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BRIEF COMMUNICATION

Working memory in posterior cortical atrophy

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Abstract

We used an ad hoc created neuropsychological battery to evaluate in details both verbal and visuospatial working memory (WM) in patients with posterior cortical atrophy (PCA, $n = 5$). PCA is a rare, early-onset neurodegenerative dementia, often due to Alzheimer's disease (AD) pathology. Clinically, PCA patients present with visual, visuospatial, and visuomotor deficits, and no memory complaints. PCA patients' patterns of performance were compared with those of 11 typical, amnestic AD patients matched for disease severity, as well as with 17 age-matched healthy controls. Both groups of patients had impaired WM performance compared to controls. However, PCA patients were more impaired than typical AD patients for both verbal and visuospatial WM. Moreover, PCA patients showed a more consistent impairment of visuospatial WM, as compared with verbal WM. Systematic WM evaluation should be part of the standard assessment in PCA. WM deficits affect patients' quality of life and can be detrimental to rehabilitation programs.

Keywords Neuropsychological assessment · Working memory · Posterior cortical atrophy · Alzheimer's disease · Parietal lobe

Introduction

Posterior cortical atrophy (PCA) is a rare neurodegenerative dementia, characterized by early age-of-onset and focal posterior brain damage, predominantly associated with Alzheimer's disease (AD) pathology [1]. PCA patients typically present with greater visuospatial and visuomotor deficits [2]. However, in clinical practice, we often observe major working memory (WM) problems. Such disorders affect the quality of life and often prevent PCA patients from taking full advantage of reeducation programs. Also, neurological and neuropsychological evaluations are strongly affected by WM deficits.

Here, we explored WM performance of PCA patients and typical old amnestic AD (tAD) patients, by using a comprehensive neuropsychological battery dissecting specific verbal and visuospatial aspects.

Methods

Participants

We enrolled five PCA, 11 tAD, and 17 healthy controls (HC) (Table 1, supplementary materials).

Working memory assessment

All patients and controls underwent an experimental task composed of 15 tests conceived to assess WM in depth (supplementary Table 1). We used visuospatial and verbal spans with different stimuli (numbers, cubes, or letters), presentation modalities (verbal or visual presentation), and response modes (verbal or manual pointing, forward or backward).

Verbal WM

1. *Digit span*. The examiner uttered numbers pseudo-randomly chosen from 1 to 9. In different conditions,

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Table 1 Sociodemographic, global cognitive, and clinical features of groups

	HC ($n = 17$)	PCA ($n = 5$)	AD ($n = 11$)
Age (mean ± SD)	63.6 ± 8.91†	60.8 ± 3.65†	80.6 ± 2.70
	48–82	56–65	74–84
Education (mean ± SD)	18.7 ± 3.57**	12.8 ± 4.79	12.7 ± 1.91
Gender (w/m)	11/6	5/0	9/2
Handedness (R/L)	16/1	5/0	11/0
MMSE (mean ± SD)	29.11 ± 1.07	19.2 ± 3.76*	18 ± 3.59*

Scores shown are mean (± standard deviation)

*$p < 0.0001$ vs. controls; †$p < 0.0001$ vs. AD; **$p < 0.001$ vs. AD

AD, Alzheimer's disease; *HC*, healthy controls; *L*, left; *m*, men; *MMSE*, Mini Mental State Examination; *n*, number; *PCA*, posterior cortical atrophy; *R*, right; *SD*, standard deviation; *w*, women

subjects reproduced the stimulus sequence forward or backward, either verbally or by manually pointing at numbers printed on white cards. There were the following conditions: (a) verbal presentation - verbal restitution - forward; (b) verbal presentation - verbal restitution - backward; (c) verbal presentation - restitution by pointing - forward; (d) verbal presentation - restitution by pointing - backward.

2. *Letter span*. Single letters were presented with a similar procedure to that used for the digit span, except for the following: (a) letter presentation could be either auditory or visual; (b) only verbal responses were requested; (c) sequences of phonologically similar letters (B-C-D-G-T-P-V) or of phonologically dissimilar letters (F-H-J-K-L-M-R) were used. There were the following conditions: (a) similar - verbal presentation - forward; (b) similar - verbal presentation - backward; (c) dissimilar - verbal presentation - forward; (d) dissimilar - verbal presentation - backward; (e) similar - visual presentation - forward; (f) dissimilar - visual presentation - forward.

Visuospatial WM

1. *Visual digit span.* Five visuospatial digit span sets, using either numbers or cubes (the Corsi test), were used. Subjects had to memorize numbers from "1" to "9" presented as printed in black on white cards without reading them, or to tap sequences of spatially separated cubes.
2. *Vertical cubes.* PCA patients frequently show signs of spatial neglect [3]. To avoid neglect-related errors in these patients, we designed an adaptation of the Corsi test with vertically aligned. The proposed sequences could be either with cubes "ordered" or "crossed." The cubes are numbered from 1 to 9 (numbers are only visible to the examiner). For example, the sequence "1,5,7,9" would be ordered (non-crossed), whereas the sequence "6,3,9,4" would be crossed. Subjects reproduced the stimulus sequence forward or backward as in the classic visual digit span.

The following conditions were administered: numbers (a) visual presentation - verbal restitution; cubes (a) ordered - forward; (b) ordered - backward; (c) crossed - forward; (d) crossed - backward.

This study complied with the Declaration of Helsinki and was promoted by the INSERM (C10-49) and approved by the Ile-de-France I Ethics Committee. Written informed consent has been given by all participants.

Statistical analyses

All variables were checked for normality of distribution by using the Kolmogorov-Smirnov test. The WM task scores were compared across groups by using the Kruskal-Wallis one-way analysis of variance taking into account the ordinal nature of the variable. Class mean, value of the Kruskal-Wallis rank sum statistic, p value, and adjusted p value (Bonferroni correction) are reported for each test in supplementary table 2. A p value of < 0.05 was considered significant.

Results

Verbal WM: digit span

Both patient groups recalled less digits than controls did (Fig. 1; all $K > 8.63$; all $ps < 0.05$). PCA patients performed worse than tAD patients on verbal presentation with backward verbal responses ($K = 19.58$; $p < .01$) and with backward pointing responses ($K = 23.02$; $p < 0.01$). Thus, verbal WM using numbers was more impaired in PCA patients than in tAD patients and controls.

Verbal WM: letter span

Also, on these tests, patients were impaired compared to controls (all $K > 16.96$; all $ps < 0.01$), but there was no significant difference in performance between PCA and tAD patients (all $K < 24.39$, all $ps > 0.05$), except in visual presentation of dissimilar letters, where PCA patients are more compromised than tAD patients ($p < 0.01$).

Visuospatial WM: visual digit span and vertical cubes

Patients were more impaired than controls and PCA patients recalled fewer items than tAD patients (all $Hs > 19.42$; all $ps < 0.01$). PCA performed worse than tAD in all vertical cubes conditions.

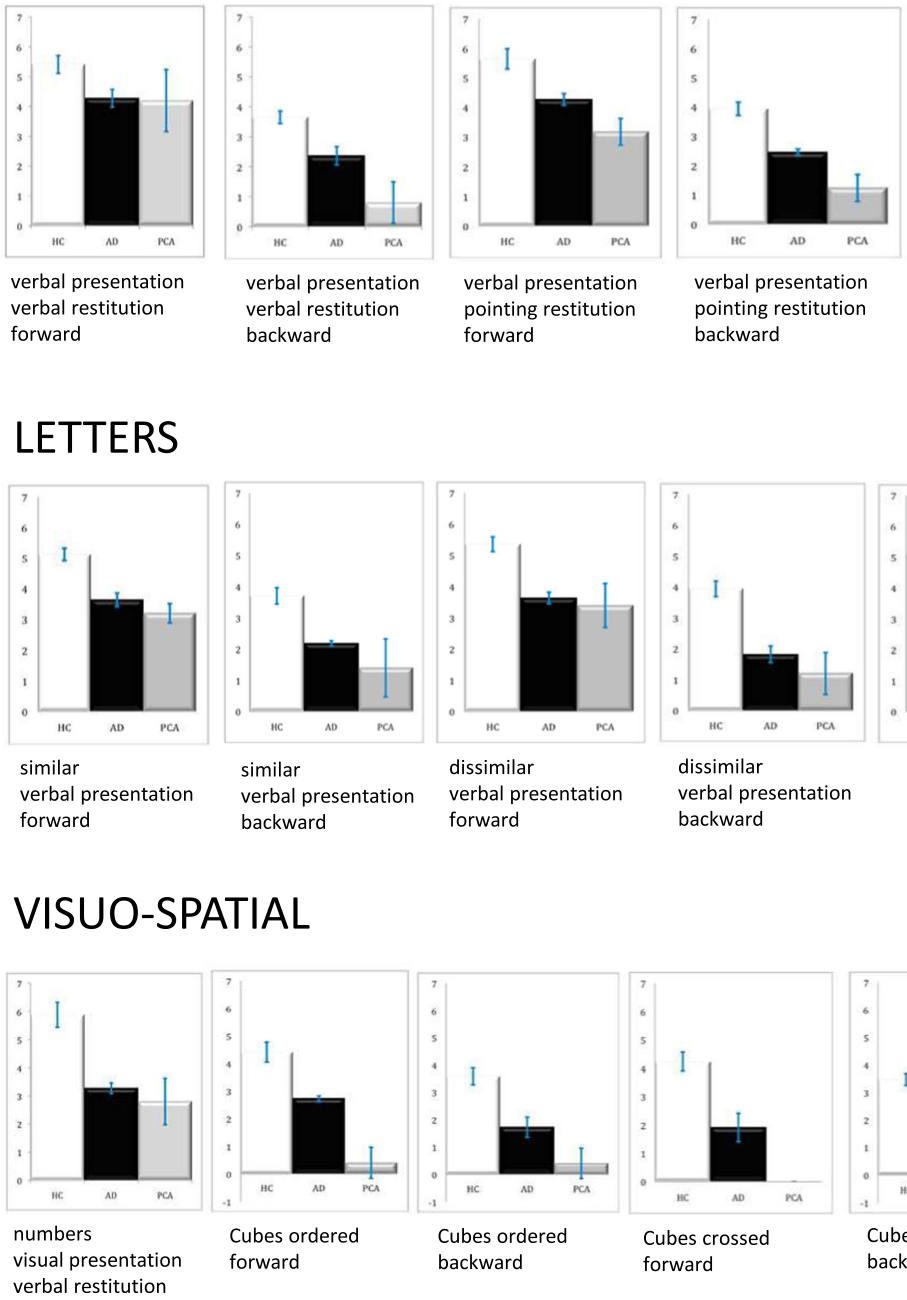

Fig. 1 For graphic representation of results, 95% inferential confidence intervals (ICIs) were calculated for all neuropsychological tests. Non-overlapping ICIs denote statistical difference, while an overlap between the ICIs indicates statistical equivalence [4]. AD, Alzheimer's disease; HC, healthy controls; PCA, posterior cortical atrophy

Discussion

We used a 15-test neuropsychological battery, including verbal and visuospatial forward and backward spans in different modalities, to assess WM in PCA and tAD. PCA patients were more impaired than tAD patients in both verbal and visuospatial WM, and showed a more consistent impairment of visuospatial WM, with respect to the verbal modality. This gradient of cognitive deficit is in agreement with the typical pattern of PCA cerebral damage mainly localized on posterior brain regions, with high right-side predominance [5]. fMRI studies during visual and spatial WM tasks in healthy subjects show stronger activations in right parieto-occipital structures

[6]. Consequently, PCA pattern predicts more severe impairment of visuospatial than of verbal WM.

We analyzed separately numbers and letters tasks, since numerical and phonological analyses seem to be supported by different brain networks, including the parietal lobe bilaterally for numbers [7], and left parietal lobe for letters [8]. PCA patients had more severely impaired performance with numbers, consistent with their predominantly right parietal involvement. Our findings are in line recently to described general memory disorders in PCA [9] and they also confirm the critical role of the posterior parietal cortex in brain networks mediating WM [10].

The finding that verbal WM in PCA was particularly impaired in backward modalities reflects perhaps a difficulty in visual imagery of the information during the task. Also, very recently, some authors have showed a specific reduction of spatiotemporal and perceptual details from PCA patients' narratives, in line with the hypothesis that PCA causes a "visual memory deficit amnesia." This finding is supported by the pattern atrophy involving posterior parietal regions, whose activity contributes to spatial mental imagery [11, 12] and memory [13].

A note of caution stems from the difference in the educational level between patients and HC in our sample. This difference might have impacted the intelligence quotient, which in turn can influence span abilities, thus perhaps contributing to the differences in performance between HC and AD patients. Future studies should control for this variable.

Summarizing, we identified a "gradient" of deficits with visuospatial WM more impaired than verbal WM; however, PCA patients were also severely impaired in verbal WM. This is in agreement with their anatomy.

A detailed evaluation of WM should be taken into account in the assessment of these patients. When clinical constraints do not permit the use of fine-grained test batteries such as the present one, at least one verbal and one visuospatial WM test should routinely be administered.

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Compliance with ethical standards

This study complied with the Declaration of Helsinki and was promoted by the INSERM (C10-49) and approved by the Ile-de-France I Ethics Committee. Written informed consent has been given by all participants.

Conflict of interest The authors declare that they have no conflict of interest.

References

1. Montembeault M, Brambati SM, Lamari F, Michon A, Samri D, Epelbaum S, Lacomblez L, Lehéricy S, Habert MO, Dubois B, Kas A, Migliaccio R (2018) Atrophy, metabolism and cognition in the posterior cortical atrophy spectrum based on Alzheimer's disease cerebrospinal fluid biomarkers. Neuroimage Clin 20:1018–1025. https://doi.org/10.1016/j.nicl.2018.10.010
2. Bartolomeo P, Migliaccio R (2016) Disorders of attentional processes. In: Husain M, Schott J (eds) Oxford textbook of cognitive neurology and dementia. Oxford University Press, Oxford, pp 161–171
3. Migliaccio R, Agosta F, Toba M, Samri D, Corlier F, de Souza L, Chupin M, Sharman M, Gorno-Tempini M, Dubois B, Filippi M, Bartolomeo P (2012a) Brain networks in posterior cortical atrophy: a single case tractography study and literature review. Cortex 48: 1298–1309
4. Tryon W, Lewis C (2008) An inferential confidence interval method of establishing statistical equivalence that correctsTryon's (2001) reduction factor. Psychol Methods 13:272–277
5. Migliaccio R, Gallea C, Kas A, Perlbarg V, Samri D, Trotta L, Michon A, Lacomblez L, Dubois B, Lehericy S, Bartolomeo P (2016) Functional connectivity of ventral and dorsal visual streams in posterior cortical atrophy. JAD 51(4):1119–1130
6. Zimmer H (2008) Visual and spatial working memory: from boxes to networks. Neurosci Biobehav Rev 32:1373–1395
7. Nieder A, Dehaene S (2009) Representation of number in the brain. Annu Rev Neurosci 32:185–208
8. Baddeley A (2003) Working memory: looking back and looking forward. Nat Rev Neurosci 4:829–839
9. Putcha D, McGinnis SM, Brickhouse M, Wong B, Sherman JC, Dickerson BC (2018) Executive dysfunction contributes to verbal encoding and retrieval deficits in posterior cortical atrophy. Cortex 106:36–46. https://doi.org/10.1016/j.cortex.2018.04.010
10. Cabeza R, Nyberg L (2000) Neural bases of learning and memory: functional neuroimaging evidence. Curr Opin Neurol 13:415–421
11. Bartolomeo P, Bachoud-Lévi AC, Azouvi P, Chokron S (2005) Time to imagine space: a chronometric exploration of representational neglect. Neuropsychologia 43:1249–1257
12. Bartolomeo P, Bourgeois A, Bourlon C, Migliaccio R (2013) Visual and motor mental imagery after brain damage. In: Lacey S, Lawson R (eds) Multisensory imagery. Springer, New York, pp 249–269
13. Ahmed S, Irish M, Loane C, Baker I, Husain M, Thompson S, Blanco-Duque C, Mackay C, Zamboni G, Foxe D, Hodges JR, Piguet O, Butler C (2018) Association between precuneus volume and autobiographical memory impairment in posterior cortical atrophy: beyond the visual syndrome. Neuroimage Clin 10(18):822–834. https://doi.org/10.1016/j.nicl.2018.03.008