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(Martina Rios Silva)

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Awareness of Subjective Memory Assessment in Patients with Mild Cognitive Impairment, Alzheimer´s Disease and Parkinson´s Disease

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Abstract (English)

Awareness of subjective memory assessment is an important factor for adequate treatment of patients with mild cognitive impairment (MCI), Alzheimer´s disease (AD) and Parkinson´s disease (PD). This study served to find out whether awareness of subjective memory assessment complies with objective performance, if differences in realization are observed longitudinally and whether decrease of awareness can serve as a predictor of AD in MCI and PD patients. Forty-three patients with MCI and PD seeking help in a memory outpatient clinic were included. All participants underwent thorough neuropsychological examination. Awareness of subjective memory assessment was obtained by calculating difference scores between patient and informant ratings on a 16-item questionnaire concerning complaints about loss of memory in every-day life. Retesting was performed after a mean follow-up period of 24 months. Whole group analyses showed that awareness remained relatively stable across time. Self-reported memory complaints correlated with episodic memory at baseline and with performance on concentration and language tasks at follow-up. Retests displayed decrease of awareness of overall cognitive ability. At group level differences in awareness between both times of assessment were not significant for PD, MCI and MCI patients turning to mild AD at follow-up. The predictive value of awareness could not be proven by the present study. Awareness of subjective memory assessment is linked to episodic memory function and decreases with decline of cognitive ability. Further studies evaluating its predictive power might possibly address to more patients with proceeding AD at follow-up by including short forms of neuropsychological test batteries.

Keywords: anosognosia, awareness, subjective memory assessment, Alzheimer´s disease, mild cognitive impairment, Parkinson´s disease

Abstract (Deutsch)

Die Awareness (Gewahrsein) der subjektiven Einschätzung des Gedächtnisses spielt eine bedeutsame Rolle bei der adäquaten Behandlung von Patienten mit leichter kognitiver Beeinträchtigung (engl. „mild cognitive impairment“, MCI), Alzheimer-Krankheit (AD) und Morbus Parkinson (PD). Diese Studie diente dem Zweck, herauszufinden, ob die Awareness der subjektiven Gedächtniseinschätzung der objektiven Testleistung entspricht, ob Unterschiede im Laufe der Zeit beobachtet werden und ob sich mangelnde Awareness der subjektiven Gedächtniseinschätzung als Prädiktor für künftige AD bei Patienten mit MCI und PD eignet. Dreiundvierzig Patienten mit MCI und PD, welche in einer Gedächtnisambulanz Hilfe suchten, nahmen an der Studie teil. Alle Studienteilnehmer unterzogen sich einer gründlichen neuropsychologischen Untersuchung. Die Awareness der subjektiven Gedächtniseinschätzung wurde errechnet, indem Unterschiedswerte zwischen Selbst- und Fremdwahrnehmung auf einem Fragebogen bestehend aus 16 Fragen über Gedächtnisprobleme im Alltag gebildet wurden. Nachtests wurden nach einem durchschnittlichen Zeitraum von 24 Monaten durchgeführt. Gesamtgruppen-Analysen zeigten, dass die Awareness der subjektiven Gedächtniseinschätzung über die Zeit hinweg relativ stabil blieb. Selbstberichtete Gedächtnisprobleme korrelierten mit episodischer Gedächtnisleistung beim ersten und mit Testleistungen bei Gedächtnis- und Sprachaufgaben beim nachfolgenden Testtermin. Nachtests zeigten eine Abnahme der Awareness für allgemeine kognitive Leistungsfähigkeit. Innerhalb der einzelnen Diagnosegruppen unterschied sich die Awareness zwischen beiden Testzeitpunkten nicht signifikant in Bezug auf PD-, MCI- Patienten und der Gruppe von MCI-Patienten, welche zu einer Frühform der AD konvertierte. Die Vorhersagekraft der Awareness konnte anhand dieser Studie nicht nachgewiesen werden. Awareness der subjektiven Gedächtniseinschätzung ist mit episodischer Gedächtnisleistung verbunden und sinkt mit abnehmender kognitiver Leistungsfähigkeit. Weitere Studien zur Untersuchung ihrer Vorhersagekraft könnten sich vermehrt an Patienten mit fortschreitender AD zum zweiten Testzeitpunkt wenden, indem nach Möglichkeit auch Kurzformen neurologischer Testbatterien inkludiert werden.

Keywords: Anosognosia, Awareness, subjective Gedächtniseinschätzung, Alzheimer-Demenz, Mild Cognitive Impairment, Morbus Parkinson

Awareness of Subjective Memory Assessment in Patients with Mild Cognitive Impairment, Alzheimer´s Disease and Parkinson´s Disease

Introduction

Elderly people often experience cognitive decline with aging. The reasons for cognitive dysfunctions can range from normal mild forgetfulness described by many older individuals to mild cognitive impairment until the severe effects of Alzheimer´s disease. (Saxton, Morrow, Eschman, Archer, Luther & Zuccolotto, 2009). Many patients with considerable subjective memory complaints (SMC) seek help at a memory outpatient clinic, and complaints advance from cognitive healthy elderly to patients with amnestic mild cognitive impairment (Lehrner et al., 2014; Pußwald et al., 2013). On the other hand, there are patients who suffer from serious memory impairment, but do not present their symptoms to their general practitioner during their visits (Waldorf, Siersma, Vogel & Valdemar, 2012). A lot of people with mild cognitive impairment (MCI) and Alzheimer´s disease (AD) are not even able to recognize cognitive, functional or behavioural impairment (Vogel et al., 2005, Zamboni & Wilcock, 2011). But this anosognosia (Ecklund-Johnson & Torres, 2005) can have serious effects on health, because patients eventually deny adequate treatment due to their unawareness of deficits. Daily functioning may be compromised, because they lack adequate judgement of situations. (Aalten, van Valen, Clare, Kenny & Verhey, 2005; Shaked et al., 2014). Especially patients suffering from Parkinson disease (PD) require early identification of inherent dementia, because dementia in PD patients often leads to caregiver distress, at-home assistance and reduced quality of life (Janvin, Aarsland & Larsen, 2005).

Subjective memory complaints (SMC) are supposed to be an early symptom of dementia and therefore are often applied in the diagnostic process. The most frequent types of questions used in order to determine SMC are: 1) Use of a single question, such as “Do you have trouble with your memory?” 2) Use of scales with a set of questions, 3) use of a questionnaire or subscale of various questions (Abdulrab & Heun, 2008).

The following study is based on the use of the “Forgetfulness Assessment Inventory” (FAI) in order to assess subjective memory complaints in individuals with MCI, AD and PD. The questions of this 16-item scale focus on subjective evaluation of memory problems in daily life, especially concerning episodic memory, which is very sensitive in the early detection of MCI and AD (Lehrner et al., 2014). The current paper gives a short overview about the characteristics of memory assessment in MCI, AD and PD, examining the impact of

associated awareness in literature. The empirical part includes a longitudinal study about awareness in relation to cognitive decline and conversion to AD.

Mild Cognitive Impairment

The concept of MCI describes as a transitional stage between cognitive normal function and the earliest stage of dementia and is characterized by cognitive decline above age and education (Petersen et al., 1999). The diagnostic criteria according to Petersen et al. (1999), revised by Winblad et al. (2004) are following: 1) The person is neither normal nor demented; 2) self or informant complaint about cognitive decline exist in combination with objective performance evidence of cognitive impairment or a measured decline in objective performance over time; 3) basic activities of daily living are preserved and complex instrumental activities are intact or minimal impaired. Extensive research on MCI led to the introduction of the new DSM-5 (American Psychiatric Association, 2013) diagnosis of mild neurocognitive disorder (Sachs-Ericsson & Blazer, 2015).

On the basis of a diagnosis of MCI, the patient can be classified by subtype: MCI with or without memory impairment (amnestic or nonamnestic MCI). Patients with nonamnestic MCI show deficits in other cognitive domains (e.g. executive function, visuospatial skills or language). Amnestic impairment (aMCI) as well as nonamnestic impairment (naMCI) can again be divided into two subtypes: single-domain MCI with deficit in only one cognitive domain (memory in aMCI or an isolated deficit in a nonmemory domain concerning naMCI), and multiple-domain MCI with mild deficits in different cognitive domains with or without memory component (Petersen, 2004; Winblad et al., 2004). The presence of an episodic memory disorder is characteristic for aMCI, which leads to a reduced ability to intentionally recollect previously encountered information (Dubois, 2007). Cerebrovascular diseases as well as neurodegenerative features were shown to contribute to MCI (Petersen et al., 2009).

Some individuals with MCI appear to remain stable or return to normal over time, but more than half reveal progression to dementia within 5 years (Gaulthier et al., 2006). Several studies found out, that patients with aMCI have an increased risk of progressing to Alzheimer´s disease (AD), while patients with naMCI are more likely to develop a non-AD dementia like vascular dementia or dementia with Lewy bodies. (e.g. Petersen, 2004; Gauthier et al., 2006). But a review of thirty-two cohort studies since 2006 (Ward, Tardiff, Dye & Arrighi, 2013) could not confirm significant differences in comparing conversion rates from aMCI and naMCI to AD due to extensive variation observed in conversion rates. Prevalence rates of MCI impairment subtypes and conversion rates from MCI or aMCI to AD vary due to

lack of standardization in diagnostic criteria and testing, different source of population (i.e. clinic or community) as well as length of follow up (Pusswald et al., 2013; Ward et al., 2013).

Alzheimer´s Disease:

Alzheimer´s Disease (AD) is the most common neurodegenerative disorder and the most widespread type of dementia. Dementia describes a variety of diseases and conditions that develop when neurons in the brain die or no longer function normally (Thies & Bleiler, 2013). According to DSM-5 (American Psychiatric Association, 2013) AD belongs to the group of major neurocognitive disorders. They are characterized by multiple cognitive deficits that include impairment in memory. AD differs from other major neurocognitive disorders (e.g. Frontotemporal lobar degeneration, Lewy body disease) in its presumed aetiology.

Memory impairment is a prominent early symptom and is required for the diagnosis of AD. Individuals with dementia become impaired in their ability to learn new material or they forget previously learned material. The development of multiple cognitive deficits is manifested by both, memory impairment, and one (or more) of the following cognitive disturbances: Aphasia, apraxia, agnosia and disturbance of executive functioning (i.e., planning, organizing, sequencing, abstracting) (Saß, Wittchen, Zaudig & Houben, 2003). Dubois et al. (2007) present the consensus of a working group discussing the opportunity for developing a diagnostic framework for revised research of AD including the integration of biomarkers. The core diagnostic criteria contains an early and significant episodic memory impairment (either isolated or in association with other cognitive changes), that includes gradual and progressive change in memory function reported by patients or informants over more than 6 months and objective evidence of significantly impaired episodic memory on testing.

The two core neuropathological characteristics of AD are amyloid plaques and neurofibrillary tangles. According to the amyloid cascade hypothesis neuronal dysfunction and death in the brain are triggered by deposition of amyloid β (Aβ). Tau, a microtubule-associated protein is the major constituent of neurofibrillary tangles (Ballard et al., 2011).

Parkinson´s Disease:

Parkinson´s disease (PD) is the second most common neurodegenerative disorder after AD. The cardinal motor manifestations of PD are resting tremor, bradykinesia, rigidity, and postural instability. (Schulman, De Jager & Feany, 2011; Van Den Eeden et al., 2001). Nonmotor manifestations, including urinary symptoms, constipation, impaired olfaction, sleep

disorder, and dementia can also accompany PD and may precede the development of cardinal motor manifestations. (Sitek, Soltan, Wieczorek, Robowski & Slawek, 2011; Ziemssen & Reichmann, 2007). Analogue to AD, pathologically PD is defined by neurodegeneratgion of dopaminergic cells within the substantia nigra in association with with α–synuclein pathology, resulting in dysfunction of the basal ganglia that are involved in movement initiation and execution. (Shulman, Jager & Feany, 2011). PD is often accompanied by cognitive impairment and neuropsychiatric symptoms, with an incidence rate of 70 % for developing dementia in PD (PDD).

Caviness et al. (2007) propose that the clinical stage of cognitive impairment between cognitively normal patients with PD and patients with PDD can be described as PD-MCI applying diagnostic criteria analogous to Petersen et al. (1999) and Winblad et al. (2004). Two forms of PD are known to date: Pure dopaminergic PD without MCI and PD with non dopaminergic lesions, which correlates with cognitive changes and may lead to PD-MCI. (Caviness et al., 2007). Factors that lead to faster progression of cognitive impairment in PD are late onset of disease, advanced age and severity of PD. Severe initial impairments to visuospatial functions can serve as early neuropsychological predictors for development of cognitive impairment in PD (Liu et al., 2011). According to Levy et al. (2002) verbal memory impairment (total immediate and delayed recall) and executive dysfunction predict progression to dementia in PD. Deficits in working memory, learning, planning and cognitive flexibility occur early in PD and are consistently assumed to be prodrome to dementia (Kehagia, Barker & Robbins, 2010). Impairments of visuospatial and executive functions as well as attention seem to be common nonamnestic deficits in PD-MCI patients. Though nonamnestic single-domain PD-MCI has turned out to be the most frequent type, there is heterogeneity within PD-MCI concerning the number and types of cognitive domain impairments. Therefore the Movement Disorder Society (MDS) recruited a task force in order to publish uniform definitions and formal diagnostic criteria for PD-MCI (Goldman & Litvan, 2011; Litvan et al., 2011)

Awareness:

Cognitive decline is often accompanied by change of awareness of deficits. Even in the earliest stages of AD and actually MCI, insight can be impaired and this lack of awareness (also termed as anosognosia) is most common in severe AD (Vogel et al., 2004). Vogel et al. (2004) compared awareness of cognitive deficits in patients with MCI and mild AD and came to the conclusion, that impaired awareness was equally frequent in both groups with

individual significant heterogeneity in the degree of impaired insight. Different studies about awareness in MCI demonstrate a great variability among this patient group. While some people with MCI show limited awareness, others seem to overestimate their dysfunction (also declared as reflecting heightened or hyper-awareness). This overestimation can also be observed in people with AD (Roberts, Clare & Woods, 2009). These differences in awareness levels raise discussions about the validity of subjective memory complaints (SMC) as diagnostic criterion for MCI as proposed by Petersen et al. (1999). In some studies memory complaints are detected as an early predictor for cognitive decline or dementia, while other studies find more associations with negative affect, such as depression, anxiety or neuroticism (Jorm, Christensen, Korten, Jacomb & Henderson, 2001).

Depressions can have negative influence on the expression of awareness and increase negative attributions, making memory problems seem more severe than they are (Lehrner et al., 2014; Roberts, Clare & Woods, 2009). Sevush and Leve (1993) found out, that denial of deficits might protect against depression in Alzheimer´s disease, because unawareness was inversely related to depressed mood. Therefore informants are often involved in diagnosis and assessment of subjective memory awareness (Schinka, 2010). The three main categories that are usually used to measure awareness are:

- measurements based on the examiner´s judgement;
- discrepancy scores between patients and informants (caregivers) on parallel forms of questionnaires assessing certain symptoms;
- discrepancy scores between self-rating and actual performance on an objective task
- a combination of the three methods

(Clare, Wilson, Carter, Roth & Hodges, 2002; Roberts et al., 2009; Vogel et al., 2004; Zamboni & Wilcock, 2010). Discrepancy scores between patients and informants, showing grater decline on informant ratings, should not remain the only diagnostic instrument measuring awareness. According to Roberts et al. (2009) they indicate only “weak” evidence of impaired awareness and should correlate highly with objective evidence of actual change, e.g. cognitive performance measures, neuropsychological and functional tests and biomarkers.

A review of comparisons between MCI patient and informant reports illustrates that informant ratings display greater loss of cognitive competency and everyday functional ability and a greater correlation with objective measures of patient cognitive performance and characteristics of probable conversion to dementia (Schinka, 2010). Ecklund-Johnson and Torres (2005) reviewed studies about unawareness of deficits in AD and resume, that unawareness of deficits progresses over time, meanwhile awareness discrepancies between

patients and their caregivers increase. Although informant reports might be influenced negatively by caregiver burden, informant ratings have turned out to be a strong predictor of an underlying dementia. The authors also conclude that memory deficits alone neither explain nor predict unawareness of deficits in AD. Brain correlates of unawareness in dementia were mainly detected in frontal and tempo-parietal regions, but further research is needed (Zamboni & Wilcock, 2011).

Comparisons of awareness between individuals with AD and Parkinson´s disease resulted in reduced awareness of motor and other deficits in both groups and impaired awareness of cognitive functioning in AD patients, which was comparatively intact in the PD group (Seltzer, Vasterling, Mathias & Brennan, 2001). Individuals with PD have a relatively intact self-awareness of memory function, but it can be negatively influenced by depressive symptoms. Depression affects 40-50 % patients with PD and leads to overestimation of memory problems (Sitek et al., 2011; Ziemssen & Reichmann, 2007). Analogue to AD, increase of cognitive deficits leads to decline of awareness in PD (Leritz, Loftis, Crucian, Friedmann & Browers, 2004; Rosen, 2011). The current research succeeds a previous cross-sectional study by Lehrner et al. (2015), who concluded that awareness decreases along the naMCI → aMCI → AD continuum, with PD patients revealing accurate self-appraisals as long as memory is well-preserved.

Current Study

The main objective of this longitudinal study was to find out, whether awareness of subjective memory assessment in patients with MCI and PD has predictive value for future conversion to AD. The methods were based on precedent studies using additional informant ratings (e.g. Vogel et al., 2004). The first aim was to explore correlations between subjective memory assessment and objective results of neuropsychological testing. Correlation analyses comprised neuropsychological test results and demographic data. Two variables measuring depressive symptoms were also included in order to examine the influence of depression on awareness (Lehrner et al., 2014; Roberts et al., 2009). The second aim was to figure out differences in awareness longitudinally. We hypothesized that small differences across time would indicate an intact awareness system, while large differences would reveal loss of awareness. It was assumed that decline of cognitive performance combined with decline of awareness between both times of assessment would imply anosognosia as observed in inherent dementia (Ecklund-Johnson & Torres, 2005). The final intent was to find out, if

unawareness of memory deficits could serve as a predictor of future AD in patients with MCI and PD.

Methods

Subjects and procedure

The current study is part of two larger research projects, the Vienna Conversion to Dementia Study and the Vienna Mild Cognitive Impairment and Cognitive Decline in Parkinson´s Disease Study. The data of this quasi-experimental longitudinal study were collected at the Department of Neurology of the Medical University Vienna. The study protocol has been approved by the Ethical Committee of the Medical University of Vienna and written informed patient consent to perform this study was received.

Patients

The study is based on a sample of 43 consecutive patients aged 50 years or older, who came to the memory outpatient clinic of the Medical University of Vienna due to self or informant reported memory problems and who fulfilled the inclusion criteria. They were either referred by physicians, by the Department of Neurology, or they were self-referrals. All patients went through clinical examination and neuropsychological testing. Exclusion criteria were evidence of stroke, traumatic head injury in the past, current psychiatric diagnosis according to ICD-10 (Dilling, Mombour & Schmidt, 2000) and any medical condition leading to cognitive deterioration. Patients with (sub-) depressive symptoms were included, because these frequently appear in elderly people (Lehrner et al., 2014).

By means of a multi-group design, patients were divided into the subgroups aMCI, naMCI, PD and AD after completion of the evaluation. MCI-subtypes were chosen according to Petersen et al. (2009), using a cut-off score of 1, 5 standard deviations below age and education. AD was diagnosed according to DSM-IV criteria (Saß et al., 2003) and the NINCDS-ADRDA (McKhann et al., 1984). All PD patients received clinical diagnosis of PD according to the UK Parkinson´s Disease Society Brain Bank criteria (Gibb & Lees, 1988) and were taking anti-Parkinson medication. Additional informant ratings about subjective assessment of memory were included in the study.

Measures

Screening

After a detailed anamnesis interview including standard questions about memory functions (Reisberg, Ferris, De Leon & Crook, 1988), and a short survey of the accompanying person, the Mini Mental Status Examination (MMSE, Folstein, Folstein & McHugh, 1975) was used to identify a possible inherent dementia. The screening lasts about 5-10 minutes and includes the categories orientation, memory, attention and numeracy. The maximal score at the MMSE is 30, scores of less or equal 23 indicate cognitive decline. The Clockdrawing-test (Sunderland, Hill, Mellow & Lawlor, 1989) and the "Test zur Erfassung der Visuokonstruktion" (VVT) (Lehrner et al., 2015) help to reveal visual constructive deficits.

Neuropsychological Test Battery Vienna (NTBV)

All patients were subjected to the Neuropsychological Test Battery Vienna (NBTV) (Lehrner, Maly, Gleiß, Auff & Dal-Bianco, 2007). Patients with a MMSE score of less or equal 23 were given the short form of the Test Battery and were excluded from the study. The NBTV includes tests for attention, executive functioning, language, and memory domains with corresponding z-scores and was found to have very good discrimination power in detecting dementia (Lehrner et al., 2007). Attention is assessed using the Alters-Konzentrationstest (AKT) (Gatterer, 1990), a geriatric cancellation test, the digit symbol subtest of the German WAIS-R (Tewes, 1994) and the symbol counting subtest from the cerebral insuffiency test (C.I.) (Lehrl & Fischer, 1997). The Trail Making Test B (Reitan, 1979) and the score difference of the Trail Making Test A and B are also used to measure attention. The Trail Making Test A (Reitan, 1979) is applied to investigate the executive function, which was also assessed by the Five-Point-Test (Regard, Strauss & Knapp, 1982), the Maze Test and the Stroop Test from the NAI Battery (Oswald & Fleischmann, 1997) and the interference test from the C.I. (Lehrl & Fischer, 1997). Lexical verbal fluency is investigated by naming as many words beginning with the letters b, f, and l that come to mind within one minute for each task. Language functions are tested by use of a verbal fluency tasks and a confrontation naming task (Goodlglass & Kaplan, 1983). Semantic and verbal fluency is assessed by naming as many animals, supermarket items and tools that came to mind within one minute for each task. The modified Boston Naming Test (mBNT) (Morris, et al., 1989) is submitted for testing naming capabilities. Episodic memory is applied using the

Verbal Selective Reminding Test (VSRT) with the subtests of immediate recall, total recall, delayed recall, and recognition (Lehrner, Gleiß, Maly, Auff & Dal-Bianco, 2006).

Cognitive functioning (intelligence-quotient; IQ)

The Wortschatztest (WST, Schmidt & Metzler, 1992), a standardized vocabulary test was applied to assess crystallized intelligence of all participants. The WST is a standardized vocabulary test, which is commonly used to examine verbal comprehension in patients with brain damage or dementia.

Assessment of subjective memory complaint

Subjective memory problems were assessed by use of the Forgetfulness Assessment Inventory (FAI) scale (Lehrner et al. 2014). The questionnaire consists of 16 questions concerning subjective memory difficulties in daily life within the past four weeks. Measurement is based on a 5 point Likert scale. Questions are e.g. "How often did you have problems during the past 4 weeks remembering ... e.g. names of people. 1 = never, 2 = rarely, 3 = sometimes, 4 = often, 5 = very often. " Other items include memory difficulties concerning telephone numbers, faces, birthdays or shopping lists (for specific items see table A, appendix). The average of all 16 items represents a global score of memory complaints, which ranges from 0 to 5. Higher scores indicate worse subjective memory performance and greater complaints. Accompanying persons were asked to fill in the informant version of the FAI in order to appraise memory functioning of the concerned patient (www.meduniwien.ac.at/Kpfs).

The FAI was developed at the Department of Neurology at the Medical University Vienna and has been used there since 2000 for research purpose. It has shown to discriminate above-average between cognitive healthy and aMCI-patients with or without PD (Kogler, 2013) and to be internally consistent with an evaluated Cronbach alpha of 0.85 (Lehrner et al., 2014).

Assessment of depressive symptoms

Depressive symptoms in were detected by use of the Beck Depression Inventory (BDI-II) and the Geriatric Depression Scale (GDS). The BDI-II (Hautzinger, Keller & Kühner, 2006) consists of 21 items that ask about how often one felt certain ways within the past two weeks, rating on a four-point scale. Scores above 10 are consistent with clinical depressive symptoms. The GDS (Sheikh & Yesavage, 1986) is a 15-item self-assessment questionnaire, which was developed to identify depression in the elderly. Participants are asked how they

felt over the past week. The questions can be answered yes or no, with higher scores representing higher depressive symptoms and a cut-off score of five-points.

Awareness

Awareness scores were assessed by subtraction of FAI informant rating scores from self rating scores. Positive signs imply that participants underestimated their memory functions in relation to their caregivers, negative signs suggest patients´ overestimation. It is assumed that higher discrepancy scores indicate greater unawareness. (Clare et al., 2002; Roberts et al., 2009; Vogel et al., 2004).

Statistical Methods

Demographic variables are described by median and range due to skewed distribution. At first step, correlations were calculated to compare whole-group FAI self, informant and awareness scores with objective performance measures and non-cognitive factors. Spearman correlations were chosen, because most of the NTBV-variables were not normally distributed. Second, whole-group comparisons of subjective memory assessment between baseline and follow-up were made using Pearson correlations. Normal distribution was verified by Kolmogorov-Smirnov test. At third step, differences across time were calculated at group-level. Within the PD patient group, paired-samples t-tests and additional Pearson correlations were conducted in order to compare both times of FAI assessment. Wilkoxon signed-rank test was used to calculate differences across time within the MCI and AD diagnoses groups, because the assumptions of equal group-sizes and normal distribution for calculating repeated measures ANOVA were violated. Finally, Receiver operator characteristics analysis (ROC) was conducted in order to evaluate predictive value of FAI variables. Statistical analyses were performed using SPSS (version 22). The reported p-values result from two-tailed tests and are statistically significant at the level of $p < 0.05$. Effect-sizes are reported according to Cohen (1988), interpreting a correlation coefficient of $r < .10$ as small effect, $r < .30$ as medium effect and $r > .50$ as large effect.

Results

Descriptive data

A total of 43 patients between 55 and 85 years (*Mdn* = 70 years) were assessed at a 2-year follow-up (*Mdn* = 28 months). Altogether, 25 males (58.1 %) and 18 females (41.9%)

were included in the study. Mean duration of formal education was 8 years, ranging from 5 to 17 years. At the baseline 34 patients were diagnosed as MCI, 19 of them were classified as aMCI, 15 as naMCI according to Petersen et al. (2009). Nine PD patients took part at the study. See Table 1 for details.

Table 1

Demographic Characteristics of Basic Sample (N = 43)

	naMCI	aMCI	PD
N	15	19	9
Age	70 (55-79)	72 (57-85)	69 (66-75)
Male/Female	8/7	9/10	8/1
Education	9 (5-15)	9 (8-17)	9 (8-15)

Note. Median (Range)

Table 2 presents conversion rates to AD. At follow up 13 patients (30, 2 %) turned out to be diagnosed as AD, 4 of them were male, 9 female. None of the PD patients turned to PDD over time. Figure 1 displays the distribution of conversion rates within the two MCI subgroups aMCI and naMCI. Within the group of baseline diagnosis aMCI, 11 people (57, 9%) turned to AD, while only 2 of the initial naMCI patient group (13, 3%) were diagnosed as AD at follow up.

Table 2

Rates of Conversion in aMCI, naMCI and PD (N=43)

		Follow-up			
		MCI	AD	PD	Total
Baseline	aMCI	8 (18,6 %)	11 (25,6%)	0	19 (44,2%)
	naMCI	13 (30,2%)	2 (4,7%)	0	15 (34,9%)
	PD	0	0	9 (20,9%)	9 (20,9%)
Total		21 (48,8%)	13 (30,2%)	9 (20,9%)	43 (100%)

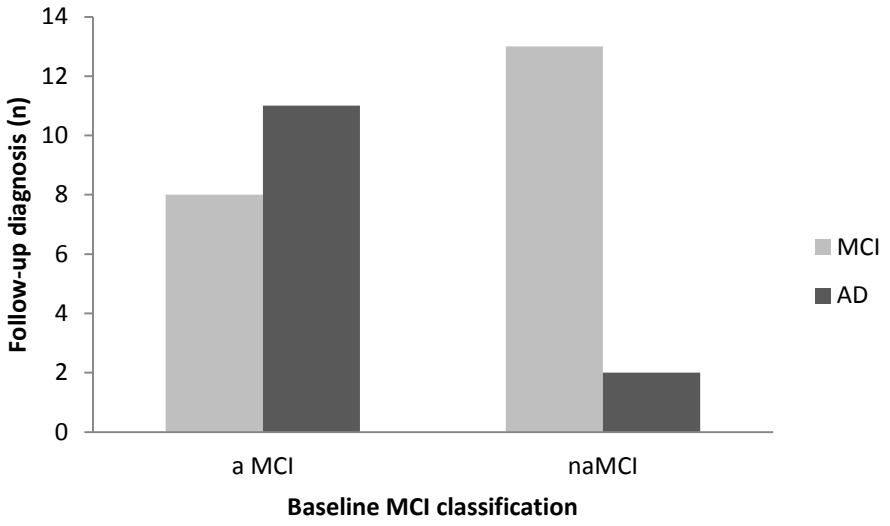

*Figure1***.** Number of conversions to AD within MCI subgroups

Correlations whole group with objective test data

Spearman correlations were performed to compare FAI self, informant and awareness scores with objective performance measures and non-cognitive factors at both times of testing. The results including the single NTBV subtests are presented in Table 3. They show a variation of 45 negative and 31 positive correlations of FAI self and informant ratings with objective performance scores (NTBV, MMSE and WST), but only 5 of them are significant. Negative correlations indicate that lower objective performance scores were in line with higher memory complaints concerning self and informant questionnaires or vice versa.

Regarding self assessment at the baseline, there was one significant negative correlation with the NTBV subtests *Verbal Selective Reminding Test – delayed recall* (VSRT), which belongs to the domain memory. At follow-up two negative correlations were found in the domains attention and language. Informant baseline questionnaires revealed one positive significant correlation at the *modified Boston Naming Test* (mBNT) within the domain language, which turned to a negative but not significant one at follow-up. At the second time of assessment, informant scores correlated significant negatively with MMSE results. All previously mentioned correlation coefficients showed moderate effects (all r_s: .30 to .50) according to Cohen (1988).

Correlation analyses of FAI awareness scores revealed 23 negative and 15 positive correlations with objective performance scores (NTBV, MMSE and WST). There was one significant positive correlation with the MMSE at follow up. The positive association indicated that overestimation was associated with lower performance on MMSE. Its

correlation coefficient showed the only large effect (r_s >.50, Cohen, 1988) of all, including self and informant correlations.

Concerning non-cognitive factors, one significant positive correlation with moderate effect was found between informant scores and the Geriatric depression scale (GDS) at follow up, indicating that higher informant estimated memory complaints were associated with an increase of patient´s depression. The demographic variables sex, age at onset and education did not reveal significant correlations to FAI self, informant and awareness scores.

Table 3

Spearman´s Correlation Coefficients (r_s) between FAI Self, Informant and Awareness Scores, Objective Performance Measures and Non-Cognitive Factors

	FAI - BASELINE			FAI - FOLLOW-UP		
	self	informant	awareness	self	informant	awareness
NTBV Domain Attention						
AKT	.06	.15	-.05	-.41*	.03	- .30
Digit-Symbol	.05	.05	.06	.02	-.15	.02
Symbols (c.I.)	.17	-.08	.12	.18	.28	-.10
TMT B	-.02	-.14	.07	.05	.26	-.17
TMT B – A	-.01	-.14	.07	.04	.31	-.21
NTBV Domain Language						
mBNT	.10	.31*	-.16	-.35	-.03	-.05
SWT	-.20	.16	-.25	-.47*	-.21	-.06
NTBV Domain Executive Function						
TMTA	-.05	-.14	.03	.05	.16	.05
5-point	.05	.12	-.00	-.33	-.05	-.25
Stroop (total/time)	-.02	.12	-.02	-.26	-.06	-.12
Labyrinth	-.05	-.06	.05	-.31	-.28	-.20
Interference (c.I.)	-.05	-.10	.02	.32	.26	-.10
PWT	-.09	.10	-.12	-.16	-.16	-.03
NTBV Domain Memory						
VSRT Immediate Recall	.04	.08	.000	.08	.02	.12
VSRT Total Recall	-.25	-.06	-.07	-.14	-.09	-.07
VSRT Delayed Recall	-.38*	.12	-.29	-.26	-.03	-.09
VSRT Recognition	-.27	.12	-.23	-.17	-.00	.07
MMSE	.17	-.06	.21	.15	-.38*	.51**
WST-IQ	.15	-.07	.17	-.31	.30	-.27
BDI	-.00	.03	.07	.29	.04	.20
GDS	.08	-.03	.10	.02	.37*	-.12

Table 3 (continued)

	FAI - BASELINE			FAI - FOLLOW-UP		
	self	informant	awareness	self	informant	awareness
Sex	-.21	.01	-.20	.15	-.14	.03
Age	.11	-.01	.04	.10	.12	-.16
Education	.07	-.15	.07	-.18	-.03	-.27

Note. AKT, Alters-Konzentrations-Test; WAIS-R, Wechsler Adult Intelligence Scale – Revised; TMTA, Trail Making Test Version A; TMTB, Trail Making Test Version B; PWT, Phonematische Wortflüssigkeit; C.I., Cerebral Insufficiency Test; SWT, Semantische Wortflüssigkeit; VSRT, Verbal Selective Reminding Test; mBNT, modified Boston Naming Test; MMSE, Mini Mental State Examination; WST, Wortschatztest; BDI, Beck Depression Inventory; GDS, Geriatric depression scale;

* $p < .05$. **$p < .01$

Correlations whole group across time

Whole group Pearson correlations were calculated to compare FAI self, informant and awareness scores between both times of testing. All correlation coefficients were statistically significant (all $p < .01$) with large effect (all $r > .50$). See Table 4 for details.

Table 4

Pearson Correlations between Baseline and Follow-up for FAI Self, Informant and Awareness Scores; Means and Standard Deviations

	r	*M*	*SD*	*n*	
Self	.61**	2.81	0.77	41	T1
		2.90	0.71	28	T2
Informant	.54**	3.05	0.86	43	T1
		3.02	0.97	41	T2
Awareness	.54**	-0.26	1.11	41	T1
		-0.07	1.15	26	T2

Note. T1 – baseline, T2 – follow-up

**p < .01

Comparisons Parkinson patient group across time

Correlation and difference analyses were performed in order to compare FAI self, informant and awareness scores of Parkinson patients between baseline and follow-up. Pearson correlations and paired-samples t-tests were calculated. The results including mean scores and standard deviations are displayed in Table 5. Only FAI informant scores correlated significantly between both times of testing. The correlation coefficients of the awareness scores were close to zero yielding no effects. Paired-samples t-tests did not reveal significant differences between the two dates of assessment. Figure 2 displays mean score distribution of FAI self, informant and awareness ratings at baseline and follow-up within the PD group. The distribution shows, that self and informant ratings remained stable over time, and that patients complained more than informants at both times of assessment. Discrepancy scores between both groups remained close to zero with a slight increase at follow-up.

Table 5

Pearson Correlations (r) and Paired-samples t-Tests (t) between PD Baseline and Follow-up for FAI Self, Informant and Awareness Scores; Means and Standard Deviations

	r	*t (df)*	*M*	*SD*	*n*	
Self	.63	.02 (5)	3.21	0.95	6	T1
			3.20	1.05	6	T2
Informant	.82**	-.08 (8)	2.99	0.67	9	T1
			3.01	0.97	9	T2
Awareness	-.04	-.77 (5)	0.43	0.54	6	T1
			0.68	0.56	6	T2

Note. T1 – baseline, T2 – follow-up

**p < .01

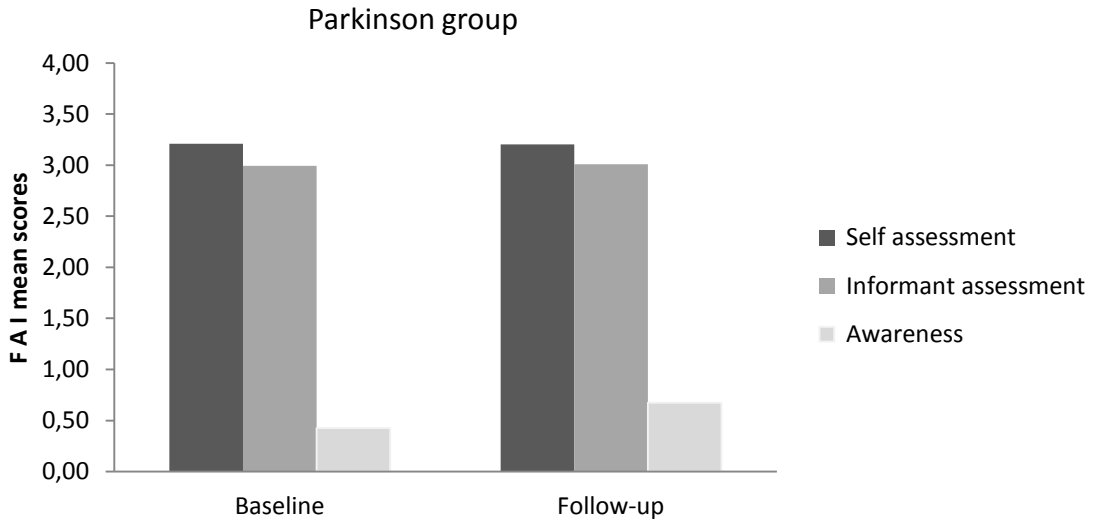

Figure 2. Mean score distribution for FAI self , informant and awareness ratings across time. *Higher self and informant scores indicate greater complaints. Awareness scores close to zero reveal close similarity between patients and their caregivers*

Differences among MCI and AD patient groups across time

The diagnosis groups of MCI patients, who turned to AD and those whose remained MCI at follow-up, were examined for overall differences in FAI scores between both times of assessment by use of a Wilcoxon signed-rank test, the non-parametric equivalent of the dependent t-test (Field, 2009). Median scores are presented at table 6. Wilcoxon signed-rank tests did not reveal significant differences for patients who remained diagnosed as MCI for FAI self (Z = -1.23, p = .22), informant (Z = -1.07, p = .29), and awareness (Z = -1.03, p = .30) ratings between both times of assessment. Those patients who turned to AD at follow-up, also did not reveal significant difference scores between baseline and follow-up for FAI self (Z = -0.37, p = .72), informant (Z = -0.73, p = .46), and awareness (Z = -0.73, p = .47) ratings. Regarding self and informant assessment median scores, memory complaints raised in the MCI group and decreased for those patients, who turned to AD at follow up. Figure 3 shows that informant ratings changes were negligible in the AD group. Concerning awareness, discrepancy scores between self and informant questionnaires decreased slightly for the MCI group and increased for those, who were diagnosed as AD at the second time (see Figure 3). In summary the results of the presented difference analyses could not provide evidence that

awareness changes longitudinally within the diagnosis subgroups of MCI or MCI converting to AD.

Table 6

Median Scores of FAI Self, Informant and Awareness Ratings for MCI and AD across Time

	Baseline				Follow-up			
	MCI		MCI-AD		MCI		AD	
	Mdn	*n*	*Mdn*	*n*	*Mdn*	*n*	*Mdn*	*N*
Self	2.75	18	3.01	4	2.81	18	2.60	4
Informant	2.88	19	3.75	13	3.00	19	3.69	13
Awareness	- 0.10	16	- 0.61	4	0.17	16	-1.31	4

Note. MCI-AD = MCI patients at baseline, converting to AD at follow-up

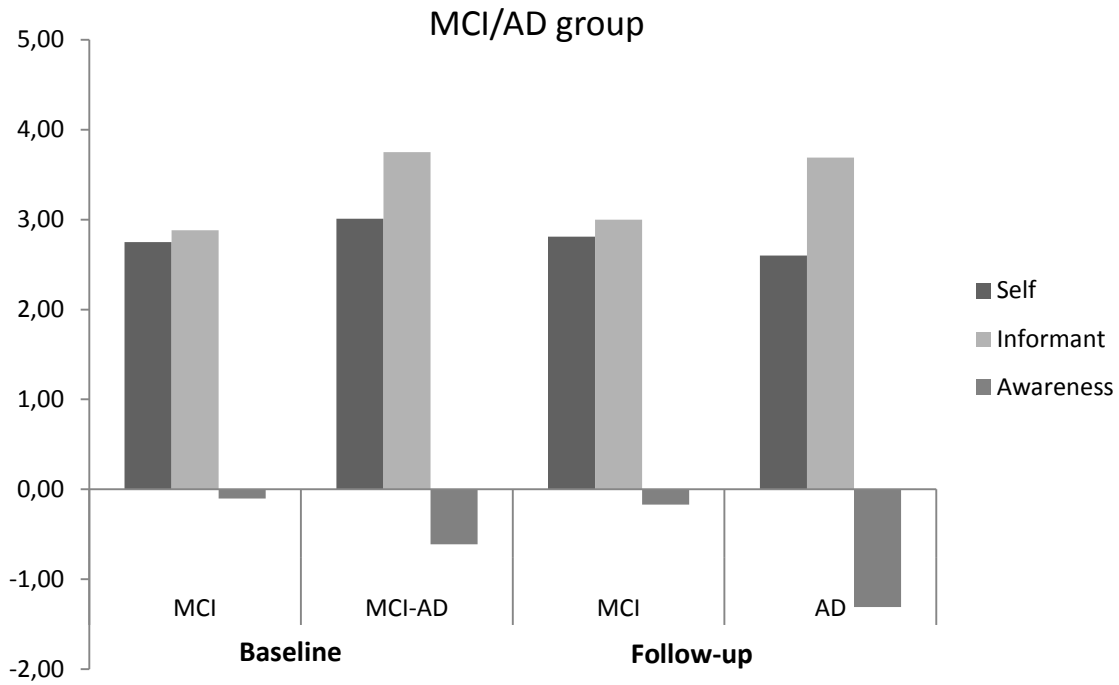

Figure 3. Mean score distribution for FAI self, informant and awareness ratings across time.

Higher self and informant scores indicate greater complaints. Negative awareness scores indicate overestimation of patients compared to informants

Prediction of AD

Finally Receiver-Operating-Characteristics (ROC) analysis was performed to explore the relative predictive power of FAI self, informant and awareness ratings to detect dementia onset in the following 2 years. Sensitivity indicates the probability that AD patients are correctly classified as demented, while specificity represents the likelihood that non demented patients are correctly identified as healthy. The error rate as counterpart of specificity (1-specifity) implies the percentage of healthy patients, who were incorrectly classified as demented. The ROC graph displays relative tradeoffs between true positives (sensitivity) and false positives (1-specifity). The Area under the ROC curve (*AUC*) is used as an indicator of the discriminative utility of each type of awareness assessment. Optimal cut-off points are calculated by selecting the point on the ROC curve that maximises sensitivity and minimizes the error rate. An area of 1 represents a perfect test, while random guessing produces an area of .5, representing a worthless test (Fawcett, 2006; Metz, 1978). The ROC graph of the current study is presented in Figure 4.

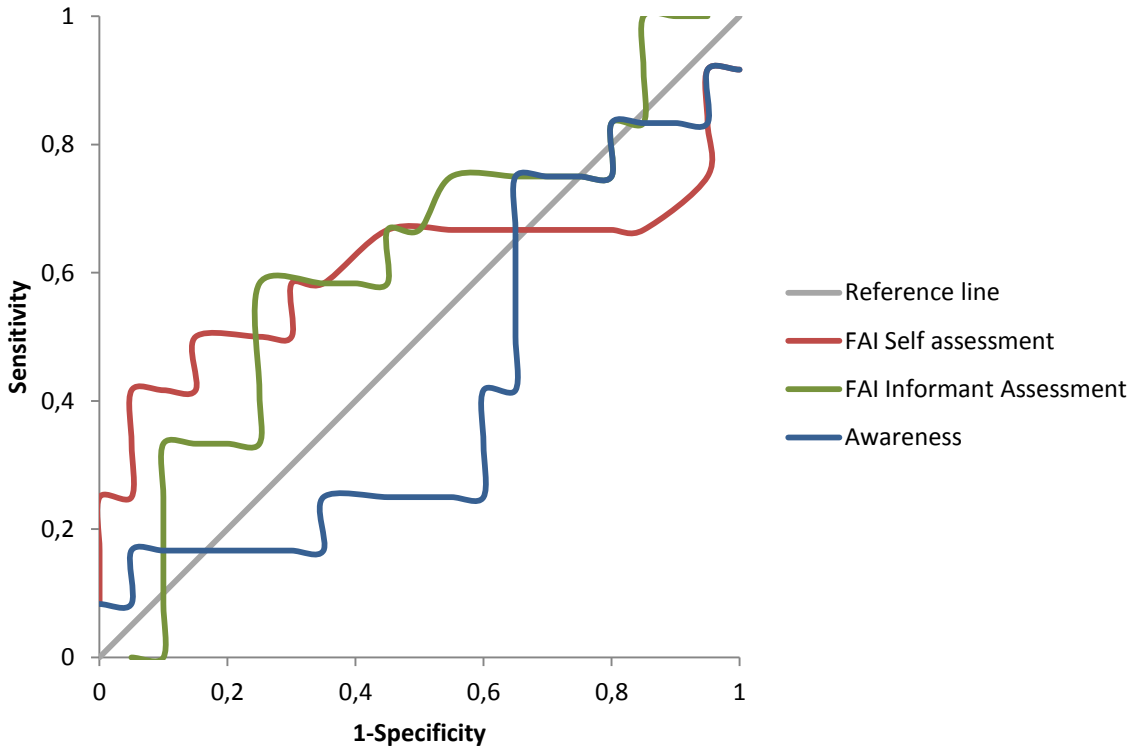

Figure 4. ROC-Graph for FAI self, informant and awareness, MCI conversion to AD

The predictive power of FAI assessment was examined by comparing self, informant and awareness ratings of MCI patients at the baseline with AD conversion-rates at follow-up. The results of the ROC analyses revealed an *AUC* of .60 for self and .62 for informant questionnaires indicating poor discriminative utility. Awareness discrepancy scores had worse predictive power (*AUC* = .42). See Table 7 for details.

Table 7

ROC-Analyse, MCI conversion to AD

				95 % KI	
	AUC	*s*	*p*	-	+
Self assessment	.60	.12	.33	.36	.85
Informant assessment	.62	.11	.29	.41	.82
Awareness	.42	.11	.46	.21	.64

Note. AUC – Area under the ROC Curve

Discussion

The main intention of the present study was to explore awareness of subjective memory assessment in patients with MCI, AD and PD and to determine if unawareness can serve as a predictor for future conversion to AD in MCI and PD. For this purpose, objective performance measures were compared to patient and caregiver memory appraisals and to awareness scores on two times of assessment with a mean interval of two years. Awareness was assessed by subtracting informant- from self-rating scores of the FAI questionnaire. Whole-group comparisons of awareness with objective test data revealed one significant correlation concerning overall cognitive ability (MMSE), which became significant with large effect at follow-up (r_s = .51). Patients with decline of cognitive performance overestimated their memory function compared to their caregivers. This outcome supports studies indicating that unawareness increases with cognitive decline (Ecklund-Johnson & Torres, 2005; Lehrner et al. 2015). FAI informant correlation with MMSE was significant at follow-up (r_s = -38), while association with self report remained small (r_s = .15). Caregivers rated higher forgetfulness when cognitive ability of participants decreased, while patients´ memory estimations did not correspond to their actual cognitive competence. These findings support the hypotheses that discrepancy scores increase with progressing unawareness and that

informant-ratings display a greater correlation to objective measures of patient cognitive performance (Ecklund-Johnson & Torres, 2005; Schinka, 2010). Whole-group comparisons between self-assessment FAI scores and the results of the NTBV revealed significant correlations with subtests of the domains memory, attention and language. At baseline self-ratings yielded one significant association with moderate effect to the VSRT-subtest *Delayed Recall* of the domain memory (r_s = -.38), revealing intact self estimation. This subtest is very sensitive to age related memory changes and assesses loss of episodic memory, which is a core diagnostic criterion for later conversion to AD (Bäckman, Jones, Berger, Laukka & Small, 2004; Dubois et al., 2007). Lehrner et al. (2015) used this subtest as a measure of objective memory in order to obtain awareness scores. Its association with self-assessment scores at baseline supports studies stating that memory complaints are supposed to be an early manifestation of memory impairment (Jorm et al., 2001). At follow-up, this correlation was not significant anymore, instead self assessment correlated significantly with the *Age Concentration Test* (AKT, r_s = -.41) of the domain attention and the *Semantic Word Fluency Test* (SWT, r_s = -.47) of the domain language. People who had worse performance on these tests complained more about loss of memory than patients with decrease on memory tasks. One reason might be a decline of insight for memory impairment in patients with proceeding MCI and those who converted to AD, while insight to dysfunctions in other cognitive domains remains relatively intact in early stages of dementia (Vogel et al. 2004). Nevertheless, correlations with awareness scores, as observed in anosognosia, were not significant for these subtests of the NTBV (Ecklund-Johnson & Torres, 2005). One probable explanation is that patients, who converted to dementia at follow-up, showed symptoms of mild AD only. People scoring 23 or less on the preceding MMSE, performed the short version of the NTBV or the screening only and were excluded from the study. Informant FAI scores correlated significantly with the modified Boston Naming Test (mBNT, r_s = .31) of the domain language. At the baseline caregivers estimated patients´ memory worse than their actual performance on this language task, but this correlation diminished close to zero at follow-up. These results might indicate that the semantic performance of MCI and PD patients remained quite intact, while memory deficits were already corroborated by informants. Unlike expected, informant memory appraisals did not correlate significantly with memory tasks at any time of assessment. As mentioned above, their follow-up ratings rather reflected decline of overall cognitive ability. Besides, difference scores at group level showed that informant FAI scores revealed better memory appraisals for the AD group at follow-up than at the baseline. Nevertheless, discrepancy scores increased, because patients overestimated their memory functions even more (Vogel et al., 2004). These findings might

be influenced by several aspects like sample size, patient-informant relationship and characteristics of informants. Moreover, the current study does not include patients with progressing AD, where memory deficits can easily be detected by caregivers. Memory tasks identify subtle changes like observed in MCI which might be beyond the competence of informants (Schinka, 2010).

In the field of non-cognitive factors, sex, age and education did not reveal any effect on awareness. Depression was assessed by two questionnaires, but only one correlation between informant FAI scores and the Geriatric Depression Scale (GDS) turned out to be significant with moderate effect at follow-up (r_s = .37). Informant-reported memory problems were associated to higher rates on depression in the elderly. Self-assessment and awareness scores as well as correlations with the Beck Depression Inventory (BDI) did not yield any significance. In general whole-group comparisons of the underlying sample could not reveal evident influence of depression on awareness. Maybe further examination of diagnostic group differences would display longitudinal effects like hyper-awareness or underestimation (Roberts et al., 2009).

It was further examined, whether awareness changed over time regarding the whole sample and each diagnostic group separately. Whole-group correlation analyses between baseline and follow-up were performed to investigate, whether awareness of subjective memory assessment remained stable over time. Significant correlation coefficients with large effect (all r_s > .5) revealed that patients as well as their caregivers estimated patient-concerned memory functions consistently between baseline and follow-up. These results suggest that awareness of subjective memory assessment remains relatively intact in cognitively healthy PD, MCI and early AD. Separate group analyses also revealed that neither MCI nor AD-converted patients differed significantly across time in the field of self, informant and awareness scores. These findings are supported by previous studies claiming that the level of awareness does not differ significantly between patients with MCI and mild AD (Vogel et al., 2004). Median-score comparisons were made in order to explore tendencies and it turned out, that subjective memory complaints increased in those people who maintained the MCI diagnosis and decreased in later AD patients. The raise of discrepancy scores within the AD group indicates a decline of awareness in AD patients who tend to overestimate their memory functions. Although not significant, these findings correspond to the significant correlates of awareness with MMSE scores. They agree with precedent studies indicating that decline of overall cognitive ability is associated with decrease of awareness (Lehrner et al. 2014; Clare et al, 2002). Regarding conversion rates within the MCI patient group, 11 of 13 people who

turned to AD at follow-up, were diagnosed as aMCI at the baseline. Only 2 initial naMCI patients received the diagnosis of AD at the second time of assessment. These results are in line with previous studies claiming that people with aMCI are at higher risk of conversion to AD (Gaulthier et al., 2006; Lehrner et al., 2005).

PD patients revealed high awareness at both times of assessment, though discrepancy scores to informants increased slightly but not significant at follow-up. They constantly complained more than their caregivers, while memory was estimated worse at follow-up by both groups. Only FAI informant-scores correlated significantly between both times of testing, indicating that caregivers´ ratings seemed more stable than self-reports. In general, neither patients nor caregivers displayed significant changes in estimating memory functions of the study participants in the course of time. Though, it has to be considered, that only nine PD patients were included in the study and that none of them converted to dementia at follow-up. In agreement to previous studies about PD, their awareness remained intact with a small tendency to decrease with cognitive decline (Leritz et al., 2004; Rosen, 2011).

One major objective of the present study was to find out the predictive power of subjective memory assessment. FAI self, informant and awareness ratings of MCI patients who converted to AD or remained MCI were subject to ROC analyses. But the area under the ROC curve revealed that all ratings were close to random guessing (all $AUC < .65$). Therefore the present study could not confirm the hypothesis that awareness of subjective memory assessment serves as predictor for future dementia. Regarding the small sample size of self and awareness scores these results have to be interpreted with caution.

The present study has some limitations. First, the number of subjective memory self-assessments and as a consequence the total of awareness scores decreased at follow-up, especially in the group of AD patients, which had an influence on the statistical power. The probable reason for this decline lies in the duration of the neuropsychological examination, which lasts about 2 to 3 hours. The long version of the NTBV was submitted to all patients before they filled in self-assessment questionnaires. It was observed that mainly those with severe cognitive decline were too weary to continue self assessment after having completed the NTBV. Second, the sample size was generally limited due to the design of the study. Patients with proceeding AD could not be included in the study, because they were not capable of filling in the long version of the NTBV respectively self assessment questionnaires. At this point it has to be mentioned, that it is a clinical study, which is basically not generalizable. Finally, information about cognitive trainings, drug or other

treatments against probable progression to AD between both times of testing, that might have influenced the outcome (Gauthier et al. 2006), was not assessed in the study.

The strengths of the study are the profound neuropsychological examination of all participants and the satisfactory sample size despite clinical limitations. Given the fact that cognitively well-preserved MCI and PD patients usually come alone to the clinical assessment at the memory clinic, the number of participants plus informants performing pre- and post-tests is remarkable.

In conclusion, our study demonstrates that cognitive healthy PD and MCI patients have a relatively intact awareness of memory performance and a good self estimation of dysfunctions in episodic memory. In the longer term, cognitive decline leads to a decrease of complaints about memory loss, and to a raise of discrepancy scores between patients and their caregivers. Generally speaking, unawareness of subjective memory assessment increases to some extent in patients with incipient AD, but further long-term research is needed in order to prove its predictive power. Future studies might include patients with proceeding cognitive decline scoring less than 24 on the MMSE, who are still able to fill in the short form of the Neuropsychological test battery plus the required self assessment questionnaires.

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Appendix

Table A. *Forgetfulness Assessment Inventory (FAI) self-report*

Here are a few questions regarding your memory. Please answer each question by selecting the appropriate digit (1, 2, 3...). If you are not sure how to answer the question, give your best possible answer and make a remark on the left side of the page. Please do not hesitate to ask for support if you need help reading or filling in the questionnaire.
How often did you have problems during the past 4 weeks remembering...

		Never	Rarely	Sometimes	Often	Very often
1	... Names of people?	1	2	3	4	5
2	... Telephone numbers?	1	2	3	4	5
3	... Faces?	1	2	3	4	5
4	... Birthdays?	1	2	3	4	5
5	... Poems?	1	2	3	4	5
6	... Book titles?	1	2	3	4	5
7	... Content of TV broadcasts?	1	2	3	4	5
8	... Shopping list?	1	2	3	4	5
9	... Directions?	1	2	3	4	5
10	... Discussion topics?	1	2	3	4	5
11	... Content of radio broadcasts?	1	2	3	4	5
12	... Content of news broadcasts?	1	2	3	4	5
13	... Arrangements?	1	2	3	4	5
14	... Prices of bread and milk?	1	2	3	4	5
15	... Numbers?	1	2	3	4	5
16	... Lyrics?	1	2	3	4	5

Note. Adapted from "Subjective memory complaints, depressive symptoms and cognition in patients attending a memory outpatient clinic," by Lehrner et al., 2014, *International Psychogeriatrics / IPA*, *26*(3), 463–73. Copyright 2014 by Johann Lehrner. Adapted with permission.

Curriculum Vitae

Personal Data

Name: Martina Rios Silva

Date of birth: February 6th, 1969

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Family status: Married, one child (son, born 2010)

Education

Since 2002 Diploma study of Psychology (extra-occupational), University of Vienna,

1988 – 1990 Apprenticeship as Travel Agent, Wagonlit Travel, Vienna

1987 – 1988 Study of Translation and Interpretation French/Spanish, University of Vienna

1979 – 1987 Bundesgymnasium Klosterneuburg

Work Experience

2014 – 2015 Student apprentice (graduand) at the memory outpatient clinic,
Department of Neurology, Medical University of Vienna

2013 – 2014 Österreichische Autistenhilfe, Vienna
Assistance of children with autism under supervision, SPZ Klosterneuburg,

2012 – 2013 Internship at Österreichische Autistenhilfe, Vienna
Assistance of a boy with autism under supervision, Primary School, Vienna

2009 – 2010 Participation as student advisor at the Cascaded Blended Mentoring (CBM)
Project for student beginners, Faculty of Psychology, University of Vienna

2000 – 2013 Doctor´s assistance at an orthopaedic surgery, Dr. Johann Jagenbrein, Vienna
(2010 – 2013 maternity leave and leave for internship)

1994 – 2000 Travel agent business travel, Cosmos Travel, Vienna
Reservation and ticketing, Air Canada (cooperative partner of Cosmos), Vienna

1988 – 1994 Apprenticeship and travel agent business travel, Wagonlit Travel, Vienna

Additional Qualifications

Foreign Languages: English, French: written and spoken language
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Computer Literacy: MS Office: Word, Excel, Power Point,
Statistical Software: SPSS