

## Episodic memory and neuroimaging of hippocampus and fornix in chronic schizophrenia

Paul G. Nestor<sup>a,b,\*</sup>, Marek Kubicki<sup>c</sup>, Noriomi Kuroki<sup>c</sup>, Ronald J. Gurrera<sup>b</sup>, Margaret Niznikiewicz<sup>b,c</sup>, Martha E. Shenton<sup>b,c</sup>, Robert W. McCarley<sup>b,c</sup>

<sup>a</sup>*Department of Psychology, University of Massachusetts, Boston, MA, United States*

<sup>b</sup>*Clinical Neuroscience Division, Laboratory of Neuroscience, Boston VA Health Care System-Brockton Division, Department of Psychiatry, Harvard Medical School, Boston, MA, United States*

<sup>c</sup>*Surgical Planning Laboratory, MRI Division, Department of Radiology, Brigham and Women's Hospital, Harvard Medical School, Boston, MA, United States*

Received 16 December 2006; accepted 27 December 2006

### Abstract

A group of 44 patients with schizophrenia and 43 age-matched controls completed psychometrically-matched tasks of recall and recognition. The patients showed similarly depressed scores across both recall and recognition matched tasks, independent of their reduced IQ and executive functioning scores. In addition, reduced memory scores correlated in the expected direction with magnetic resonance imaging (MRI) of the hippocampus and diffusion tensor imaging (DTI) of the fornix for subsets of both patients and controls that had available these structural imaging measures. Reduced executive functioning also correlated with lower fornix integrity for the patient subset. However, increased hippocampal volume correlated, in the negative direction, with lower scores for executive functioning and IQ in the control subset. Implications of these results are discussed.

© 2007 Elsevier Ireland Ltd. All rights reserved.

*Keywords:* Hippocampus; Fornix; Recall; Recognition

### 1. Introduction

Cognitive disturbance is thought to be a central and enduring characteristic of schizophrenia that can predate illness onset, almost always accompanying and then outlasting acute symptom expression (Heinrichs, 2005). A key component of this disturbance is a deficit in declarative episodic memory for both encoding and

retrieval of newly acquired information. Typically accompanied by a general diminution in other higher-order cognitive functions of working memory, generalized intelligence, and executive functions (Mohamed et al., 1999; Bilder et al., 2000), memory deficit in schizophrenia may be the best cognitive predictor of poor outcome (Heinrichs and Zakzanis, 1998), especially vocational (Green, 1996). As such, a better understanding of memory impairment in schizophrenia may contribute to developing therapies for improving cognition and functional outcome in patients (Green and Nuechterlein, 2004).

\* Corresponding author. Department of Psychology, University of Massachusetts-Boston, Boston, MA 02125-3393, United States.

E-mail address: [paul.nestor@umb.edu](mailto:paul.nestor@umb.edu) (P.G. Nestor).

The current study aimed principally to examine declarative episodic memory in schizophrenia using the Doors and People Test (DPT). The DPT provides standardized, psychometrically-matched recognition and recall measures of equivalent difficulty as well as quantitative, age-norm forgetting rates (Baddeley et al., 1994). The DPT thus allows for two important dimensions of episodic memory in schizophrenia to be investigated comprehensively within the same behavioral paradigm. First is the question of recall and recognition, which Baddeley (1996) found to be similarly impaired on the DPT, in contrast to earlier findings of a differential impairment in recall for patients on experimental tasks of equivalent difficulty (Calev, 1984). Second is the question of whether DPT forgetting rates are unaffected in schizophrenia as have been reported in other behavioral experimental studies of neuropsychiatric disorders (Lewis and Kopelman, 1998) as well as studies of subjects with impaired memory emanating from lesions of the diencephalon and the temporal lobe (Freed et al., 1987; Kopelman and Stanhope, 1997).

The current study also aimed to investigate episodic memory disturbance in schizophrenia in relation to other well-known neuropsychological deficits in executive functioning and intelligence. While clearly related, schizophrenic disturbances in memory, executive functioning, and intelligence are typically studied in isolation. By examining the relationship among these deficits, the current study addressed the extent to which impaired recall and recognition in schizophrenia may be attributed to memory per se or to other disease-related deficits in executive functions and generalized intelligence.

In a similar vein, in the current study, subsets of both patients and controls had available structural imaging measures of particular brain regions, the fornix and the hippocampus, which are thought to play important roles in declarative episodic memory (Kuroki et al., 2006). In fact, several case studies of amnesia patients with hippocampal lesions have now demonstrated the sensitivity of recall and recognition deficits on the DPT (e.g., Reed and Squire, 1997; Manns and Squire, 1999). In addition, considerable evidence also has shown that transection of the fornix, a subcortical white matter tract carrying axons to and from the hippocampus, can have similar deleterious effects on memory in monkeys and in humans (Gaffan, 2005). Both these regions are thought to be critical nodes in a network that is essential for remembering new information, with the fornix serving as an important connective output pathway with axons originating from cells in the subiculum

traveling to terminal sites of the nucleus accumbens, medial prefrontal cortex and septal regions (Brasted et al., 2003).

For patients with schizophrenia, lower scores on neuropsychological tests of memory have correlated with reduced magnetic imaging resonance (MRI) volumes of the left parahippocampal gyrus (Nestor et al., 1993), and the left hippocampus (Kuroki et al., 2006), and reduced diffusion tensor imaging (DTI) of fractional anisotropy of the uncinate fasciculus (Nestor et al., 2004). We now examine the neuropsychology of episodic memory in schizophrenia, with recall and recognition tests of equivalent difficulty that have been consistently linked to medial temporal regions, particularly the hippocampus, and we examine various aspects of memory within the context of both intelligence and executive functions, as well as structural neuroimaging of the hippocampus and the fornix.

## 2. Methods

### 2.1. Subjects

All subjects ( $n=87$ ) were male between the ages of 18 and 55 years, right-handed, native speakers of English, without histories of ECT, neurological illness, and without alcohol or drug abuse in the past 5 years, as assessed by the Addiction Severity Index (McClellan et al., 1992). Diagnoses were ascertained by the Structured Clinical Interview for DSM-IV Axis I Disorders-Patient Edition (SCID-P) (First et al., 1997), along with chart review. All patients were part of an ongoing comprehensive, longitudinal study of schizophrenia, and all were receiving neuroleptic medication; the mean chlorpromazine (CPZ) equivalent daily dose was 381.04 mg (S.D.=304.07). The mean duration of illness was 14.67 years (S.D.=8.51). Normal comparison subjects, recruited from newspaper advertisement, underwent the SCID-NP, and were matched to patients on the basis of age, sex, handedness, and parental SES. After the study was described to them, all subjects provided written informed consent. For the neuropsychological assessment, 43 normal controls and 44 schizophrenic patients completed the Wisconsin Card Sorting Test (WCST; Heaton, 1981) and the Wechsler Adult Intelligence Test-Third Edition (WAIS-III; Wechsler, 1997). For the WCST, 21 patients and 25 normal controls had available magnetic resonance imaging (MRI) volume measures of the hippocampus and diffusion tensor imaging (DTI) of the fornix, and for the WAIS-III, 21 patients and 24 normal controls had available MRI/DTI measures (Kuroki et al., 2006).

متن کامل مقاله

دریافت فوری ←

**ISI**Articles

مرجع مقالات تخصصی ایران

- ✓ امکان دانلود نسخه تمام متن مقالات انگلیسی
- ✓ امکان دانلود نسخه ترجمه شده مقالات
- ✓ پذیرش سفارش ترجمه تخصصی
- ✓ امکان جستجو در آرشیو جامعی از صدها موضوع و هزاران مقاله
- ✓ امکان دانلود رایگان ۲ صفحه اول هر مقاله
- ✓ امکان پرداخت اینترنتی با کلیه کارت های عضو شتاب
- ✓ دانلود فوری مقاله پس از پرداخت آنلاین
- ✓ پشتیبانی کامل خرید با بهره مندی از سیستم هوشمند رهگیری سفارشات