

Thinking through delusions in Alzheimer's disease

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The recent finding in a cohort of patients with Alzheimer's disease and predominantly 'factual' delusions that the clinical severity of abnormal beliefs correlated with right frontal brain perfusion (Sultzer *et al*, 2003) has again highlighted the problematic relationship between clinical phenomenology and cognitive neuropsychiatry. The classical definition of delusion and the traditional clinical hierarchy of form and content have been of value in establishing a descriptive consensus for syndrome-based studies of mental disorders. As a phenomenal account, however, these descriptions seem inadequate to inform experimental design, case selection and interpretation when abnormal beliefs are studied using the methods of cognitive neuroscience and functional neuroimaging (Halligan & David, 2001). Delusions are common, disabling and persistent in the course of Alzheimer's disease and are likely to relate to a range of specific cognitive failures with regional associations as much as to an interaction between neurological and psychosocial factors. It can be suggested that Alzheimer's disease, far from being a diffuse degenerative disease in the course of which poorly differentiated psychotic symptoms emerge from global neurological causes, offers an opportunity to increase our understanding of higher cognitive functions including normal and abnormal belief formation.

TRADITIONAL NEUROBIOLOGICAL STUDIES OF ABNORMAL BELIEFS

Differences between cohorts of patients with and without psychotic symptoms have regularly emerged from both structural and functional neuroimaging studies. Neuropathological studies have suggested a particular role for cortical dysfunction in the neurobiology of delusions in Alzheimer's disease.

Structural findings in patients with delusions have shown that pronounced

degenerative atrophy of the right frontal and temporal areas, and subcortical white-matter hyperintensities in anterior brain regions, are associated with the presence or severity of the psychotic symptoms. Functional neuroimaging studies of patients either with a history of delusions or with contemporary abnormal beliefs have also primarily implicated anterior brain structures, although the specific focus of presumed cortical hypoperfusion or metabolic change has varied. Significant bilateral blood flow deficits in the right temporal cortex, left frontal region, and right frontal and limbic structures were all identified. The findings from metabolic studies have implicated a more widespread network of cerebral dysfunctions including the orbitofrontal and cingulate cortex bilaterally and the left medial temporal areas. The dimensional aspects of the correlation reported by Sultzer *et al* (2003) may be difficult to interpret, but the association of 'factual' or content-specific delusions with frontal and in particular right hemisphere dysfunction was again supported.

The disparity of these findings is likely to relate, at least in part, to the design and implementation of the different studies. Factors likely to influence outcomes include the variable ascertainment, contemporary presence and definition of abnormal beliefs, as well as medication status during imaging and the method of imaging data analysis. The most important factor, however, is likely to be the batching of relatively unselected patients with a range of abnormal beliefs and experiences whose phenomenology had not been well characterised.

HETEROGENEITY OF DYSFUNCTION AND RELATED SYMPTOMS

The dementias have been classified from clinical presentations, patterns of gross anatomical change and parenchymal neuropathology together with what is known of

more fundamental genetic and other aetiological factors. At clinical threshold diagnosis, however, Alzheimer's disease is not uniform in presentation, natural history, rate and mode of progression or age of onset. In some cases, the onset of the dementia is heralded by the selective progressive loss of individual cognitive skills; in others, by asymmetrical brain degeneration predominantly affecting visuospatial or linguistic abilities. Distinctive and various neuropsychiatric symptoms may also emerge at minimal or mild stages of the disease (Venneri *et al*, 2000; Breen *et al*, 2001). The first case published by Alois Alzheimer in 1907 described a woman with delusional jealousy as one of her first symptoms.

Heterogeneity characterises the metabolic and blood flow abnormalities as well as the clinical and neuropsychological features detected early in the disease. Neuropathological heterogeneity may promote clinical variance because of an interaction between the pattern of brain damage and the 'cognitive architecture' of a given patient. The result is the appearance of more subtle cognitive failures and dissociations at higher levels of cognitive processing than might be seen after focal lesions due to vascular or traumatic causes. Cognitive studies with patients with Alzheimer's disease have already made substantial contributions to the formulation of testable models of normal cognitive function. In a similar way, the study of different psychotic symptoms in case and cohort studies in Alzheimer's disease can provide, through natural variance in clinical phenotype, a way of achieving a deeper understanding of the biological and cognitive determinants of abnormal belief formation and persistence.

DECONSTRUCTING DELUSIONS

There is a growing acknowledgement that a procedurally uniform account of delusions may conceal the phenomenological and potentially neurobiological heterogeneity of these symptoms (Middlemost *et al*, 2002). When species of abnormal belief with distinctive contents have been studied, in both 'functional' and organic disorders, persuasive cognitive accounts have emerged. In very brief outline, studies of Capgras syndrome (Ellis & Young, 1990) and other types of reduplicative phenomena have benefited from the ready availability

of well-argued and experimentally supported cognitive models of face identification and affectivity as much as from the focal nature of the symptoms. In the same way, contemporary theories about persecutory delusions depend on demonstrable anomalies in attention and reasoning (Blackwood *et al*, 2001). The variety of neuropsychiatric symptoms associated with Alzheimer's disease offers many more opportunities for the illustration and potential explanation of higher-order mental dysfunctions. From the cognitive perspective, for example, symptoms that at a superficial level might be considered as 'delusions' or as reports of 'hallucinations', on analysis are frequently found to arise from processes of invention or faulty retrieval of imaginal contents that are believed and reported as real experience. It follows that umbrella classifications of psychotic symptoms arising in Alzheimer's disease run the risk of obscuring meaningful variations in the population being studied to the point that only general associations emerge. A detailed understanding of specific symptoms would not be solely of academic interest, but would inform studies of social and pharmacological interventions in the organic psychoses.

A MULTIFACETED APPROACH TO PSYCHOTIC SYMPTOMS

Designs that address individual symptoms in case studies, and in smaller cohorts of patients who share – or differ in respect of – carefully characterised symptoms, might be adopted. The combination of detailed phenomenological analysis with neuroimaging and neuropsychological assessment in Alzheimer's disease has led to interesting preliminary findings. Using a multiple single-case strategy, significantly reduced perfusion in areas of the right dorsolateral prefrontal cortex with an associated deficit in episodic autobiographical memory was described in patients presenting with persistent delusions about autobiographical facts (Venneri *et al*, 2000). These findings were confirmed in a larger cohort study of people with Alzheimer's disease, in which 10 patients with similar autobiographical delusions were contrasted with 20 patients without delusions and 16 patients with other types of delusion (Staff *et al*, 2000).

A study of patients with Alzheimer's disease who had delusions of theft showed a group-specific perfusion deficit in the

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right medial posterior parietal region, and suggested a link with the attentional deficits contingent on local cortical damage (Fukuhara *et al*, 2001). Mirrored-self misidentification delusion has been linked to perceptual and reasoning deficits arising from right hemisphere dysfunction in two patients with mild disease, the delusion appearing as an onset symptom (Breen *et al*, 2001). A common cerebral blood flow defect in right frontoparietal cortex and severe visuoperceptual processing deficits were found in three patients with Alzheimer's disease who had animistic delusions about soft toys (Shanks & Venneri, 2002). The data from all of these studies are consistent with hypotheses about the role of the right brain in reality monitoring and the exertion of a pathoplastic influence by regional cognitive deficits on the content of abnormal belief formation. Such findings do not necessarily conflict with more socially based and interpersonal interpretations of the abnormalities that emerge. It often appears that the underlying neurological damage merely facilitates, in a changed cognitive and perceptual environment, the realisation in a more concrete form of what may be unfulfilled needs.

CONCLUSIONS

The findings outlined above are clearly preliminary. It should be emphasised again (and most clinicians will have observed this) that the mental disintegration in mild and minimal Alzheimer's disease is often discrete. The phenomena of mental disorder may appear in relative isolation, albeit against a background of mild cognitive impairment. This allows the comparative analysis of patient groups with or without the symptom in question, using the combined approach outlined above. The investigation of delusions in this disease, compared with studies of the functional psychoses, has the advantage that a population is studied whose abnormal beliefs appear in a context often relatively free from overlapping

psychopathological and treatment effects, perhaps in a form less integral with the individual psyche and against a background of normal cognitive development. Such studies of the breakdown in higher mental functions in the course of Alzheimer's disease can clarify the fundamental mechanisms involved in delusional thinking and abnormal experience and inform qualitative comparisons with the phenomena seen in the schizophrenias and other delusional disorders. The 'purer' culture of individual symptoms in Alzheimer's disease may, in the end, help provide the basis for a more truly scientific psychopathology.

REFERENCES

- Blackwood, N. J., Howard, R. J., Bentall, R. P., et al (2001)** Cognitive neuropsychiatric models of persecutory delusions. *American Journal of Psychiatry*, **158**, 527–539.
- Breen, N., Caine, D. & Coltheart, M. (2001)** Mirrored-self misidentification: two cases of focal onset dementia. *Neurocase*, **7**, 239–254.
- Ellis, H. D. & Young, A. W. (1990)** Accounting for delusional misidentifications. *British Journal of Psychiatry*, **157**, 239–248.
- Fukuhara, R., Ikeda, M., Nebu, A., et al (2001)** Alteration of rCBF in Alzheimer's disease patients with delusions of theft. *Neuroreport*, **12**, 2473–2476.
- Halligan, P. W. & David, A. S. (2001)** Cognitive neuropsychiatry: towards a scientific psychopathology. *Nature Reviews Neuroscience*, **2**, 209–215.
- Middlemost, M., Mullins, S., Brown, A., et al (2002)** Current problems with the concept of delusion. *Progress in Neurology and Psychiatry*, **6**, 10–13.
- Shanks, M. F. & Venneri, A. (2002)** The emergence of delusional companions in Alzheimer's disease: an unusual misidentification syndrome. *Cognitive Neuropsychiatry*, **7**, 317–328.
- Staff, R. T., Venneri, A., Gemmell, H. G., et al (2000)** HMPAO SPET imaging of Alzheimer's disease patients with a similar content specific autobiographical delusion: a comparison using Statistical Parametric Mapping. *Journal of Nuclear Medicine*, **41**, 1451–1455.
- Sultzer, D. L., Brown, C. V., Mandelkern, M. A., et al (2003)** Delusional thoughts and regional frontal/temporal cortex metabolism in Alzheimer's disease. *American Journal of Psychiatry*, **160**, 341–349.
- Venneri, A., Shanks, M. F., Staff, R. T., et al (2000)** Nurturing syndrome: a form of pathological bereavement with delusions in Alzheimer disease. *Neuropsychologia*, **38**, 213–224.