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Specific Features of Executive Dysfunction in Alzheimer-Type Mild Dementia Based on Computerized Cambridge Neuropsychological Test Automated Battery (CANTAB) Test Results

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Data Interpretation D
Manuscript Preparation E
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Background: The primary manifestation of Alzheimer's disease (AD) is decline in memory. Dysexecutive symptoms have tremendous impact on functional activities and quality of life. Data regarding frontal-executive dysfunction in mild AD are controversial. The aim of this study was to assess the presence and specific features of executive dysfunction in mild AD based on Cambridge Neuropsychological Test Automated Battery (CANTAB) results.





Material/Methods: Fifty newly diagnosed, treatment-naïve, mild, late-onset AD patients (MMSE ≥ 20 , AD group) and 25 control subjects (CG group) were recruited in this prospective, cross-sectional study. The CANTAB tests CRT, SOC, PAL, SWM were used for in-depth cognitive assessment. Comparisons were performed using the *t* test or Mann-Whitney U test, as appropriate. Correlations were evaluated by Pearson *r* or Spearman *R*. Statistical significance was set at $p < 0.05$.

Results: AD and CG groups did not differ according to age, education, gender, or depression. Few differences were found between groups in the SOC test for performance measures: Mean moves (minimum 3 moves): AD (Rank Sum=2227), CG (Rank Sum=623), $p < 0.001$. However, all SOC test time measures differed significantly between groups: SOC Mean subsequent thinking time (4 moves): AD (Rank Sum=2406), CG (Rank Sum=444), $p < 0.001$. Correlations were weak between executive function (SOC) and episodic/working memory (PAL, SWM) ($R = 0.01 - 0.38$) or attention/psychomotor speed (CRT) ($R = 0.02 - 0.37$).

Conclusions: Frontal-executive functions are impaired in mild AD patients. Executive dysfunction is highly prominent in time measures, but minimal in performance measures. Executive disorders do not correlate with a decline in episodic and working memory or psychomotor speed in mild AD.

MeSH Keywords: **Alzheimer Disease • Cognition • Executive Function • Frontal Lobe • Memory • Neuropsychological Tests**

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Background

Alzheimer's disease (AD) is a chronic neurodegenerative disorder associated with progressive neuronal loss, especially in limbic regions and temporo-parietal cortex, leading to atrophy of the brain [1,2]. AD is the most common form of dementia and may contribute to 60–70% of all cases [3]. Primary and early clinical manifestation of typical Alzheimer's disease is cognitive decline in episodic declarative memory and visuospatial abilities [1,2]. The obvious decline of recognition and retrieval memory, language, praxis, attention, and executive functions usually are evident in moderate and severe stages of typical Alzheimer's dementia [4,5]. It is established that executive dysfunction is earlier and more prominent in some variants of Early-onset Alzheimer's disease (EOAD), which frequently is familial and may be ascribed to atypical AD [5], but only 4% to 5% of AD cases are early-onset Alzheimer's disease [6]. In 95% to 96% of cases, AD dementia begins in people over 65 years of age and is classified as late-onset Alzheimer's disease (LOAD). The percentage of familial cases in LOAD is much lower than in EOAD [1,2,6]. The accepted opinion is that the executive functions are relatively preserved in patients with mild, sporadic, late-onset Alzheimer's disease [4]. The problem of executive dysfunction in mild typical AD is important, because there are numerous studies indicating that executive disorders could have even more disastrous effect on activities of daily living (ADL) and quality of life than memory disorders [7–9]. Nevertheless, the amount of research dealing with this problem is quite limited. Published reports about executive dysfunction in mild late-onset AD reaches discrepant conclusions. Data regarding the nature, specific features, and the very existence of executive dysfunction in mild AD remain unequivocal and controversial. There are abundant neurobiological arguments for the existence of executive dysfunction in mild AD, available from positron emission tomography (PET) and functional magnetic resonance imaging (fMRI) studies, but data from neuroimaging studies do not necessarily and completely coincide with the results of direct cognitive testing or evaluation of functional abilities (ADL and instrumental ADL) [10–12]. Executive functions are cognitive processes, such as attentional and inhibitory control, cognitive flexibility, and problem solving [13]. Some previous neuropsychological studies suggest that AD patients may have impairment of executive functions early in the course of the disease [14–17]. However, there are also reports that contradict positive findings and show that executive impairment is not typical for mild AD patients [18,19]. These contradictory results may be explained by a variety of reasons: different tests were used to evaluate executive functions, there were significant differences in severity of Alzheimer's dementia, and conflicting opinion of the researchers about the influence of other cognitive functions, especially memory, on the performance in tests, used to evaluate executive functions [14].

It seems that more reproducible and comparable results could be achieved by using strictly standardized, very sensitive, but inter-rater stable tests, which could provide multiple different measures for any cognitive test in order to allow selective assessment of mild decline in various specific aspects of the cognitive function under investigation. Possibly, such a solution could be provided by the computerized cognitive tests. Computerized cognitive tests provide numerous advantages over classical pencil-paper tests, such as automatic administration, recording, and scoring, which increase data accuracy and reliability [20]. The Cambridge Neuropsychological Test Automated Battery (CANTAB) is a widely used, validated, and reliable neuropsychological battery [21,22].

We used the computerized CANTAB battery tests to investigate executive functions, especially problem solving abilities, and their relationship with other cognitive functions in mild AD patients in hope that the advantages of computerized cognitive tests may enable us to acquire novel information and new insights into the problems described above.

In addition, there is a need for reliable, reproducible, but powerful tests with simple administration for assessment of various aspects of executive dysfunction, not only due to the above-mentioned relationship between executive dysfunction and activities of daily living in mild AD. Greater executive deficits in AD are associated with more expressed and more frequent aggressive behavior and agitation, as well as more severe psychotic and depressive symptoms [23,24]. There is some evidence that there may be a link between the severity of executive deficits and rapid clinical progression of AD dementia [25]. Thus, the early and reliable detection of executive disorders in patients with mild AD could contribute significantly to more accurate assessment of the patient's degree of disability, may help to determine how dependent the patient is on support from caregivers, and enable the medical personnel to provide timely and adequate management and treatment of neuropsychiatric complications.

The aim of this study was to investigate the presence and specific features of frontal-executive dysfunction in mild Alzheimer's disease based on the computerized CANTAB battery tests results.

Material and Methods

Study participants

The prospective, cross-sectional study was performed at the Memory Disorders Unit of the Center of Neurology, Vilnius University Hospital Santariskiu Klinikos; 75 subjects were enrolled in the study. We recruited 50 newly diagnosed,

treatment-naïve AD patients and 25 healthy controls (Control group, CG) matched according to age, education, and gender.

Participants of the Control group voluntarily agreed to participate in the study. Informed consent forms (ICF), approved by the Vilnius Regional Biomedical Research Ethics Committee, were obtained from all participants. Screening evaluation (MMSE, GDS, Hachinski ischemic index (HII), and others) was started after the ICF was signed. Inclusion/Exclusion criteria were verified. MMSE, GDS, and computerized CANTAB testing were performed on the same day, before the AD patients took their first dose of prescription medication. Control group participants were recruited from volunteers with no medical or familial history of AD or other dementia. Volunteers could not be working at or related to the Santariskiu hospital or Vilnius university in any other way.

Approval by Ethics Committee

The study Protocol and Informed Consent Form were approved by the Vilnius Regional Biomedical Research Ethics Committee. Written Informed consent has been obtained from all participants.

Inclusion and exclusion criteria

Strict and detailed inclusion and exclusion criteria were applied for enrollment in the study with the intent to exclude any other dementia, except Alzheimer's disease, to avoid significant vascular comorbidity or severe depression, or any other medical condition, which could confound the participant groups.

Inclusion criteria for Alzheimer's disease patients were:

1. The patient has late-onset sporadic probable Alzheimer's disease, diagnosed according to the National Institute of Neurological and Communicative Disorders and Stroke and the Alzheimer's Disease and Related Disorders Association (NINCDS-ADRDA) criteria;
2. The patient has mild dementia, defined as Mini-Mental State Examination (MMSE) score of at least 20;
3. The patient has newly diagnosed Alzheimer's disease;
4. The patient is treatment-naïve and the patient has never been treated with Cholinesterase inhibitors or/and Memantine;
5. The patient had CT or/and MRI performed at the time when Alzheimer's disease was diagnosed for the first time. The results of the CT or/and MRI should be consistent with the diagnosis of probable Alzheimer's disease and without evidence of significant vascular disease;
6. The patient is aged at least 65 years;
7. Hachinski Ischemic Index is 4 or less;
8. 30-item Geriatric Depression Scale (GDS) score is 19 or less;

9. Education level is 8 years or more;
10. The patient's sight, hearing, and movement functions should be sufficient for compliance with the study procedures.

Exclusion criteria for Alzheimer's disease patients were:

1. The patient is receiving or has taken within 6 months prior to the assessment any cognitive-enhancing medication;
2. The patient has any kind of evidence of any neurodegenerative disease or any other disease, which could be associated with cognitive decline, or any signs or symptoms of other significant neurological disorders other than Alzheimer's disease;
3. The patient has a DSM-IV-TR Axis I disorder other than Alzheimer's disease, including delirium, schizophrenia, schizoaffective disorder, psychosis, bipolar disorder, and major depressive episode;
4. The patient has evidence of clinically significant comorbidities, including but not limited to pulmonary, cardiovascular, gastrointestinal, hepatic, renal, endocrine disease, or vitamin B₁₂ deficiency;
5. Current or past alcohol or drug abuse.

Inclusion criteria for Control group participants were:

1. Normal cognitive functioning (MMSE score 27–30);
2. The participant is aged at least 65 years;
3. Hachinski Ischemic Index is 4 or less;
4. 30-item Geriatric Depression Scale (GDS) score is 19 or less;
5. Education level is 8 years or more;
6. The patient's sight, hearing, and movement functions should be sufficient for the compliance with the study procedures.

Exclusion criteria for Control group participants were the same as for Alzheimer's disease patients.

Neuropsychological assessment instruments

The global cognitive performance of the study participants was assessed by means of the Mini-Mental State Examination (MMSE). Cambridge Neuropsychological Test Automated Battery (CANTAB®, Cambridge Cognition Ltd., United Kingdom) was used for more comprehensive, detailed, and sensitive assessment of cognitive performance.

After an initial explanation and training provided by some tests, the subjects were given the following tests in the same order for all participants:

1. Choice reaction time (CRT): a test for 2 stimuli discrimination, attention, and psychomotor speed;
2. Stockings of Cambridge (SOC): The task is similar to the Tower of London test and evaluates many different aspects of the study participant's problem solving ability. SOC is mainly a test of frontal-executive functions. Testing

Table 1. Demographic and clinical characteristics in participant groups.

	AD group	CG group	t-value	p
Number of subjects, N	50	25	–	–
Age (years), Mean \pm SD	76.9 \pm 5.20	76.8 \pm 6.61	0.071	0.94* ns
Education (years), Mean \pm SD	13.4 \pm 4.57	13.2 \pm 3.37	0.194	0.85* ns
Gender, Women/Men, N	25/25	15/10	Chi-square=0.67	0.41** ns
MMSE score, Mean \pm SD	21.9 \pm 1.16	29.5 \pm 0.50	31.3	<0.001*
Depression (GDS score), Mean \pm SD	7.00 \pm 4.48	6.92 \pm 4.47	0.073	0.94* ns

* t-test; ** Chi square test; ns – not significant.

software records and provides multiple measures of performance (performance-type measures) and time (time-type measures);

3. Paired associate learning (PAL): The PAL test is for the assessment of visuospatial associative learning and episodic recall memory;
4. Spatial working memory (SWM): SWM test evaluates the participant's spatial working memory.

Statistical analysis

Normal distribution of data was verified using the Shapiro-Wilk test. Levene test was used to assess the homogeneity of variances in participant groups. Comparisons between groups for continuous variables were performed using parametric *t* test or nonparametric Mann-Whitney U test, as appropriate. The chi-square test was used to compare frequencies of categorical variables. Correlation of CANTAB test measures was evaluated by using parametric Pearson *r* or nonparametric Spearman rank *R*, as appropriate. Statistical significance value was accepted at $p < 0.05$.

Results

Demographic characteristics, depression level, and overall cognitive function

AD patients and controls did not differ according to age ($p=0.94$), duration of education ($p=0.85$), or gender ($p=0.41$). Demographic characteristics, depression level by 30-GDS, and MMSE scores for both participant groups are presented in Table 1.

The Stockings of Cambridge (SOC) test results in Alzheimer's disease and Control groups are provided in Table 2. The results of SOC performance-type measures and time-type measures are presented separately for the sake of clarity. Nonparametric Mann-Whitney U test was used to compare AD and CG groups

due to violation of normal distribution or heterogeneity of variances in some SOC test measures.

As nonparametric Mann-Whitney U test was used, rank sums and statistical significance indicators, which have been shown in the Table 2, do not provide the possibility to match the metric differences between AD and CG groups and do not provide a possibility to appreciate the stark disparity between group differences in performance-type and time-type SOC measures. The descriptive statistics of untransformed raw scores of the main performance-type indicator – “Mean moves” and the main time-type indicator “Mean Subsequent Thinking Time” have been presented in metric form accordingly in Figures 1 and 2. Means and 95% Confidence Intervals of Stockings of Cambridge (SOC) test performance-type measure “Mean Moves” in AD and Control groups in tasks of different difficulty are provided in Figure 1. Means and 95% Confidence Intervals of Stockings of Cambridge (SOC) test time-type measure “Mean Subsequent Thinking Time” in AD and Control groups in tasks of different difficulty are provided in Figure 2. While “performance-type” Stockings of Cambridge (SOC) test results differ significantly only for tasks, which can be solved in minimum 3 moves, “time-type” SOC test measures of AD and Control groups demonstrate a very significant difference in all tasks of different difficulty (minimum 2, 3, 4, 5 moves), which is especially apparent when comparing unranked metric results of both types in Figures 1 and 2.

Correlation analysis between the scores of frontal-executive function tasks (SOC test measures) and episodic recall memory (PAL test measures) and working memory (SWM test main measure) was performed for AD participants. We found very few significant correlations between Stockings of Cambridge (SOC) test measures and episodic recall memory, evaluated by means of Paired associate learning (PAL) test results, and working memory, evaluated by Spatial working memory (SWM) test results in mild Alzheimer's disease patients. And even significant correlations were very weak; none were more than 0.4. Spearman Rank Order Correlations *R* are provided in Table 3.

Table 2. Comparison of performance-type and time-type measures of Stockings of Cambridge (SOC) test in AD and control groups*.

Type of measure	Minimum number of moves needed to solve the problem	SOC Test Measure	Rank Sum AD group	Rank Sum CG group	U	Z adjusted	p	
Performance	2	SOC Mean moves (2 moves minimum)	2000.5	849.5	524.5	1.82	0.067 ns	
		SOC Problems solved in minimum moves (2 moves)	1799.5	1050.5	524.5	-1.83	0.067 ns	
	3	SOC Mean moves (3 moves minimum)	2227.0	623.0	298.0	4.06	<0.001	
		SOC Problems solved in minimum moves (3 moves)	1592.5	1257.5	317.5	-3.92	<0.001	
	4	SOC Mean moves (4 moves minimum)	2018.0	832.0	507.0	1.33	0.183 ns	
		SOC Problems solved in minimum moves (4 moves)	1855.5	994.5	580.5	-0.51	0.605 ns	
	5	SOC Mean moves (5 moves minimum)	2023.5	826.5	501.5	1.38	0.165 ns	
		SOC Problems solved in minimum moves (2 moves)	1775.0	1075.0	500.0	-1.44	0.148 ns	
	Time	2	SOC Mean initial thinking time (2 moves)	2129.0	721.0	396.0	2.57	0.010
			SOC Mean subsequent thinking time (2 moves)	2074.5	775.5	450.5	1.98	0.047
3		SOC Mean initial thinking time (3 moves)	2240.5	609.5	284.5	3.82	<0.001	
		SOC Mean subsequent thinking time (3 moves)	2225.5	624.5	299.5	3.66	<0.001	
4		SOC Mean initial thinking time (4 moves)	2183.0	667.0	342.0	3.17	0.001	
		SOC Mean subsequent thinking time (4 moves)	2406.0	444.0	119.0	5.68	<0.001	
5		SOC Mean initial thinking time (5 moves)	2408.0	442.0	117.0	5.70	<0.001	
		SOC Mean subsequent thinking time (5 moves)	2454.0	396.0	71.0	6.22	<0.001	

* Mann-Whitney U Test; ns – not significant.

Correlation analysis between the scores of frontal-executive function tasks (SOC test “time-type” measures) and attention/psychomotor speed (CRT test measures) was also performed. This correlation analysis also showed very few significant correlations between Stockings of Cambridge (SOC) test measures and attention/psychomotor speed, evaluated by means of Choice reaction time (CRT) test results in mild Alzheimer’s disease patients. In this correlation analysis, significant correlations were also very weak; – none were more than 0.4. Spearman Rank Order Correlations R are provided in Table 4. Only SOC test measures of “time-type” were included in this correlation analysis, seeking to compare the

so-called AD patients’ cognitive slowness in simple (CRT) and complex (SOC) tasks.

Discussion

The Stockings of Cambridge (SOC) test assesses various aspects of complex executive functions, such as spatial planning, thinking, and problem solving ability [26]. The Paired Associates Learning (PAL) test assesses visual episodic recall memory and new learning and is very sensitive to medial temporal lobe dysfunction [26]. The Spatial Working Memory (SWM) test is

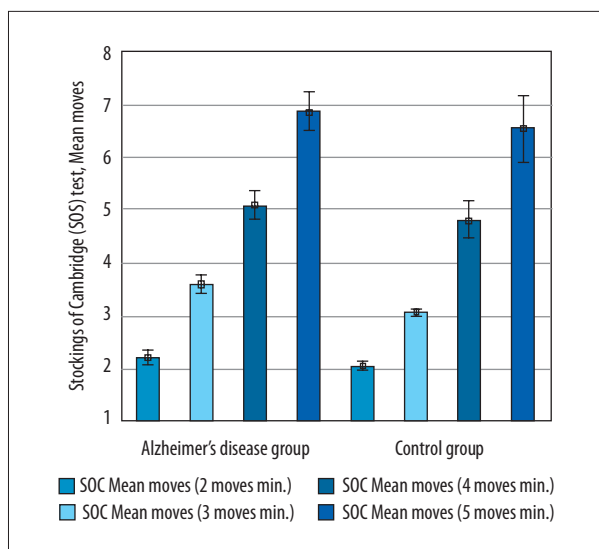


Figure 1. Means and 95% Confidence Intervals of Stockings of Cambridge (SOC) test performance-type measure Mean moves in AD and control groups.

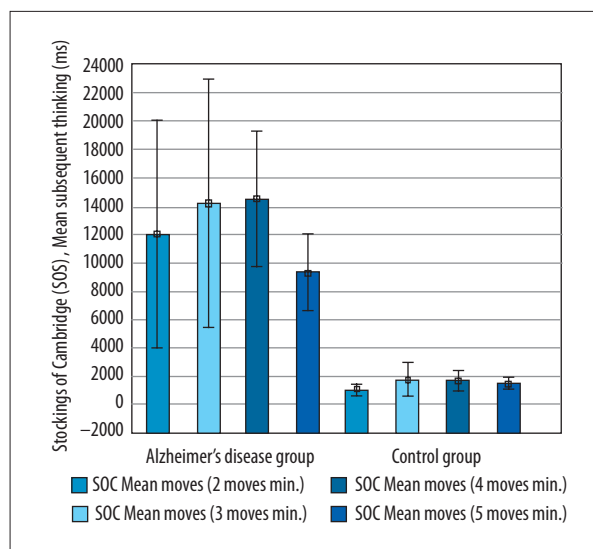


Figure 2. Means and 95% Confidence Intervals of Stockings of Cambridge (SOC) test time-type measure mean subsequent thinking time in AD and control groups.

an instrument for assessment of working memory [26]. The Choice Reaction Time (CRT) test measures speed and errors of response in a simple 2-choice paradigm and is used to assess attention and psychomotor speed [26].

Our results are in line with other reports supporting early frontal-executive dysfunction in Alzheimer's disease patients [27,28]. Some other reports, which used CANTAB, did not show a difference between AD and normal controls in the performance of the SOC test [29]. Still other authors contend that executive dysfunction may be an early feature in a subgroup of patients with mild Alzheimer's disease [30]. These reports may seem contradictory, but the tests and measures used by their authors were very different. Also, the severity of Alzheimer's dementia varied significantly in different studies. Binetti et al. used the Wisconsin card sorting test, the Stroop test, and other traditional tests to assess frontal-executive dysfunction [30]. Swanberg et al. found executive dysfunction in AD patients by using letter cancellation and maze tests, but AD patients with executive dysfunction had mean MMSE=17.2 (moderate dementia), while another group of AD patients with MMSE=21.4 (mild dementia) were classified as AD patients with normal executive function [24].

Based on our results, we are able to argue that executive dysfunction is present in mild AD, whether executive impairment is noticed during testing depends on the nature of employed tests, measures, complexity of tasks, and time limitations of the tests.

Mild AD patients appear to be able to achieve almost normal performance in not very complex frontal tests, due to the

allocation of much more extensive processing resources and if allowed to use tests for much longer time periods, and this supposition agrees with Buckner [31]. Our results showed that when performing frontal function tests of the same complexity, AD patients need much more time compared with the Control group, probably due to the difficulties in information integration in wide-spread cortical networks required by these tasks [32]. Another explanation of the disparity between the results of performance-type and time-type measures in executive tasks could be the concept of cognitive reserve and available information processing resources [33]. Even much smaller information processing resources in AD may lead to final results comparable to CG, if enough time is assigned for patients to solve the problems presented in cognitive tests.

Our results have shown that executive impairment is not significantly related with or dependent on episodic and working memory disorders, which again is in accordance with some previous observations [14,30] but contradict others [19]. What we observed could also be attributed to the so-called phenomenon of cognitive slowing in AD [33], but in our study the cognitive slowing was evident only in tasks sufficiently demanding to require significantly more brain operational resources than needed for very simple tasks like choice reaction time (CRT). Therefore, the cognitive slowing in mild AD cannot be observed in the simple tasks of psychomotor speed. On the contrary, very significant cognitive slowing was observed in complex problem-solving tasks like the SOC, which may explain why we did not find high or even medium correlations between CRT test results and time-type measures in SOC in Alzheimer's disease patients. The very term "cognitive slowing" seems to be ambiguous and complex. At least 2 different

Table 3. Spearman Rank Order Correlations R between Stockings of Cambridge (SOC) test measures and episodic recall memory, evaluated by means of Paired associate learning (PAL) test, and working memory, evaluated by – Spatial working memory (SWM) test in mild AD patients.

Test and it's measure	PAL Mean errors to success (N)	PAL Mean trials to success (N)	PAL Stages completed (N)	PAL Total errors adjusted (N)	PAL Total trials adjusted (N)	SWM Total errors (N)
SOC Mean initial thinking time (2 moves)	0.105	0.059	0.072	-0.025	-0.006	0.089
SOC Mean moves (2 moves minimum)	0.136	0.104	0.023	-0.007	0.064	0.086
SOC Mean subsequent thinking time (2 moves)	0.026	-0.091	0.072	-0.136	-0.159	0.275
SOC Problems solved in minimum moves (2 moves)	-0.145	-0.085	-0.023	0.001	-0.050	-0.065
SOC Mean initial thinking time (3 moves)	0.227	0.137	0.109	-0.077	-0.097	0.165
SOC Mean moves (3 moves minimum)	-0.129	-0.041	-0.387*	0.326*	0.240	0.057
SOC Mean subsequent thinking time (3 moves)	0.012	0.044	0.027	-0.034	-0.015	0.281*
SOC Problems solved in minimum moves (3 moves)	0.236	0.135	0.343*	-0.251	-0.145	-0.021
SOC Mean initial thinking time (4 moves)	0.347*	0.233	0.097	0.021	0.101	0.024
SOC Mean moves (4 moves minimum)	-0.231	-0.029	-0.120	0.047	0.113	0.059
SOC Mean subsequent thinking time (4 moves)	0.244	0.231	-0.010	0.014	0.096	0.377*
SOC Problems solved in minimum moves (4 moves)	0.141	0.023	0.121	-0.086	-0.071	-0.075
SOC Mean initial thinking time (5 moves)	0.026	0.053	-0.012	-0.010	-0.046	-0.042
SOC Mean moves (5 moves minimum)	-0.142	0.089	-0.188	0.130	0.179	-0.038
SOC Mean subsequent thinking time (5 moves)	0.088	0.258	0.038	-0.101	0.106	0.278
SOC Problems solved in minimum moves (5 moves)	0.140	-0.027	0.304*	-0.253	-0.239	0.157

* Statistically significant.

kinds of cognitive slowing may be identified based on the results of our study: cognitive slowing in simple tasks, which may be associated with the psychomotor slowing, and cognitive slowing in complex problem solving tasks, which may be related to the significantly reduced brain information processing resources.

When the complexity of the tests or level of dementia reaches the limit at which allocation of larger processing resources cannot compensate for the disintegration of information processing networks, then even performance-type measures are worse in AD than in normal controls, as was found by previous research with the Stroop test, Raven progressive matrices, and some other tests [14,30]. The inability to compensate for

Table 4. Spearman Rank Order Correlations R between Stockings of Cambridge (SOC) test “time-type” measures and attention/psychomotor speed, evaluated by means of Choice reaction time (CRT) test in mild Alzheimer’s disease patients.

Test and it’s measure	CRT Mean correct latency (ms)	CRT Median correct latency (ms)	CRT Total correct trials (N)	CRT Total incorrect trials (N)
SOC Mean initial thinking time (2 moves)	0.279*	0.307*	0.123	-0.129
SOC Mean subsequent thinking time (2 moves)	0.046	0.064	-0.021	0.026
SOC Mean initial thinking time (3 moves)	0.057	0.085	0.242	-0.254
SOC Mean subsequent thinking time (3 moves)	0.159	0.156	-0.108	0.062
SOC Mean initial thinking time (4 moves)	0.187	0.227	-0.013	0.018
SOC Mean subsequent thinking time (4 moves)	0.362*	0.344*	0.028	-0.023
SOC Mean initial thinking time (5 moves)	0.311*	0.375*	0.107	-0.116
SOC Mean subsequent thinking time (5 moves)	0.166	0.149	0.052	-0.061

* Statistically significant.

near-to-normal frontal-executive performance most probably occurs in moderate or mild-to-moderate stages of typical amnesic late-onset Alzheimer’s disease, although there is some evidence that a quite similar pattern of performance-type SOC measures is found in mild-to-moderate AD [34]. In addition, various non-AD factors may influence the cognitive phenotype of AD. Concomitant vascular factors may have a significant impact on cognitive phenotype of AD [35]. Depression, age, education level, and gender are all demographic and clinical factors associated with specific features of cognitive disorders and response to treatment [36]. Vice versa, symptomatic treatment for AD itself may not only produce the modified phenotype of cognitive disorders, but also can cause an atypical pattern of electrophysiological responses in Alzheimer’s disease [37]. Regardless of various kinds of obstacles, studies of executive dysfunction in AD are worth the effort, because earlier detection of dysexecutive syndrome in AD can improve the potential benefit of treatment, reduce the burden on caregivers and residential care services, and provide better quality of life for AD patients [38]. An appropriate evaluation and categorization of executive dysfunction, when employed together with the longitudinal assessment of the intellectual, physical, and social level of activity, may be useful in determining the prognosis for the future course of mild cognitive impairment (MCI) [39]. Deeper understanding of executive dysfunction may provide new insights in closely interconnected problems of neurodegenerative non-fluent aphasia [40], and elucidate the close interdependence of executive function, activities of daily living, and emotion [41].

It should be noted that our study has some limitations. Executive functions are a very wide set of quite different cognitive processes, and more extensive testing with inclusion of more tests is needed to determine when impairment of different executive functions appears in Alzheimer’s disease patients. The problem is that extensive testing requires a lot of effort from the AD patient. The very large battery may provide results in which some effects may occur simply due to tiredness or unwillingness of the AD patient to proceed with testing. Ideally, the research should not be limited to typical amnesic AD in order to provide the data regarding different subtypes of highly heterogeneous Alzheimer’s disease. Such endeavors would require a much larger number of participants, as subtypes of atypical AD are much rarer than typical amnesic late-onset AD.

Conclusions

Executive functions are impaired in mild AD patients. Executive impairment is much more pronounced in time-type measures than in performance-type measures. Executive disorders are not correlated with a decline in episodic and working memory in mild AD. Cognitive slowing in complex tasks is not correlated with simple cognitive slowing of psychomotor reactions.

Conflict of interest

The authors declare they have no conflicts of interest.

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