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 focused 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]. However, the evidence is inconclusive[5,6,7].

- To our knowledge these suggested functional preferences for PM vs. SMA have not yet been investigated in a non-motor sequencing framework.

Table 1: patient data

<table>
<thead>
<tr>
<th>Patient</th>
<th>Gender</th>
<th>Age</th>
<th>Lesion site</th>
<th>Etiology</th>
</tr>
</thead>
<tbody>
<tr>
<td>PM1</td>
<td>m</td>
<td>30</td>
<td>L frontal</td>
<td>infection</td>
</tr>
<tr>
<td>PM2</td>
<td>m</td>
<td>48</td>
<td>L frontal</td>
<td>infection</td>
</tr>
<tr>
<td>PM3</td>
<td>m</td>
<td>64</td>
<td>L frontal</td>
<td>infection</td>
</tr>
<tr>
<td>PM4</td>
<td>m</td>
<td>47</td>
<td>L frontal</td>
<td>trauma/injury</td>
</tr>
<tr>
<td>PM5</td>
<td>m</td>
<td>40</td>
<td>L frontal</td>
<td>infarction</td>
</tr>
<tr>
<td>PM6</td>
<td>m</td>
<td>49</td>
<td>L frontal</td>
<td>infarction</td>
</tr>
<tr>
<td>PM7</td>
<td>m</td>
<td>23</td>
<td>L frontal</td>
<td>infarction</td>
</tr>
<tr>
<td>PM8</td>
<td>m</td>
<td>65</td>
<td>L frontal</td>
<td>infarction</td>
</tr>
<tr>
<td>PM9</td>
<td>m</td>
<td>49</td>
<td>R frontal</td>
<td>infection</td>
</tr>
<tr>
<td>PM10</td>
<td>m</td>
<td>74</td>
<td>L frontal</td>
<td>infarction</td>
</tr>
</tbody>
</table>

LPM patients made significantly more errors than the control group while PF patients did not differ from their controls.

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).

- In the third condition (baseline) the “rule” consisted simply of a no sequence manipulation (baseline).

- To our knowledge these suggested functional preferences for PM vs. SMA have not yet been investigated in a non-motor sequencing framework.

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).

Analysis:

Through comparison of the two reorganisation conditions with the baseline condition, the experiment allows to isolate the effect of sequential 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.

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.

Premotor patients and healthy controls

Error rates

- No significant group effect, existing trend does not reach significance
- No significant interaction between group and condition

Completion time

- No significant group effect, existing trend does not reach significance
- No significant interaction between group and condition

Prefrontal patients and healthy controls

Error rates

- Within-subjects factor CONDITION (baseline/easy/difficult) and between-subjects factor GROUP (patients/controls)

Completion time

- PF patients were significantly slower than their controls (main effect for group, p < .05)
- No significant interaction between group and condition

Discussion

1. 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.

2. Regarding completion times in the LPM sample, there were no significant effects. However, the 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 this result.

3. 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.

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.

References