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2015

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Sandberg-Smits, L. L. (2015). *A cognitive perspective on clinical manifestations of Alzheimer s disease*. [PhD-Thesis - Research and graduation internal, Vrije Universiteit Amsterdam].

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Apraxia in Mild Cognitive Impairment and Alzheimer's disease: validity and reliability of the Van Heugten test for apraxia

Dementia and Geriatric Cognitive Disorders, 2014

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Abstract

Objective: To assess reliability and validity of Van Heugten test for apraxia (VHA), developed for and used in stroke patients, in a memory clinic population. To assess presence and severity of apraxia in Mild Cognitive Impairment (MCI) and Alzheimer's disease (AD) and to investigate which AD patients were likely to have apraxia.

Methods: We included 90 controls (age:60±9 years,MMSE:28±2), 90 MCI patients (age:65±7 years,MMSE:26±2) and 158 AD patients (age:66±8 years,MMSE:20±5). Apraxia was evaluated by VHA assessing ideational and ideomotor praxis. We retested 20 patients to assess reliability.

Results: Intrarater reliability was 0.88 and interrater reliability was 0.73. AD patients performed worse on VHA (median:88;range:51-90) than controls (median:90;range:88-90) and MCI patients (median:89;range:84-90) (both $p<0.001$). Apraxia was prevalent in 35% of AD patients, 10% of MCI and not in controls (0%;$p<0.001$). In AD, dementia severity was the main risk for apraxia; 15% of mildly versus 52% of moderately demented patients had apraxia (OR(95%CI)=6.7(2.9-15.6)). The second risk factor was APOE genotype; APOE Ɛ4 non-carriers (47%) were at increased risk compared to carriers (30%) (OR(95%CI)=2.1(1-4.7)).

Conclusion: Apraxia can be reliably measured with VHA. Apraxia is present in a proportion of patients with MCI and AD. Presence of apraxia in AD is related to dementia severity and APOE Ɛ4.

Introduction

Apraxia is defined as the inability to carry out learned movements, not caused by motor or sensory impairments, comprehension or cooperation [1]. Apraxia can traditionally be subdivided in ideomotor and ideational apraxia. Ideomotor apraxia refers to the inability to perform gesture pantomimes and imitations correctly, while the actual use of tools is less affected [2,3]. Ideational apraxia refers to the inability to carry out a sequence of actions, but it is also associated with a deficit in tool selection and use, even in single object use [3-5]. A patient with ideomotor apraxia knows what to do but doesn't know *how*, while a patient with ideational apraxia doesn't know *what* to do with a tool.

Before the new clinical criteria for Alzheimer's disease (AD) were proposed, memory impairment followed by impairment in other cognitive domains was considered the core feature of AD [6]. The new criteria recognize that in a subset of atypical patients cognitive domains other than memory may be the core presenting symptom [7]. In a former study, we found that among these atypical patients apraxia/visuo-spatial presentation is the most common non-amnestic presentation [8]. In AD, the presence of apraxia is most often based on clinical judgement or simple bedside tests, since a widely used, validated test is lacking.

Table 1 provides a short overview of the literature on apraxia in AD. Only a small number of studies has been performed, most decades ago and in small samples. Interest seems to increase as evidenced by some recent papers. Two of those former studies showed that roughly one third of mildly demented AD-patients had apraxia on testing [9,10] and the frequency increased with disease severity [9]. Another small study in AD and healthy controls showed that patients performed worse on both ideomotor and ideational apraxia than controls, and especially pantomimes of tool use were most impaired [11]. Furthermore, it has been suggested that patients with early onset AD were more impaired on praxis than late onset patients [12]. As can be appreciated from table 1, tests were not validated. Moreover, the test that was used was often not described in detail [12].

Van Heugten and colleagues developed and validated an apraxia test in a stroke population [13]. We aimed to study its reliability and validity in our memory clinic population. Secondly, we investigated presence and severity of apraxia in MCI, AD and examined which patients with AD were most likely to have apraxia.

Table 1. Overview of studies to apraxia in Alzheimer's disease

Study	N	Apraxia test	Reliability/Validity	Results
Van Heugten et al., 1999 [13]	44 stroke patients with apraxia 35 stroke patients without apraxia 50 older controls Apraxia was based on clinical evaluation.	The Van Heugten test for apraxia, based on tests by De Renzi [28,47].	H coefficient: 0.72 Rho-value: 0.97 Cut off of 86 points: sensitivity: 0.91 specificity: 0.90 positive predictive value: 0.89 negative predictive value: 0.92	The test is a simple and consistent instrument and can sufficiently differentiate between persons with and without apraxia.
Della Sala et al., 1987 [10]	18 Mild AD (not further specified) with 7±2 months follow up	Assesses ideomotor apraxia through the imitation movement test by De Renzi [28].	--	6 (33%) patients were apraxic. Ideomotor apraxia is not an early feature.
Rapcsak et al., 1989 [11]	28 AD (mean MMSE: 12) 23 HC	Assesses ideomotor and ideational apraxia through 33 tasks, partly based on Liepmann [43].	--	AD performed worse than HC on ideomotor and ideational apraxia tasks. Patients with AD were most impaired on pantomimes of tool use (ideomotor apraxia).
Edwards et al., 1991 [9]	142 AD 113 HC Dementia severity based on Clincal Dementia Rating	Assesses ideomotor and ideational apraxia. Standardized motor performance battery designed for school children, selected from Slaon, DeRenzi & Lucchelli and De Renzi, Goodglass and Kaplan and common clinical usage [5,28,48,49].	Cronbach's α: 0.92 Interrater reliability: r=0.81	Apraxia: 35% mild AD (CDR 1) 58% moderate AD (CDR 2) 98% severe AD (CDR 3) Ideomotor apraxia was apparent in mild AD, ideational only in moderate and severe AD.
Dobigny-Roman et al., 1998 [31]	55 AD (MMSE: 15±6) 26 HC	Assesses and validates the ideomotor apraxia test (IAT) consisting of imitating 10 gestures. Based on Ajuriaguerra and clinical usage [50].	Interrater agreement: ICC=0.99 sensitivity: 0.95 specificity: 0.88 correlation MMSE: r=0.83	IAT is an easy and quick to perform and could contribute to an early diagnosis of AD. It correlates with severity of cognitive impairment.
Derouesné et al., 2000 [32]	22 AD (MMSE: 20±4) 10 HC	Assesses ideomotor and ideational apraxia through eight tasks.	--	77% of patients showed ideomotor apraxia. All patients showed ideational apraxia.
Crutch et al., 2007 [51]	35 AD (MMSE: 21±4) 75 HC	Qualitative praxis: three traditional gesture production tasks, to ensure some patients were apraxic. Quantitative praxis: developed and based on two sequential movements tasks by Kimura; meaningful and meaningless movements.	Meaningful task dominant hand; sensitivity: 0.35 specificity: 0.99, AUC: 0.76 Meaningless task dominant hand, sensitivity: 0.74 specificity: 0.93, AUC: 0.89	Sequential movements (quantitative praxis) were validated as measures of praxis and found to be more sensitive than qualitative methods. Disease severity had minimal and inconsistent influence upon apraxia in AD.
Study	**N**	**Apraxia test**	**Reliability/Validity**	**Results**
Musicco et al., 2010 [30]	154 AD (MMSE: 18±4) with 2y follow up	Praxis was measured by Rey Figure Copy Test and the Freehand Copy of Drawings test [52].	--	More severely impaired praxis was associated with more rapid progression. Note: visuo-constructive praxis.
Sa et al., 2012 [12]	109 Early onset AD (MMSE: 22±5) 171 Late onset AD (MMSE: 21±4)	Not specified: part of neuropsychological test battery.	--	Early onset AD had a major impairment in praxis compared to late onset AD.
Falchook et al., 2012 [46]	10 AD (MMSE: 15±5) 12 amnesticMCI (MMSE: 26±2) 18 HC	Conceptual praxis was measured by the in-house developed Alternative tool selection test, Tool selection test	--	Patients with AD had conceptual apraxia and this was associated with impaired knowledge of

		Taxonomic relations test Ideomotor praxis was measured by pantomimes.		semantic taxonomic relations.
Serra et al., 2014 [45]	24 AD with apraxia (MMSE: 18±4) 24 AD no apraxia (MMSE: 20±2) 20 HC	Constructional praxis was measured by the Freehand Copy of Drawings test [52].	--	Constructional apraxia in AD is more often associated with an early onset, a different neuropsychological profile and gray matter distribution.

N: Number of subjects included, AD: Alzheimer's disease,HC: Healthy controls, MMSE: Mini-Mental State Examination, CDR: Clinical Dementia Rating, ICC: Intraclass correlation Coefficient, AUC: Area Under the Curve

Methods

Subjects

338 Patients (90 controls, 90 MCI and 158 AD) were included from the Amsterdam Dementia Cohort at the Alzheimer Center of the VU University Medical Center (VUmc) Amsterdam, between October 2010 and September 2012. All patients underwent a standardized one-day assessment including medical history, informant-based history including the disability assessment for dementia (DAD) [14], physical and neurological exam, neuropsychological assessment, laboratory tests, magnetic resonance imaging (MRI) of the brain and electroencephalogram (EEG).

The neuropsychological assessment included Mini-Mental State Examination (MMSE) [15], Cambridge Cognitive Examination (CAMCOG) [16], the Visual Association Test (VAT) [17], total immediate recall and delayed recall of the Dutch version of the Rey auditory verbal learning task (RAVLT) [18,19], category fluency (animals) [20], the Dutch version of Controlled Oral Word Association Test (COWAT) (letter fluency) [21], three subtests of the Visual Object and Space Perception Battery (VOSP): incomplete letters, dot counting and number location [22], Trail Making Test (TMT) A and B [23] and the forward and backwards condition of Digit Span (extended version) [24] and Stroop [25].

In multidisciplinary consensus meetings diagnoses were made. Patients with Mild Cognitive Impairment (MCI) fulfilled the Albert-criteria and patients with probable AD fulfilled the diagnostic criteria of Mckhann [7,26]. When the results of clinical examinations were normal, patients were considered to have subjective memory complaints and were included in the study as controls. Age at diagnosis of 65 years or younger was considered as early onset. Level of education was classified according to the system of Verhage ranging from 1 to 7 (low to highly educated) [27]. The local Medical Ethics Committee approved the study and all patients gave written informed consent for their clinical data to be used for research purposes.

Apraxia

The Van Heugten test for apraxia is based on tests described by De Renzi [5,13,28]. It consists of two subsets: ideational apraxia is tested by the demonstration of object use and ideomotor apraxia is tested by imitation of a set of gestures. The Van Heugten tests takes only a couple of minutes to perform [13].

Ideational apraxia is tested in three different conditions with the same instruction: “show me how you would use… (this object)”. In the first condition the objects (key, hammer and toothbrush) are presented by verbal request, without the object present. In the second condition the set of objects (spoon, hammer and scissors) are presented visually; the patient may look at the object, but not touch them. In the third set of objects (eraser, comb and screwdriver) actual use is tested: the objects are handed to the patient, who may see and feel them. The test for ideomotor apraxia contains six gestures demonstrated by the test leader, which the patient has to imitate: sticking out one’s tongue, blowing out a candle, closing one’s eyes, waving goodbye, saluting and making a fist.

The scoring procedure is as follows: performance is correct and appropriate (3 points); performance resembles the correct one, but is somewhat imprecise or the patient uses a body part as object (2 points); performance only weakly resembles the correct one but is executed in the correct place, or is correct but carried out in a wrong place (i.e., moving the toothbrush in front of the forehead; 1 point); and performance is not correct or so incomplete that it is not recognizable (0 points). The patient is allowed to try one more time if the first attempt was not correct or appropriate. When the patient at the first attempt used a body part as an object, they were before

the second attempt instructed to act as if they were using the object. Scores of both attempts are added so the maximum score of per item is six points. When the participant performs correctly at the first attempt, six points are given immediately. For the ideational subtest the maximum sub score is 54 points and 36 points for the ideomotor subtest. The maximum total score is 90 points and the cut-off for apraxia is ≤86 points.

Reliability

In 20 patients, the praxis test was administrated again one week after the first assessment. The rater that performed the Van Heugten test for apraxia at baseline, performed the test again. At this repeated measurement, two raters independently rated the performance, allowing estimates of both inter- and intrarater reliability.

APOE

DNA was isolated from10 ml blood samples in ethylenediaminetetraacetic acid (EDTA). apolipoprotein (APOE) genotype was determined at the Neurological Laboratory of the Department of Clinical Chemistry of the VUmc with the LightCycler APOE mutation detection method (Roche Diagnostics GmbH, Mannheim, Germany). APOE data were available for 307 (91%) patients; 87 (97%) of controls, 79 (88%) of MCI patients and 141 (89%) of AD patients and were analysed according to the presence or absence of an APOE Ɛ4 allele.

Statistical analysis

PASW Statistics 18.0 for Mac was used. To quantify inter- and intra-rater reliability we calculated Cohen's kappa (dichotomous) and intraclass correlation (ICC) (continuous) between and within the two raters. Degree of reliability was defined according to Landis and Koch; 0.00-0.20 slight, 0.21-0.40 fair, 0.41-0.60 moderate, 0.61-0.80 substantial and 0.81-1.00 almost perfect [29].

Univariate analysis of variance (ANOVA) was performed with diagnosis as between-subjects factor and the Van Heugten test as dependent variable. Sex, age and education were entered as covariates. Subsequently, we used ANOVA's to compare performance on the Van Heugten test in AD patients according to age at onset (early onset: ≤65 years versus late onset: >65 years), dementia severity (mildly demented: MMSE>21 versus moderately demented MMSE≤21) and APOE Ɛ4 (non-carrier: no APOE Ɛ4 alleles versus carrier: 1 or 2 APOE Ɛ4 alleles), with the same covariates, except for the ANOVA according to age at onset; sex and education.

Finally, we used logistic regression to investigate the associations in AD between age of onset, sex, education, dementia severity and APOE Ɛ4 and apraxia. First, we entered each variable separately (model 1) and secondly, we entered the five variables using the backward stepwise (likelihood ratio) method (model 2). For all analyses, the significance level was set at $p<0.05$.

Results

Based on 20 subjects, intrarater reliability was substantial with a Cohen's Kappa (dichotomous scores) of 0.69 and good with an ICC (continuous score) of 0.88. Interrater reliability was substantial with a Cohen's Kappa of 0.69 and an ICC of 0.73.

Table 2 describes the demographics of patient groups. Controls were younger than patients with MCI and AD. As expected, patients with AD performed worse on MMSE and CAMCOG than patients with MCI and controls, and patients with MCI performed intermediate. Patients with AD performed worse on the Van Heugten test for apraxia (median:88, range:51-90) than controls (median:90, range:88-90) and patients with MCI (median:89, range:84-90) ($p<0.001$). Based on the cut-off score of 86 points; 0% of the controls, 10% of MCI-patients and 35% of the patients with AD presented with apraxia ($p<0.001$).

Table 2. Demographics and test performance of controls and patients with Mild Cognitive Impairment and Alzheimer's disease.

	Controls	MCI	AD
Number of patients, N	90	90	158
Number of women, N (%)	38 (42%)	28 (31%)	77 (49%)#
Age in years	60±9	65±7§	66±8*
Level of education $	5±1	5±2§	5±1*
APOE Ɛ4 carrier, N (%)	32 (37%)	45 (52%)§	88 (62%)*
DAD (N=300)	93±10	91±6	82±17*#
MMSE	28±2	26±2§	20±5*#
CAMCOG	93±6	86±8§	67±15*#
Van Heugten test for apraxia	90 (88-90)	89 (84-90)	88 (5190)*#
Ideational praxis	54 (52-54)	54 (50-54)	53 (26-54)*#
Ideomotor praxis	36 (34-36)	36 (32-36)	35 (25-36)*#
Percentage of apraxia, N (%)	0 (0%)	9 (10%)§	56 (35%)*#

Age, education and tests scores presented as mean±standard deviation. Scores on the Van Heugten test for apraxia are presented as median and range. For baseline demographics independent samples T-test and $\chi 2$-tests were performed when appropriate. Note that we report the significances derived from Univariate analysis of variance (ANVOA) so that we could correct for covariates (sex, age and education). ANOVA was performed with diagnosis as between-subjects factor.

N: Number of patients, DAD: Disability Assessment for Dementia, MMSE: Mini-Mental State Examination, CAMCOG: Cambridge Cognitive Examination, $ According to the Verhage-system.

§ = significance difference MCI versus controls; $p<0.05$ * = significance difference AD versus controls; $p<0.001$ # = significance difference AD versus MCI; $p<0.001$.

The Van Heugten test for apraxia correlated moderately with MMSE ($r=0.53$, $p<0.001$) and CAMCOG ($r=0.56$, $p<0.001$). The correlation with memory tasks was $r=0.30$, $p<0.01$ for the RAVLT immediate recall, $r=-0.24$, $p<0.01$ for the RAVLT delayed recall and $r=0.42$, $p<0.01$ for the VAT. In patients with AD, the Van Heugten test for apraxia correlated moderately with MMSE ($r=0.44$, $p<0.001$) and CAMCOG ($r=0.49$, $p<0.001$). The correlation with memory tasks was $r=0.09$, $p=0.31$ for the RAVLT immediate recall, $r=-0.06$, $p=0.50$ for the RAVLT delayed recall and $r=0.26$, $p<0.01$ for the VAT. Table 3 lists correlations with other neuropsychological tests, illustrating that the Van Heugten test adds information that is not completely covered in the remainder of the neuropsychological assessment.

Table 3. Correlations of the Van Heugten test for apraxia with neuropsychological tests of all patient and of patients with Alzheimer's disease.

	Total group			Alzheimer's disease		
	N	**Pearson's correlation**	**p-value**	**N**	**Pearson's correlation**	**p-value**
MMSE	338	0.54	<0.001	158	0.44	<0.001
CAMCOG	338	0.56	<0.001	158	0.49	<0.001
VAT	337	0.42	<0.001	157	0.26	<0.01
RAVLT total immediate recall	327	0.30	<0.001	147	0.09	0.31
RAVLT delayed recall	326	0.24	<0.001	147	-0.06	0.50
Category Fluency	338	0.41	<0.001	158	0.35	<0.001
Letter Fluency	331	0.35	<0.05	151	0.33	<0.05
Incomplete Letters	312	0.54	<0.001	137	0.49	<0.001
Dot Counting	311	0.33	<0.001	137	0.26	<0.01
Number Location	318	0.23	<0.001	139	0.12	0.15
Digit Span forward	337	0.26	<0.001	157	0.20	<0.05
Digit Span backward	334	0.39	<0.001	154	0.35	<0.001
TMT A	328	-0.45	<0.001	148	-0.34	<0.001
TMT B	254	-0.33	<0.001	79	-0.23	<0.05
Stroop card III	289	-0.46	<0.001	112	-0.36	<0.001

N: Number of patients, MMSE: Mini-Mental State Examination, CAMCOG: Cambridge Cognitive Examination, VAT: Visual Association Task, RAVLT: Rey auditory verbal learning task, TMT: Trail Making Test.

We used ANOVA's to compare subgroups of AD patients with respect to their performance on the Van Heugten test for apraxia; based on dementia severity, age at onset and APOE Ɛ4 status. Moderately demented patients (N=72) performed worse on the Van Heugten test for apraxia than mildly demented patients (N=86); 84±7 versus 88±2 ($p<0.001$), which was attributable to worse performance in both ideomotor and ideational praxis (data not shown). There was no difference in total score according to age at onset (86±5 versus 86±6; $p=0.44$). Patients with early onset AD performed worse than patients with late onset AD on ideomotor praxis however (34±2 versus 35±2; $p<0.05$), while such an effect was not found on ideational praxis (52±3 versus 52±5; $p=0.96$). For APOE Ɛ4 status there were no differences between carriers (N=88) and non-carriers (N=53) on the Van Heugten test for apraxia (86±5 versus 86±4; $p=0.32$), ideational praxis ($p=0.68$) or ideomotor praxis ($p=0.10$)

Finally, we used logistic regression to identify which AD patients were most likely to present with apraxia, see also table 4. The first model in which the variables were entered separately showed that patients with moderate dementia more often had apraxia; 45 (52%) versus 11 (15%) of mildly demented patients (OR(95%CI) = 6.1 (2.8-13.1)). Patients who did not carry an APOE Ɛ4 allele had more often apraxia; 25 (47%) versus 26 (30%) APOE Ɛ4 carriers (OR(95%CI) = 2.1 (1-4.3)). Patients with an early age at onset tended to have more often apraxia; 33 (42%) versus 23 (29%) patients with late onset AD (OR(95%CI) = 1.7 (0.9-3.4); $p=0.07$). Sex and education were not associated with prevalence of apraxia. In the second model, we used the stepwise backward method and found that dementia severity (OR(95%CI) = 6.7 (2.9-15.6)) and APOE Ɛ4 genotype (OR(95%CI) = 2.1 (1-4.7); $p=0.05$) were independently associated with presence of apraxia.

Table 4. Results of logistic regression in patients with Alzheimer's disease.

	Presence of apraxia	**Logistic Regression**	
		Model 1	**Model 2**
Age of onset (early, late)	42%, 29%	1.7 (0.9-3.4)	-
Sex (women, men)	39%, 32%	1.4 (0.7-2.6)	-
Education (low, high)	37%, 34%	1.1 (0.6-2.2)	-
Dementia severity (mild, moderate)	15%, 52%	6.1 (2.8-13.1)	6.7 (2.9-15.6)
APOE Ɛ4 (non-carrier, carrier)	47%, 30%	2.1 (1 -4.3)	2.1 (1-4.7)

Model 1: all variables were entered separately, Model 2: Backward Stepwise (Likelihood Ratio).

Discussion

The main finding of our study was that the Van Heugten test for apraxia was reliable and easy to use in a memory clinic setting. Furthermore, we showed that apraxia is a common feature of AD, as it is present in more than one out of three patients with AD and in one of 10 patients with MCI. Patients with moderate to severe dementia and APOE Ɛ4 non-carriers are at increased risk of having apraxia.

The Van Heugten for apraxia was originally developed for a stroke population. We demonstrated that it is also a reliably measure of apraxia in AD and MCI. The few former studies of apraxia in AD mostly included small patient samples and sometimes tests were not well validated [10-12,30-32]. One of the major issues of some of the earlier studies is that it is hard to replicate them, because it is unknown how, or which test was used to assess praxis [12]. Furthermore, in some cases the tests used to measure deficits in praxis seem more likely to measure executive functioning and visuo-construction [30]. Our study adds to the small but growing body of evidence concerning the role of apraxia in AD. We show that the Van Heugten test for apraxia is easy and quick to assess and therefore easy to incorporate in neuropsychological work-up.

Overall, we found 35% of AD patients to have apraxia. Two former studies found apraxia in mild AD in around 33% of patients [9,33]. Prevalence increased with disease progression: 58% of moderate and 98% of severe demented patients had apraxia [9]. We found that 15% of mild demented patients had apraxia, a lower percentage than the former studies. The number of patients with apraxia in moderate AD (52%) was in agreement with an earlier study. It is very well possible that dementia nowadays is earlier diagnosed than in the eighties and therefore we found a lower percentage of patients with mild AD to have apraxia. Apraxia in MCI has hardly been studied before; it has been found that MCI patients who converted to AD were just slower on a sequential movement task [34]. Another study showed that MCI patients performed intermediate between controls and AD on a praxis task [35]. We extend on these findings by showing that 10% of MCI patients had apraxia. From this perspective, we provide further support for the notion that in some patients apraxia is an early rather than a late feature of AD.

The correlations of the Van Heugten test for apraxia with MMSE and CAMCOG in all patients were moderate, indicating a test dedicate to apraxia adds value to a global cognitive screening. The correlations with other neuropsychological tests ranged from low: 0.23 (number location) to moderate: 0.54 (Incomplete letters). In patients with AD the correlations were even lower, implying that the Van Heugten test for apraxia measures different aspects of cognition. Furthermore, it suggests that the cognitive domain of apraxia is not adequately covered in the standard test battery and deserves a dedicated test.

We found that dementia severity was the main risk factor for the presence of apraxia in AD. This is an expected finding, as with disease progression more cognitive domains get impaired and the impairment gets more severe. Absence of the APOE Ɛ4 allele was the second risk factor for apraxia in AD. APOE Ɛ4 is known to be a genetic risk factor for sporadic AD [36]. Former studies have shown that APOE Ɛ4 carrier ship is associated with prominent memory impairment while non-carriers more often have a non-amnestic presentation [37,38]. In line with these findings we found that APOE Ɛ4 non-carriers more often had apraxia than APOE Ɛ4 carriers. Pathology of the left parietal cortex has been associated with apraxia, especially impairment in usage of tools or objects and the imitation of meaningless hand gestures [39]. Former studies have shown that APOE Ɛ4 carrier ship is associated with more hippocampal atrophy and APOE Ɛ4 non-carrier ship with more atrophy of the frontal

and parietal cortex [40,41]. This would fit with our finding and would suggest that the APOE Ɛ4 non-carriers have more parietal atrophy than the APOE Ɛ4 carriers, resulting in a higher prevalence of apraxia.

Since early onset AD has been associated with a higher prevalence of non-amnestic presentations [8,42], we expected patients with early onset AD to score worse on the praxis test than patients with late onset AD. We found that patients with early onset were more than one and a half times more likely to have apraxia, but this effect did not reach significance. When we evaluated continuous scores, patients with early onset AD appeared more impaired at ideomotor praxis. These results are in line with a study showing that early onset AD is associated with major impairment in praxis [12].

About 100 years ago Liepmann was the first to describe apraxia; he described ideomotor and ideational praxis [43]. Since then, there is debate in literature about the nature and exact definition of apraxia and its subtypes. Most researchers use Liepmann's subdivision, but there are also other definitions and operationalizations [2,3]. As a consequence, the term 'conceptual apraxia' was introduced, meaning that the concept of the object or action is lost [2,44]. Conceptual apraxia can affect the ability to select and use individual tools, but it is not the same as ideational apraxia.

The different practice of definitions seems to make it more difficult to design a proper test to measure apraxia. This is also a limitation of the current study; the subtest of the Van Heugten test for apraxia assessing ideational apraxia might be considered by some to assess ideomotor apraxia. Nonetheless, our study shows apraxia in a substantial proportion of patients with AD and we hope it serves as a starting point for further studies on the topic of (subtypes of) apraxia in AD [45,46]. As can be appreciated from table one, literature on apraxia in AD is scarce.

To conclude, apraxia is a common feature of AD, and is already prevalent in a fair proportion of patients with MCI. Praxis is closely related to the ability to carry out activities of daily living and a diagnosis of AD requires interference of activities of daily living. Therefore is it highly relevant to measure apraxia in (diagnostic) work-up. The Van Heugten for apraxia appears a reliable tool for a memory clinic population and easy to incorporate in standard work-up and could for fill the role of reliable tool to assess apraxia.

Acknowledgements

Research of the VUmc Alzheimer Center is part of the neurodegeration research program of the Neuroscience Campus Amsterdam. The Alzheimer Center VUmc is supported by Alzheimer Nederland and Stichting VUmc Fonds. The clinical database structure was developed with funding from Stichting Dioraphte.

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