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Reduced neuron density, enlarged minicolumn spacing and altered ageing effects in fusiform cortex in schizophrenia

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Abstract

Structural and functional MRI studies report reduced volume and activation of the fusiform gyrus in schizophrenia. The fusiform cortex is involved in object naming and face recognition. Neuron cell size, shape and density, glial cell density and minicolumn spacing in layers III and V of the fusiform cortex were assessed following systematic random sampling from 13 controls and 11 schizophrenic patients. Pyramidal cell density was reduced in schizophrenia. Non-pyramidal cell density was reduced in layer III of the left hemisphere in schizophrenia, mostly in females. Non-pyramidal cells were larger in schizophrenia. Glial cell density was unaltered. Fusiform minicolumn spacing was asymmetrically wider in the right hemisphere of normal control subjects. Minicolumns were less dense in schizophrenia, particularly in the left hemisphere of females and the right hemisphere of males. Reduced neuron density in the fusiform cortex in schizophrenia contributes to evidence of functional–anatomical abnormalities from neuroimaging and neuropathology studies. Anatomical sex differences in schizophrenia may relate to anatomical and cognitive sex differences associated with fusiform cortex in the normal population. Wider minicolumn spacing is consistent with reduced cell density and is linked to altered ageing in schizophrenia.

Keywords: Temporal lobe; Pyramidal cells; Neuron size; Asymmetry; Neuroplasticity; Ageing

1. Introduction

Brain-imaging studies find reduced volume of the fusiform gyrus (FG) in schizophrenia (Onitsuka et al., 2006), but the microscopic basis has not yet been identified. Forming the inferior surface of the temporal lobe, the FG plays a central role in face processing, object and word recognition (Moore and Price, 1999), and it is part of a system that integrates perception, memory and emotion (Powell et al., 2004). Anomia (deficit in naming common objects) and prosopagnosia (deficit in identity discrimination of human faces) as well as difficulties in naming objects and colours, and in reading are associated with brain lesions in FG

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cortex (Greenblatt 1990; Hudson and Grace, 2000; Whatmough et al., 2002).

Multiple studies have identified facial processing abnormalities in schizophrenia (Addington and Addington, 1998; Edwards et al., 2001; Gruzelier et al., 1999; Gur et al., 2002; Habel et al., 2000; Johnston et al., 2005; Kohler et al., 2000; Penn and Combs, 2000; Phillips and David, 1995; Whittaker et al., 2001; Wolwer et al., 1996) as well as worse performance in object naming compared with the normal population (Gabrovska et al., 2003).

The deficit of memory for faces in schizophrenia has been correlated with the degree of volume reduction of the anterior FG (Onitsuka et al., 2003). Lateral ventricle enlargement has also been correlated with the decrease in fusiform grey matter volume (Chance et al., 2003), and asymmetric volume reductions have been found, with greater reduction in the left FG, by magnetic resonance imaging (MRI) (Paillere-Martinot et al., 2001) and post-mortem studies (McDonald et al., 2000). Further clinical correlates include an association between FG volume and Liddle's "disorganisation" factor (Chua et al., 1997) and a negative correlation between poverty of speech and left fusiform gyrus activation (Kircher et al., 2003).

Face and object recognition neurons in the inferotemporal region of monkey cortex are clustered in functional columns that extend across the cellular layers forming a mosaic of macrocolumnar modules, each approximately 400 μm in diameter (Tanaka, 1996). Structurally, they consist of groups of smaller minicolumns that emerge from the migration of cells towards the brain's surface during embryonic formation of the cerebral cortex. We have previously shown that minicolumn spacing is altered in the planum temporale in schizophrenia (Chance et al., 2006a,c). Casanova et al. (2005) have shown subtle alterations in the columnar cell spacing in prefrontal cortex. This may be consistent with a developmental anomaly.

Since facial identification is essential for empathic social interaction (Schultz, 2005), abnormalities of the fusiform region may contribute to the social disturbances observed in schizophrenia. Although several neuroimaging studies report macrostructural alterations and functional abnormalities in the fusiform gyrus in schizophrenia, only one histological study has been reported, which found no difference in the apical and basal dendritic arborisation of neurons in fusiform cortex (Rosoklija et al., 2000). The anterior fusiform has been the object of functional MRI (fMRI) studies focusing on its specificity for face recognition. However, we aimed to investigate the whole of the fusiform, which has previously been shown to be defective in schizophrenia suggesting a role of the whole fusiform cortex in the pathophysiology of the schizophrenia spectrum (Onitsuka et al., 2005, 2006; Takahashi et al., 2006; Ha et al., 2004). Layers III and V of the human brain cortex are of particular interest as they are the major pyramidal cell layers involved in intra- and inter-hemispheric connections found to be altered in schizophrenia (Sweet et al., 2004, 2007; Simper et al., 1996). The present study investigated microstructural changesnot previously examined in the fusiform gyrus including cell density, size and shape, and minicolumnar organisation.

2. Materials and methods

2.1. Subjects

Formalin-fixed brain tissue was sampled from 13 normal controls (6 females and 7 males) and 11 patients with schizophrenia (5 females and 6 males). Following assessment of cell morphology two subjects were no longer available for density measurement because this study was not contiguous with the morphological study. However, these subjects were not demographic outliers and being unable to include them did not alter the homogeneity of the group studied (details are given in Table 1).

Tissue was collected with consent in accordance with standard neuropathological practice and is registered with UK national investigations on organ retention. All cases are catalogued and none has been recalled. Control subjects had no history of neuropsychiatric illness; patients with schizophrenia had been diagnosed by specialists (Stephen J. Cooper, Belfast and T.J.C.) according to DSM IV criteria. Cases were selected to yield comparable group mean fixation times and ages at death as far as possible, although pair matching was not possible. Demographic details and potentially confounding variables, including age at death (in years), fixation time (in months) and post-mortem interval (in hours), were subjected to statistical analysis (see below) (Table 1).

No comorbidity of alcohol or illicit drug misuse was detected in our sample's records. Patients had received long-term anti-psychotic medication. Unfortunately, insufficient detail on lifetime medication was available for subsequent statistical analysis; however, we note that Benes et al. (2001) found no structural changes in cortical areas when comparing patients that had been exposed to neuroleptics with drug-naive patients. Pathological assessment of tissue samples used CERAD criteria to exclude brains with pathological evidence, such as Alzheimer's or cerebro-vascular diseases, from the study.