Neuropsychopharmacology (2003) 28, 1014–1015

www.neuropsychopharmacology.org

Letter to the Editor

Immunoglobulins as an Alternative Strategy of Psychopharmacological Treatment of Children with Autistic Disorder

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Neuropsychopharmacology (2003) **28,** 1014–1015, advance online publication 26 March 2003; doi:10.1038/sj.npp.1300130

Sir

Autistic disorder is a chronic pervasive developmental disorder, characterized by qualitative impairments in reciprocal social interaction, verbal and nonverbal communication, and imaginative activity with a markedly restricted repertoire of activities and interests. Additionally, hyperactivity, poor attention span, and impulsivivity are often prominent associated clinical features and have been target symptoms in previous medication trials (Campbell *et al*, 1951). In an earlier open trial of dextroamphetamine, autistic children had an adverse response (Campbell *et al*, 1972) and Jaselskis *et al* (1992) report good efficiacy of clonidine treatment of autistic children. An open trial (Birmaher *et al*, 1988) suggested that methylphenidate use in autistic hyperactive children may ameliorate hyperactivity, inattention, and impulsivity in children with autistic disorder. Neuroleptics are somewhat effective in reducing hyperactivity, impulsivity, and inattention in children with autistic disorder (Perry *et al*, 1959). However, chronic use of neuroleptics may be complicated by cognitive blunting and the often irreversible side effect of tardive dyskinesia (Campbell *et al*, 1985). The development of efficacious and safe therapeutic interventions remains an area of significant need in this disorder. Therapeutic effects in other disorders with similar target symptoms may guide the development of treatments for children with autistic disorder. Intravenous immunoglobulin has been reported to be effective in the treatment of central nervous system disorders such as intractable epilepsy (Gross-Tsur *et al*, 1993), Guillain–Barré syndrome (Van Doom *et al*, 1990), myasthenia gravis (Cosi *et al*, 1991), and multiple sclerosis (Achiron *et al*, 1992). Autistic patients also had an abnormal lymphocyte proliferative response to mitogens and to autologous lymphocytes and monocytes (Fudenberg *et al*, 1987; Plioplys *et al*, 1994, 1998).

Given the current widespread interest in the use of intravenous immunoglobulin for autism, and recent pronouncements of its curative nature in the lay literature, the authors feel compelled to publish these results as a strong cautionary word against the growing indiscriminate use of intravenous immunoglobulin in treating autistic children.

We performed a double-blind and placebo-controlled crossover study. Immunoglobulins (tested for possible Hepatitis C contamination) and identical placebo injections were administered once in a 0.4 g/kg strength. In all, 12 outpatient male children (age range 4.2–14.9 years; mean = 7.3 years; SD = 3.3 years) meeting ICD-10 criteria for autistic disorder were recruited from the community and clinic. Full-scale IQs ranged from 52 to 84 (65 ± 11), and were obtained from several tests, including the Wechsler Intelligence Scale for Children Revised, the Leiter International Performance Scale, or the Cattell Infant Intelligence Scale. Parents provided written informed consent for their children after the procedures and possible side effects were explained to them. The subjects had no history of identified medical or neurologic illnesses and had been off medications for at least 1 month before the study. All of them showed a normal red and white blood count, and no immunological (IgG, IgM) abnormalities. All of these children had been treated with either methylphenidate (10 mg daily for 4 weeks), neuroleptics (100 mg Zotepine daily for 3 weeks), or Amitryptiline (50 mg daily for 3 weeks) before entry into the study. In each case, these medications had either not been effective or caused intolerable side effects like increased activity or extrapyramidal symptoms. Weekly parent and teacher ratings included the Aberrant Behavior (ABC) and Symptom Checklist (Amman *et al*, 1985a, b). The responses were summed after a 6-week and a 13-week treatment period. Weekly clinician ratings consisted of videotaped observations at baseline, 6 weeks, and 13 weeks using the modified Children's Psychiatric Rating Scale (CPRS). Side effects monitored included increased thirst, drowsiness, sleep disturbance, sadness, dizziness, irritability, appetite change, and decreased activity. All raters

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Received 23 October 2002; accepted 17 December 2002
Online publication: 20 December 2002 at http://www.acnp.org/citations/Npp122002446

Table 1 Improvement of ABC and Symptom Checklist Factors

Subscale	Immunoglobulins	Placebo	p
ABC			
Irritability	11.9 ± 7.2	14.3 ± 5.2	0.041*
Hyperactivity	19.7 ± 11.8	22.9 ± 11.7	0.036*
Inadequate eye contact	7.4 ± 3.6	8.2 ± 5.4	0.041*
Inappropriate speech	4.9 ± 3.7	6.4 ± 2.3	0.042*
Symptom checklist			
Drowsiness	3.2 ± 3.5	1.3 ± 2.0	0.020*
Decreased activity	4.3 ± 3.2	2.8 ± 3.1	0.034*

*< 0.05.

(parents, teachers, and clinicians) were blind to drug order until ratings were completed. Subjects continued to receive educational and behavioral interventions such as psychomotoric therapies or supported communication in school during the course of the study. Most of the ratings on the ABC factors and the symptom checklist scores were significantly improved on Immunoglobulins (Table 1). None of the clinician ratings showed significant differences between placebo and Immunoglobulins. None of the subjects appeared to have headaches or stomachaches, although the report of such side effects was limited by the expressive language and social skills of these subjects. Our results show that immunoglobulin treatment may be effective only for selected autistic patients. This fact could be an area of future direction of research. For that reason, our results should be understood as a strong cautionary word against the growing indiscriminate use of intravenous immunoglobulin in treating autistic children.

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