

Sequence manipulation in patients with lesion of the ventrolateral premotor cortex



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Introduction

Research in both monkeys and humans provides evidence for the involvement of the premotor cortex in the planning and execution of sequential tasks. While animal and much of imaging and clinical research has focussed on motor tasks, recent imaging studies have established that the premotor cortex is also involved in sequence processing (or sequencing) in non-motor tasks, such as the prediction of sequential patterns[1].

AIM

- Lateral premotor cortex (LPM)** hereafter has been suggested to primarily mediate externally (i.e. stimulus-) based actions, while its medial part (supplementary motor area, SMA) seems to be mostly engaged in internally (e.g. memory-) based processes[2,3,4,5]. However, the evidence is inconclusive[6,7,8].
- To our knowledge these suggested functional preferences for PM vs. SMA have not yet been investigated in a non-motor sequencing framework.

Taking up these two issues, the present study aimed to determine whether, in a non-motor task, lesions of the ventral LPM cause deficits not only in externally based sequencing but also in internally driven sequencing.

Methods

Task: Computer-based non-motor sequencing (see Figure 2)

- 3 conditions (20 trials each), all of which required subjects to memorise a sequence of three letters and to match this memorised sequence to a test sequence presented afterwards (= externally based sequencing)
- 2 of the conditions required an additional mental rearrangement of the sequence according to a given rule before matching it against the test sequence (= internally driven sequential reorganisation). Easy rule: 1-3-2, difficult rule: 3-1-2
- In the third condition (baseline) the “rule” consisted simply of the sequence presented previously (order 1-2-3) so that no sequence reorganisation was necessary
- 50% of test sequences were incorrect, i.e., did not match the reorganised sequence
- Instruction: Indicate whether or not the test sequence was correct by pressing one of two buttons

Behavioral performance measures:

- completion time, i.e. self-paced amount of time a subject needed to rearrange the sequence, as indicated by button pressed as soon as the sequence was mentally rearranged
- error rates (matching between mentally rearranged and presented test sequence)

Participants

- 10 patients with lesions comprising the ventral LPM (LPM patients; see Table 1 / Figure 1a)
- 7 patients with prefrontal (frontopolar) lesions (PF patients), in order to rule out that functional deficits in the LPM sample are due to the patients' clinical status as such (see Table 1 / Figure 1b)
- 2 healthy control groups (n=10 and n=7) matched to the respective clinical samples with regard to age, gender, and education.

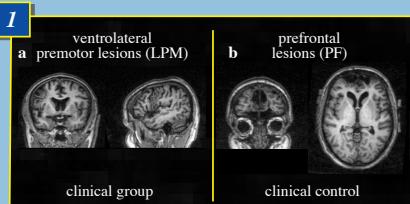


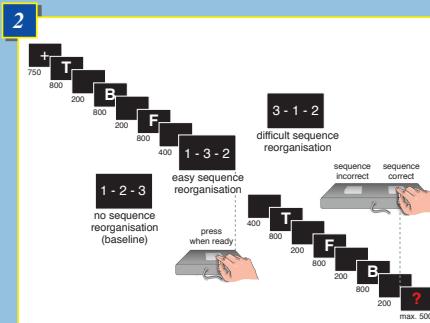
Table 1

patient data

Patient	Gender	Age	MsL	H	Lesion site	Etiology
PM1	m	30	49	L	lateral-frontal	infarction
PM2	w	48	92	L	lateral-frontal	infarction
PM3	m	64	54	L	lateral-frontal	infarction
PM4	m	47	50	L	lateral-frontal	traumatic brain injury
PM5	w	46	28	L	lateral-frontal	infarction
PM6	m	49	33	L	lateral-frontal	infarction
PM7	w	23	69	L	lateral-frontal	infarction
PM8	m	65	61	L	lateral-frontal	infarction
PM9	w	49	35	R	lateral-frontal	infarction
PM10	m	74	55	L	lateral-frontal	infarction
PF1	m	44	91	R	orbitofrontal	ruptured aneurysm
PF2	m	45	292	B	anterior-prefrontal	traumatic brain injury
PF3	m	33	108	B	anterior-prefrontal	traumatic brain injury
PF4	m	33	38	R	anterior-prefrontal	traumatic brain injury
PF5	w	55	147	B	anterior-prefrontal	tumor
PF6	w	44	70	L	anterior-prefrontal	infarction / ruptured aneurysm
PF7	w	67	36	B	anterior-prefrontal	tumor

TABLE 1 - Note: MsL = months since lesion, H= hemisphere, L = left, R = right, B = bilateral. Mean age 49.5 yrs (range 23 – 74 yrs) in PM patients; 45.9 yrs (range 33 – 67 yrs) in PF patients. Average time since lesion 47.9 months (SD 22.27) in PM patients; 117.9 months (SD 88.6) in PF patients.

Methods



Analysis:

Through comparison of the two reorganisation conditions with the baseline condition, the experiment allows to isolate the effect of sequence reorganisation (i.e. an internally driven sequencing process) on the measures of performance and thus to investigate internal sequencing ability as compared to performance in externally based sequencing.

Pretest

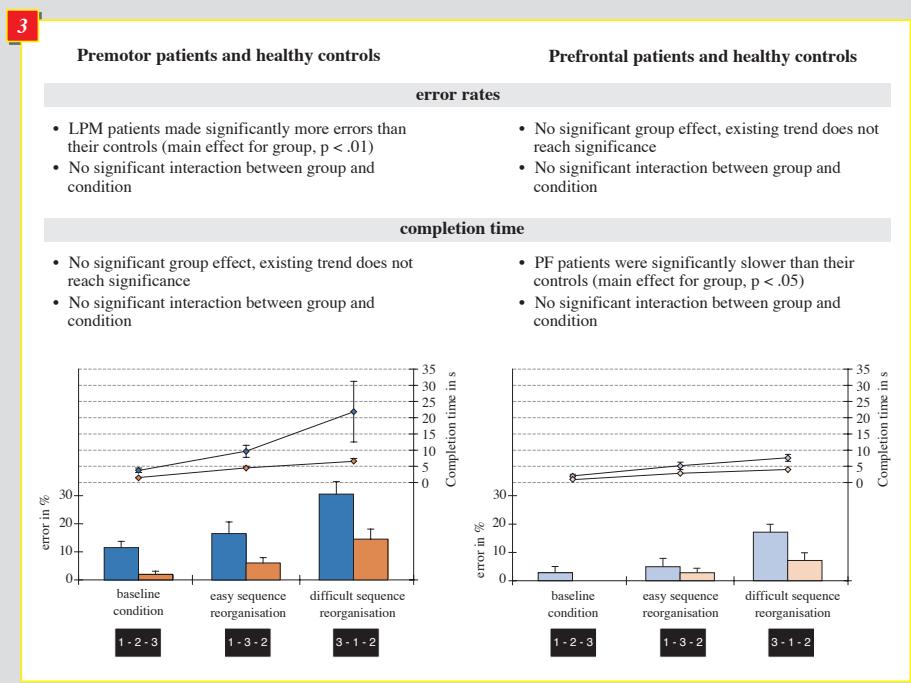
- Aim: Ascertain that patients were able to memorise a three-letter sequence
- Match-to-sample task (60 trials): three-letter sequence - 4s delay - test item
- Task: Indicate whether test item had been part of the sequence (50%)
- Results: Error rates were significantly above chance for all subjects, thus the aim was met; however, LPM patients made significantly more errors than the control group while PF patients did not differ from their controls (see Discussion).

Hypotheses

- LPM patients should be significantly impaired as compared to their control group on account of a deficit in externally based sequencing which is required in all experimental conditions (**main effect GROUP**)
- LPM patients should exhibit an additional impairment in internally driven sequencing in those conditions which require sequence rearrangement (**interaction GROUP x CONDITION**)
- There should be no such differences in performance between PF patients and their controls

Results

- 4 separate mixed ANOVAs so as to evaluate both error rates and completion times for LPM patients vs. controls and PF patients vs. controls, respectively
- Within-subjects factor CONDITION (baseline/easy/difficult) and between-subjects factor GROUP (patients/controls)



Discussion

- Error rates for the LPM patients displayed the expected deficit in externally based sequencing. As there was no indication of an impairment in internally driven sequencing the pattern of error rates confirms the tendencies in the literature pointing to a preferential involvement of LPM in externally based sequencing.
- Regarding completion times in the LPM sample, there were no significant effects. However, the results displayed trends which would strongly indicate an impairment in internally based sequencing despite not reaching statistical significance. The high degree of variance commonly associated with relatively small and inhomogeneous clinical samples may explain for this result.
- The significant slowing of PF patients across conditions was unexpected. However, their error rates were not significantly higher than those of their healthy control subjects. The slowing may be due to specific lesion-related problems of the PF sample with complex task management [9].
- Further investigation is needed regarding the deficit displayed by LPM patients in the pretest as it pertains to the relation between sequencing and working memory.

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