Zhurnal Nevropatologii i Psikhiatrii imeni S. S. Korsakova, vol. 69, no. 11, pp. 1679-1682, 1969

PRINCIPLES GOVERNING APPEARANCE OF ANTI-BRAIN ANTIBODIES IN SERUM OF SCHIZOPHRENICS

G. I. KOLYASKINA and S. G. KUSHNER

Institute of Psychiatry,
Academy of Medical Sciences of the USSR, Moscow

Previous investigations showed that tissue antibodies, notably antibodies against brain antigens, are present in the blood of patients with schizophrenia and certain other psychoses (1-7).

At the present time, antibody formation in the diseased organism is regarded as an expression of complex immunopathological processes. Facts have recently been obtained concerning the appearance of autoantibodies in pathological states associated with tissue destruction, with aging, and so on. In all these cases the autoimmune reactions either contribute to the pathological process or result from it. The organism is immunized by endogenous substances, i.e., by its own tissue proteins. Such immunization can take place in reaction not only to components of normal tissues, but also of tissues which have been modified by the action of various factors. After injury to the "barrier" organs, if their tissues enter the blood stream, this can act as an antigenic stimulus for the lymphoid system. Structural changes characteristic of the immune response take place in the lymphoid tissue and antibodies appear in the blood stream.

Although the hypothesis concerning the role of autoimmune processes in schizophrenia was formulated long ago, no definitive evidence has yet been obtained that they play an essential role in the pathogenesis of this disease.

One possible approach to the study of this problem is to examine the relationship between the immunologic changes and the severity and special features of the clinical course of the disease. The object of the investigation described below was to study the relationship between the appearance of brain antibodies in the blood of patients with schizophrenia and the various clinical parameters of the disease: the clinical course of the disease, its duration, the age of the patients, the degree of malignancy of the disease, and the treatment given.

The patients' sera were tested by the cold complement fixation test (CFT) (5). The antigens used were saline extracts of human brain and liver tissues. The brain and liver were taken from the cadaver of a person dying accidentally and not later than 6 hr after death. The minced tissues were carefully ground in a mortar with continuous addition of physiological saline (10 ml/g brain and 5 ml/g liver). The resulting suspension was thrice frozen and thawed, and then centrifuged (10,000 rev/min for 30-40 min). The supernatant was collected and its protein content determined by Lowry's method; after dilution with physiological saline to a final concentration of 0.332 mg protein/ml it was used as the antigen. This content of protein ensured activity of the antigen and also that the sera studied were free of anticomplement properties. In each experiment rabbit antisera against analogous protein extracts of human brain and liver were used as the control. The results of the reaction were taken as positive if the antibody titer of the patient's serum against brain antigen was 1:40 or above, to give a reaction of intensity +, ++, +++, or ++++. If the serum reacted with specific antigens up to a dilution of 1:20, the result was regarded as doubtful, and if to a lower dilution than this, as negative.

Clinically homogeneous groups of schizophrenic patients were investigated. Division into subgroups was based on the clinical course of the disease, in accordance with the classification of schizophrenia adopted at the Institute of Psychiatry, Academy of

ISSN 0012-4966, Doklady Biological Sciences, 2007, Vol. 412, pp. 18–19. © Pleiades Publishing, Ltd., 2007.
Original Russian Text © I.P. Ashmarin, G.Sh. Burbaeva, R.A. Danilova, M.F. Obukhova, 2007, published in Doklady Akademii Nauk, 2007, Vol. 412, No. 6, pp. 832–833.

PHYSIOLOGY

Schizophrenia and Autoantibodies Against the Regulatory Peptide 5HT-modulin

I. P. Ashmarin, G. Sh. Burbaeva, R. A. Danilova, and M. F. Obukhova

Presented by Academician N.F. Myasoedov June 26, 2006

Received July 3, 2006

DOI: 10.1134/S0012496607010061

The role of the immune system in the pathogenesis and progress of mental illnesses attracts increasingly much attention. Regarding schizophrenia, numerous factual data on the subject have been accumulated [1]. Autoimmune processes are of special interest. To date, it is obvious that autoantibodies may fulfill both negative and positive functions. They may, in particular, change the levels of regulatory peptides [2]. We attempted to determine the possible role of autoantibodies against the neuroregulator peptide 5HT-modulin. This tetrapeptide (Leu–Ser–Ala–Leu) is an important specific modulator of serotonergic transmission and indirectly affects dopaminergic transmission. It serves as an internal inducer of anxiety and depressive behavior, taking part in the development of stress [3, 4].

The purpose of this study was to determine the level of autoantibodies against 5HT-modulin in schizophrenics and healthy subjects and estimate the effect of treatment on this parameter. We detected anti-5HT-modulin autoantibodies only in schizophrenics. The antibody titer increased in the course of treatment for schizophrenia. The data obtained allow us to make some assumptions on the possible role of autoantibodies in the mechanisms of compensation of the pathological process.

A difficulty with this study was the necessity to measure low titers of antibodies and, hence, to use the most reliable statistical methods for treating the obtained data.

We measured the titers of anti-5HT-modulin autoantibodies in 31 patients with shift-like paranoid schizophrenia and 12 physically and mentally healthy subjects. A combination of haloperidol and clozapine (2.5 and 12.5 mg/day, respectively) was used for treatment. Blood tests were performed before the treatment (untreated patients, U) and after 8 and 20–28 weeks of treatment (T-I and T-II, respectively).

The concentrations of antibodies against 5HT-modulin were determined by means of enzyme-linked immunosorbent assay (ELISA). Hereinafter, the antibody titers are shown as serum dilution factors instead of fractions.

5HT-modulin was synthesized in the Institute of Molecular Genetics of the Russian Academy of Sciences. Statistical treatment of the results was performed with the use of a set of both parametric and nonparametric tests. We calculated geometric mean values for control subjects, untreated patients, and treated patients, and estimated the significance of differences between them with the use of classical statistical tests. Test for differences between proportions were used to compare samples of data grouped according to titers exceeding specified levels. Finally, the Mann–Whitney test was used. The significances of differences estimated using all the above tests were similar. Here, we show the data on the proportion difference test as the most illustrative ones.

Of special interest are data on anti-5HT-modulin autoantibodies in "pure" (untreated) patients. Although the titers of these autoantibodies were low, they differed from the control values according to all tests used at $p < 0.05$. Diagrams showing the comparison with respect to titers ≤40 and >80 (experiment, $n = 31$; control, $n = 12$) are especially illustrative. In the patients treated with haloperidol and clozapine, the autoantibody titers were considerably increased, especially at the second stage, with the significance of difference from the control corresponding to $p < 0.01$ (Fig. 1). In addition to these data, we observed a trend towards larger changes in the autoantibody titers in the patients that positively responded to treatment. This result, however, requires confirmation using lager samples of patients.

Moscow State University, Leninskie gory, Moscow, 119899 Russia

Research Institute of Normal Physiology, Russian Academy of Medical Sciences, Bol'shaya Nikitskaya ul. 6, Moscow, 103009 Russia

Mental Health Center, Russian Academy of Medical Sciences, Moscow, Russia

Schizophr Res. 1994 Dec;14(1):15-22.

Increased prevalence of antibrain antibodies in the sera from schizophrenic patients.

Henneberg AE, Horter S, Ruffert S.

Department of Neurology, University of Ulm, Germany.

Abstract

The pathogenesis of schizophrenia is still unknown. In a previous study we found antibrain antibodies in the sera of schizophrenic patients, but not in normal controls. Therefore we have further examined the sera of schizophrenic patients versus normal controls, increasing the number of brain areas, to explore whether certain areas were involved more often than others in the antibody binding process. The sera of 50 patients suffering from an acute episode of schizophrenia (classified by DSM III-criteria) were tested. 70% of the patients showed antibody binding, while only 12% of the age- and sex-matched controls were positive. The binding was mediated by IgG- as well as IgM-antibodies. Amygdala, frontal cortex, cingulate gyrus, and septal area were the prominent targets, while hippocampus, parahippocampal gyrus, entorhinal cortex, putamen, mamillary bodies and head of the caudate nucleus were involved to a lesser degree. Binding was not present to nucleus olivaris, to the thyroid gland or to HEp-2 cells, which we included to test for unspecific antinuclear factors. Longterm studies of schizophrenic patients and biochemical analyses of the antigen(s) involved are in progress.

PMID: 7893617 [PubMed - indexed for MEDLINE]

Autoantibodies to DNA in Multicase Families with Schizophrenia

Pinkhas Sirota, Michael A. Firer,* Klara Schild, Amir Tanay, Avner Elizur, Dina Meytes, and Hanoch Slor

In an attempt to define the autoimmune status of members of multicase families with schizophrenia, sera of both patients and healthy relatives from 28 such cases were tested for antinuclear antibodies, anti–double-strandedDNA, and anti–single-strandedDNA autoantibodies. These autoantibodies were significantly more frequent in both schizophrenic patients and healthy relatives than in normal subjects. Immunoglobulin (Ig) M anti-DNA antibodies were more common in patients, whereas in healthy relatives, IgG anti-DNA antibodies were more common. No significant differences were found between schizophrenic patients and their healthy relatives. The data indicate that an autoimmune process may be involved in the etiology of a subset of patients with schizophrenia.

Key Words: Autoimmunity, schizophrenia, immunology, autoantibodies, DNA, families

Introduction

The nature of the association between autoimmune phenomena and schizophrenia is not entirely clear (Sirota 1990). Antibodies to nuclear antigens (ANA), for instance, are almost invariably found in patients with systemic lupus erythematosus, a subset of whom have a variety of psychiatric abnormalities (Abel et al 1980; Adelman et al 1986; Avinoach et al 1990). ANA have also been found in schizophrenic patients treated with chlorpromazine and other psychotropic drugs (Hald 1964; Berglund et al 1970; Fabius and Gaulhofer 1971; Quismorio et al 1972; Alacron-Segovia et al 1973; Gallien et al 1975; Johnstone and Whaley 1975; Presley et al 1976). Zarrabi et al (1979) found that ANA-positive schizophrenic patients treated with chloropromazine had antibodies to native DNA and nucleoprotein. In an earlier study, ANA occured more often and in higher titers in psychiatric patients (including schizophrenia) than in control subjects, but anti-DNA antibodies were not found (Johnstone and Whaley 1975). Whereas similar results were also reported by Villemain et al (1988), another study (DeLisi and Wyatt 1982) found that prior to neuroleptic treatment, ANA titers were elevated in a group of patients with acute schizophrenia. These conflicting results with regard to the presence of anti-DNA antibodies in schizophrenia are disturbing, although they may be explained by technical variations in the Farr assay used for antibody detection or the possible variable effects of neuroleptic drugs on antibody production (Hald 1964; Fabius and Gaulhofer 1971; Gallien et al 1975; Johnstone and Whaley 1975; Presley et al 1976). The work of DeLisi and Wyatt (1982) is pertinent because

From the Abarbanel Mental Health Center (PS, KS, AE), Bat Yam; Department of Human Genetics (HS), Sackler School of Medicine (PS, KS, AE, DM), Tel Aviv University, Tel Aviv; Biohytech (Israel) Ltd. (MAF); Clinical Immunology and Allergy Unit (AT) and Department of Hematology (DH), Wolfson Hospital, Holon, Israel.
Address reprint requests to P.Sirota, M.D., Department 6A, Y. Abarbanel Mental Health Center, 15 Keren-Kayemet Street, Bat Yam, Israel.
Received November 25, 1991; revised November 9, 1992.
*Current address: Biotechnology Program, Technical College of Judea and Samaria, Ariel, Israel.

0006-3223/93/$06.00

Neuropsychopharmacology (2009) 34, 2489–2496

www.neuropsychopharmacology.org

Anti-Brain Autoantibodies and Altered Excitatory Neurotransmitters in Obsessive–Compulsive Disorder

Sagnik Bhattacharyya[1,*], Sumant Khanna[2], Koushik Chakrabarty[3], Anita Mahadevan[4], Rita Christopher[5] and SK Shankar[4]

[1]Division of Psychological Medicie and Psychiatry, Section of Neuroimaging, Institute of Psychiatry, King's College London, London, UK; [2]The Psychiatric Clinic, Vasant Vihar, New Delhi, India; [3]Department of Molecular Neurobiochemistry, International Graduate School of Neuroscience, Ruhr University Bochum, Universitatsstrasse 150, Bochum, Germany; [4]Department of Neuropathology, National Institute of Mental Health and Neurosciences, Bangalore, India; [5]Department of Neurochemistry, National Institute of Mental Health and Neurosciences, Bangalore, India

Although serum autoantibodies directed against basal ganglia (BG) implicate autoimmunity in the pathogenesis of obsessive–compulsive disorder (OCD), it is unclear whether these antibodies can cross the blood–brain barrier to bind against BG or other components of the OCD circuit. It is also unclear how they might lead to hyperactivity in the OCD circuit. We examined this by investigating the presence of autoantibodies directed against the BG or thalamus in the serum as well as CSF of 23 OCD patients compared with 23 matched psychiatrically normal controls using western blot. We further investigated CSF amino acid (glutamate, GABA, taurine, and glycine) levels and also examined the extent to which these levels were related to the presence of autoantibodies. There was evidence of significantly more binding of CSF autoantibodies to homogenate of BG as well as to homogenate of thalamus among OCD patients compared with controls. There was no significant difference in binding between patient and control sera except for a trend toward more bands to BG and thalamic protein corresponding to 43 kD among OCD patients compared with controls. CSF glutamate and glycine levels were also significantly higher in OCD patients compared with controls, and further multivariate analysis of variance showed that CSF glycine levels were higher in those OCD patients who had autoantibodies compared with those without. The results of our study implicate autoimmune mechanisms in the pathogenesis of OCD and also provide preliminary evidence that autoantibodies against BG and thalamus may cause OCD by modulating excitatory neurotransmission.
Neuropsychopharmacology (2009) **34,** 2489–2496; doi:10.1038/npp.2009.77; published online 12 August 2009

Keywords: autoantibodies; glutamate; glycine; OCD; basal ganglia; thalamus

INTRODUCTION

Obsessive–compulsive disorder (OCD) is a chronic disorder with a lifetime prevalence of 1.9–2.5% (Weissman *et al*, 1994) worldwide. Neuroimaging studies suggest that OCD involves hyperactivity of the ventral cognitive circuit specifically involving the basal ganglia (BG) and thalamus (Saxena *et al*, 1998; Friedlander and Desrocher, 2006). Recent evidence has also linked glutamatergic abnormalities with OCD (Rosenberg *et al*, 2000, 2004; Chakrabarty *et al*, 2005; Arnold *et al*, 2006; Dickel *et al*, 2006; Whiteside *et al*, 2006; MacMaster *et al*, 2008; Yucel *et al*, 2008), glutamate being one of the predominant excitatory neurotransmitters in the OCD circuit, with beneficial effects of glutamate-modulating agents noted in OCD (Coric *et al* 2005; Grant *et al*, 2007).

*Correspondence: Dr S Bhattacharyya, Section of Neuroimaging, Box PO67, Institute of Psychiatry, King's College London, De Crespigny Park, London SE5 8AF, UK, Tel: (+44) 20 7848 0955, Fax: (+44) 20 7848 0976, E-mail: s.bhattacharyya@iop.kcl.ac.uk
Received 23 February 2009; revised 24 May 2009; accepted 26 May 2009

However, the cause of OCD is still unclear with both genetic and environmental factors implicated in the causation (Hoekstra and Minderaa, 2005). Although accumulating evidence implicates autoimmunity in the causation of OCD (Pavone *et al*, 2004; Dale *et al*, 2005), it is unclear whether autoantibodies shown in the sera of OCD patients can actually cross the blood–brain barrier to bind to epitopes in the brain and whether they are causally related to OCD, particularly in light of conflicting reports from studies investigating serum antibodies in OCD and related disorders (Singer *et al*, 2005; Morer *et al*, 2008). It is also unclear whether they can cause hyperactivity in the brain pathways implicated in OCD and how that might be mediated at the neurotransmitter level.

As both BG and thalamus have a central position as per current understanding regarding the neurobiological substrate for OCD, we hypothesized that any autoantibodies would need to target either the BG or thalamus in order to cause OCD and should be detectable in the CSF of OCD patients. We also hypothesized that, independent of the presence of autoantibodies, there would be evidence of abnormal excitatory neurotransmission in OCD. We further

Table 1 Sociodemographic and Clinical Profile of Probands

	Patient probands	Control probands	*P*-value
Age in years (SD)	24.65 (8.95)	32.00 (12.95)	***<0.05*** (*t*-test)
Sex (M/F)	18:5	18:5	
Number of years of education (SD)	10.30 (4.86)	9.22 (3.52)	NS (*t*-test)
Mean duration of illness (years)	4.7 ± 4.2	NA	
Mean Y-BOCS score	26 ± 5.6	NA	
Psychiatric comorbidity in OCD patients			
Dysthymia	1	NA	
Social phobia	4	NA	
Tic disorder	3	NA	

Statistically significant '*p*' values have been depicted with bold, italicized fonts.

Autoantibodies

Molecular weight distribution of bands and thus the antigenic determinants in BG and thalamus, observed on western blot using the CSF of patients and controls (Figure 1) is shown in Table 2. There were significantly more bands, suggesting binding of CSF autoantibodies to homogenate of BG corresponding to molecular weight of 97, 43, and between 6.5 and 3 kD, among OCD patients in contrast to controls. Similarly, there were significantly more bands, suggesting binding of CSF autoantibodies to homogenate of thalamus corresponding to molecular weight of 97, 43, and between 6.5 and 3 kD, among OCD patients compared with controls.

Although there was evidence of binding of serum to BG and thalamic homogenate, this was not significantly different between the patients and controls, except for binding of serum to BG and thalamic homogenate corresponding to molecular weight of 43 kD, which was increased in OCD patients compared with controls at a trend level of significance (Table 3).

CSF Neurotransmitter Levels

On MANOVA, CSF glutamate and glycine levels were significantly higher in OCD patients compared with controls, while there was no significant difference in GABA and taurine levels (Table 4; Figure 2). There was no effect of age or gender on CSF levels of the amino acids. Furthermore, MANOVA showed evidence of a significant effect of presence of antibody against BG and thalamic antigen (OCD patients with autoantibody, $n = 20$; controls with autoantibody, $n = 14$) on CSF glycine levels in the entire group ($F(1,39) = 8.186$, $p = 0.007$) and a significant interaction effect between the presence of autoantibody and diagnosis of OCD on CSF glycine levels ($F(1,39) = 5.073$, $p = 0.030$) (Figure 3). There was no significant effect of presence of autoantibody on CSF glutamate levels in OCD patients, which was in fact slightly higher in OCD patients without autoantibody compared with those patients who had positive autoantibody status. Finally, there was no correlation between the severity of obsessive–compulsive symptoms as indexed by YBOCS score and levels of glutamate and glycine in the CSF in the OCD patients.

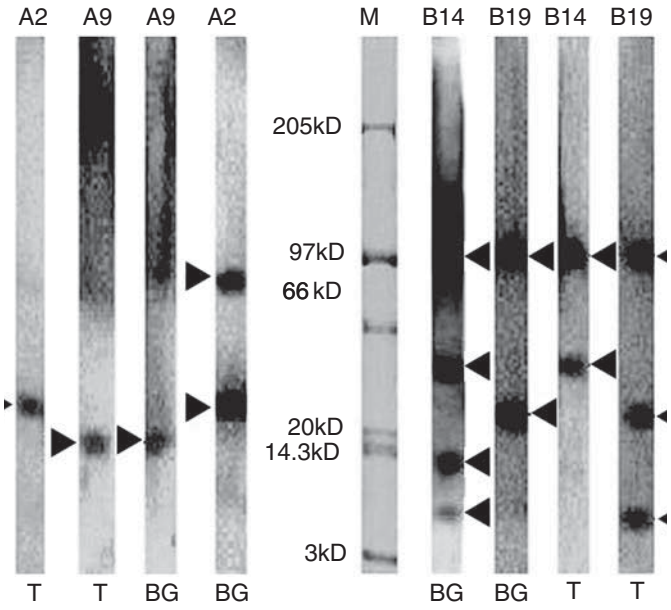

Figure 1 Representative immunoblots reacted with CSF of OCD patients and controls. Immunoblots of two patients and two controls were developed by chemiluminescence. A quantity of 85 μg of BG and thalamic homogenate in PBS was loaded in the lanes. The blots were reacted with control (A2 and A9) and patient (B14 and B19) CSF. The lane in between represents molecular weight markers (M). Lanes A2 and B14 were from the same gel, whereas lanes A9 and B19 were also from the same gel.

DISCUSSION

This study examined the presence of autoantibodies directed against the BG and thalamus in the sera and CSF and measured CSF amino acid (glutamate, GABA, taurine, and glycine) levels in a sample of psychotropic drug-naïve OCD patients compared with matched controls. Furthermore, the study examined the extent to which the CSF amino acid levels were related to the presence of the autoantibodies.

Autoantibodies

First, this study found significantly increased CSF autoantibody binding to one or more BG and thalamic antigenic proteins in the psychotropic drug-naïve OCD patients compared with psychiatrically healthy controls. To our knowledge, this is the first report implicating CSF autoantibodies in a sample of psychotropic drug-naïve OCD patients compared with psychiatrically healthy controls. The results of this study are consistent with the only previous study that has examined CSF autoantibodies in a smaller sample ($n = 6$) (Kirvan *et al*, 2006), as well as with other studies that implicate serum autoantibodies in the causation of OCD and related disorders (Pavone *et al*, 2004; Dale *et al*, 2005). The presence of autoantibodies in the CSF but not in the serum in this study might indicate intrathecal synthesis or might be a function of dilution in the larger volume of sera. Similar binding profiles against both brain

Incidence of anti-brain antibodies in children with obsessive–compulsive disorder

RUSSELL C. DALE, ISOBEL HEYMAN, GAVIN GIOVANNONI and ANDREW J. CHURCH

Background Obsessions and compulsions may occur in the post-streptococcal disorders Sydenham's chorea and paediatric autoimmune neuropsychiatric disorders associated with streptococcus (PANDAS). The proposed mediators are anti-basal ganglia antibodies (ABGA).

Aims We tested the hypothesis that post-streptococcal autoimmunity may have a role in 'idiopathic' obsessive–compulsive disorder (OCD).

Method We examined 50 children with OCD for ABGA using enzyme-linked immunosorbent assay (ELISA) and western immunoblotting. The findings were compared with paediatric autoimmune (n=50), neurological (n=100) and streptococcal (n=40) controls.

Results The mean ABGA binding on ELISA was elevated in the patient cohort compared with all control groups ($P<0.005$ in all comparisons). Western immunoblotting revealed positive antibody binding (as seen in Sydenham's chorea) in 42% of the patient cohort compared with 2–10% of control groups ($P<0.001$ in all comparisons).

Conclusions Our findings support the hypothesis that central nervous system autoimmunity may have a role in a significant subgroup of cases of OCD. Further study is required to examine whether the antibodies concerned are pathogenic.

Declaration of interest None. Funding detailed in Acknowledgements.

Obsessions and compulsions commonly occur in the post-streptococcal movement disorders Sydenham's chorea and paediatric autoimmune neuropsychiatric disorders associated with streptococcal infections (Swedo *et al*, 1998; Mercadante *et al*, 2000). These disorders are thought to be autoimmune in origin, in that antibodies raised in response to streptococcus cross-react with the basal ganglia. We have recently described serum anti-brain antibodies that bind to basal ganglia proteins in patients with post-streptococcal brain syndromes (Church *et al*, 2002, 2003*a*; Dale *et al*, 2004). The recognition that obsessions and compulsions may occur after streptococcal infection has led to the hypothesis that a subgroup of obsessive–compulsive disorder might be secondary to post-streptococcal autoimmunity. We tested this hypothesis by measuring anti-basal ganglia antibodies in a cohort of unselected individuals with obsessive–compulsive disorder, and comparing the findings with paediatric control groups.

METHOD

Patients

Fifty children and adolescents with obsessive–compulsive disorder were recruited from a specialist clinic between August 2001 and August 2002. Ethics approval was granted by the local committee. Consecutive patients were screened for probable obsessive–compulsive disorder before attending the clinic, and all underwent a detailed clinical assessment by child psychiatrists and psychologists. All those meeting DSM–IV criteria for the disorder (American Psychiatric Association, 1994) were invited to participate in the study. All patients were assessed with a structured diagnostic interview, the Children's Yale–Brown Obsessive Compulsive Scale (CY–BOCS; Scahill *et al*, 1997), at the time of serological examination (mean score 19.5, range 5–33). The symptom characteristics of the total cohort are presented in Table 1, including medication status (56% of the sample). Patients were taking paroxetine (n=9), fluoxetine (n=7), sertraline (n=9) or clomipramine (n=3) at the time of sampling. The mean age at symptom onset (retrospectively) was 8.9 years and the mean age at the time of assessment was 13.0 years (range 6–16). After complete description of the study to the participants, written informed consent was obtained from the family.

Controls

For comparison in the serological study, we recruited paediatric control groups: a neurological control group with stroke, metabolic movement disorders and encephalitis (n=100, mean age 8.2 years, range 1–16 years, 50 males); a group with uncomplicated streptococcal infections, defined as laboratory-confirmed streptococcal pharyngitis without autoimmune or invasive complications (n=40, mean age 9.8 years, range 2–15 years, 25 males); and a third group of children with autoimmune disorders without neurological involvement, including rheumatic carditis and post-streptococcal glomerulonephritis (n=50, mean age 9.2 years, range 2–16 years, 25 males). Some of these control groups had been previously reported (Church *et al*, 2003*b*). The control groups were recruited during the same period as the obsessive–compulsive disorder cohort (between August 2001 and August 2002).

Serology

All serum samples were coded and stored at −80 °C prior to streptococcal serological investigation, in which anti-streptolysin O titres were measured using the Dade Behring BN II nephelometer (http://www.dadebehring.com). All control group levels were within acceptable parameters. Titres greater than 200 IU/ml were considered significant according to World Health Organization guidelines (Spaun *et al*, 1961). Streptococcal serological measurements took place in a different laboratory from the other tests, with investigators masked to the anti-basal ganglia antibody results.

The methods for assaying anti-basal ganglia antibodies have been described by Church *et al* (2002). All participants in the patient and control groups had their antibody levels measured using both

New from Selene River Press!

Closed Head Injuries, Mental Illness, Dementia: Dr. Royal Lee—Sixty Years On

A lecture presented by Mark R. Anderson