV**).

The answer "Yes, I feel depressed" has high sensitivity (94%). When the patient himself recognises his mood problems, then the sensitivity of one question is high and the clinical diagnosis is easily made. In other words, without additional tests it is highly likely that the person has depression and the treatment recommendations could be given. According to our study one question test detects depression effectively in a group of persons with MS who feel depressed and express it. If the person gives negative answer then the sensitivity is much lower, only 70%. Therefore the main importance and the practical value of our study is that the persons with MS who answer anything else than "Bad" to the one item interview should be treated with bigger caution and should be referred to further testing in spite of the given answer (**IV**).

The specificity of the one item interview was 84% so in these cases the one question "Are you depressed?" had positive predictive value as these persons with multiple sclerosis answered the question concurrently to the clinical opinion of the clinical psychologist and treating physician (**IV**).

In the group of persons with MS (study group **IV**) 66% of persons with MS were depressed. Our study confirms that depression is very common among persons with MS as reported earlier (Arnett et al. 2008, Siegert, Abernethy 2005, Joffe et al. 1987, Schiffer, Babigian 1984). MS serves as an excellent example of a disease that causes many different problems and all should be addressed during the clinical interview.

The group of persons with MS (study **IV**) who gave the non-concurrent answers were more likely people living with their families and having children below 18 years. It is beyond the reach of the study to explore the reasons for this discrepancy. Our study also showed that there were no statistically significant differences in the levels of depression in the groups with concurrent and not concurrent opinions. Therefore earlier data that people "deny" milder forms of depression published by Simon and colleagues (Simon, Goldberg, Tiemens, Ustun 1999) was not confirmed in our study. The study was relatively small and has only investigated an in-patient population. The antidepressant treatment can have influence to the quality of life of these people, but further investigation is needed.

### 3.2.2. The effectiveness of one item interview "Are you depressed?" (*"Kuidas Teie meeleolu on*?") in persons with hereditary spastic paraplegia

Our study (**II**) is to our knowledge the first describing the possible prevalence of depression in the persons with hereditary spastic paraplegia (HSP). Also how subjective complaints may reflect the actual state of mood in this group is not known (Nielsen et al. 2004).

According to our results more than half (54%, 26/48) of persons with HSP in Estonia had subjective complaints about depression (**II**). Depression was confirmed in 81% (21/26) in persons who answered "Yes" to the single item interview "Are you depressed?" and not confirmed in 19% (5/26) of persons feeling depressed. 46% (22/48) of the study group answered "No" to the single item interview. In 68% (15/22) of these persons with hereditary spastic paraplegia depression was not confirmed. Depression was still confirmed despite the negative answer in 32% (7/22) in this group.

The implication to the everyday clinical practice is similar to the previous study (**II**) that if the person with hereditary spastic paraplegia answers anything else than "Bad" to the one item interview then he should be treated with bigger caution and should be referred to further testing in spite of the given answer. The sensitivity of the interview was 75% and the specificity of the one item interview in this study group was 75%.

According to the results of our study the overall prevalence of depression in persons with hereditary spastic paraplegia (HSP) was confirmed in 58 % which is in good correlation with earlier reports (Nielsen et al. 2004). In our study almost half of patients (44%) had mild, 13% (6/48) moderate and one had severe depression. There were no statistically significant correlations between Beck Depression Inventory scores and the clinical course of the disease. The major triggers to explain the prevalence of the depression in HSP population need further evaluation. The early detection and treatment implication of depression can improve significantly the quality of life of these persons (**II**).

We can conclude that one item interview "Are you depressed?" is a reliable screening instrument for the patients with different chronic neurologic disorders. It has to be underlined that one item interview is extremely time saving and at the same time very informative. If the person indicates to the possible depression he could be referred to the treatment, if the answer is negative then more profound evaluation should be carried out (**II, IV**).

### 3.3. THE CORRELATIONS BETWEEN SUBJECTIVE COMPLAINTS AND DEPRESSION IN PERSONS WITH EPILEPSY

Subjective cognitive complaints can affect the patient's quality of life and be one of the most important signs for the clinician. The results of our study (**III**) confirmed that in general, with some exceptions, subjective cognitive complaints are not strongly associated with the results of objective cognitive functioning measures in epilepsy patients. Correlation analysis indicated that the majority of subjective complaints had a strong correlation with the Beck Depression Inventory (BDI) score. As presented, the distribution of subjective complaints in two groups of patients – with or without depressive symptoms – differed on a statistically significant level. Depression does not only influence the general subjective complaint rate but may also have some deteriorating influences on objective neuropsychological functioning.

The results indicate that subjective complaints may be the sign of concurrent mood disorder. Comparable results have been found in studies of subjective and objective functioning and depression in other chronic disorders as multiple sclerosis (Maor et al. 2001) or after moderate to severe head injury (Lannoo et al. 1998) (**III**).

In conclusion we may say that according to our study in persons with epilepsy the majority of subjective complaints are correlated with the possible depressive state of the mood (**III**).

# CONCLUSIONS

1. Our study confirmed that majority of persons with MS are able to learn clean intermittent self catheterization and therefore profoundly improve their quality of life. The time needed to acquire learn clean intermittent self-catheterization skills differed considerably depending on physical disability but not on cognitive dysfunction (**I**).

2. The results of our study demonstrate that all patients need individual training time for acquiring clean intermittent self-catheterization. Other possible factors influencing the effectiveness of bladder management need further investigation (**I**).

3. It is important to pay more attention to persons with MS with more severe cognitive decline during follow-up, and these patients might need special programs for their rehabilitation (**I**)

4. The one item interview "Are you depressed?/ *Kuidas Teie meeleolu on?*" is useful and effective as a screening question to define persons with different chronic neurological disorders who are depressed. It is also sensitive to detect people who may have the need for more profound evaluation, management and treatment of depression (**II, IV**).

5. The major finding of the studies **II** and **IV** is that the positive answer to the single item interview "Are you depressed? /*Kuidas Teie meeleolu on*?" carries a very sensitive predictive value. Therefore, the major importance of our study for everyday clinical work is that a clinical diagnosis of depression may be easily made if a person reveals possible mood problems. Unfortunately negative answer does not exclude the possibility of depression, therefore in case of clinical suspicion it is necessary to still refer patients for further evaluation even if the patient denies mood problems. (**II**, **IV**).

6. In multiple sclerosis group the sensitivity of positive answer to the one item interview "Are you depressed? */Kuidas Teie meeleolu on*?" was 94% when the person gave positive answer and 70% when the answer was negative. The overall specificity of the one item interview in this group was 84% (**IV**).

7. There were no demographic or disease related factors reliably differentiating between patients with concurrent and not concurrent answers in the study group of the MS patients (**IV**).

8. In persons with hereditary spastic paraplegia group the sensitivity of the positive answer of the one item interview "Are you depressed?" was 81%. The sensitivity was only 68% when the answer was negative. The overall sensitivity of the one item interview was 75% and specificity of the one item interview in this group was 75% (**II**).

9. Our results confirmed that in persons with HSP depression is prevalent among 58% persons with hereditary spastic paraplegia in our study group. Depression

needs evaluation and treatment when people express their opinion even during one item interview only (**II**).

10. The results of study of persons with epilepsy (**III**) show that self-reported functioning appears to be affected by the presence of depressive symptoms. The need to investigate different subjective complaints and not only memory problems and depressive symptoms is stressed (**III**).

## Summary

Cognitive dysfunction may be a common feature in persons with multiple sclerosis. The results of our study show that the presence of cognitive problems does not automatically exclude the possibility to improve the quality of life by learning the clean intermittent self catheterization. Depression is common in persons with different neurological disorders frequently in combination with many other problems that need attention. Therefore it is very valuable in practice to take into account that asking only one question about the person's mood may lead to the diagnosis of depression in multiple sclerosis, hereditary spastic paraplegia and epilepsy.

# ERINEVATE NEUROLOOGILISTE HAIGUSTE KORRAL ESINEVAD SUBJEKTIIVSED KAEBUSED – SEOSED TEGELIKE PROBLEEMIDEGA JA MÕJU IGAPÄEVAELUGA TOIMETULEKULE

## Kokkuvõte

Neuropsühholoogiline hindamine on muutunud pelgalt diagnostikast aja jooksul teaduseks, mis on võimeline mõõtma inimese mõtlemise tugevaid ja nõrku külgi (Goldstein, McNeil 2004). Paljudes uuringutes on kirjeldatud neuroloogiliste haigustega kaasneda võivaid psüühikahäireid ja neuropsühholoogilisi muutusi (Ketterer, Knyz 2009, Patti 2009, Nielsen jt 2004, Marino jt 2009), kuid selle kohta, millised on seosed subjektiivsete kaebuste ja tegelike probleemide olemasolu vahel, ei ole palju teada (Maor jt 2001, Piazzini jt 2001).

Käesolevas töös uuritakse *sclerosis multiplex*i, hereditaarse spastilise parapleegia ja epilepsiaga kaasneda võivaid psühholoogilisi ja neuropsühholoogilisi muutusi ning inimeste poolt esitatavate subjektiivsete kaebuste esinemise määra. Eelnimetatud diagnoosid on headeks näideteks haiguste kohta, millega võib kaasneda nii depressioon kui ka kognitiivne düsfunktsioon, kuid mitte dementsus, aga sellest hoolimata võib neuropsühholoogiliste probleemide olemasolu tõttu muutuda oluliselt inimese elukvaliteet.

*Sclerosis multiplex* on kesknärvisüsteemi demüeliniseeriv krooniline neuroloogiline haigus, mille sagedamini esinevateks sümptomiteks on erinevad halvatused, tundlikkuse häired, liikumisraskused, lihaste spastilisus ja nõrkus, väsimus, põieprobleemid, depressioon ja kognitiivne düsfunktsioon (McDonald jt 2001).

Hereditaarsed spastilised parapleegiad on pärilikud neurodegeneratiivsed motoorikahäired, mida iseloomustab peamiselt jalgade spastilisus (Harding 1983). Selle haigusega kaasneb erinevaid psüühika muutusi kirjanduse andmetel harva (Fink jt. 1996). Need andmed on esitatud peamiselt juhtumite kirjelduste või väikeste valimitega läbi viidud uuringutena (Nielsen jt 2004).

Epilepsia võib tekkida seoses peaajus esineva elektrilise aktiivsuse häiritusega. Epilepsia diagnoositakse siis, kui inimesel on esinenud kaks vähemalt 24-tunnise intervalliga epileptilist hoogu (Fisher, Leppik 2009). Epilepsiaga kaasnevad tihti erinevad psüühika muutused nagu depressioon ja ärevus, samuti esineb nendel inimestel sageli kognitiivset düsfunktsiooni (Meador 2002).

## UURIMUSE EESMÄRGID

Käesoleva uurimistöö eesmärkideks on:

- uurida *sclerosis multiplex*i diagnoosiga inimeste grupis seoseid puhta enesekateteriseerimise õppimiseks kuluva aja ja kognitiivse düsfunktsiooni olemasolu vahel (**I**);

- hinnata üheküsimuselise intervjuu “Kuidas Teie meeleolu on?” tundlikkust depressiooni sõelumisel kahes erinevas kliinilises grupis (*sclerosis multiplex* ja hereditaarne spastiline parapleegia) (**II**, **IV**);
- uurida seoseid subjektiivsete kaebuste ja depressiooni esinemise vahel epilepsia diagnoosiga inimestel (**III**).

## TULEMUSED JA ANALÜÜS

### Kognitiivse düsfunktsiooni mõju *sclerosis multiplex*i diagnoosiga inimeste ravistrateegia üle otsustamisele – seosed puhta enesekateteriseerimise õppimise ja kognitiivse düsfunktsiooni vahel

Igapäevasest kliinilisest praktikast on teada, et osal juhtudel ei hakata neile *sclerosis multiplex*i diagnoosiga inimestele, kellel on väljendunud kognitiivne düsfunktsioon, puhast enesekateteriseerimist õpetama. Taolistel juhtudel võidakse samadele inimestele paigaldada epitsüstostoom, mis tekitab neile ja nende omastele olulisi lisaprobleeme (Petersen jt 1997). On arusaadav, et selle protseduuri omandamine sõltub füüsilise puude määrast, kuid kirjanduses on vähe andmeid selle kohta, kuidas kognitiivne düsfunktsioon mõjutab õppimise protsessi edukust. Artikkel **I** mõõtis käesolevas töös seoseid puhta enesekateteriseerimise õppe ning kognitiivse düsfunktsiooni vahel.

Uurides *sclerosis multiplex*iga inimeste võimet õppida ära puhas enesekateteriseerimine, selgus, et enamik (87%, 20/23) uuringus osalenud inimestest suutis omandada puhta enesekateteriseerimise (**I**). Selles protsessis ei ole võimalik üle hinnata kogemustega, kõrge motivatsiooniga ja eesmärgile pühendunud õe rolli. Patsiente treeniv õde ei olnud teadlik neuropsühholoogiliste testide tulemustest ning planeeris õpet vastavalt iga patsiendi vajadustele. Meie uuringu tulemused näitasid, et õppimise aeg korreleerus füüsilise puude määraga, aga mitte kognitiivsete võimete tasemega. Seda peaks edaspidi kindlasti ravi planeerimisel arvesse võtma.

Puhta enesekateteriseerimise õppimise kirjeldamine on neuropsühholoogilises kontekstis tõeline väljakutse. Uuringus osalenud inimeste neuropsühholoogiliste testide profiilid varieerusid normtulemustest kuni sügava kognitiivse düsfunktsioonini. Kõige sagedamini esinesid kahjustused mälu, infotöötlemise kiirust ning täidesaatvaid funktsioone hindavates testides, mida on kirjeldanud ka teised uurijad (Patti 2009, Rao jt 1991, Kujala jt 1994, Fisher jt 1994, Rao, Aubin-Faubert, Leo 1989, Elpern jt 1984, Heaton jt 1985). Meie uuringu tulemustes leiduv huvitav seos protseduuri õppimiseks kuluva aja ning nägemis-ruumitaju hindavate mälu mõõtvate testide tulemuste vahel kinnitab vajadust töötada välja kirjalikud abivahendid patsientidele. See aitaks protsessi omandamist kergendada (**I**).

Kõige olulisem faktor, mis mõjutas meie töö tulemusi, oli see, kui palju on professionaalil võimalik inimese väljaõpetamiseks aega kulutada. Meie tulemused kinnitavad, et puhta enesekateteriseerimise omandamiseks vajalikku õppetundide arvu

peab kohandama vastavalt inimese võimetele. Sügavama kognitiivse düsfunktsiooniga inimesed vajavad pikemat õppeperioodi ja suuremat tundide arvu, et protseduuri omandada ja seda iga päev iseseisvalt sooritada (**I**).

Hilisem järeluuring näitas, et kuus inimest (6/20) olid puhta enesekateteriseerimise lõpetanud. Kahel inimesel olid põieprobleemid lahenenud, ülejäänud neli, kes protseduuri ei jätkanud, olid sügava kognitiivse düsfunktsiooniga, mis väljendus peamiselt täidesaatvaid funktsioone hindavates testides (**I**).

Puhta enesekateteriseerimise läbiviimine kolm kuud hiljem ei sõltunud uuringu alguses hinnatud neuropsühholoogiliste testide tulemustest, statistiliselt olulised seosed puudusid ka füüsilise puude raskuse, haiguse kulu ja protseduuri omandamiseks kulunud ajaga. Meie uuring kinnitas seda, et enam väljendunud kognitiivse düsfunktsiooniga inimesed vajavad hilisemal järelkontrollil lisaks telefonikõnele näiteks lisakülastust keskusesse või spetsialiseeritud õe koduvisiiti, et protseduuri jätkamine õnnestuks (**I**).

Kognitiivse düsfunktsiooniga SM diagnoosiga inimestel kulus enam õppetunde puhta enesekateteriseerimise omandamiseks, mis on mõnevõrra vastuolus varasemas kirjanduses leiduvate andmetega (Chiaravalloti jt 2003), kelle tulemuste kohaselt ei õnnestunud hilisem meenutamine neil, kellel kulus õppimiseks enam aega. Meie uuringu tulemused näitasid ka, et kahjustus täidesaatvates funktsioonides ei ennusta kõige paremini ette seda, kuidas inimene hiljem protseduuri läbiviimisega toime tuleb. Puhta enesekateteriseerimise omandamiseks kuluv aeg varieerub inimeseti oluliselt ja seda peaks raviplaane tehes kindlasti silmas pidama (**I**).

Meie uuringu tulemuste põhjal on võimalik järeldada seda, et vaatamata erinevatele kognitiivsete düsfunktsiooni tasemetele, olid *sclerosis multiplex*i diagnoosiga inimesed võimelised omandama puhast enesekateteriseerimist. Hoolimata sellest, et sügavama kognitiivse düsfunktsiooniga inimesed on võimelised protseduuri haiglasoleku jooksul omandama, on neile siiski vajalik oluliselt sagedasem järelkontroll (**I**).

### Üheküsimuselise intervjuu efektiivsus krooniliste neuroloogiliste haigustega inimeste depressiooni sõeluuringus

1. Üheküsimuselise intervjuu "Kuidas Teie meeleolu on?" ("*Are you depressed*?") efektiivsus *sclerosis multiplex*i diagnoosiga inimeste depressiooni sõeluuringul

Meie uuringu tulemuste kohaselt osutus üheküsimuseline intervjuu *sclerosis multiplex*i (SM) diagnoosiga inimeste depressiooni sõeluuringul tundlikuks vahendiks (**IV**).

Positiivne vastus ("Mu meeleolu on halb") omas meie uuringu tulemuste kohaselt kõrget tundlikkust (94%), mistõttu saab kliinilise diagnoosi kergesti välja panna juhul, kui inimene ise meeleolu langust tunnistab. Kui inimene annab üheküsimuselisele intervjuule "Kuidas Teie meeleolu on?" vastuseks kõike muud kui "halb", siis oli selle küsimuse tundlikkus palju madalam (70%). Meie töö peamine

praktiline väärtus väljendub selles, et kui inimene vastab üheküsimuselisele intervjuule positiivselt, siis on peale seda suhteliselt kerge depressiooni diagnoosida. Kui inimene annab negatiivse vastuse, siis on tundlikkus oluliselt madalam ning sellisel juhul tuleks ta enne kindla diagnoosi väljapanekut ja ravi alustamist kindlasti suunata edasistele uuringutele. Üheküsimuselise intervjuu üldine tundlikkus selles uuringugrupis oli 91% ja spetsiifilisus 84% (**IV**).

*Sclerosis multiplex*i näol on tegemist väga hea näitega krooniliseset neuroloogilisest haigusest, mis võib põhjustada inimesele palju erinevaid probleeme. Kliinilise intervjuu eesmärk on saada kõigist probleemidest ülevaade. Meie uuringugrupis esines depressioon 66% SM diagnoosiga inimestel. See on kooskõlas varasemate uuringutega (Arnett et al. 2008, Siegert, Abernethy 2005, Schiffer, Babigian 1984, Joffe et al. 1987), kus samuti kirjeldatakse sagedast depressiooni esinemist SM diagnoosiga inimeste hulgas (**IV**).

Need inimesed uuringugrupist, kelle vastused üheküsimuselisele intervjuule ei olnud kooskõlas hilisema depressiooni diagnoosiga, elasid koos oma pereliikmetega ja nende lapsed olid alla 18 aasta vanused. Seetõttu on võimalik, et oluline roll stabiilse meeleolu säilitamisel on perel. Meie uuring näitas, et uuringugrupis ei esinenud muid statistiliselt olulisi sotsiodemograafilisi ja kliiniliste näitajatega seotud erinevusi nende gruppide vahel, kes andsid vastuseid, mis olid kooskõlas kliinilise hinnanguga, ja nende vahel, kelle vastus hilisema diagnoosiga kooskõlas ei olnud. See oli mõnevõrra vastuolus varasemate uuringutega (Simon, Goldberg, Tiemens, Ustun 1999), mis näitasid, et SM diagnoosiga inimesed depressiooni kergemaid vorme pigem eitavad. Uuringu tulemusi võis mõjutada ka see, et uuringugrupp oli suhteliselt väike ja uuringus osalesid ainult statsionaarsel ravil viibivad patsiendid. Kas antidepressantravi oleks nende inimeste elukvaliteeti parandanud, vajab edasist uurimist (**IV**).

2. Üheküsimuselise intervjuu "Kuidas Teie meeleolu on?" ("*Are you depressed*?") efektiivsus hereditaarse spastilise parapleegia diagnoosiga inimeste depressiooni sõeluuringul

Meile teadaolevatel andmetel on käesolev uuring (artikkel **II**) esimene, mis kirjeldab depressiooni esinemise sagedust hereditaarse spastilise parapleegia diagnoosiga inimestel. Kirjanduses ei leidu ka olulisi andmeid selle kohta, kui adekvaatselt selle diagnoosiga inimeste subjektiivsed kaebused nende tegelikku meeleolu peegeldavad (Nielsen et al. 2004).

Meie uuring näitas, et enam kui pooltel (58%, 26/48) meie uuringugrupis osalenud hereditaarse spastilise parapleegiaga inimestest oli depressioon, mis on kooskõlas varasemates töödes kirjeldatuga (Nielsen et al. 2004). Meie uuringugrupis oli enamikul (44%) patsientidest kerge, 13%-l mõõdukas ja ühel inimesel sügav depressioon. Becki Depressiooniküsimustiku skoorid ei korreleerunud ühegi haigusega seotud kliinilise näitajaga. Edasist uurimist vajavad need tegurid, mis võiksid olla seotud depressiooni esinemisega hereditaarse spastilise parapleegia grupis, sest võimalikult varajane sekkumine peale depressiooni väljakujunemist parandaks oluliselt nende inimeste elukvaliteeti (**II**).

Enam kui pooltel (58%, 26/48) meie uuringugrupis osalenud hereditaarse spastilise parapleegia diagnoosiga inimestest oli kaebusi meeleolu languse esinemise suhtes (**II**). Depressiooni diagnoos leidis kinnitust 81%-l (21/26) juhtudest nende inimeste hulgas, kes vastasid üheküsimuselisele intervjuule "Kuidas Teie meeleolu on?" "Halb". Selles grupis ei leidnud depressioon kinnitust 19%-l (9/26) juhtudest.

46% (22/48) vastasid üheküsimuselisele intervjuule negatiivselt. 68%-l (15/22) nendest inimestest ei esinenud depressiooni. Hoolimata negatiivsest vastusest leidis depressioon kinnitust 32%-l (7/22) juhtudel. Selle uuringu praktiline väärtus sarnaneb eelmise uuringu (**II**) omaga, mis tähendab seda, et kui inimene vastab üheküsimuselisele intervjuule "Kuidas Teie meeleolu on?" positiivselt, saab jätkata raviga. Kui inimene vastab kõike muud kui "halb", siis tuleb ta sellest hoolimata kliinilise hinnangu täpsustamiseks siiski suunata edasisele hindamisele. Üheküsimuselise intervjuu üldine tundlikkus selles grupis oli 75% ja spetsiifilisus oli 75%.

Kokkuvõtvalt võib öelda, et üheküsimuseline intervjuu "Kuidas Teie meeleolu on?" on tundlik vahend erinevate krooniliste neuroloogiliste haigustega inimeste sõeluuringul depressiooni edasiseks diagnostikaks (**II**, **IV**). Veel kord tuleks rõhutada fakti, et tegemist on äärmiselt vähe aega nõudva ja samal ajal väga informatiivse töövahendiga. Kui inimene väljendab meeleolu langust üheküsimuselise intervjuu käigus, siis tuleks talle koostada raviplaan. Juhul, kui vastus on negatiivne, tuleks see inimene diagnoosi täpsustamiseks suunata edasistele uuringutele.

### Seosed subjektiivsete kaebuste ja depressiooni esinemise vahel epilepsia diagnoosiga inimestel

Subjektiivsed kaebused on klinitsisti jaoks oluline märk sellest, milline võib olla kroonilise haigusega inimese elukvaliteet.

Meie läbi viidud uuringu (**III**) tulemuste kohaselt ei ole epilepsia diagnoosiga inimeste subjektiivsed kaebused neuropsühholoogiliste võimete languse kohta seotud tegeliku testisooritusega. Korrelatsioonanalüüs näitas, et seosed esinesid hoopis Becki Depressiooniküsimustiku tulemustega. Uuringu tulemuste kohaselt erines kaebuste hulk statistiliselt olulisel määral depressiivsete ja mittedepressiivsete epilepsia diagnoosiga inimeste hulgas. Depressiooni esinemine ei mõjuta mitte ainult kaebuste esinemise hulka, vaid võib omada mõju ka neuropsühholoogiliste testide sooritusele. Läbi viidud uuringu (**III**) tulemused kinnitavad väidet, et subjetiivsete kaebuste hulk võib olla märk kaasnevast meeleolulangusest. Võrreldavaid tulemusi on leitud ka teiste krooniliste neuroloogiliste haiguste korral – näiteks *sclerosis multiplex*i diagnoosiga inimestel (Maor et al. 2001) või pärast keskmist kuni rasket peaaju traumat (Lannoo et al. 1998).

Kokkuvõtteks võib öelda, et meie uuringus saadud tulemuste kohaselt on epilepsia diagnoosiga inimestel subjektiivsed kaebused seotud pigem depressiooni esinemisega (**III**).

## JÄRELDUSED

Käesoleva uurimistöö tulemuste põhjal saab järeldada järgmist:

1. Meie uuringu tulemused tõestasid, et *sclerosis multiplex*i diagnoosiga inimesed on võimelised omandama puhta enesekateteriseerimise protseduuri olenemata nende neuropsühholoogilise hindamise tulemustest ning said seeläbi parandada oluliselt oma igapäevaelu kvaliteeti. Õppimiseks kuluv aeg korreleerus füüsilise puude määraga, aga mitte kognitiivse düsfunktsiooni tasemega (**I**).

2. Läbi viidud uuringu tulemused näitavad, et kõik inimesed vajavad puhta enesekateteriseerimise omandamiseks individuaalset õppetundide arvu. Ülejäänud efektiivset põiehäirete ravi mõjutavad tegurid vajavad edasist põhjalikku uurimist (**I**).

3. Oluline on teada, et hilisema korduva hindamise käigus on vajalik pöörata tähelepanu sügavama kognitiivse düsfunktsiooniga *sclerosis multiplex*i diagnoosiga inimestele, sest nad võivad vajada raviks spetsiaalset programmi (**I**).

4. Üheküsimuseline intervjuu "Kuidas Teie meeleolu on?" osutus väga efektiivseks depressiooni tuvastavaks sõelküsimuseks erinevate krooniliste neuroloogiliste haigustega inimeste gruppides (**II, IV**).

5. Käesoleva uurimuse üheks olulisemaks järelduseks on see, et kui inimene annab küsimusele "Kuidas Teie meeleolu on?" positiivse vastuse, siis on võimalik üsna kiiresti jõuda depressiooni kliinilise diagnoosini ja sealt edasi alustada raviga. Kui vastus on negatiivne, siis tuleks ta kindlasti lõpliku diagnoosi selgitamiseks suunata täpsustavale hindamisele (**II, IV**).

6. *Sclerosis multiplex*i diagnoosiga inimeste grupis oli positiivse vastuse tundlikkus üheküsimuselisele intervjuule ("Kuidas Teie meeleolu on?") 94%, negatiivse vastuse oma oli madalam (70%). Üheküsimuselise intervjuu tundlikkus selles uuringugrupis oli 91% ja spetsiifilisus 84% (**IV**).

7. *Sclerosis multiplex*i diagnoosiga inimestega läbi viidud uuringus ei selgunud sotsiodemograafilisi või haigusega seotud tegureid, mis oleksid eristanud seda gruppi, mille subjektiivne arvamus oli kooskõlas kliinilise hinnanguga sellest grupist, kus need kaks tegurit kooskõlas ei olnud (**IV**).

8. Hereditaarse spastilise parapleegia diagnoosiga inimeste grupis oli üheküsimuselise intervjuu "Kuidas Teie meeleolu on?" positiivse vastuse tundlikkus 88%. Samale küsimusele antud negatiivse vastuse tundlikkus oli 68%. Üheküsimuselise intervjuu tundlikkus oli selles uuringugrupis 75% ja spetsiifilisus 75% (**II**).

9. Meie uurimuse tulemused näitasid, et depressioon esineb hereditaarse spastilise parapleegia (HSP) diagnoosiga inimeste hulgas sageli (58% juhtudest) ning see vajab kindlasti edasist hindamist ja ravi juhtudel, kui inimesed avaldavad seda üheküsimuselise intervjuu käigus (**II**).

10. Epilepsia diagnoosiga inimeste hulgas läbi viidud uuringust selgus, et nende inimeste subjektiivsed kaebused on oluliselt seotud depressiooni esinemisega. Sellest tulenevalt on oluline subjektiivsete kaebuste olemasolul hinnata nii neuropsühholoogilisi muutusi kui ka depressiooni esinemist (**III**).

**Kokkuvõte**

*Sclerosis multiplex*i korral võib kognitiivne düsfunktsioon esineda sageli. Meie töö tulemused näitavad, et hoolimata neuropsühholoogiliste probleemide olemasolust saab inimene oma elukvaliteeti puhta enesekateteriseerimise omandamise läbi oluliselt parandada. Nii *sclerosis multiplex*i, hereditaarse spastilise parapleegia kui ka epilepsiaga kaasneb tihti depressioon. Seetõttu on äärmiselt oluline üheküsimuselise intervjuu ("Kuidas Teie meeleolu on?") vastuste märkamine ja arvesse võtmine raviplaani koostamisel või meeleoluhäirete edasisel uurimisel.

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