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## Environmental reduplicative paramnesia in a case of atypical Alzheimer's disease

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Sirs: In environmental reduplicative paramnesia (RP), one or more environments are believed to exist simultaneously in two or more locations. We report a clinical and

neuropathological description of a patient presenting with the remarkably rare association of atypical Alzheimer's disease (AD) and RP.

A 75-year old man in good physical health presented with delirium caused by flupentixol/melitracene and nitrazepam given for a minor depressive syndrome that disappeared after stopping medication and introducing clomethiazole. Neuropsychological assessment revealed moderate memory and executive deficits (Case summary in Table 1). Nine months later, difficulties in activities of daily living arose. His cognitive performance was unchanged or better except for delayed recall. A further nine months later, both his cognitive impairment and functional dependency increased dra-

matically. Within the interval of a few weeks, the patient developed RP. When asked where he was he would say he was in another town, in an apartment identical to the one where he lived. He believed his apartment and building had been transported to that other town and were now located in both places. He was unable to explain how this could be possible although he wondered why someone had rebuilt his house elsewhere. He was afraid he would have to pay two rents for the two identical houses, apartments, and TV sets. He died ultimately of bronchopneumonia 4 years after his first presentation with delirium in a stage of advanced dementia.

Tissue samples from 32 brain regions were stained with hematoxylin-eosin, luxol-fast-blue-van Gieson, and Gallyas-silver tech-

**Table 1** Short case summary

| Cognitive domain                        | Assessment at presentation  | Assessment 9 months after 1 <sup>st</sup> assessment  | Assessment 18 months after 1 <sup>st</sup> assessment                |
|---|---|---|--|
| Orientation                             | normal  | normal  | Minor difficulty   |
| Attention/Memory                        |   |   |  |
| Clinical global impression              | slight attention deficit<br>performance fluctuating                     | unchanged<br>unchanged  | worsened<br>worsened   |
| AVLT immediate recall                   | 6-1-7; 14/30  | 6-8-8-9-8; 22/30  | –  |
| AVLT delayed recall                     | 4/10  | 0/10  | –  |
| Delayed recall of prose story           | 9/22  | 32/36   | –  |
| Language                                |   |   |  |
| Boston naming                           | 14/20   | 17/20   | –  |
| Visuospatial and visuoperceptive skills |   |   |  |
| Famous faces                            | 6/15  | major difficulty recognizing familiar persons   | –  |
| Correctly placed Swiss cities           | 2/5   | 4/8   | –  |
| Poppelreuter picture                    | 4/4   | 4/4   | –  |
| Imitations of non-significant gestures  | 5/5   | 5/5   | –  |
| Executive performances                  |   |   |  |
| Stroop errors                           | 8   | 3   | –  |
| Literal fluency                         | 6   | 3   | –  |
| Neurological examination                | normal  | Slightly increased muscular reflexes, slight paratonia, mild dysarthria for guttural sounds   | slowed gait, stooped posture, intermittent coarse tremor, paratonia, |
| Activities of daily living              | Independent for all activities  | Difficulties preparing meals; demotion from function as president of military society; administrative duties taken over by guardian | Activities of daily living partially impaired                        |
| CT-scan                                 | Mild cortical and subcortical atrophy and moderate leuco-encephalopathy | Slightly increased cortical and subcortical atrophy, unchanged leucoencephalopathy  | –  |

nique. Immunostaining was performed using monoclonal antibodies against the amyloid beta peptide (A $\beta$ ), tau protein, ubiquitin, and  $\alpha$ -synuclein.

Histological analysis confirmed the neuropathological diagnosis of definite AD. Severe neurofibrillary tangle (NFT) formation was observed in the frontal and temporal association cortex whereas NFT density was very low in the entorhinal and occipital cortices and the hippocampus. There were no NFTs in the parietal association cortex. Senile plaque (SP) distribution in this patient was similar to that reported in typical AD cases (cf. Table 2). No Lewy bodies or Lewy neurites were seen.

The regional distribution of NFTs in the hippocampus, the entorhinal and neocortical association areas was atypical and suggested a frontotemporal variant of AD [9]. The gradient of the NFT load may reflect the timing of neocortical NFT invasion. The clinical evolution lends support to this hypothesis: the initial stages were characterized by the predominance of dysexecutive and behavioral impairment and correlated with the highest NFT load in the frontal cortex. The consecutive deterioration may reflect the high NFT load in the temporal association cortex as the progression of NFT within

this particular brain area has been shown to be associated with clinically overt dementia [6].

RP is rare in AD and published cases were either not clearly identified as suffering from RP or the link between the presence of RP and AD was uncertain [4, 5, 11, 13].

Perceptual and memory problems may not be sufficient to account for the phenomenon of RP in AD [3, 7]. In fact, RP may include an interpretative component through which patients attribute failure to identify correctly places to the outer world rather than to their own self [12]. This delusional interpretation of RP may be due to the frontal lobe impairment frequently linked to RP [1, 4, 5, 12].

The NFT distribution in our patient suggests the possibility of corticocortical disconnection of the frontal lobes from parietal or temporal areas that may have contributed to the occurrence of RP by disrupting brain circuits that link parietal or temporal areas responsible for place recognition and for similarity and familiarity matching to frontal lobe regions [10, 14, 15], or connections between closely located areas in the right temporal lobe which are required for the visual recognition of faces and scenes [2, 8].

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## References

1. Benson DF, Gardner H, Meadows JC (1976) Reduplicative paramnesia. *Neurology* 26:147–151
2. Edelstyn NM, Oyebode F, Barrett K (2001) The delusions of Capgras and intermetamorphosis in a patient with right hemisphere white matter pathology. *Psychopathol* 34:299–304
3. Filley CM, Jarvis PE (1987) Delayed reduplicative paramnesia. *Neurology* 37:701–703

4. Fisher CM (1982) Disorientation for place. *Arch Neurol* 39:33–36
5. Förstl H, Almeida OP, Owen AM, Burns A, Howard R (1991) Psychiatric, neurological and medical aspects of misidentification syndromes: a review of 260 cases. *Psychol Med* 21:905–910
6. Giannakopoulos P, Hof PR, Michel JP, Guimon J, Bouras C (1997) Cerebral cortex pathology in aging and Alzheimer's disease: a quantitative survey of large hospital-based geriatric and psychiatric cohorts. *Brain Res Rev* 25:217–245
7. Hakim H, Verma PV, Greiffenstein M (1988) Pathogenesis of reduplicative paramnesia. *J Neurol Neurosurg Psychiatry* 51:839–841
8. Hudson AJ, Grace GM (2000) Misidentification syndromes related to face specific area in the fusiform gyrus. *J Neurol Neurosurg Psychiatry* 69:645–648
9. Jackson M, Lowe J (1996) The new neuropathology of degenerative frontotemporal dementias. *Acta Neuropathol (Berl)* 91:127–134
10. McFie J, Piercy ME, Zangwill OL (1950) Visual spatial agnosia associated with lesions of the right hemisphere. *Brain* 73:167–190
11. Mentis MH, Weinstein EA, Horwitz B, McIntosh AR, Pietrini P, Alexander GE, Furey M, Murphy DGM (1995) Abnormal brain glucose metabolism in the delusional misidentification syndromes: a positron emission tomography study in Alzheimer's disease. *Biol Psychiatry* 38:438–449
12. Moser DJ, Cohen RA, Malloy PF, Stone WM, Rogg JM (1998) Reduplicative paramnesia: longitudinal neurobehavioral and neuroimaging analysis. *J Geriatr Psychiatry Neurol* 11:174–180
13. Pick A (1901) On reduplicative paramnesia. *Prag med Wochenschrift* 39/40:260–267
14. van Lancker D, Ohnesorge C (2002) Personally familiar proper names are relatively successfully processed in the human right hemisphere; or, the missing link. *Brain Lang* 80:121–129
15. Whatmough C, Chertkow H, Murtha S, Hanratty K (2002) Dissociable brain regions process object meaning and object structure during picture naming. *Neuropsychologia* 40:174–186

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**Table 2** The severity of AD-type cortical changes are entered in four grades: absence of lesion –; discrete +; moderate ++; severe ++++; according to the CERAD criteria. SP senile plaques; NFT neurofibrillary tangles

| Brain region<br>(Brodmann's areas) | Right hemisphere |     | Left hemisphere |     |
|------------------------------------|------------------|-----|-----------------|-----|
|                                    | SP               | NFT | SP              | NFT |
| Entorhinal (28)                    | +                | +   | +               | +   |
| Hippocampus                        | +                | +   | +               | +   |
| Temporal (21)                      | +++              | +++ | +++             | +++ |
| Frontal (9)                        | +++              | +++ | +++             | +++ |
| Parietal (39)                      | +++              | –   | +++             | –   |
| Occipital (19)                     | +++              | +   | +++             | +   |

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