The cerebral correlates of the Subjective Experience of Time. A VLSM study in focal brain-damaged patients.

C. CRISCI (1), L. TROJANO (2), M. CACCAVALE (2), F. DE BELLIS (2)
(1) Clinic Center S.p.A. Rehabilitation Institute, Viale Maria Bakunin, 171 Napoli
(2) University of Campania Luigi Vanvitelli, Department of Psychology, Viale Ellittico, 31 Caserta

INTRODUCTION

Subjective experience of time (SET) implies the sense of self across the time [1], and is involved in evaluating duration of daily life events, ranging from seconds and minutes to months [2]. SET relies on multiple cognitive and neural mechanisms related to time cognition, attention, memory and emotional processess [1, 3].

We searched for the neural correlates of SET by voxel-based lesion-symptom mapping (VLSM) in a sample of focal brain-damaged patients.

PARTICIPANTS AND MATERIALS

33 patients suffering from single focal stroke (19 with right-hemisphere lesion -RBD- and 14 with left-hemisphere lesion –LBD) and 28 non-neurological controls (NNC) were recruited from Clinic Center, Rehabilitation Institute, Naples. All participants completed the Revised QUestionnaire for the Subjective experience of Time (QUEST-R), a 12-item inventory requiring retrospective (e.g., *"How many days ago did you enter this hospital?"*) or prospective (e.g.,*"Could you drop a hint in 4 min?"*) time estimations on self-relevant time intervals. A short screening battery for general cognitive abilities and affective state, including Mini Mental State Examination (MMSE), Frontal Assessment Battery (FAB), Clock Drawing Test, Hospital Anxiety and Depression Scale (HADS), and the Apathy Evaluation Scale (AES), was administered to all participants. Only patients who did not show impairment in language comprehension or severe mental deterioration were included in the study.

METHODS

Responses on QUEST-R items were checked against 'correct' values and then Error Indexes for Retrospective (RET-EI) or Prospective (PRO-EI) items were calculated. A MANOVA with Group (RBD, LBD, NNC) as fixed factor was conducted on demographic data, neuropsychological scores and QUEST-R error indexes. We performed a Crawford's analysis [4] to assess whether Ret-EI and Pro-EI of individual patients were significantly higher than those of NNC (at $p<.001$).

Lesions were manually drawn directly on patients' CT using Mricron, then both structural scans and lesion maps were registered to a standard (MNI space) stroke-control CT template using Clinical Toolbox [5], running with SPM8. Voxel-based Lesion Symptom Mapping (VBLSM) analyses were conducted to identify lesioned voxel significantly predicting larger PRO-EI or RET-EI scores. For both error indexes, subtraction analyses were performed between lesion overlays of RBD patients with and without significant impairments as assessed by Crawford's analysis.

RESULTS

RBD and LBD scored worse than matched NNC on QUEST-R indices and in all dependent measures but FAB and Anxiety subscales of HADS, but no difference was found between each other. Differences on QUEST-R were still observed when controlling for covariate effect of MMSE, Clock Drawing Test and Depression subscale of HADS. In both patient groups Crawford's analysis identified individuals with selective impairment in either prospective or retrospective estimations.

VBLSM on PRO-EI [Fig. 1] revealed voxels significantly associated with larger errors in white matter underlying the right inferior parietal lobule (IPL). Subtraction-analyses [Fig. 2] revealed distinct patterns associated with lower accuracy in prospective (right IPL, rolandic operculum, posterior middle temporal gyrus) and in retrospective items (right superior middle temporal gyrus, white matter posterior to insula).

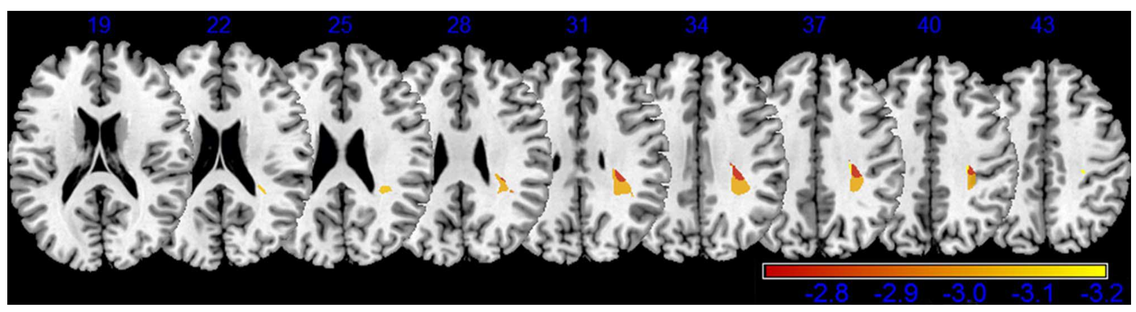

FIGURE 1. *Results of VLSM analysis on error index in prospective estimations. Statistical map shows voxels wherein comparison of error scores of patients with and without lesion yielded a significant t-test (converted into Z-scores) at $p<0.05$ with FDR correction. Significant voxels are rendered in red ($Z = -2.71$) to bright yellow ($Z = 3.199$) scale.*

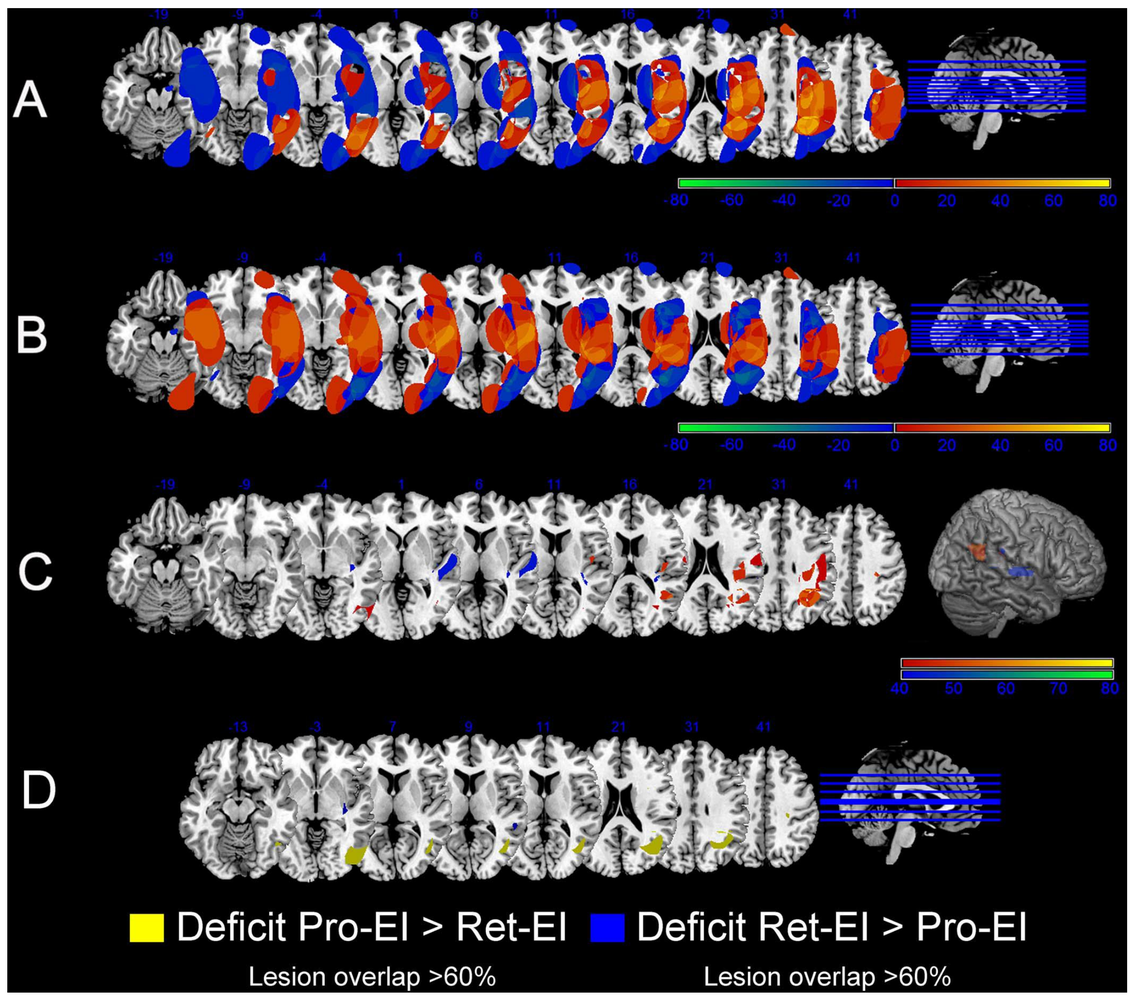

FIGURE 2. ***Panels A*** *and* ***B*** *show subtraction of lesion overlay of RBD patients with impaired performance from lesion overlay of RBD patients with normal performance in prospective estimations (Panel A) and in retrospective estimations (Panel B). Colours from red to yellow indicate brain regions more frequently damaged in the group of patients with low accuracy; colours from dark blue to green represent regions more frequently damaged in the group with high accuracy.* ***Panel C*** *shows brain regions more frequently damaged in patients with low accuracy in prospective estimations (n=5; red to yellow) or in retrospective estimations (n=7; dark blue to green) superimposed on the same MNI template, and rendered in 3D.* ***Panel D*** *shows subtraction plot of lesion overlays of patients with a selective impairment for prospective estimations (n=3) vs retrospective estimations (n=5) and vice-versa.*

DISCUSSION

Both left and right focal brain lesions affect time estimation suggesting that SET involves bilateral, widespread neural systems. Nonetheless, lesion analyses suggested that different aspects of SET are related to distinct neural networks in the right hemisphere. Consistent with previous findings [6,7], prospective judgments, mostly involving attentional and executive processes, seem to depend on IPL and rolandic operculum, whereas retrospective judgments, mostly implying memory processes, could rely on connections between temporal and posterior insular regions. Such distinction was also supported by clinical observation of double dissociations between prospective and retrospective time processing in our patients.

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