Available online at www.sciencedirect.com
ScienceDirect
Psychiatry Research 151 (2007) 1–10
PSYCHIATRY RESEARCH
www.elsevier.com/locate/psychres

Stereologic analysis of the lateral geniculate nucleus of the thalamus in normal and schizophrenic subjects

Lynn D. Selemon *, Anita Begovic´

Department of Neurobiology, Yale University School of Medicine, PO Box 208001, New Haven, CT 06520-8001, USA

Received 11 December 2005; received in revised form 29 October 2006; accepted 2 November 2006

Abstract

Reduction of volume and neuronal number has been found in several association nuclei of the thalamus in schizophrenic subjects. Recent evidence suggests that schizophrenic patients exhibit abnormalities in early visual processing and that many of the observed perceptual deficits are consistent with dysfunction of the magnocellular pathway, i.e. the visual relay from peripheral retinal cells to the two ventrally located magnocellular layers of the lateral geniculate nucleus (LGN). The present study was undertaken to determine whether abnormalities in cell number and volume of the LGN are associated with schizophrenia and whether the structural alterations are restricted to either the magnocellular or parvocellular subdivisions of the LGN. Series of Nissl-stained sections spanning the LGN were obtained from 15 schizophrenic and 15 normal control subjects. The optical disector/fractionator sampling method was used to estimate total neuronal number, total glial number and volume of the magnocellular and parvocellular subdivisions of the LGN. Cell number and volume of the LGN in schizophrenic subjects were not abnormal. Volume of both parvocellular and magnocellular layers of the LGN decreased with age. These findings do not support the hypothesis that early visual processing deficits in schizophrenic subjects are due to reduction of neuronal number in the LGN.

Keywords: Vision; Magnocellular; Parvocellular; Postmortem; Human; Aging

1. Introduction

The lateral geniculate nucleus (LGN) of the thalamus is the major target of retinal ganglion cells and relays visual information from the contralateral visual field to the primary visual cortex. The LGN is comprised of six cellular layers, i.e., two magnocellular layers lying ventrally and four parvocellular layers located dorsally, as well as cell-sparse intralaminar layers and a cell-poor superficial layer that is ventral to the magnocellular layers. Parvocellular layers transmit information about color and object form from the fovial retina to the visual cortex whereas magnocellular layers carry retinal signals from peripheral retinal cells that are involved in spatial recognition and motion detection (Lennie, 1980; Kaplan and Shapley, 1986; Livingston and Hubel, 1988). The magnocellular and parvocellular pathways correspond loosely to the transient and sustained channels of visual processing that have been derived from psychophysical experimentation in human subjects (Breitmeyer, 1992). These pathways travel in parallel through the LGN but interact at the level of the primary visual cortex and in subsequent relays through the dorsal and ventral visual streams. Thus, although the magnocellular and parvocellular pathways project primarily

* Corresponding author. Tel./fax: +1 508 540 5306.
E-mail address: ldselemon@aol.com (L.D. Selemon).

0165-1781/$ - see front matter © 2006 Elsevier Ireland Ltd. All rights reserved.
doi:10.1016/j.psychres.2006.11.003

into the dorsal and ventral visual streams, respectively, these functionally distinct visual streams represent an integrated signal from the two LGN pathways that encode object localization (dorsal) and object recognition (ventral).

The most prominent symptoms of schizophrenia are thought disorder, psychosis, and cognitive dysfunction (for review, see Carpenter and Buchanan, 1994). Somewhat surprisingly, recent evidence suggests that schizophrenic subjects also have subtle deficits in early visual processing (Butler et al., 2001, 2002; Green et al., 2003; Schecter et al., 2003). Moreover, several lines of evidence suggest that perceptual abnormalities associated with schizophrenia may be channel-specific. The majority of findings in schizophrenic subjects suggest that deficits are more prominent in the magnocellular pathway or in the dorsal stream which would also implicate magnocellular processing (Green et al., 1994a,b; O'Donnell et al., 1996; Cadenhead et al., 1998; Butler et al., 2001, 2005; Doniger et al., 2002; Schecter et al., 2003; Kim et al., 2005;) although some recent evidence implicates the parvocellular pathway in visual processing abnormalities associated with schizophrenia (Butler et al., 2002; Green et al., 2003).

Several abnormalities in structural and neurochemical composition of the visual cortex have emerged despite its inclusion in many studies only as a "control" comparison region for the dorsolateral prefrontal cortex (for review, see Selemon, 2001). These abnormalities include increased neuronal cell packing density (Selemon et al., 1995), decreased expression of synaptophysin protein and mRNA (Perrone-Bizzozero et al., 1996; Eastwood et al., 2000), and decreased expression of RSG4 mRNA, a gene that regulates G-coupled intracellular signaling (Mirnics et al., 2001). All of these findings are consistent with reduced connectivity and diminished synaptic signaling in the visual cortex.

Presently, it is not known whether there are corresponding structural changes in the LGN, and in particular, whether the LGN may have fewer projection neurons in schizophrenic patients in comparison to normal subjects. *In vivo* neuroimaging studies of schizophrenic subjects have found smaller whole thalamic volume and altered thalamic shape (Ettinger et al., 2001; Gilbert et al., 2001; Csernansky et al., 2004), altered metabolic activity (Buchsbaum et al., 1996; Hazlett et al., 1999) and reduction of volume in subregions or specific nuclei of the thalamus (Andreasen et al., 1994; Byne et al., 2001; Kemether et al., 2003). In addition, postmortem studies of brains from schizophrenic subjects have reported a reduction in total neuronal number and volume of individual thalamic nuclei, e.g., the mediodorsal, anterior, pulvinar and ventral lateral posterior nuclei (Pakkenberg, 1990; Popken et al., 2000; Young et al., 2000; Byne et al., 2002; Danos et al., 2002, 2003). It should be noted, however, that several studies have not found evidence of thalamic pathology in schizophrenic subjects (Portas et al., 1998; Arciniegas et al., 1999; Deicken et al., 2002; Cullen et al., 2003; Dorph-Petersen et al., 2004; Preuss et al., 2005). Moreover, all of the thalamic nuclei that have been implicated in schizophrenia are reciprocally connected with higher association cortices; therefore, it is not clear whether thalamic neuronal deficits in schizophrenia extend to sensory thalamic nuclei, such as the LGN.

The present study was undertaken to determine whether subjects with schizophrenia had an altered number of neurons or glia in the LGN and whether, if structural differences were found, the pathology would be limited to either the parvocellular or magnocellular subdivisions of the LGN.

2. Methods

2.1. Brains and histology

Thirty brains from the Stanley Foundation Consortium Collection, 15 schizophrenic and 15 matched normal control brains, were examined in this study (Table 1). Schizophrenic patients were diagnosed by retrospective review of medical records using DSM-IV criteria by two senior psychiatrists associated with the Stanley Foundation. A detailed description of donor selection has previously been reported (Torrey et al., 2000). Normal control subjects did not have a history of

Table 1
Subject demographics[a]

	Normal subjects ($N=15$)	Schizophrenic subjects ($N=15$)	Student's *T*-test
Gender	9M/6F	9M/6F	
Age	48.07±10.66	44.53±13.11	$t_{1,28}=0.810$, $P=0.425$
PMI	23.73±9.95	33.80±14.55	$t_{1,28}=-2.212$, $P=0.035$
TF	338.27±234.32	620.73±233.11	$t_{1,28}=-3.310$, $P=0.003$
Brain wt	1501.00±164.12	1471.67±110.89	$t_{1,28}=0.578$, $P=0.568$
pH	6.18+0.25	6.16+0.26	$t_{1,28}=1.175$, $P=0.250$
Hemisphere	8R/7L	9R/6L	

PMI = postmortem interval in hours.
TF = storage time in formalin in days.
Brain wt = brain weight in grams.
[a] Means±S.D.