MEMORY FOR SERIAL ORDER IN PATIENTS WITH FRONTAL LOBE LESIONS

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INTRODUCTION

In daily life it is often the case that when we have to remember a list of items, we can remember the items but not the order in which they occurred. In activities as language comprehension or cognitive reasoning, order is essential. Thus the phone number 212-962006 is not the same as 212-692600. Many models of frontal-lobe functioning propose that frontal cortex plays a critical role on memory for temporal order. The objective of the present study was to measure the ability of patients with frontal lesions on learning a fixed sequence of unrelated words according to a different rate of presentation and stimulus-modality, in a controlled set of administration.

DESIGN/METHODS

Subjects : 21 patients with frontal lobe lesions (8 left, 9 right, 4 bilateral) and 21 normal controls, matched for age and educational level (Table 1).

Table 1. Demographic profile

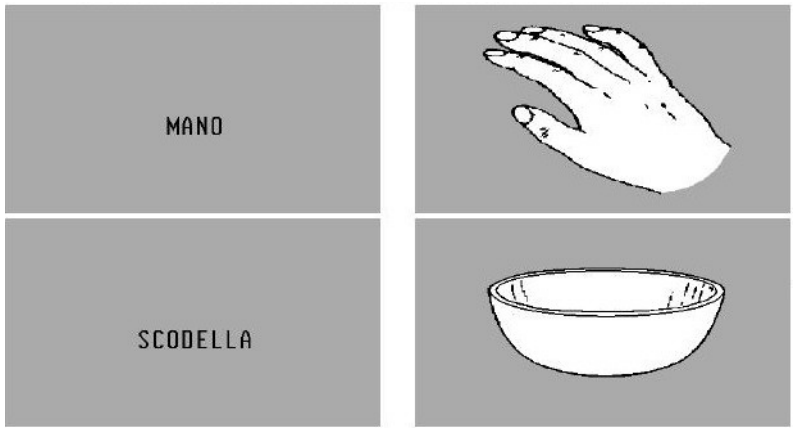
	CONTROLS		FRONTALS	
	Mean	SD	Mean	SD
AGE	49.0	16.2	49.7	17.1
EDUCATION	10.1	3.5	9.40	3.8
MMSE	30.0	0.0	28.2	2.1

All subjects underwent a standard neuropsychological investigation (with special emphasis to frontal tests)(Table 2).

Table 2. Neuropsychological battery

Variable	CONTROL		FRONTAL		
	MEAN	SD	MEAN	SD	P=
DIGIT forward	6.5	1.6	5.9	1.5	
DIGIT backward	5.0	1.6	3.7	1.1	0.003
CORSI	5.9	1.8	4.6	0.9	0.004
WCST Cat	6.9	0.7	4.7	1.7	0.000
WCST Err	4.4	2.9	13.6	7.5	0.000
LONDON	30.2	3.1	24.8	4.6	0.000
WAIS P.Arr	23.7	5.7	13.9	6.7	0.000

Experimental test for serial memory: it consists of seven unrelated, high-frequency words or equivalent drawings displayed for 200 msec on a video screen at a rate of one every 2 sec (normal rate of presentation) (NP) or every 5 sec (slow rate of presentation)(SP). Words and drawings were checked for complexity, familiarity, name and image agreement and frequency index for italian language (see figure 1 below).



Subjects were invited to verbally recall in 30 sec. as many words or pictures as possible in the same order they were presented, until the criterion or at the end of 12 trials. Intrusions and duplications were recorded. Four lists were presented in a balanced order, according to a latin square design.

Performance was evaluated through two levels of analysis: a) number of trials needed to learn the correct sequence and b) measures of separate indices as illustrated in Table 3.

Table 3. Storage and organizational measures

Index	
A:	number of correct elements recalled for each repetition independently of their order
B:	number of stimuli placed in the correct position
O3:	pairs of items recalled in the correct order
D:	distance between each pairs of stimuli recalled, matched to the original position of the list (relative deviation score)
ITR:	sum of pairs of correct items recalled in two sequential repetitions

Index A can be considered as a simple storage index, since the correct sequence of elements is not taken into account. **Indices B, O3** and **D** are considered by Vrieze & Moscovitch (1990) as temporal order index. The latter **(ITR)** reflects the observation that when a list is presented several times in the same order, items presented together across repetitions, are also recalled together.

RESULTS 1

REPETITIONS and STORAGE (index A)

Analyses were performed with ANOVA considering three factors: materials (words and drawings), rate of presentation (NP vs SP) and groups (control and frontal).
Number of repetitions for learning is greater for frontal patients ($F(1,27)=11.453$, $p=002$), material presented ($F(1,27)=7.672$, $p=.010$) and rate of presentation ($F(1,27)=55.149$, $p=000$). No interactions were found (Table 4).
For index A (number of correct elements reported) there were significant differences between groups ($F(1,40)=20.9$, $p=.000$), material presented ($F(1,40)=9.6$, $p=.004$) and rate of presentation ($F(1,40)=21.6$, $p=.000$). Moreover a significant interaction groups/materials emerged ($F(1,40)=7.5$, $p=.009$).

Table 4. Repetitions and Storage

	NORMAL RATE OF PRESENTATION				SLOW RATE OF PRESENTATION			
	CONTROLS		FRONTALS		CONTROLS		FRONTALS	
WORDS	MEAN	SD	MEAN	SD	MEAN	SD	MEAN	SD
Index A	1.0	0.0	0.8	0.1	1.0	0.0	0.9	0.1
REPETITIONS	3.5	1.9	6.2	3.2	1.8	1.4	4.5	2.9
Learners #	21		9		21		15	
DRAWINGS	MEAN	SD	MEAN	SD	MEAN	SD	MEAN	SD
Index A	1.0	0.0	0.9	0.1	1.0	0.0	0.9	0.1
REPETITIONS	2.7	1.2	5.0	2.5	1.2	0.8	3.6	2.5
Learners #	21		13		21		18	

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RESULTS 2

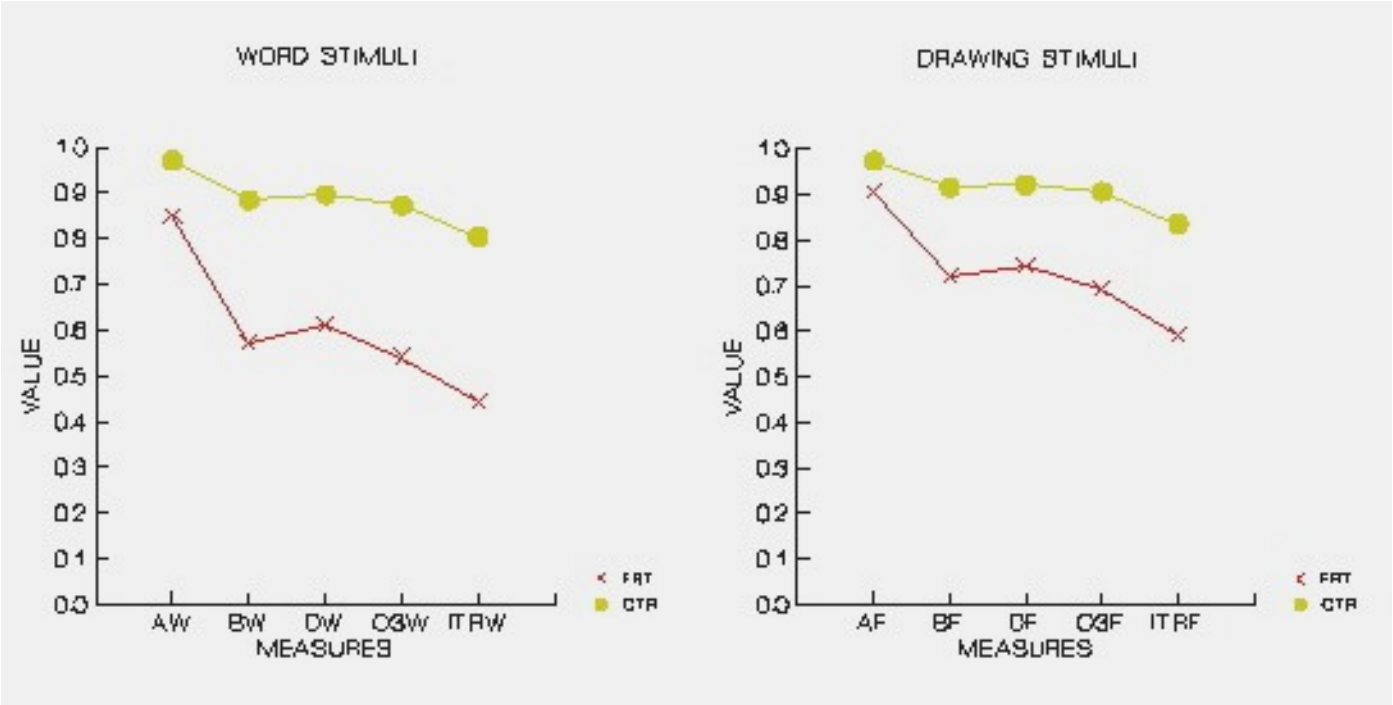
ORGANIZATION

These analyses were performed matching information storage and organisation. Since preliminary data revealed no interaction between rate of presentation and groups, data were averaged across the first factor (rate of presentation). See Table 5 and figure 2 for means and SD for each condition and group; significant differences ($p<.005$) are present across all measures.

Table 5 Storage and organization measures

	Controls		Frontals		Group Difference	General Means (Words and drawings)	
Words	Mean	SD	Mean	SD		Controls	Frontals
A	0.97	0.02	0.85	0.10	0.12	0.97	0.88
B	0.88	0.08	0.57	0.22	0.31	0.90	0.65
D	0.90	0.07	0.61	0.21	0.28	0.91	0.68
O3	0.87	0.09	0.54	0.24	0.33	0.89	0.62
ITR	0.80	0.10	0.44	0.24	0.36	0.82	0.52
Drawings	Mean	SD	Mean	SD			
A	0.97	0.02	0.91	0.10	0.07		
B	0.92	0.04	0.72	0.21	0.20		
D	0.92	0.04	0.74	0.20	0.18		
O3	0.91	0.05	0.69	0.22	0.21		
ITR	0.83	0.07	0.59	0.24	0.24		

Figure 2. Means for each condition and group



RESULTS 3

Distinct ANOVA has been made comparing the index A with other indices. All ANOVA showed group, materials and measure as main effect (p=.000), with two-way significant interactions (Table 6).

Table 6. Statistical results

	A vs B		A vs D		A vs O3		A vs ITR	
	F(1,40)	P=	F(1,40)	P=	F(1,40)	P=	F(1,40)	P=
Stimulus * group	8.89	0.005	7.94	0.000	7.81	0.008	7.59	0.009
Measure * group	31.80	0.000	29.49	0.000	32.32	0.000	34.04	0.000

Since groups are different for all measures considered, the two-way interaction seems to indicate that frontal patients are worse than control, mainly in their organisational recall. Our measures differ one from each other ($F(1,40)=180.575$, $p=0.000$), suggesting that they detect different aspects of memory.

CONCLUSIONS

1. The global storage deficit (index A) or the greater number of trials needed to learn a list of words shown by frontal patients, does not help elucidating the nature of their memory difficulties.
2. Frontal patients exhibited poor performance on the ability to retrieve the sequential order of information, not only when they have to recall the relationships among the stimuli (indices B, O3 and D), but also when the information following each repetition becomes crucial for learning (index ITR).
3. Frontal lobes are probably important in monitoring and coding the temporal appearance in time and place of events in working memory.
4. Both controls and frontal subjects increased their performance under slow presentation rate.
5. Future studies with non-frontal brain damage controls are in progress to demonstrate that this pattern was not a consequence of brain lesion alone or a general processing deficit.

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Lack of Visual Field Defects with Long-Term Use of Tiagabine

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OBJECTIVE: To evaluate visual field changes in patients on long-term treatment with tiagabine.

BACKGROUND: Vigabatrin, a GABAergic AED, has been found to be associated with visual field constricton with long-term use. This raised concern that tiagabine, also a GABAergic drug through a different mechanism, might produce similar changes.

DESIGN/METHODS: Patients were selected if they had received tiagabine for at least one year with no prior exposure to vigabatrin. Data were collected for age, gender, seizure frequency, concurrent and past antiepileptic drug (AED) therapy, duration of treatment with tiagabine, dose of tiagabine, and the presence of any visual symptoms. Patients were also questioned for any previous brain surgery, including surgery for epilepsy. Visual acuity was obtained prior to testing. Visual fields were tested with both the Goldman's and Humphrey's methods. Because of long travel distances, both tests had to be performed consecutively.

RESULTS: Eight patients (4 males, 4 females) with a mean age of 41 years were tested. All but one patient taking concurrent AEDs (3 carbamazepine, 3 phenytoin). The mean duration of tiagabine therapy was 43 months and the mean daily dose was 56 mg. The visual acuity was 20/20 OU in 6 patients and 20/30 in 1 patient. There were no unexpected visual field defects. Three patients who had temporal lobe resections for intractable epilepsy had contralateral superior quadrantinopsis. One patient, who had resection of a brain tumor in childhood and placement of a ventriculoperitoneal shunt, had contralaterial inferior quadrantinopsis. Four patients had slight nonspecific constrictions. All had further ophthalmologic evaluation which were normal, indicating that the noted changes were secondary to fatigue and inattention.

CONCLUSIONS: Long-term therapy with tiagabine showed no effect on visual fields in these patients. Fatigue and inattention accounted for minor nonspecific findings.

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Memory for Serial Order in Patients with Frontal Lobe Lesions

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OBJECTIVE: To measure the ability of patients with frontal lobe damage on learning a fixed sequence of unrelated words, according to a different time presentation and verbal-pictorial modality.

BACKGROUND: Patients with frontal lesions develop memory problems qualitatively different from those of classical amnesias. Cognitive deficits involve problem-solving, metamemory, verbal fluency, category shifting, planning of complex sequence of actions, cognitive estimation and memory for serial order. These deficits have been attributed to disruption of learning caused by an increased susceptibility to interference, retrieval strategies and impaired organization of the material to be learned.

DESIGN/METHODS: 21 patients with frontal lobe lesions (8 left, 9 right, 4 bilateral) and 21 controls matched for age and educational level, underwent a standard neuropsychological examination (MMSE, PM47, Stroop test, WCST, Digit and spatial span, Logical Memory, Tower of London, Fluency tests, WAIS Picture Arrangement subtest and Dual Task) and an experimental test for serial memory. It consisted of seven unrelated, high-frequency words or equivalent figures displayed for 200 msec on a videoscreen at a rate of one every two seconds (normal presentation) or every five seconds (slow presentation). Subjects were invited to recall as many words or figures as possible in the same order they appeared until the criterion or at the end of 12 trials. Four lists were presented on a balanced order: 2 word and 2 figure lists for both normal and slow presentation rate. Performance was evaluated taking into account the number of repetitions needed to learn the correct sequence and the following indices: index A, related to the number of items correctly recalled independently of their order and index ITR (Sternberg and Tulving,1977)based on the sum of pairs of correct items in two adjacent repetitions.

RESULTS: Analysis of variance revealed significant differences between patients and controls in most of the neuropsychological tests, with the exception of digit span and PM47. On serial memory test, frontal patients needed more trials [$F(1,27)=11.453$; $p=.002$] to reach the criterion than controls. A significant group difference for index A (storage) and ITR (organization) [$F(1,40) = 32.85$; $p < .001$] and measure x group interaction [$F(1,40) = 34,036$; $p = .000$]and types x group interaction [$F(1,40) = 7.593$); $p = .009$] was found. For verbal memory test, frontal patients were more impaired on index A and ITR, with greater difference on the latter, while on pictorial task the difference was smaller.

CONCLUSIONS: Frontal patients were impaired on most of the neuropsychological measures, according to the previous literature (cognitive flexibility, interference effect, planning). On serial memory task, patients had more difficulties for item organization than for storage. However, such a difficulty was attenuated when figures were presented or when list items were displayed at a slow frequency rate. Thus, the present study seems to suggest that a) the frontal lobe play a critical role on memory for temporal order and b) performance may be changed by manipulating the rate of presentation and the target modality.

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Implicit Memory and Estrogen: Aging and Alzheimer's Disease

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OBJECTIVE: To evaluate estrogen effects on two implicit memory tasks: procedural learning and priming in older healthy women and women with dementia due to Alzheimer's disease.

BACKGROUND: Estrogen has clear effects on brain and brain function, and some studies in humans and animals indicate that estrogen improves performance on certain explicit memory tasks. Potential estrogen effects on implicit memory (ie, memory for which a person has no consciousness awareness) have not been examined.

DESIGN/METHODS: Volunteers were recruited from among healthy older women and women meeting criteria for probable Alzheimer's disease. Volunteers included women currently receiving oral estrogen therapy and women not currently receiving estrogens. Procedural learning was assessed with a pursuit rotor paradigm in which subjects attempted to maintain contact between a stylus and a rotating metal disc. Subjects were also administered a naming task within which three priming conditions were embedded: identity (eg, apple/apple), related (eg, apple/orange), and unrelated (eg, apple/bear). Voice-activated reaction time-to-name was recorded.

RESULTS: Complete datasets were available for 28 (procedural task) and 31 (priming task) healthy women and 12 Alzheimer's patients. Among both healthy and Alzheimer's disease women, there were no between-group differences on the pursuit rotor task (% time on target). On the priming task, median difference scores between priming conditions for healthy women showed a trend toward increased priming among estrogen users (unrelated minus identity reaction times, Mann-Whitney $U=164.0$, $p=0.08$). Among Alzheimer's women, between-group differences were not significant; however, reaction times were longer and number correct less for nonusers vs users of estrogen. Finally, 7 of 11 patients (including both estrogen users and non-