DELUSIONS IN ALZHEIMER'S DISEASE: SPET EVIDENCE OF RIGHT HEMISPHERIC DYSFUNCTION

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Abstract

Delusional thinking and related behaviours are common symptoms in Alzheimer's disease (AD). The aim of the study was to determine if any consistent cerebral image pattern can be identified using Tc99m-hexamethylpropyleneamine (HMPAO) SPET in AD patients with and without delusions. 18 AD patients with delusion and 15 AD patients without delusion underwent neuropsychological testing and regional cerebral blood flow imaging using Tc99m-HMPAO SPET. The reconstructed data was compared using regions of interest drawn over each cerebral lobe and a statistical parametric mapping (SPM) approach. The neuropsychological testing showed that there was no difference in the profiles of the deluded and non deluded AD patients. The imaging results showed a significant degree of image asymmetry. This took the form of a right hemisphere hypoperfusion mainly in the right frontal and limbic regions. The results do not indicate a specific focal site of hypoperfusion in the patients with delusion. They do, however, indicate that delusions in AD may be associated with areas of hypoperfusion in the right anterior hemisphere.

Key words: SPET, delusion, Alzheimer disease, SPM, HMPAO

Introduction

Research into delusions in Alzheimer's Disease (AD) has mainly concentrated on the phenomenology of these disorders rather than on an understanding of their neurobiological and cognitive mechanisms. Delusions have been reported in up to 70% of patients with AD (Wragg and Jeste, 1989; Binetti, Padovani, Bianchetti et al., 1993) and these symptoms frequently do not respond to pharmacological treatment. When AD patients have been followed up longitudinally, 50% have delusions at some stage of the disease (Rubin, 1992).

The onset of delusional thinking in AD can be distressing for patients and their carers (Morris, Morris and Britton, 1988) and is an important reason for transfer to institutional care (Deimling and Bass, 1986; Morriss, Rovner, Folstein et al., 1990; Steele, Rovner, Chase et al., 1990). In the past, research has been carried out to identify the functional and structural causes of progressive deterioration in memory, language and visuospatial skills in AD. Research aimed at understanding the underlying neurological failure responsible for delusional symptoms is scant. These symptoms have traditionally been considered an

emergent complication of global neurological dysfunction and have often been referred to as 'non cognitive symptoms'. More recently some authors have reconsidered the possible cases of delusional symptoms in AD in terms of specific abnormalities of the brain. Binetti, Padovani, Magni et al. (1995) looked for brain morphological anomalies using CT and showed a significant association between isolated white matter lesions in the frontal areas and the presence of delusions. An earlier study (Förstl, Burns, Jacoby et al., 1991) found an association between a pronounced degeneration of the right frontal lobe, with relative sparing of the left frontal lobe, and the presence of delusions and misidentifications in patients with AD. Evidence is also available from studies evaluating blood flow with SPET or glucose metabolism with PET. Using Tc99m-hexamethylpropyleneamine (HMPAO) SPET, Starkstein, Vazquez, Petracca et al. (1994) found a significant bilateral deficit in the inferior and superior temporal areas, whereas Ponton, Darcourt, Miller et al. (1995) localised cerebral blood flow deficits in the right temporal regions. A more widespread network of cerebral dysfunction was associated with delusional behaviour in a PET study by Mentis, Weinstein, Horwitz et al. (1995) who reported finding significant hypometabolism in the orbitofrontal and cingulate areas bilaterally and in the left medial temporal areas. More recently, a study using HMPAO SPET reported a deficit in blood flow localised in the right frontal regions in two AD patients whose primary 'non-cognitive' onset symptom of dementia was a previously unreported content specific delusion consisting of fixed delusional beliefs about their dead spouse (Venneri, Shanks, Staff et al., 1998). These studies while inconsistent in their findings, indicate, in contrast to earlier views (Rubin, 1992), that delusional symptoms in AD may be associated with discrete and localised brain anomalies. These findings do not point to any specific site for this organic deficit, but all of these studies included AD patients with different types of delusion and this might contribute to the variety of dysfunctional neuronal systems identified.

Observations in patients showing delusions following other neurological disorders have also yielded inconsistent findings, but lend support to the view that delusions may be associated with specific regional dysfunction. A variety of anatomical correlates have been reported including: bilateral frontal lesions (Lebert, Pasquier, Steinling et al., 1994), damage in the right parietal or temporal areas (Lebert et al., 1994; Quinn, 1981; Levine and Finklestein, 1982; Levine and Grek, 1984) and left temporo-parietal damage (Benson, 1973). A recent review, by Malloy and Richardson (1994), has highlighted an association between frontal and right sided lesions and persistent content specific abnormal beliefs.

Previous research with AD patients can also be criticised for not imaging all of the patients while delusions were present and for grouping together patients with single and multiple delusions, as well as including patients with a range of delusional content. The latter are potential confounding variables since there is evidence that single content specific delusions are distinct from other types of delusion (Malloy and Richardson, 1994).

The aim of this study was to ascertain whether there is a consistent SPET perfusion pattern characterising AD patients with single content specific