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The volumes of the fornix in schizophrenia and affective disorders: A post-mortem study

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Abstract

Structural and functional pathology of limbic structures including the hippocampus are frequently replicated in schizophrenia. Although the fornix is the main afferent system of the hippocampus to the septal nuclei and the hypothalamus (especially the mammillary bodies), relatively few studies have investigated structural changes of the fornix in schizophrenia. We measured the volume of the fornix in post-mortem brains in 19 patients with schizophrenia, 9 patients with bipolar disorder, 7 patients with unipolar depression, and 14 control subjects by planimetry of serial sections. The volumes, the mean cross-sectional areas, and the anterior to posterior distances of the fornix did not differ among patients with schizophrenia, bipolar disorder, unipolar depression, and control subjects. No lateralization existed between the right and the left fornices in among patients in the diagnostic groups and the control subjects. The fornix does not show morphometrical abnormalities in patients with schizophrenia, bipolar disorder and unipolar depression compared with control subjects, which might indicate that the fornix is not a primary focus of structural changes in these diseases.

Keywords: Volumes; Fornix; Lateralization; Schizophrenia; Affective disorders

1. Introduction

Although several studies show that parts of the limbic and cortical systems such as the hippocampus (Bogerts et al., 1985; Bogerts et al., 1990a; Schmajuk, 2001), the thalamus (Byne et al., 2002; Danos et al., 2003; Danos et al., 2005; Mitelman et al., 2005a; Mitelman et al., 2006), the hypothalamus (especially the mammillary bodies) (Bernstein et al., 2007), the cavum septi pellucidi (Degreef et al., 1992a,b; DeLisi et al., 1993; Nopoulos et al., 1998; Brisch et al., 2007), and the temporal and association cortices are involved in the pathophysiology

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of schizophrenia (Hirayasu et al., 1998; Heckers, 2001; Kasai et al., 2003; Szeszko et al., 2003; Mitelman et al., 2005b,c), only a few studies with conflicting results have addressed the role of the fornix as part of the limbic system in schizophrenia. These studies report conflicting results. Several magnetic resonance imaging (MRI) studies measured the volumes and the cross-sectional areas of the fornix in schizophrenia (Cirillo et al., 2000; Davies et al., 2001; Zahajszky et al., 2001; Kubicki et al., 2005; Kuroki et al., 2006). However, only one post-mortem study by Chance et al. (1999) considered the cross-sectional areas and the total fiber number of the fornix in schizophrenia. The fornix plays a major role in functions that are assumed to be disturbed in schizophrenia such as memory retrieval (Gaffan, 1993; Calabrese et al., 1995), verbal memory (Calabrese et al., 1995; McMackin et al., 1995), spatial memory (Gaffan, 1994; Parker and Gaffan, 1997; Murray et al., 1998; Galani et al., 2002; Buckley et al., 2004), increased motor activity (Weiner et al., 1998) and transitive inference (Dusek and Eichenbaum, 1997).

Morphologically, near the splenium of the corpus callosum the fimbria of the hippocampus becomes the crus of the fornix which sends fibers forward at the inferior edge of the septum pellucidum to the interventricular foramen. The fornix is located inferiorly and posteriorly and diverges into the column of the fornix. The column of the fornix divides at the anterior commissure into a postcommissural projection to the mammillary body and a precommissural projection to the septal region.

It was the aim of this study to measure the volumes of the fornix in 3-D (or three dimensions) in a post-mortem study in patients with schizophrenia, bipolar disorder, and unipolar depression and to compare these results to control subjects matched for age, sex, and other confounding variables.

2. Material and methods

2.1. Subjects

All brains used in this study were from the New Magdeburg Brain Collection from 1987 to 2003 (Bernstein et al., 1999). The collection of the human brain material was performed according to German law and after approval by the local ethical commission. The mean demographic data of all individual cases (all were Caucasian) including brain weight, postmortem delay, and duration of the disease are given in Table 1. Post-mortem brains of 14 subjects (8 males, 6 females) without any signs of neurological or psychiatric symptoms were used as the control group. Brains of 19 patients (11 males, 8 females) with a clinical diagnosis of schizophrenia according to the Diagnostic and Statistical Manual of Mental Disorders (DSM-IV) were included. All patients with schizophrenia had received antipsychotic treatment for at least several years before death.

Additionally, brains of 16 patients with affective disorders (8 males, 8 females) according to DSM-IV were studied. Seven of these patients were diagnosed with unipolar depression and nine patients had bipolar disorder. Patients with affective disorders received antidepressant medication for several years before death. The degree of typical neuroleptic and antidepressant medication in the last 3 months before death was assessed from medical records and was categorized as little, average, or much as described in a previous study of the fornix by Chance et al. (1999). In all cases a complete medical history was available. Information for clinical diagnosis was obtained by the careful study of clinical records and/or by structured interviews with either the physicians involved in the treatment and with persons who either lived with or had frequent contact with the subjects before death. Exclusion criteria were (i) organic

Table 1
Demographic data of control subjects, patients with unipolar depression, bipolar disorder, and schizophrenia

Demographic Data	Control Subjects	Unipolar Depression	Bipolar Disorder	Schizophrenia	Three-Group-Comparison Values	
	$N=14$	$N=7$	$N=9$	$N=19$	ANOVA	
					F	P
Age (years)	53.64±9.61	46.71±14.31	51.78±11.90	51.37±7.85	0.724	0.543
Brain weight (mg)	1280.71±145.63	1301.14±137.73	1447.00±148.74	1295.00±149.93	2.768	0.054
Postmortem delay (h)	33.93±20.68	37.00±20.02	47.44±29.16	40.05±19.90	0.718	0.546
Duration of illness (years)	–	3.60±4.16	14.88±7.68	19.00±10.64	5.435	0.010
Frequency					χ^2 - test	
Males / Females	8 / 6	2 / 5	6 / 3	11 / 8	χ^2	P
					2.562	0.464