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Brain gray and white matter transverse relaxation time in schizophrenia

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Abstract

Recent in vivo diffusion brain imaging studies of schizophrenic patients have revealed microstructural abnormalities, with low diffusion anisotropy present throughout much of cortical white matter. Brain anisotropy is produced when proton movement reflects physically restricted water movement, for example, by myelin sheaths. Conditions that increase self-diffusion, such as edema, may also alter the longitudinal and transverse relaxation time of protons, and it is possible that such changes could explain the observed anisotropy diminution seen in schizophrenia. To test this possibility, we calculated pixel-by-pixel transverse relaxation time (T2) and proton density (PD) maps for gray matter and white matter across eight 5-mm-thick axial slices of fast spin echo MRI in 10 control men (age 30–57 years) and 10 men with schizophrenia (age 32–64 years). Schizophrenics had significantly longer mean white matter T2 (84.0 vs. 81.9 ms, $P < 0.03$) and gray matter T2 (95.1 vs. 92.2, $P = 0.003$); their mean white and gray matter PD values were not significantly different from those of controls. Correlations were not significant between anisotropy and T2 in either grey or white matter but were significant between anisotropy and PD in white matter. T2 relaxation times are longer in schizophrenics than in controls in both gray and white matter whereas anisotropy reduction is restricted to white matter. Taken together, these results suggest that the process producing prolonged T2 does not fully account for the abnormally low anisotropy observed selectively in white matter in this group of schizophrenic patients.

Keywords: Schizophrenia; Magnetic resonance imaging; Diffusion tensor imaging; Transverse relaxation time; T2; White matter

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1. Introduction

Over the last decade, numerous controlled in vivo magnetic resonance imaging (MRI) studies have examined the brain's macrostructure and have reported volume abnormalities in patients with schizophrenia [reviewed by Marsh et al. (1996) and Shenton et al. (1997)]. The general consensus is that the lateral and third ventricles are enlarged and that cortical gray matter deficits occur; less frequently reported are white matter volume deficits [e.g. gray matter (Harvey et al., 1994; Schlaepfer et al., 1994; Sullivan et al., 1998; Zipursky et al., 1992); white matter (Breier et al., 1992; Buchanan et al., 1998; Wolkin et al., 1998)].

Recently, diffusion weighted imaging, or diffusion tensor imaging (DTI) (Basser and Le Bihan, 1992; Basser et al., 1992, 1994), which can quantitate the magnitude and directionality of tissue water mobility (i.e. self-diffusion) in three dimensions (Moseley et al., 1991; Basser et al., 1994), has been used to examine the brain's white matter microstructure. When diffusion is constrained by a regular and orderly microstructure, such as white matter fibers, the water molecules tend to move faster and further along the fibers than perpendicular to them, and the diffusion is termed 'anisotropic'. Contrarily, the diffusion of water molecules that move equally in all directions is 'isotropic'. Buchsbaum et al. (1998) reported evidence of lower diffusion anisotropy in inferior portions of prefrontal white matter in schizophrenic patients than controls. In the study of Lim et al. (1999), schizophrenic patients exhibited lower anisotropy in white matter than controls, despite absence of a white matter volume deficit. In contrast to white matter, gray matter anisotropy did not distinguish the groups even though the schizophrenic patients had significant gray matter volume deficits. The abnormal white matter anisotropy in the schizophrenic patients was present in both hemispheres and was widespread, extending from the frontal to occipital brain regions.

Decreased anisotropy and increased self-diffusion are seen in edema, demyelination and white matter hyperintensities (Spielman et al., 1996; Makris et al., 1997; Arnold et al., 1998; Miller et al., 1998; Jones et al., 1999). Also seen in these conditions and phenomena are prolonged longitudinal and transverse relaxation times (T1 and T2) of water protons. It is possible that a common process is responsible, at least in part, for all three findings: decreased anisotropy, increased diffusion, and prolonged relaxation times. In addition to decreased anisotropy, prolonged T2 times have been reported in patients with schizophrenia in gray matter (Andreasen et al., 1991) and white matter (Williamson et al., 1992), including fornix (Supprian et al., 1997). Prolonged transverse and longitudinal relaxation times both occur in frontal and temporal cortex in patients with schizophrenia (Yurgelun-Todd et al., 1995, 1996; Yurgelun-Todd et al., in review).

The purpose of this study was to examine the transverse relaxation time of brain gray matter and white matter separately in schizophrenics compared to controls and to examine the relationship of transverse relaxation time and proton density (PD) to diffusion anisotropy. Accordingly, we calculated pixel-by-pixel T2 and PD maps for gray matter and for white matter from the structural MRIs of the control subjects and schizophrenic patients collected in our previous study (Lim et al., 1999).

2. Methods

2.1. Subjects

As described previously (Lim et al., 1999), all subjects gave written informed consent for study participation and underwent physical and psychiatric examinations. The patients were 10 men, veterans of the United States Armed Services, who met DSM-IV criteria for schizophrenia. They were 47.7 ± 7.8 years old (range = 32–64) and had 13.9 ± 1.9 years of education. Exclusion factors were DSM-IV criteria for Alcohol or Substance Abuse or Dependence within 3 months prior to scanning; Posttraumatic Stress Disorder; significant medical illness; or head injury resulting in loss of consciousness exceeding 30 min. DSM-IV diagnoses were determined by consensus between a psychiatrist or clinical psychologist,