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## ORIGINAL ARTICLE

# Abnormal serotonin transporter availability in the brains of adults with conduct disorder

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**KEYWORDS**

conduct disorder;  
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**Background/Purpose:** The aims of the current study were to determine whether patients with conduct disorder (CD) showed an abnormal availability of serotonin reuptake transporter (SERT), and if their hyperkinetic symptoms, impulsivity, and quality of life were correlated with the availability of SERT.

**Methods:** We recruited 14 drug-naïve patients with CD and eight age-matched healthy controls (HCs). The adult attention-deficit/hyperactivity disorder (ADHD) self-report scale (ASRS), Barrett impulsivity scale (BIS), and the World Health Organization quality of life-brief version (WHOQOL-BREF) scale were administered. Positron emission tomography (PET) of the brain with 4-<sup>[18F]</sup>-ADAM was arranged for SERT imaging.

**Results:** SERT availability was significantly reduced in the striatum and midbrain of patients with CD. Quality of life and inattention symptoms were also significantly correlated with the availability of SERT in the prefrontal cortex.

**Conclusion:** The study suggested that a reduction in the availability of SERT might be associated with CD and could potentially predict poor quality of life or symptoms of inattention

Conflicts of interest: The authors have no conflicts of interest relevant to this article.

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for these patients. The implications of our results might be limited to individuals with CD; a future study with a larger sample to validate our preliminary results is warranted.

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## Introduction

Conduct disorder (CD) and oppositional defiant disorder are the disorders most frequently comorbid with attention-deficit/hyperactivity disorder (ADHD).<sup>1</sup> CD is a relatively more severe behavioral problem, and occurs in 20% of patients with ADHD and can alter the course and prognosis of ADHD.<sup>2</sup> It also accounts for the greatest cost in terms of psychological, psychiatric, and social services.<sup>3</sup> CD may be associated with an increase in the severity of symptoms of both learning and disruptive behavior disorders,<sup>4</sup> which may affect patients' educational outcomes. Likewise, CD has been identified as the most relevant risk factor predisposing to substance use disorders in adulthood.<sup>5</sup> The presence of CD in adolescents doubles their risk of substance use,<sup>6</sup> and also influences the risk of other psychiatric comorbidities, such as higher baseline rates of major depression, bipolar disorder, and multiple anxiety disorders.<sup>7</sup> Finally, CD also negatively affects self-reported health-related quality of life among children and adolescents, with less warmth and closeness and more conflict in familial relationships.<sup>8,9</sup> These children may inflict serious physical and psychological harm on others, and are also at increased risk for self-injury and death by homicide or suicide.<sup>10,11</sup>

Comorbid CD also complicates treatment for ADHD, and may diminish the effectiveness of some medications<sup>12</sup>; the effect of disruptive behavior disorders on adherence to prescribed medication regimens may also occur.<sup>13</sup> Clinicians should therefore attempt to identify the presence of CD as early as possible, and provide potentially effective behavioral and pharmacologic interventions.

It has been reported that lower serotonergic responsivity in hyperkinetic children may predict the development of conduct and antisocial personality disorders.<sup>14</sup> It has also been suggested that impulsive aggressive symptoms are associated with reduced serotonin uptake, increased synaptic levels of serotonin, and reduced postsynaptic receptor responsiveness.<sup>15</sup> Previous studies using positron emission tomography (PET) found that abnormal levels of serotonin in the brain were associated with aggressive/impulsive behaviors.<sup>16</sup> Other studies found that the availability of serotonin reuptake transporter (SERT) was not significantly different between hyperkinetic patients and healthy controls (HCs),<sup>17</sup> but there have been inconsistent findings that showed increased rather than decreased serotonin, as measured by CSF 5-HIAA, a metabolite of serotonin, was associated with aggression in children.<sup>18</sup> Moreover, there are limited disorder-specific biomarkers for symptoms including poor impulse control, aggression, and emotional dysregulation. We hypothesized that

serotonergic dysfunction plays a role in the vulnerability of patients with CD. We measured SERT availability in male CD patients with PET using 4-<sup>[18F]</sup>-ADAM as a tracer. The aims of this study were to investigate abnormalities in the availability of SERT in the brain, and to determine potential correlations of this abnormality with symptom severity and quality of life.

## Methods

### Participants

Fourteen adult males (mean age, 26.71 ± 4.32 years) whose symptoms met the DSM-IV TR criteria for conduct disorder were recruited into our study from the outpatients at the Tri-service General Hospital in Taipei, Taiwan. The patients were assessed by trained clinicians using the Kiddie Schedule for Affective Disorders and Schizophrenia-Epidemiology version (K-SADS-E). All of the patients with CD had both childhood and current symptoms of ADHD. The control group (mean age, 29.38 ± 2.83 years) was made up of eight healthy men whose comparable scans were available in the PET Centre of the Tri-service General Hospital. All patients were first-time visitors at our psychiatric clinic and their medication status was evaluated by direct report and chart review. The experimental protocol was approved by the Institutional Review Board for the Protection of Human Subjects at the Tri-Service General Hospital, National Defense Medical Center in Taipei, Taiwan. All participants gave written informed consent.

Exclusion criteria, including ongoing psychiatric or somatic comorbidity or other neurodevelopmental disorders, were assessed using the mini-international neuropsychiatric interview of the DSM-IV. We did not specifically exclude patients with substance exposure because comorbidity with substance use is prevalent in this group of patients.

The CD patients were evaluated using the adult ADHD self-report scale (ASRS), the Barrett impulsivity scale (BIS), and the World Health Organization Quality of Life-brief version scale (WHOQOL-BREF). All patients in the CD group were drug naïve in that they had never been treated with mood stabilizers, antidepressants or methylphenidate, or other psychotropic agents.

### Radiopharmaceutical and PET procedure

The 4-<sup>[18F]</sup>-ADAM was synthesized in an automated synthesizer.<sup>19</sup> All the 4-<sup>[18F]</sup>-ADAM formulations used in this study were prepared in our PET cGMP laboratory, which is inspected regularly by the Council of Atomic Energy and the Department of Health, Taiwan.

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