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Investigation of frontal lobe subregions in first-episode schizophrenia ☆

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Abstract

The evidence for frontal lobe structural abnormalities in schizophrenia using magnetic resonance (MR) imaging has been mixed, but most studies used either single slice measures or total volumes of a single frontal region, neither of which is sensitive to potential volume differences in more specific subregions. This study employed reliable methods for parcellation of the frontal lobes from MR images based on the sulcal anatomy. Following a cytoarchitectonic theory that distinguishes dorsomedial (archicortically derived) from ventrolateral (paleocortically derived) frontal subregions, we measured the superior frontal gyrus, anterior cingulate gyrus, and orbital frontal region in 19 first-episode schizophrenia patients and 26 healthy comparison subjects. Results indicated that male patients had significantly larger right orbital frontal volume compared to their left orbital frontal volume and compared to healthy men. Among male patients larger right orbital frontal volume was significantly correlated with smaller right 'archicortical' (i.e. anterior cingulate and superior frontal gyri) volume. Furthermore, the ratio of right orbital frontal to right 'archicortical' volume was significantly and positively correlated with level of delusions among male patients. These findings suggest that there may be reciprocal controls on 'archicortical' and 'paleocortical' neurodevelopment among men with schizophrenia, and that larger paleocortical relative to archicortical volumes may be associated with increased delusions. © 1999 Elsevier Science Ireland Ltd. All rights reserved.

Keywords: Magnetic resonance imaging; Frontolimbic; Cerebral sulci; Parcellation; Sex differences

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1. Introduction

Emil Kraepelin (1919) and Eugen Bleuler (1950) postulated that at least some symptoms of schizophrenia could be due to abnormalities in either the structure or function of the frontal lobes, which are widely regarded to play a major role in attention, affect regulation, executive functioning and metacognition. Despite consistent findings of frontal lobe dysfunction in schizophrenia, however, the evidence for frontal lobe structural abnormalities from magnetic resonance (MR) imaging studies has been mixed. While some studies have reported structural abnormalities in the frontal lobes (Andreasen et al., 1986; Jernigan et al., 1991; Breier et al., 1992; Raine et al., 1992; Zipursky et al., 1992; Buchanan et al., 1993, 1998; Harvey et al., 1993; Bilder et al., 1994; Schlaepfer et al., 1994; Nopoulos et al., 1995; Woods et al., 1996; Hege et al., 1997) others have not (Kelsoe et al., 1988; Suddath et al., 1989, 1990; Andreasen et al., 1990; Rossi et al., 1990; Corey-Bloom et al., 1995; Wible et al., 1995), and methodologic problems prevent firm conclusions. Most studies included patients who had chronic illness and/or long-term exposure to antipsychotic medication. In addition, frontal measures were either from a single slice, or reflected the total volume of a large frontal region (e.g. the entire prefrontal lobe), which may be insensitive to subtle differences in the volumes of more specific subregions.

Assessment of cortical subregions is potentially important because it is known that the frontal lobes are both structurally and functionally heterogeneous. The lack of MR imaging investigations of discrete frontal lobe subregions in schizophrenia may be due to the complicated sulco-gyral patterning in the frontal lobes (Ono et al., 1990), which makes it difficult to reliably identify sulcal boundaries for subregions. Despite these difficulties, several notable methods have been developed for parcellation of the prefrontal cortex (Buchanan et al., 1998; Rademacher et al., 1992; Wible et al., 1997). Few studies, however, have investigated anatomically relevant frontal lobe subregions in patients with schizophrenia. Buchanan et al. (1998) reported decreased inferior prefrontal volume in patients whereas Wible et al. (1994) reported no volume differences in subregions between patients and comparison subjects.

A current challenge in cognitive neuroscience is to define those frontal subregions that are most functionally relevant, and so far there is no clear consensus regarding either the anatomic divisions that are most appropriate, or the functional distinctions that these systems subserve. The ‘evolutionary cytoarchitectonic trends’ model of cerebral cortex originally elaborated by Sanides (1969, 1972) provides a possible anatomic framework to investigate frontal lobe subregions. Using comparative anatomic methods to examine patterns of cytoarchitectonic differentiation, Sanides (1969, 1972) provided evidence for a fundamental duality in the origins of the cerebral cortex in mammals. According to this theory, the frontal neocortex is derived from two cellular primordia, comprising hippocampal (‘archicortical’) and olfactory (‘paleocortical’) moieties. The ‘archicortical’ trend is more dorsally and medially positioned, and includes the hippocampal formation (most primitive), cingulate gyrus (intermediate) and dorsal/medial aspects of prefrontal cortex (most developed, true six-layered isocortex). This trend is isomorphic with the ‘medial frontolimbic system’, in which the frontal lobes and limbic system are linked by the cingulate bundle (Bilder and Degreef, 1991). The ‘archicortical’ trend is distinct from the ‘paleocortical’ trend, which is more ventrally and laterally placed, and in which the most primitive cytoarchitectonic representative is the olfactory cortex, with higher levels of development reflected in the peri-insular (intermediate) and ventral neocortices including the orbital frontal cortex (most developed). Sanides’ early studies have been supported by modern anatomical studies of both long- and short-range connectivity patterns, and by patterns of laminar organization (Pandya and Barnes, 1987; Yeterian and Pandya, 1988). With the aid of anterograde and retrograde tracers, Pandya and colleagues have detailed the efferent and afferent projections of the ventral (‘paleocortical’) and dorsal (‘archicortical’) subdivisions (Pandya and Yeterian, 1985; Barbas and Pandya, 1989) and demon-