Neuropsychologia 44 (2006) 1909–1913

NEUROPSYCHOLOGIA

www.elsevier.com/locate/neuropsychologia

Isolated numerical skills in posterior cortical atrophy—An fMRI study

Margarete Delazer[a,*], Thomas Benke[a], Thomas Trieb[b], Michael Schocke[b], Anja Ischebeck[a]

[a] *Clinical Department of Neurology, Innsbruck Medical University, Innsbruck, Austria*
[b] *Department of Radiology I, Innsbruck Medical University, Innsbruck, Austria*

Received 13 December 2005; received in revised form 1 February 2006; accepted 10 February 2006
Available online 4 April 2006

Abstract

Posterior cortical atrophy (PCA) is characterized by bilateral parieto-occipito-temporal atrophy and hypometabolism. Neuropsychological impairments include complex visual disturbances, alexia, agraphia, finger agnosia, right–left disorientation and dyscalculia. A recent case study reported severe numerical deficits with some selectively preserved numerical skills in a patient affected by PCA [Delazer, M., Karner, E., Zamarian, L., Donnemiller, E., & Benke, T. (2006). Number processing in posterior cortical atrophy—a neuropsycholgical case study. *Neuropsychologia*]. In a functional magnetic resonance imaging (fMRI) study brain activation patterns related to these selectively preserved numerical skills were analyzed. Recitation of multiplication tables and counting forward were contrasted to word recitation in a block design. Contrasts between experimental conditions and control condition yielded significant activation of inferior and medial temporal structures. Since numerical processing is generally associated with parietal activation, it was hypothesized that preserved brain structures would compensate for the functional deficits.

Keywords: Dementia; Compensation; Degeneration; fMR; Number processing

1. Introduction

Posterior cortical atrophy (PCA) is a rare syndrome of dementia characterized by early onset, bilateral parieto-occipito-temporal atrophy and hypometabolism (Nestor, Caine, Fryer, Clarke, & Hodges, 2003; Freedman et al., 1991; Pietrini et al., 1996). Neuropsychological deficits include complex visual disturbances, alexia, agraphia, finger agnosia, right-left disorientation and dyscalculia (Benson, Davis, & Snyder, 1988; Mendez, Ghajarania, & Perryman, 2002). Language and memory are typically better preserved. A recent case study reported severe numerical deficits, but also selectively preserved numerical skills in a patient affected by PCA (Delazer, Karner, Zamarian, Donnemiller, & Benke, 2006). The present functional magnetic resonance imaging (fMR) study assesses brain activation patterns related to these selectively preserved numerical skills.

The assessment of preserved numerical skills in PCA is of particular interest, since brain imaging studies with healthy subjects reliably show the activation of parietal areas in simple calculation (e.g., Menon, Rivera, White, Glover, & Reiss, 2000; Dehaene, Piazza, Pinel, & Cohen, 2003; Delazer et al., 2003). In particular, the intraparietal sulcus consistently yields significant activation in numerical tasks. This intraparietal activation is thought to reflect the use of an internal quantity representation to compute the answer or to monitor the results initially retrieved from verbal memory (e.g., Chochon, Cohen, van de Moortele, & Dehaene, 1999). However, not only the IPS is involved in the skilled retrieval of multiplication facts. Similar to other arithmetic operations, multiplication activates also prefrontal areas bilaterally (e.g., Delazer et al., 2003). Training studies indicate that the retrieval of over-learned multiplication facts (trained multiplication) activates the angular gyrus more than untrained multiplication (Delazer et al., 2003), whereas no such activation was observed for trained subtraction problems (Ischebeck et al., in press). The angular gyrus activation is also related to the type of arithmetic training (stronger activation after drill training; Delazer et al., 2005a). Neuropsychological case studies reported multiplication deficits not only after left parietal lesions (e.g., Delazer & Benke, 1997), but also after left medial frontal lesion (Lucchelli & De Renzi, 1993) and basal ganglia dysfunction (Delazer et al., 2004). Though the serial recitation of multiplication tables might differ from the task of retrieving the specific multiplication result for two operands, Kazui,

* Corresponding author at: Anichstrasse 35, 6020 Innsbruck, Austria. Tel.: +43 512 504 23870.
E-mail address: margarete.delazer@uibk.ac.at (M. Delazer).

0028-3932/$ – see front matter
doi:10.1016/j.neuropsychologia.2006.02.007

Kitagaki and Mori (2000) reported similar activations as for the solution of multiplication problems along the left intraparietal sulcus, the premotor and supplementary motor areas and the left inferior frontal gyrus.

Few studies investigated brain activation patterns in elderly subjects or in patients affected by degenerative disease. Bondi, Houston, Eyler, and Brown (2005) proposed a compensatory hypothesis to account for greater magnitude and extent of BOLD response in medial temporal areas in older adults at genetic risk for dementia of the Alzheimer type (DAT). Subjects at risk for DAT would invest additional effort in order to achieve a performance level comparable to controls. In the present study we investigate preserved numerical skills in a patient with severe parietal hypoperfusion. Since numerical processing is generally associated with parietal activation, it was hypothesized that other brain structures would compensate for the functional deficits.

2. Case description

HR is a 63-year-old, right-handed woman with 12 years of formal education (for a detailed case description and neuropsychological assessment see Delazer et al., 2006). Disease onset was approximately 5 years before the present investigation. SPECT evidenced a severe reduction of cortical perfusion in the superior and posterior parietal, and posterior temporal lobe, more pronounced on the right side. Neuropsychological assessment showed an above average score (percentile 96.5) in verbal intelligence. Impairments included the typical symptoms of parietal dysfunction, that means, deficient visuo-spatial processing, simultanagnosia, apraxia, dysgraphia, and finger agnosia. Deficits were also found in several numerical tasks assessing transcoding, approximation, estimation, mental number bisection, dot counting, and positioning on an analog number scale. In simple arithmetic, a striking dissociation between operations was found between preserved retrieval of multiplication and addition facts (operands smaller than 10) and impaired subtraction and division. The recitation of the conventional counting sequence was preserved.

HR gave written informed consent to participate in the study. The study was approved by the ethical commission of the Innsbruck Medical University.

3. Task

Due to HR's severe simultanagnosia, no visual stimuli could be used. Thus, two conditions were tested in the fMR session, the recitation of the multiplication sequence of five (from 5 to 50) and the recitation of the canonical counting sequence (from 1 to 20). The recitation of a two-syllable word (hallo) served as a control condition for verbal processing and articulation. Four activation blocks alternated with five resting blocks (30 s each) per condition. In three separate scanning runs of 4.5 min duration each HR was instructed via headphones to start (multiplication, counting or repeating 'hallo') and to stop. Experimental instructions were trained in two sessions before the fMRI to ensure that the patient understood and remembered the procedure (pre-scanning sessions). Experimental tasks (counting, recitation of the multiplication sequence) were performed without any difficulty in the pre-scanning sessions. Two further tasks were trained and measured in the scanner (recitation of the months of the year in their correct order and counting backwards). However, these tasks are excluded from the analysis due to the considerable difficulties of HR with these tasks in the pre-scanning sessions.

4. Scanning procedure and data analysis

fMRI measurement was performed on a 1.5 T Siemens Symphony scanner with a bird-cage head-coil. Functional measurement: EPI, TE = 60 ms, flip angle = 90°, 3 × 3 mm inplane (FOV = 190 mm, matrix = 64 × 64), 4 mm thickness, 1 mm gap, 24 axial slices. Anatomical scan: MPRAGE, TE = 3.49 ms, TR = 1610 ms, flip angle = 12°, matrix = 256 × 256, FOV = 220 mm, 112 slices, 0.86 mm inplane, 1.5 mm thickness, no gap. The functional data were analyzed using SPM2 software (Wellcome Department of Cognitive Neurology, London, UK). The data were motion-corrected and normalized. Normalization parameters were calculated for the anatomical scan and then applied to the functional data. Because of HR's atrophy normalization was affin only. Finally, the functional images were smoothed using a Gaussian kernel of 9 mm FWHM. Data were analyzed as a block design on the basis of the General linear model as implemented in SPM2. The canonical form of the hemodynamic response function was used to generate the model time courses for the rest and activation blocks. A high-pass filter (cut-off frequency: 1/125 Hz) was used to remove low frequency drifts. No global normalization was used. All scanning runs were analyzed and compared using a fixed effects analysis. For the comparisons between experimental conditions significantly activated voxels were identified using an initial *p*-value threshold of less than 0.001 (uncorrected), reporting only clusters with a corrected *p*-value of less than 0.05 on cluster level. Contrasts between experimental conditions were masked with the respective baseline contrast to avoid artefacts due to the subtraction of deactivations. Due to HR's cognitive problems overt articulation was chosen instead of silent articulation. This caused motion artefacts that are highly correlated with the on/off paradigm and that can therefore not be regressed out of the analysis. Motion artefacts were therefore identified visually (areas not in the brain or activations at high contrast boundaries) and discarded from the results.

5. fMR results

Baseline contrasts (Table 1). Recitation of a two-syllable word as compared to rest showed significant activation bilaterally in the pars triangularis of the inferior frontal gyrus, left insula, right middle temporal gyrus and right hippocampus. Counting minus rest showed left sided activations in the inferior frontal region, precentral gyrus, parahippocampal gyrus, inferior temporal gyrus, middle occipital gyrus and pallidum. Right sided activations included middle frontal gyrus, superior temporal gyrus and fusiform gyrus. Multiplication minus rest showed significant left sided activation of superior temporal gyrus, precentral gyrus, paracentral lobule and cerebellum, extending to