Comprehension of complex instructions deteriorates with age and vascular morbidity

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Received: 22 November 2009 / Accepted: 14 June 2010 / Published online: 30 June 2010
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Abstract Verbal comprehension is critical to the success of medical counseling. Here, we tested how age and vascular risk factors affect the ability to understand complex instructions. Verbal comprehension, cognitive functions, and vascular risk factors were assessed in 39 mid- and 38 late-life community-dwelling individuals (48 to 59 years and >59 years of age, respectively). To test for verbal comprehension, we used a modified version of the Token Test (TT). In midlife individuals, education ($\beta=0.572$, $p<0.05$) was the only predictor for extended-TT performance. In late-life individuals, age ($\beta=-1.015$, $p<0.001$) and

body mass index ($\beta=-0.651$, $p=0.003$) were significantly correlated with extended-TT performance and explained 50% of the variance in extended-TT performance (adjusted $R^2=0.503$). This relation is only partly explained by conventional neuropsychological measures as the ones used in our test battery. These results indicate that aging and overweight impair comprehension of complex instructions. Therefore, medical counseling appropriate for midlife individuals may be less successful in elderly people and particularly in those with metabolic disturbances.

Keywords Token test · Language comprehension · Age · Vascular risk factor · Medical counseling

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Introduction

Recent evidence suggests that older age and comorbidities negatively affect medication adherence (Munger et al. 2007). One cause of non-adherence is the impaired comprehension of medical instructions (Morrell et al. 1989). Language comprehension is critical for patient education and counseling and consequently for adherence (Park and Jones 1996). Comprehension deficits are further associated with decreased medical decision-making capacity (Okonkwo et al. 2007). Researchers have suggested that consultation process should be adapted to the specific needs of mentally ill (Grisso and Appelbaum 1991) and cognitively impaired (Okonkwo et al. 2007) or demented (Marson et al. 1996) patients.

In clinical practice, recognition of non-adherence as a result of subtle cognitive changes in otherwise mentally healthy individuals is relatively low. There is controversial evidence about the effects of aging on language understanding, including literature that suggests an age-related decline in language comprehension (Kemper 2006) and evidence supporting age constancy in understanding (Burke and Mackay 1997). Empirically, clinicians communicate with healthy elderly individuals perhaps in a louder voice and a slower pace. The actual quality of communication does not differ much from that with younger ones with regard to information load and complexity of given instructions. This is not necessarily justifiable as several conditions like hypertension, atrial fibrillation, hyperlipidemia, diabetes, obesity, and smoking have been associated with cognitive decline in the elderly (Duron and Hanon 2008). Furthermore, some medications have been associated with drug-induced cognitive disorders (Gray et al. 1999) and some others used for the treatment of classical cardiovascular risk factors (CVRF) have a favorable effect on risk factor associated cognitive decline (Haag et al. 2009a; Haag et al. 2009b; Nash and Fillit 2006; Shah et al. 2009). Our intention was to evaluate whether age and cardiovascular risk factors impair comprehension of complex instructions and their practical implementation.

For this purpose, we used an extended version of the Token Test (TT; De Renzi and Vignolo 1962), developed and tested so as to be adapted to the needs and performance level of community-dwelling individuals.

Methods

Study sample

From October 2007 until May 2008, we examined 79 consecutive participants of the SEARCH Health Study, a large population-based study in Muenster, Germany, designed to assess the impact of atrial fibrillation and other vascular risk factors on cognition (Knecht et al. 2008). The study population consisted of patients with atrial fibrillation and a fivefold oversampled control group. Exclusion criteria were a history of any major neurological or psychiatric illness. An informed consent was obtained from participants in the study after the nature of the procedure had been fully explained to them. All

participants underwent a clinical interview and physical examination by a trained study physician, a high resolution 3-Tesla MRI of the brain and blood sampling for biochemical and genetic analysis. Furthermore, participants were studied with a comprehensive neuropsychological test battery, designed to assess a full range of cognitive functions. The tests are listed in Table 2 and a detailed description of each test may be found in Lezak (2004). Trained technicians supervised by a clinical neuropsychologist conducted the neuropsychological assessment. All participants were native German speakers.

Independent variables

Education was assessed as categorical variable (5 vs. 7 vs. 9 years of secondary school vs. tertiary education). Body mass index (BMI) was calculated dividing body weight (kilogram) by the square of the body height (square meter). History of arterial hypertension, atrial fibrillation, diabetes, dyslipoproteinemia, current smoking status, and gender were documented as dichotomous variables. We also created one variable including medication for classical CVRF (including the number of antihypertensive, antiarrhythmic, antidiabetic, lipid-lowering, and antithrombotic agents) and another variable including drugs that have been associated with drug-induced CNS-related adverse effects (tricyclic antidepressants, benzodiazepines, digoxin, beta blockers, reserpine).

Task and procedure

The TT (De Renzi and Vignolo 1962) was designed to assess verbal comprehension of commands of increasing complexity. The patient has to choose the right token out of a set of 20 tokens of five colors (red, green, blue, yellow, and white), two sizes, and two shapes (rectangle and circle). The TT consists of five different subtests with non-redundant instructions which increase in length and complexity. In the first four parts, the patient is instructed to choose a token. According to the authors, these four parts are used to examine the patient's understanding of adjectives and nouns. In Part V, prepositions, conjunctions, adverbs, and different verbs are introduced in the commands, for example "Put the red circle on the green square." This subtest is used to examine the patient's understanding of sentence components and comprehension of syntax.

In the present study, we used ten tokens of five colors and two shapes and developed a list of ten non-redundant instructions of increasing complexity. The instructions increase in length from three units of information (“Show me the red square/and then take all the circles/except the yellow”) to ten units involving not only the tokens, but also hand- and time-components (“Put the white square on the yellow circle with your left hand, before you put the blue tokens and the white circle on top of each other in any order you wish”). The instructions were all read out loud for all participants by the same examiner, in a mild tone of voice and with the same tempo. Every instruction was read out only once. After each task, the manipulated tokens were put back in their original places so that subsequent tasks were not made easier by reducing the number of possible choices.

Scoring was based on linguistic principles: failure to respond to any one element of information transmitted by the command was scored as an error. We introduced a point-system evaluation of the correct answers for the statistical analysis, taking into account the degree of difficulty that each instruction presented: each instruction received a total of points equal to the percentage of incorrect responses to it multiplied by 100, and the score each participant achieved, was the sum of the points of his/her correct answers.

Statistical analysis

Multiple linear regression analysis was used to test independently the effect of age, gender, education, cardiovascular risk factors, and medication on extended-TT performance.

To directly compare regression coefficients, we used a simultaneous regression model. Pearson’s correlation analyses were used to compare the TT scores of the participants with the achieved scores in neuropsychological tests of linguistic function, working memory, verbal memory, attention, and executive functions (Table 2). We converted the tests that were significantly correlated with token test performance to z-scores and created a single composite variable called “executive attention.” To analyze the independent effect of cardiovascular risk factors and neuropsychological performance, we performed another regression analysis including the variable “executive attention” in the regression model.

The significance level was set at $p < 0.05$. The analyses were carried out using SPSS version 15 (SPSS Inc., Chicago, IL, USA).

Results

A total of 79 participants, aged 48 to 74 years, who took part in the SEARCH-Healthy study, consented to participate. Since the goal of our study was to assess the comprehension and implementation of complex instructions, we excluded one participant with presbycusis and one participant with severe neuropsychological deficits. These exclusions left a total of 77 participants, whose data were further analyzed (Table 1).

The average correct responses to the extended-TT were 60% (SD 16.7%). The participants scored in average 182.9 points (SD 75.5) with a minimum of 25 and a maximum of 341.3 points. A Kolmogorov–Smirnov test revealed that this measure was normally distributed ($p > 0.621$). The study sample was divided by a median split into mid- and late-life: aged 48 to 59 years and > 59 years, respectively. Midlife individuals achieved significantly higher extended-TT scores than late-life individuals (60% vs. 47%, $p < 0.05$).

Extended token test and health functioning

On multiple regression analysis education ($\beta = 0.572$, $p < 0.05$) was the only significant predictor for extended-TT performance in midlife individuals (Table 3). In late-life individuals age ($\beta = -1.015$, $p < 0.001$) and body mass index ($\beta = -0.651$, $p = 0.003$) were significantly correlated with extended-TT performance (Table 3) and explained 50% of the variance in extended-TT performance (adjusted $R^2 = 0.503$). Gender, smoking, and a history of atrial fibrillation, diabetes, hypertension, and hyperlipidemia did not show any significant association with extended-TT performance. Medication for cardiovascular risk factors was positively associated with extended-TT performance, whereas medication associated with drug-induced CNS-related adverse effects was negatively related to TT, though statistically not significant.

Extended-TT scores and cognitive functioning

Performance on the extended-TT correlated significantly with scores involving linguistic functions, working memory, attention, and executive functions (Table 2). There were no significant correlations between extended-TT performance and verbal memory scores.

Table 1 Characteristics of the participants ($n=74$)

	Midlife individuals $n=39$	Late-life individuals $n=38$
Age	54.31±2.44	63.24±4.3
Education (5/7/9/+) ^a	10/8/1/20	11/12/0/15
Female	20 (51.3)	20 (52.6)
MMSE	29.47±0.65	29.0±0.96
BDI	5.82±4.8	5.24±4.59
Body mass index (BMI)	26.2±4.7	25.96±3.38
History of hypertension	13 (33.3)	22 (57.9)
Atrial fibrillation	1 (2.6)	6 (15.8)
Cigarette smoking	4 (10.3)	3 (7.9)
Dyslipoproteinaemia	12 (30.8)	14 (36.8)
Diabetes	4 (10.3)	3 (7.9)

Data are shown as means±SD for continuous variables and as count (percentage) for dichotomous and categorical variables

MMSE Mini-Mental State Examination, BDI Beck Depression Inventory

^aEducation was assessed as categorical variable (5 vs. 7 vs. 9 years of secondary school vs. tertiary education)

After inclusion of the composite variable “executive attention” in our regression model to compare cognitive functioning and health functioning directly, education was no longer a significant predictor for extended-TT performance in midlife individuals. In late-life individuals, age and body mass index were still significant predictors, but had a smaller impact on Token Test performance: for the variable age the regression coefficient was $\beta=-0.750$ ($p=$

0.007) in the model including both cognitive and health measures vs. $\beta=-1.015$ ($p<0.001$) in the model including only health measures, and for BMI it was $\beta=-0.517$, $p<0.05$ the model including both cognitive and health measures vs. $\beta=-0.651$, $p=0.003$ the model including only health measures. “Executive attention” was positively associated with extended-TT performance, though statistically not significant.

Table 2 Pearson’s correlation coefficients between neuropsychological test scores and extended-TT performance

DOMAIN	TESTS	Extended-TT scores
Working memory	Verbal Span (AVLT 1)	$r=0.230^a$
	Digit Span Forward (WMS-R; German Version)	$r=0.193$
	Digit Span Backward (WMS-R; German Version)	$r=0.177$
Attention and executive functions	Colour–Word Interference Test (Part 3)	$r=-0.290^a$
	Colour–Word Interference Test (Part 2)	$r=-0.277^a$
	Digit Symbol Substitution Test (DSST)	$r=0.348^b$
	Trail-Making Test (TMT) Part A	$r=-0.484^b$
	Trail-Making Test (TMT) Part B	$r=-0.425^b$
	Letter Fluency	$r=0.042$
	Category Fluency	$r=0.307^a$
	Shifting Categories: Fruit–Sport	$r=0.265^b$
Linguistic functions	Boston Naming Test	$r=0.267^a$
Verbal memory	AVLT 5	$r=-0.009$
	AVLT 1–5	$r=0.114$
	AVLT 6	$r=-0.114$
	AVLT 7	$r=-0.050$

^aCorrelation is significant at the 0.05 level (two-tailed)

^bCorrelation is significant at the 0.01 level (two-tailed)

Table 3 Regression coefficients and coefficients of determination, dependent variable: extended-TT score

Variables	<i>B</i>	<i>SE</i>	Standardized β	<i>p</i> value	R^2	Adjusted R^2
Midlife group, <i>n</i> =39 ^a						
Education	34.769	14.813	0.572	<0.05	0.540	0.179
Late-life group, <i>n</i> =38 ^b						
Age	−1.275	0.256	−1.015	<0.001		
BMI	−12.705	3.620	−0.651	0.003	0.698	0.503

B raw regression coefficient, *SE* standard error, β standardized regression coefficient

^a Age, gender, BMI, smoking, atrial fibrillation, and a history of diabetes, hypertension, and hyperlipidemia did not show any significant association with extended-TT performance

^b Education, gender, smoking, atrial fibrillation, and a history of diabetes, hypertension, and hyperlipidemia did not show any significant association with extended-TT performance

Discussion

We found significant deficits in the implementation of complex instructions with advanced age and cardiovascular risk factors. The age effects concur with previous evidence showing age-related changes in linguistic abilities: elderly individuals are affected by cognitive slowing, impaired working memory capacity, and inhibitory deficits (Kemper 2006). A general slowing of perceptual and cognitive operations is an essential feature of the aging process (Salthouse 1996). Furthermore, as inhibitory mechanisms weaken with age (Hasher and Zacks 1988), older adults' comprehension may be affected by distractions or intrusive thoughts. They experience difficulties in dividing attention effectively (Anderson et al. 1998) and avoiding distraction by irrelevant stimuli (Barr and Giambra 1990) during listening. These processing declines might hinder effective speech perception and language comprehension.

Importantly, we found cardiovascular risk factors like overweight to additionally impair language comprehension in late-life individuals. Several risk factors like hypertension, atrial fibrillation, hyperlipidemia, diabetes, obesity and smoking (Duron and Hanon 2008) and some sorts of medication (Gray et al. 1999) have been shown to deteriorate cognitive functions in the elderly.

Obesity has been associated with an increased risk of dementia in late-life (Kivipelto et al. 2005). Concomitant cardiovascular disease, hypertension, hyperglycemia, hyperlipidemia, and inflammatory markers like C-reactive protein and interleukin 6 have been proposed as potential causative agents of

dementia in obesity (Barrett-Connor 2007). Although the pathway connecting obesity and cognitive decline is still unclear, studies on obesity using brain imaging have revealed cortical and subcortical changes, like regional and generalized brain atrophy and white matter lesions, which are associated with cognitive decline and dementia (Jagust 2007).

We did not find an association between extended-TT performance and vascular risk factors in midlife individuals. Education was the only significant predictor of extended Token Test performance in this age group. This can partly be explained by an age-related rise in prevalence and incidence of cardiovascular risk factors (Kivipelto et al. 2005). The aging brain is more vulnerable to vascular risk factors since there are frequently concomitant multiple risk factors present (Llewellyn et al. 2008) and a longer history of disease.

The strengths of this study are the accurate characterization of our subjects including an extensive neurocognitive assessment. Furthermore, the test we used (TT) does not only assess language comprehension but also its practical implementation. A limitation of this study is the rather small number of subjects. Furthermore, the limitations of cross-sectional studies must be kept in mind when evaluating the results. We cannot overlook the possibility that individuals with deficits in implementation of complex instructions may be the ones who tend to become overweight. But since age and body mass index were correlated with extended-TT performance only in late-life individuals, our data support the hypothesis that the metabolic consequences of a longer history of overweight and obesity lead to poor understanding and implementation of instructions.

In addition to the previously described cognitive deficits, we were able to show in a pragmatic approach that understanding and following complex instructions is limited under the influence of advanced age and vascular morbidity and this relation is only partly explained by conventional neuropsychological measures as the ones used in our test battery.

Older adults are frequently challenged by multimorbidity and polypharmacy and have to cope with new instructions involving, e.g., new treatment strategies, modification of dietary habits, or the use of self-monitoring devices. Poor understanding and implementation of instructions can lead to a vicious circle of poor medication adherence, increasing vascular morbidity, and declining language comprehension.

Acknowledgment We thank the City of Münster, Germany for supporting us in recruiting community-dwelling elderly citizens.

Funding The project is supported by several public funding sources, which had no involvement in study design, in the collection, analysis, and interpretation of data, in the writing of the report, or in the decision to submit the paper for publication. This work was supported by the BMBF-Competence Network on Atrial Fibrillation, BMBF-Research Consortium: 01GW0520, the Deutsche Forschungsgemeinschaft (Kn 285/6-1 and 6-3), Volkswagen Stiftung (Az.: I/80708), Marie Curie Research and Training Network: Language and Brain (RTN:LAB) funded by the European Commission (MRTNCT-2004-512141), and the Neuro-medical Foundation Münster.

Conflict of interest None declared.

References

- Anderson ND, Craik FI, Naveh-Benjamin M (1998) The attentional demands of encoding and retrieval in younger and older adults: 1. Evidence from divided attention costs. *Psychol Aging* 13:405–423
- Barr RA, Giambra LM (1990) Age-related decrement in auditory selective attention. *Psychol Aging* 5:597–599
- Barrett-Connor E (2007) An introduction to obesity and dementia. *Curr Alzheimer Res* 4:97–101
- Burke DM, Mackay DG (1997) Memory, language, and ageing. *Philos Trans R Soc Lond B Biol Sci* 352:1845–1856
- De Renzi E, Vignolo LA (1962) The token test: a sensitive test to detect receptive disturbances in aphasics. *Brain* 1962:665–678
- Duron E, Hanon O (2008) Vascular risk factors, cognitive decline, and dementia. *Vasc Health Risk Manag* 4:363–381
- Gray SL, Lai KV, Larson EB (1999) Drug-induced cognition disorders in the elderly: incidence, prevention and management. *Drug Saf* 21:101–122
- Grisso T, Appelbaum PS (1991) Mentally ill and non-mentally-ill patients' abilities to understand informed consent disclosures for medication: preliminary data. *Law Hum Behav* 15:377–388
- Haag MD, Hofman A, Koudstaal PJ, Breteler MM, Stricker BH (2009a) Duration of antihypertensive drug use and risk of dementia: a prospective cohort study. *Neurology* 72:1727–1734
- Haag MD, Hofman A, Koudstaal PJ, Stricker BH, Breteler MM (2009b) Statins are associated with a reduced risk of Alzheimer disease regardless of lipophilicity. The Rotterdam Study. *J Neurol Neurosurg Psychiatry* 80:13–17
- Hasher L, Zacks RT (1988) Working memory, comprehension, and aging: a review and a new view. In: Bower GH (ed) *The psychology of learning and motivation*. Academic, New York, pp 193–226
- Jagust W (2007) What can imaging reveal about obesity and the brain? *Curr Alzheimer Res* 4:135–139
- Kemper S (2006) Language in adulthood. In: Bialystok E, Craik FIM (eds) *Lifespan cognition: Mechanisms of change*. Oxford University Press, Oxford, pp 223–238
- Kivipelto M, Ngandu T, Fratiglioni L, Viitanen M, Kareholt I, Winblad B, Helkala EL, Tuomilehto J, Soininen H, Nissinen A (2005) Obesity and vascular risk factors at midlife and the risk of dementia and Alzheimer disease. *Arch Neurol* 62:1556–1560
- Knecht S, Wersching H, Lohmann H, Bruchmann M, Duning T, Dziawas R, Berger K, Ringelstein EB (2008) High-normal blood pressure is associated with poor cognitive performance. *Hypertension* 51:663–668
- Lezak MD (2004) *Neuropsychological assessment*. Oxford Univ. Press, New York, Oxford
- Llewellyn DJ, Lang IA, Xie J, Huppert FA, Melzer D, Langa KM (2008) Framingham stroke risk profile and poor cognitive function: a population-based study. *BMC Neurol* 8:12
- Marson DC, Chatterjee A, Ingram KK, Harrell LE (1996) Toward a neurologic model of competency: cognitive predictors of capacity to consent in Alzheimer's disease using three different legal standards. *Neurology* 46:666–672
- Morrell RW, Park DC, Poon LW (1989) Quality of instructions on prescription drug labels: effects on memory and comprehension in young and old adults. *Gerontologist* 29:345–354
- Munger MA, Van Tassel BW, LaFleur J (2007) Medication nonadherence: an unrecognized cardiovascular risk factor. *MedGenMed* 9:58
- Nash DT, Fillit H (2006) Cardiovascular disease risk factors and cognitive impairment. *Am J Cardiol* 97:1262–1265
- Okonkwo O, Griffith HR, Belue K, Lanza S, Zamrini EY, Harrell LE, Brockington JC, Clark D, Raman R, Marson DC (2007) Medical decision-making capacity in patients with mild cognitive impairment. *Neurology* 69:1528–1535
- Park DC, Jones TR (1996) Medication adherence and aging. In: Fisk AD, Rogers WA (eds) *Handbook of human factors and the older adult*. Academic, San Diego, pp 257–288
- Salthouse TA (1996) The processing-speed theory of adult age differences in cognition. *Psychol Rev* 103:403–428
- Shah K, Qureshi SU, Johnson M, Parikh N, Schulz PE, Kunik ME (2009) Does use of antihypertensive drugs affect the incidence or progression of dementia? A systematic review. *Am J Geriatr Pharmacother* 7:250–261