



## Familial correlates of central serotonin function in children with disruptive behavior disorders

Jeffrey M. Halperin<sup>a,b,\*</sup>, Kurt P. Schulz<sup>b</sup>, Kathleen E. McKay<sup>c</sup>, Vanshdeep Sharma<sup>b</sup>,  
Jeffrey H. Newcorn<sup>b</sup>

<sup>a</sup>Department of Psychology, Queens College of CUNY, 65-30 Kissena Boulevard, Flushing, NY 11367, USA

<sup>b</sup>Department of Psychiatry, Mount Sinai School of Medicine, One Gustave L. Levy Place, New York, NY 10029, USA

<sup>c</sup>Westchester Jewish Community Services, Hartsdale, NY 10530, USA

Received 12 September 2002; received in revised form 30 April 2003; accepted 16 May 2003

### Abstract

Previous findings suggest a relationship between childhood aggression, parental history of aggression and central serotonin (5-HT) function. The present study extended these findings by examining the impact of childhood aggression and central 5-HT function on the incidence of psychopathology in first- and second-degree relatives of pre-pubertal children with disruptive behavior disorders. Family history of psychopathology was obtained for 58 aggressive and 44 non-aggressive clinically referred children who were further sub-divided based on central 5-HT function. Central 5-HT function was assessed by measuring the prolactin response to a 1 mg/kg oral dose of *d,l*-fenfluramine. Aggressive children with low-prolactin responses to fenfluramine had a significantly greater incidence of first- and second-degree relatives with aggressive and antisocial characteristics compared to both non-aggressive children and aggressive children with high-prolactin responses. No group differences were found in the frequency of relatives with symptoms of cognitive impairment or inattention and hyperactivity. These data suggest that there are both familial and non-familial forms of aggression in children, and that only the familial type is associated with reduced 5-HT function.

© 2003 Elsevier Ireland Ltd. All rights reserved.

**Keywords:** Serotonin; Aggression; Familial psychopathology; Disruptive behavior disorders; Children; Development

### 1. Introduction

The relationship between diminished central serotonin (5-HT) function and impulsive-aggressive behavior in animals and human adults has been among the most consistently reported findings in biological psychiatry over the past two

decades. Studies in non-human primates indicate inverse correlations between cerebrospinal fluid (CSF) levels of the 5-HT metabolite 5-hydroxyindoleacetic acid (5-HIAA) and aggressive behavior (Higley et al., 1996; Mehlman et al., 1994). Similar studies in human adults assessing CSF 5-HIAA concentrations or neuroendocrine response to acute administration of 5-HT agonists have also consistently reported either inverse correlations

\*Corresponding author. Tel.: +1-718-997-3254; fax: +1-718-997-3257.

E-mail address: [jeffrey\\_halperin@qc.edu](mailto:jeffrey_halperin@qc.edu) (J.M. Halperin).

with indices of aggression (Brown et al., 1982; Coccaro et al., 1989; Manuck et al., 1998) or reduced function in a wide array of aggressive individuals (Linnoila et al., 1983; O'Keane et al., 1992; Stanley et al., 2000).

Central 5-HT function has also been postulated to play a role in the manifestation of childhood aggression, but the few studies conducted in children have yielded inconsistent results that are largely at odds with the adult literature. An early series of studies in disruptive children reported inverse correlations between CSF 5-HIAA concentration and aggression both at the time of initial assessment (Kruesi et al., 1990) and at 2-year follow-up (Kruesi et al., 1992). However, the same laboratory later found a positive correlation between CSF 5-HIAA and aggression in children with attention-deficit hyperactivity disorder (ADHD) (Castellanos et al., 1994). Discrepant results have also been found using the prolactin response to the 5-HT releaser/reuptake inhibitor fenfluramine to examine central 5-HT function in children. The prolactin response to fenfluramine was unrelated to measures of aggression in small samples of disruptive boys and adolescents (Stoff et al., 1992), but it was positively correlated with aggression in boys at-risk for antisocial behavior (Pine et al., 1997) and in aggressive relative to non-aggressive boys with ADHD (Halperin et al., 1994). This latter finding was not replicated in two subsequent samples of boys with ADHD (Halperin et al., 1997a; Schulz et al., 2001).

The source of these discrepancies in child studies has remained elusive. Attempts to reconcile the inconsistencies initially pointed to diagnostic and developmental factors (Castellanos et al., 1994; Halperin et al., 1997b; Pine et al., 1997), but further analyses cast doubt on both age and diagnostic comorbidity as possible explanations (Schulz et al., 2001). Rather, the inconsistency of neurochemical findings in children may be attributable to the heterogeneous causes of aggressive behavior in children (Halperin et al., 1997b).

Several lines of research have identified familial sociopathy and aggression as highly salient risk factors for the persistence of childhood aggression into adolescence and adulthood (Cadoret et al., 1995; Frick et al., 1992). Familial aggression and

sociopathy may also be associated with reduced central 5-HT function. Studies in child and adult samples have reported low CSF 5-HIAA concentrations in individuals with a family history of criminal and antisocial behavior (Constantino et al., 1997; Virkkunen et al., 1996). Further, a blunted prolactin response to fenfluramine was associated with high rates of impulsive aggression in the first-degree relatives of adults with personality disorders (Coccaro et al., 1994) and with parental history of aggression in aggressive children (Halperin et al., 1997b). In aggregate, these data are consistent with the hypothesis that familial transmission of aggressive behavior may be associated with low central 5-HT function.

The present study was designed to extend previous findings of a relationship between childhood aggression, parental history of aggression, and central 5-HT function by examining a wider array of relatives in a substantially expanded sample of children with disruptive behavior disorders (DBD). The incidence of aggressive and antisocial behaviors in first and second degree relatives was compared separately across aggressive and non-aggressive children who were further subdivided based upon their prolactin response to a single oral dose of *d,l*-fenfluramine. We hypothesized that the aggressive children with reduced prolactin responses to fenfluramine would have an increased frequency of relatives with aggressive and antisocial behaviors compared to both non-aggressive children and aggressive children with higher prolactin responses to fenfluramine.

## 2. Methods

### 2.1. Subjects

The participants were 102 children (91 boys and 11 girls) aged 7–11 years who were referred for significant difficulty with disruptive behavior (e.g. inattention, hyperactivity, aggression). The participants were part of three independent samples of children in whom the relationship of central 5-HT function to aggression was assessed (Halperin et al., 1994, 1997b; Schulz et al., 2001), and all for whom family history data were ascertained. These samples, which were studied sequentially

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