WORKING MEMORY FUNCTIONS AT PRESTROKE STAGE OF CADASIL

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Abstract

Cerebral Autosomal Dominant Arteriopathy with Subcortical Infarcts and Leucoencephalopathy (CADASIL) is a severe disease of midadulthood leading to variable neurological symptoms and dementia. The onset of the cognitive decline in CADASIL remains unresolved, and there is considerable debate concerning the presence of cognitive defects at prestroke stage of CADASIL. To address this issue, we examined the performance of clinically asymptomatic CADASIL patients on tests of working memory. Seven asymptomatic genetically confirmed CADASIL-gene carriers and seven matched controls were administered a battery of neuropsychological tests and computerized working memory (n-back) tests. On the standardized neuropsychological tests, CADASIL patients' performance was significantly impaired on measures reflecting the speed of processing (timed verbal fluency). On the computerized working memory tasks requiring memory for visual shapes, letters, or locations, the CADASIL group showed increased response times and decreased performance accuracy. Specifically, both the accuracy of performance and the response times of the CADASIL group were significantly impaired in the letter task compared to the controls; in all other n-back tasks the CADASIL group's test results showed a nonsignificant impairment trend. The CADASIL patients' performances, however, were not disproportionally deteriorated compared to the control group as the mnemonic load increased. The results of the present study suggest that cognitive slowing might be an early manifestation of incipient CADASIL and detectable cognitive decline can be assessed already at the prestroke stage of the disease.

Key words: CADASIL, vascular dementia, neuropsychology, n-back task, working memory

Introduction

Cerebral Autosomal Dominant Arteriopathy with Subcortical Infarcts and Leucoencephalopathy (CADASIL) is an adult-onset systemic small artery disease clinically confined to the central nervous system and it is the most frequent form of hereditary ischaemic stroke (Bousser & Tournier-Lasserve, 2001). CADASIL is an autosomal dominant form of cerebral arteriopathy and it has shown to map to chromosome 19 (Tournier-Lasserve et al., 1993). More recently, mutations of the Notch3 gene have been found responsible for the disease (Joutel et al., 1996). Along the inherited form of the disease, de novo mutation in the Notch3 gene has been identified to cause sporadic cases of CADASIL (Joutel et al., 2000). Since 1993, CADASIL has been observed in European, American, African, and Asian pedigrees (Davous, 1998). Up to day, over 400 families have been identified carrying the gene suggesting that CADASIL is not a rare disease and its prevalence might have been underestimated (Bousser & Tournier-Lasserve, 2001).

The core clinical features of CADASIL include recurrent ischaemic episodes (transient or complete), migraine with or without aura, psychiatric symptoms comprising of mood disorders, cognitive deficits and/or dementia, and epileptic seizures (Bousser & Tournier-Lasserve, 2001; Desmond, 1999). In the natural history of CADASIL, transient ischaemic attacks and/or strokes begin at about 50 years of age leading to diffuse cognitive deterioration within 10-20 years (Chabriat et al., 1995; Trojano, Ragno, Manca, & Caruso, 1998). Although CADASIL is a systemic vasculopathy, its effects are only manifested in the brain (Harris & Filley, 2001) and it has been estimated that more than 80% of the patients over 65 years of age are demented (Dichgans et al., 1998). One hallmark of the condition is the presence of magnetic resonance imaging (MRI) signal abnormalities in both symptomatic and asymptomatic patients (Bousser & Tournier-Lasserve, 2001). White matter abnormalities in MRI can be found a decade before the symptoms appear

(Desmond, 1999). A typical pattern of cerebral lesion distribution has been found: the frontal lobe is the site with the highest lesion load indicated by hyperintensities in periventricular white matter. The temporal lobe and the insula are also typically affected areas. Less frequently, deep white matter lesions are seen in the basal ganglia and brainstem (Chabriat et al., 1998; Yousry et al., 1999). Previous studies suggest that the severity of the basal ganglia involvement might be one of the most relevant factors for the occurrence of dementia in CADASIL (Taillia et al., 1998; Mellies et al., 1998).

The cognitive deficits associated with CADASIL have been found to resemble those with white matter dementia (Harris & Filley, 2001; Filley et al., 1999) or subcortical dementia (Davous, 1998). Neuropsychological evaluations of the symptomatic non-demented CADASIL patients have revealed deficits in several different types of tasks. These include impaired attentional processes, cognitive slowing, impaired learning, reduced fluency, and increased perseveration (Taillia et al., 1998; Filley et al., 1999). The onset of the cognitive decline in CADASIL, however, remains unknown (Taillia et al., 1998), and there is considerable debate concerning the presence of cognitive defects at the prestroke stage of CADASIL. Trojano and coworkers (1998) did not find any significant differences in cognitive performance between asymptomatic subjects and normal controls. In their study, the cognitive performance of the asymptomatic subjects did not deteriorate either during a two-year follow-up (Trojano et al., 1998). In a recent study, however, Dichgans and coworkers (1999) found a significant negative correlation between MRI total lesion volume and overall cognitive performance (Mini-Mental State Examination) in CADASIL. Yet, there is also evidence that cognitive impairment in CADASIL can appear in the absence of any major vascular event (Mellies et al., 1998; Taillia et al., 1998) and some studies (Amberla, Mononen, Repo & Viitanen, 1998a; Amberla et al., 1998b; Taillia et al., 1998) suggest that patients with CADASIL may develop cognitive dysfunctions early in the disease, probably long before the neurological

signs emerge. Even though the rate of cognitive decline in CADASIL still remains unknown it is agreed that the cognitive decline is a progressive process precipitated and/or worsened by recurrent strokes (Trojano et al., 1988; Taillia et al., 1998).

In the present study, we were interested in investigating the working memory functions in asymptomatic CADASIL patients. As noted above, the frontal lobes are known to be the most affected areas in CADASIL (Yousry et al., 1999). The involvement of frontal brain areas has also been heavily implicated in the context of working memory functions both in non-human primates (Goldman-Rakic, 1987; Funahashi & Kubota, 1994; Levy & Goldman- Rakic, 2000) as well as in humans (Braver et al., 1997; Nyström et al., 2000; Smith & Jonides, 1999; Tranel & Damasio, 1995). In brief, the working memory has been conceptualized as a temporary storage where task-relevant information is maintained and manipulated (Baddeley, 1986). The concept of working memory has some overlap with short-term memory as they both refer to a transient type of memory processing with limited capacity (Tranel & Damasio, 1995). There is evidence that the working memory functions are compromised by frontal lobe dysfunction (Fletcher & Henson, 2001; Smith & Jonides, 1999; Stuss & Levine, 2002).

So far, a study by Trojano et al. (1998), to the authors' knowledge, is the only study where spesific short-term memory functions have been assessed in CADASIL patients. Trojano and coworkers used standardized memory span tests to assess both verbal and visual short-term memory in asymptomatic CADASIL patients. The study revealed no differences between asymptomatic CADASIL patients and controls in their short-term memory functions. It was suggested that the traditional neuropsychological tests may not detect mild cognitive defects associated with frontal lobe dysfunction in asymptomatic/preclinical CADASIL patients (Trojano et al., 1998). Particularly, the span tasks may not be useful when assessing the frontal lobe

functions. Based on a comprehensive literature review, D'Esposito and Postle (1999) argued that a simple forward verbal and spatial span performance is not dependent on frontal lobe integrity. According to their study, the span tasks can be useful when assessing working memory storage capacity, but these tasks do not provide information relating to rehearsal or executive control functions of the working memory.

Because the present study was targeted to asymptomatic patients, we anticipated that the standard neuropsychological test batteries might not be sensitive enough to reveal possible and supposedly subtle working memory dysfunctions. Recent functional neuroimaging studies indicate that a sequential stimulus task type, e.g., an n-back task, is particularly sensitive in revealing working memory related brain activation (Braver et al., 1997; Carlson et al., 1998; Fletcher & Henson, 2001; Nyström et al., 2000; Smith, Jonides, & Koeppe, 1996). Therefore, in this study, we measured working memory performance in CADASIL patients and matched control subjects using both standardized neuropsychological tests and computerized n-back tasks. We employed an n-back paradigm which has been used previously in a number of experiments studying working memory (Braver et al., 1997; Carlson et al., 1998; Nyström et al., 2000; Smith et al., 1996; Vuontela, Rämä, Raninen, Aronen, & Carlson, 1999). Three different tasks tapping on memory for visual shapes, letters, and locations were delivered in order to test the possible effect of information type on working memory functions. It was expected that there might be differences between the groups in the performance of the n-back tasks while performance differences in the standardized tests might be absent. No specific hypotheses were set regarding the effect of information type on possible working memory deterioration in CADASIL patients.

Materials and methods

Subjects

The subjects were seven (7) asymptomatic genetically confirmed CADASIL-gene carriers (3 females). The inclusion criteria were as follows: demonstration of a pathogenic mutation within the Notch3 gene (Tournier-Lasserve et al., 1993; Joutel et al., 1997), presence of white-matter changes in MRI (Skehan, Hutchinson, & MacErlaine, 1995; Dichgans et al., 1999) (MRI scans of the brain were obtained from 6 patients), absence of vascular dementia according to AIREN-NINDS criteria (Roman et al., 1993), absence of medically treated mood disorder according to DSM-IV criteria at the time of examination (absence of medication at least 12 months prior to examination) (American Psychiatric Association, 1994), absence of history of major stroke, normal neurological status at the time of examination, and no graded disability (grade 0 according to the Rankin scale) (Wade, 1998). History of migraine was not considered as an exclusion criterion. As normal controls, seven (7) sex, age, and education matched subjects were recruited. Mean age (CADASIL group 43.1 yrs vs. control group 41.4 yrs) and length of formal education (11.6 vs. 11.2 yrs) did not differ significantly between the two groups (t-tests). All subjects gave an informed consent for their participation. The study protocol was approved by the ethical committee of the Middle-Ostrobothnia Central Hospital. Neuropsychological assessment was performed by one of the authors (M.W., February 1999 to December 2000). All affected individuals had a neurological examination conducted by a neurologist (S.T.) before the neuropsychological assessment.

Neuropsychological assessment

Standardized neuropsychological tests. All subjects were tested with a battery of standardized neuropsychological tests chosen to assess such cognitive functions that are sensitive to frontal lobe dysfunction according to previous CADASIL studies (Taillia et al., 1998; Trojano et al., 1998). Digit span and visual memory span subtests from Wechsler Memory Scale -Revised (WMS-R; Wechsler, 1996) were used to assess short-term memory (raw score, range 0-24). Rey-Osterrieth Complex Figure Test (ROCFT; Rey, 1941) copy and immediate recall versions were used to assess visuoconstructive abilities and visual memory (raw score, range 0-36, and time to complete in seconds). Trail Making Test (TMT; Lezak, 1995) versions A and B were used to assess psychomotor speed and attentional functions (difference score [B-A] in seconds). Verbal fluency including both phonemic fluency (P\A\S) and semantic fluency (animals) was used to assess cognitive flexibility, verbal retrieval, and short-term memory (Lezak, 1995). Phonemic fluency score was the number of all acceptable words produced in three one-minute trials. Semantic fluency score was the number of all acceptable words produced in a one-minute trial. Wechsler Adult Intelligence Scale -Revised (Wechsler, 1992) similarities subtest was used to assess general verbal ability (raw score, range 0-34).

N-back tasks. The experiment included three versions of an n-back task. The tasks were otherwise similar except that the type of material to-be-remembered varied between the tasks. Each task was divided into three conditions that varied the mnemonic load incrementally (0-back, 1-back, 2-back).

Shape task: Six stimulus shapes were adopted from Wechsler Memory Scale -Revised visual paired associates subtest (Wechsler, 1996). The black-coloured stimuli were presented one at a time in one of sixteen (16) possible spatial locations around a centrally located fixation cross on a white

computer screen. The size of the stimuli was approximately 40 x 40 mm. In the 0-back task condition, the subjects were instructed to discriminate, independent of its location, whether or not a shape was a prespecified target shape. In the 1-back task condition, the target was any shape identical to the previous one (i.e., one trial back). In the 2-back task condition, the target was any shape that was identical to the one presented two trials back.

Letter task: The stimuli in the letter task were six black-coloured capital letters (A\B\C\H\M\T\, Chicago boldface 48 points; height 15 mm on the screen). The stimuli were presented one at the time in one of sixteen (16) possible spatial locations around the fixation cross on a computer screen. In the 0-back task condition, the subjects were instructed to discriminate, independent of its location, whether or not a letter was a prespecified target letter. In the 1-back task condition, the target was any letter identical to the previous one (i.e., one trial back). In the 2-back task condition, the target was any letter that was identical to the one presented two trials back.

Location task: In the location task, the stimuli were the same letters as in the letter task, i.e., six black-coloured capital letters, presented one at the time in one of sixteen (16) possible spatial locations around the fixation cross. The subjects responded on the basis of the location of the stimulus independent of the particular letter. In the 0-back task condition, the subjects were instructed to respond to a predetermined location. In the 1-back task condition, the subjects had to decide whether or not the location of each letter matched the location of the stimulus presented one trial back. In the 2-back task condition, the target was any letter that matched the location of the stimulus presented two trials back.

The stimulus presentation and data collection was controlled by a PsyScope software (Cohen, MacWhinney, Flatt, & Provost, 1993) running on a Macintosh Performa 5260 computer. The

subjects sat approximately 50 cm away from the screen and responded using a PsyScope button box. The button box had three response buttons; one central and two lateral buttons. The lateral buttons were labelled with Finnish words <SAMA> (same) and <ERI> (different). Half of the subjects had the left-right -order of the buttons reversed. Each task and each memory load condition commenced with instructions. Each trial began with a fixation cross exposed for 2500 ms. This indicated the subjects to press and hold down the central button until the stimulus occurred. After this, the stimulus was presented for 500 ms followed by the fixation point until the subject made his/her response. The next trial was not started before a response was made but began immediately after a response, whether correct or incorrect. All trials required the subjects to respond by pressing either one of the lateral buttons and return their finger immediately back on the central button after the response. The subjects were told that the accuracy and speed of response were of equal importance.

Each memory load condition had the same number of trials (20) of which 30% were match trials. In each task, the memory load conditions were presented twice in a reversed order (0-back-1-back- 2-back-2-back-1-back-0-back). Hence, the total number of trials for every subject was 360 (3 tasks x 3 memory load conditions x 2 repetitions x 20 trials). All the tasks had an identical structure except that the instructions and stimuli (letters vs. shapes) varied. The presentation order of the tasks was counterbalanced across the subjects. All the subjects were given a practise session which included trials from all three tasks with all memory load conditions. After practise trials, they were asked to come up with questions and were tested only after they had comprehended the rational of the tasks.

Data analysis

In the data analysis of the standardized neuropsychological tasks, Student's t-tests were used to compare the mean scores. In the n-back tasks, response times were measured from the stimulus onset to the press of the response button. Trials with incorrect responses were excluded from the data analysis. Following this, trials with response times shorter or longer than two standard deviations from the individual mean response time were also discarded from the data analysis. The proportion of correct responses (hits) were scored for each subject to characterize the accuracy of performance. Two-way analyses of variance (SPSS, split-plot design) were used to test the effects of group (CADASIL group and control group) and memory load (0-back, 1-back, and 2-back) on the response times and accuracy.

Results

Standardized neuropsychological tests

The results on the standardized neuropsychological tests are shown in Table 1. Out of the ten measures, significant between group differences were found on tasks of verbal fluency. CADASIL patients' performance was markedly impaired relative to controls on both semantic ($p < .05$) and phonemic ($p < .04$) tasks of verbal fluency. Yet, assessed by Similarities subtest of WAIS-R the CADASIL group and control group did not differ in terms of general verbal ability. There were no differences in performance accuracy between CADASIL and control groups in visuoconstructive functions. However, CADASIL patients' time to accomplish both the copy and recall version of the ROCFT was longer, yet the difference in performance times only approached statistical significance (ROCFT copy $p < .07$; ROCFT recall $p < .08$). This same tendency was present in the test of psychomotor speed (TMT B-A). Again, CADASIL patients were slower that the controls,

yet this difference was not statistically significant ($p < .12$). It is noteworthy, that the results did not show significant differences between the CADASIL and control group on standardized short-term memory tests.

Insert Table 1 here

N-back tasks

Shape task: The mean response times and accuracies of performance for the 0-back, 1- back, and 2-back memory load conditions in the shape task are illustrated in Figure 1. A two-way ANOVA revealed a significant effect of memory load on the response times, $F(2, 24) = 21.46$, $p < .001$, indicating that the reaction times lengthened when the mnemonic load increased. The CADASIL group was slower in all memory load conditions compared to the control group, yet the difference did not quite reach statistical significance, $F(1, 12) = 4.41$, $p < .06$. There was no interaction between group and memory load ($p > .1$). The performance accuracy was almost equal for both groups at the baseline level (0-back memory condition), and the accuracy deteriorated in the 2-back condition for both groups. There was no significant effect of memory load ($p < .9$) or group ($p > .1$) on the overall accuracy, nor interaction between the main effects ($p > .1$).

Insert Figure 1 here

Letter task: The mean response times for the 0-back, 1-back, and 2-back memory load conditions in the letter task are illustrated in Figure 2A. Again, both groups showed a linear

slowing of the response times with respect to mnemonic load. An ANOVA revealed a significant effect of memory load on the response times, $F(2, 24) = 14.73$, $p < .001$. In the letter task, the CADASIL group was also significantly slower than the control group, $F(1, 12) = 6.08$, $p < .03$. There was no interaction between group and memory load ($p > .1$). Memory load had a significant effect on the accuracy of performance, $F(2, 24) = 8.90$, $p < .001$ (Figure 2B). Compared to controls, CADASIL group's performance accuracy was also significantly inferior, $F(1, 12) = 11.23$, $p < .006$. There was no significant interaction between the main effects ($p > .1$).

Insert Figure 2 here

Location task: Like in the two tasks described above, the response times exhibited a linear relationship with respect to memory load (Figure 3A). There was a statistically significant effect of memory load on the response times, $F(2, 24) = 25.29$, $p < .001$. Although the CADASIL group was again slower than the control group, the effect of group ($p < .09$) or the interaction between the main effects ($p > .1$) were not statistically significant. In terms of the performance accuracy, there was a significant effect of memory load on the overall accuracy, $F(2, 24) = 5.70$, $p < .009$, but no main effect of group ($p > .1$) or interaction between the main effects ($p > .1$) (Figure 3B).

Insert Figure 3 here

Discussion

In this study, we compared the cognitive performance of seven asymptomatic CADASIL gene carriers to that of seven matched control subjects. Especially, we were interested in the working memory functions of the CADASIL patients related to that of the control group. Standardized neuropsychological tests were used to assess whether there was evidence for cognitive dysfunction at the prestroke stage of CADASIL. The working memory functions were assessed with computerized n-back tasks.

On the standardized neuropsychological tests, the CADASIL group showed a significant decline on those measures which reflect the speed of processing, i.e., on tasks measuring timed verbal fluency. This finding is in keeping with other reports in which subtle cognitive decline in non-demented CADASIL patients has been found (Amberla et al., 1998b; Taillia et al., 1998). The results did not show differences between the CADASIL and control group in standardized short term memory tests nor in any other cognitive domains assessed by standardized neuropsychological tests.

Importantly, however, the computerized working memory tasks revealed a clear tendency for performance impairment in CADASIL patients. This result was evident in both performance speed and performance accuracy measures. The CADASIL group was slower relative to the control group in all three tasks (shape, letter, and location), even though the difference was statistically significant only in the letter task. Working memory load had similar effects on the response times for both groups. The CADASIL patients were not disproportionally slowered compared to the control group as the mnemonic load increased. Also, the CADASIL patients' performance accuracy was inferior to that of the control group in all n-back tasks, even though this trend was not statistically

significant in shape and location tasks. In the letter task, however, the control group outperformed the CADASIL group.

It is now widely acknowledged that the prefrontal cortex (PFC) plays a critical role in the neural network subserving working memory (WM) functions. Much less agreement exists on the issue of segregation of WM functions within the frontal cortex. According to Goldman-Rakic (1987), PFC may be organized into modules which are devoted to specialized processing of sensory information. In some studies, support for such modality-spesific WM systems has been found offering tentative evidence for left-right lateralization of verbal versus nonverbal WM processes, respectively (Levy & Goldman-Rakic, 2000; Smith et al., 1996; Smith et al., 1995). Furthermore, it has been suggested that dorsal and ventral frontal areas are respectively involved in spatial and nonspatial WM functions (Goldman-Rakic, 1987). Nyström et al (2000), however, were unable to find convincing evidence to support either a left/right - verbal/nonverbal or a dorsal/ventral - spatial/nonspatial association in humans. According to their study, the same frontal cortical areas responded to increases in WM load despite the stimulus type (letters, shapes, locations). This result was interpreted to show that a single common WM system operates across all three stimulus types (Nyström et al., 2000). In our study, we also employed three different tasks in order to test the possible effect of information type on working memory functions. Interestingly, the CADASIL patients' performance was significantly impaired on verbal tasks both in the standardized (verbal fluency) and in the computerized neuropsychological tasks (letter task). It is tempting to interpret these results as an indication of a spesific, yet incipient, deficit in verbal working memory functions in asymptomatic CADASIL patients. Our findings are, however, preliminary and certainly need further support before such a conclusion can be made.

Even though we did not found a statistically significant difference between the CADASIL and control group's performance in all working memory tasks, the current findings suggested that the CADASIL patients were slightly impaired both in accuracy of performance and in response times. In particular, the letter task brought out the clearest, and also statistically significant, difference between the groups. Since it has been argued that working memory functions depend on intact frontal lobe structures (Lezak, 1995) it can be postulated that our test results point to an incipient frontal lobe dysfuncion already at the prestroke stage of CADASIL. The results suggest that prestroke CADASIL patients exhibit a global slowing of psycho-motor speed independent of the cognitive complexity of the task. Another possibility is, of course, that the CADASIL patients compensated their difficulties in the tests by slowing their processing rate, keeping their performance level high this way. This has also been suggested earlier in a study investigating patients with multiple sclerosis (MS) (Hämäläinen, Portin, Revonsuo, & Ruutiainen, 1995). In that study, it was found that those MS patients with mild cognitive impairment made more errors on easy tasks than the other subjects. On the other hand, on more complicated tasks, the MS patients compensated for their deficits by using slower processing rates. It should be noted that in the present study, the CADASIL patient's performance was inferior to that of the control subjects at all levels of task difficulty.

The development of cognitive defects in CADASIL has been related to the occurence of clinically relevant ischaemic episodes or to sensible variations in MRI findings (Trojano et al., 1998). All patients, in this study, were nondemented and asymptomatic. They had, however, diffuse white matter changes in MRI. The clinical significance of the white matter abnormalities seen in brain imaging studies still remains unresolved although some previous studies have demonstrated relationships between subcortical MRI abnormalities and cognitive functions (De Groot et al., 2000; Yousry et al., 1999). The relationship between MRI white matter lesions and

neuropsychological deficits in normal aging has also been controversial (Filley, 1998; Garde, Mortensen, Krabbe, Rostrup & Larsson, 2000). Our results are in accordance with previous studies demonstrating that diffuse white matter abnormalities are assosiated with slowing of information processing in tasks that involve complex processes (Junque et al., 1990). The results of our study suggest that a relationship exists between subcortical pathological changes and cognitive functions already at the prestroke stage of CADASIL. Our results demonstrate that a detectable cognitive decline can be assessed in asymptomatic patients with CADASIL and the cognitive slowing might be one indication of the incipient disease.

The prognosis of CADASIL remains poor. No therapeutic intervention has been succesful so far. Our findings are important in suggesting that it might be possible to detect the cognitive decline already at its early stages. Improved test sensitivity and specificity will be of importance also when measuring the effectiveness of the probable therapeutic interventions, in future. Prospective studies will be needed to clarify the deficits in verbal working memory and concurrent information processing in the natural history of the CADASIL disease. Developing a sensitive test for detecting subtle changes in cognitive functioning will have an important predictive, and thus subjective, value for each affected individual and will help in planning and organizing proper care and treatment for this condition.

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Table 1. Mean scores (mean) and standard deviations (SD) in the standardized neuropsychological tests. Statistical differences between the results of CADASIL and control groups were analyzed by Student's t-tests.

Neuropsychological Test	CADASIL n=7		CONTROL n=7			
	mean	SD	mean	SD	t	sig. (df=12)
WMS-R digit span	12	2.4	15	4.4	-1.50	n.s.
WMS-R visual span	16	2.7	17	3.7	-.91	n.s.
ROCFT copy/accuracy	33	1.9	34	1.9	-.57	n.s.
ROCFT copy/time (sec.)	176	57.5	128	27.8	2.01	.07
ROCFT recall/accuracy	19	6.1	20	3.9	-.29	n.s.
ROCFT recall/time (sec.)	148	63.9	99	24.1	1.90	.08
TMT B-A (sec.)	80	44.2	46	29.9	1.69	n.s.
WAIS-R similarities	27	3.8	26	3.7	.14	n.s.
Verbal fluency/phonemic	35	7.9	47	10.4	-2.38	.04
Verbal fluency/semantic	18	3.9	22	3.2	-2.21	.05

Abbr.

WMS-R = Wechsler Memory Scale - Revised, ROCFT = Rey-Osterrieth Complex Figure Test, TMT = Trail Making Test, WAIS-R = Wechsler Adult Intelligence Scale - Revised, sec. = seconds, n.s. = non significant ($p > .1$)

Figure legends

Fig. 1. The mean response times (A) and performance accuracy (B) for different memory loads in the visual task.

Fig. 2. The mean response times (A) and performance accuracy (B) for different memory loads in the verbal task.

Fig. 3. The mean response times (A) and performance accuracy (B) for different memory loads in the spatial task.

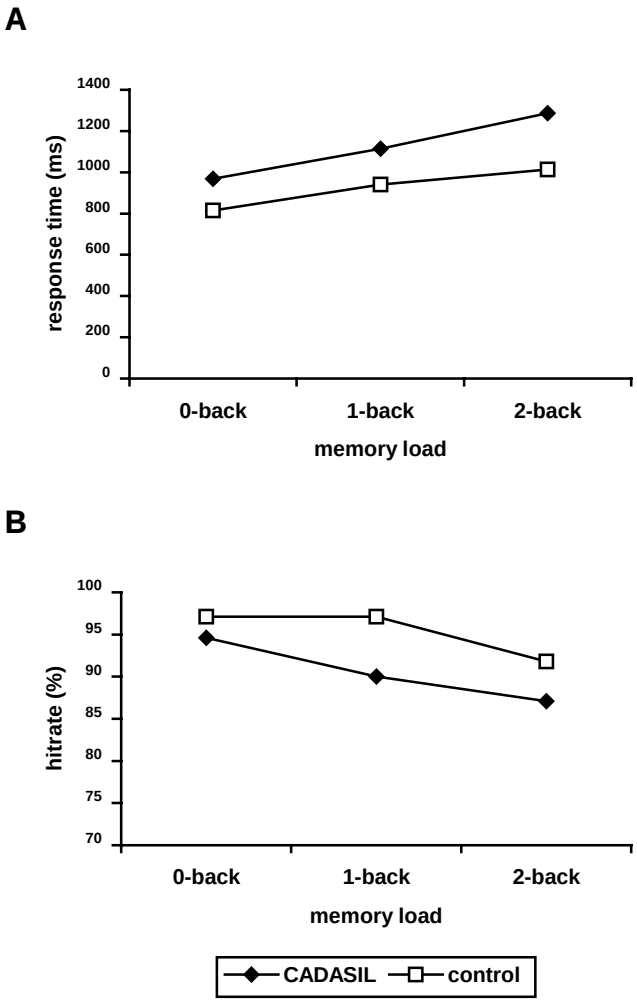

Figure 1. Wäljas et al.

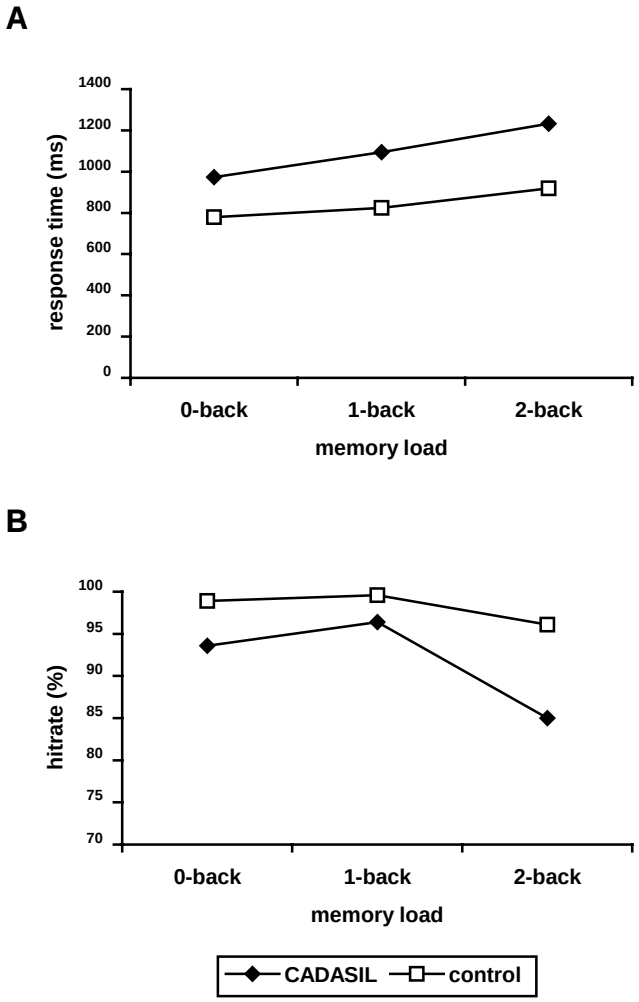

Figure 2. Wäljas et al.

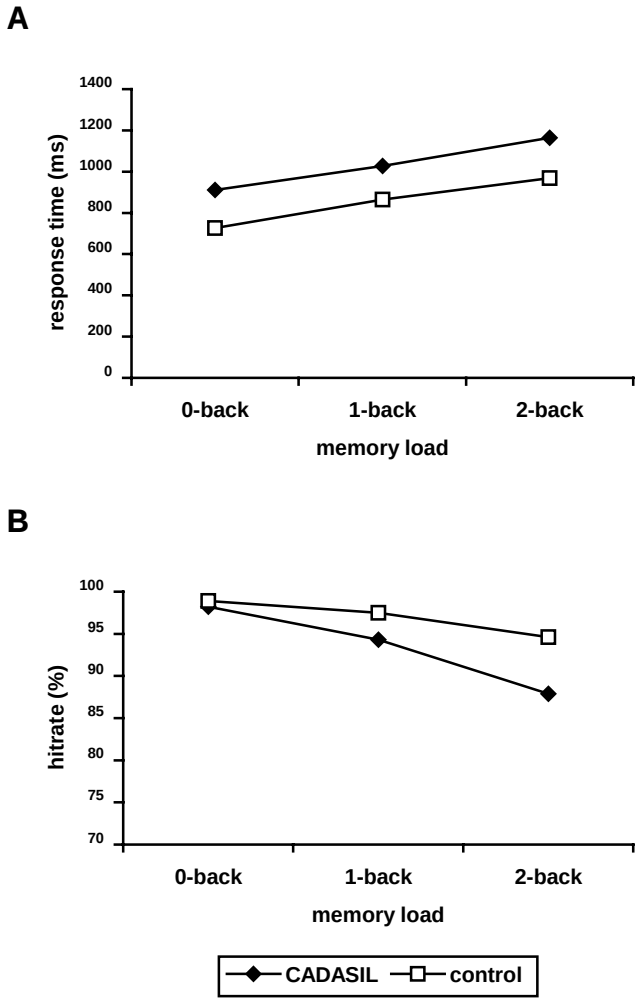

Figure 3. Wäljas et al.