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Olfactory impairment in posterior cortical atrophy

INTRODUCTION

Olfactory dysfunction develops in many neurodegenerative diseases, and is an early feature of the most common neurodegenerative disorder, Alzheimer’s disease (AD). Anatomically, the central olfactory pathways traverse brain regions implicated in the common neurodegenerative diseases, including the mesial temporal and inferior frontal lobes. Phenotypically, AD shows substantial diversity with several important variant syndromes, notably posterior cortical atrophy (PCA), which is underpinned by AD pathology in over 70% of cases across series. Olfactory impairment in PCA might act as an early signal of underlying AD pathology in these clinically atypical cases; while if olfactory processing were spared in PCA, this would imply that olfaction depends chiefly on disease topography. However, there is presently very little information concerning olfaction in PCA.

METHODS

Fifteen patients fulfilling consensus criteria for PCA, patients fulfilling The National Institute of Neurological and Communicative Disorders and Stroke and the Alzheimer’s Disease and Related Disorders Association (NINCDS-ADRDA) criteria for tAD and 32 healthy control (HC) subjects participated. Cerebrospinal fluid (CSF) measurements, available for four patients with PCA, revealed a raised total-β-amyloid ratio (>1) in each case, consistent with underlying AD. Informed consent was obtained from all subjects and the study had local ethics committee approval.

All subjects had a comprehensive general neuropsychological assessment which corroborated the clinical impression in both disease groups (see online supplementary table S1). Further details about the behavioural assessments are in online supplementary material.

RESULTS

For both patient groups, mean odour categorisation and identification raw scores were significantly lower than the HC group (p<0.001; figure 1A, online supplementary table S1; individual data in online supplementary figure S1). Based on published UPSIT norms, four patients with PCA (26%) and three patients with tAD (30%) scored <5th percentile. Mean raw or percentile scores did not differ significantly (p>0.1) between the PCA and tAD groups. After correction for guessing, mean odour identification scores were higher than mean categorisation scores for PCA patients as well as HC subjects (see online supplementary table S1). An error analysis of individual odour items in the identification test revealed a qualitatively similar profile of errors across all groups (see online supplementary figure S2).

DISCUSSION

Here we have demonstrated deficits of odour identification and categorisation in patients with PCA relative to HCs. A similar proportion (around 30%) of patients with PCA and tAD in this study had an absolute deficit of odour identification referenced to published age and gender norms and taking account of associated cognitive impairment. Olfactory impairment was similar quantitatively and qualitatively in the PCA and tAD groups. To the extent that PCA manifests underlying AD, the findings imply that olfactory impairment is a hallmark of AD pathology. It is noteworthy that only a minority of patients in both phenotypical groups here reported olfactory symptoms, suggesting that in many cases olfactory impairment is ‘subclinical’. Mean corrected odour identification scores were higher than categorisation scores in the HC and PCA groups: this unexpected finding might hold clues to the cognitive organisation of olfactory knowledge or the cognitive strategies engaged by these tests, and would warrant further study in larger populations. Odour identification tasks tend to be cognitively demanding and therefore potentially susceptible to executive and attentional deficits that accompany AD.
The deficit of odour identification identified here was associated with regional grey matter volume in a cerebral network focussed on the right anteromedial temporal lobe. The most robust neuroanatomical associations occurred in parahippocampal gyrus and entorhinal cortex: areas linked to odour identification performance across the combined PCA and tAD cohorts. SPMs are shown rendered on axial (left, middle panels) and sagittal (right panel) sections of the mean normalised structural T1-weighted brain MR image. The axial sections show the right hemisphere on the right; the sagittal section is through the right hemisphere. For display purposes, SPMs have been thresholded at p<0.001 uncorrected over the whole brain volume; see online supplementary table S3 for associations attaining significance after multiple-comparisons correction. The plane of each section is shown in Montreal Neurological Institute (MNI) coordinates in millimetres (mm).

Figure 1  Summary of behavioural and neuroanatomical findings. (A) Distribution plots of olfactory performance comparing mean, median, IQR and full range of odour categorisation and identification of raw scores of subjects in the healthy control (HC), posterior cortical atrophy (PCA) and typical Alzheimer’s disease (tAD) groups. (B) Statistical parametric maps (SPMs) of regional grey matter atrophy associated with odour identification performance across the combined PCA and tAD cohorts. SPMs are shown rendered on axial (left, middle panels) and sagittal (right panel) sections of the mean normalised structural T1-weighted brain MR image. The axial sections show the right hemisphere on the right; the sagittal section is through the right hemisphere. For display purposes, SPMs have been thresholded at p<0.001 uncorrected over the whole brain volume; see online supplementary table S3 for associations attaining significance after multiple-comparisons correction. The plane of each section is shown in Montreal Neurological Institute (MNI) coordinates in millimetres (mm).
experimental behavioural and neuroimaging data, and in drafting and critically revising the paper. TJS and KXY were involved in acquisition of behavioural data and in drafting and critically revising the paper. RO was involved in study design, preparation of experimental behavioural tests, and in drafting the paper. DMC was involved in study design, analysis of neuroimaging data and in drafting the paper. SJC and MNR were involved in planning the study and in critically revising the paper. JDW obtained funding for and supervised the study, and was involved in study planning and design and in drafting and critically revising the paper.

Competing interests None.

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