Research report

History of childhood attention deficit hyperactivity disorder (ADHD) features among adults with panic disorder

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Abstract

Background: The prevalence of ADHD features during childhood and its relationship to the course and presentation of panic in adults with panic disorder was examined. Methods: The presence of DSM-III-R ADHD was retrospectively ascertained in a cohort of 85 adults with panic disorder by structured interview. Results: Childhood ADHD features occurred in 23.5\% of panic subjects; 9.4\% satisfied full DSM-III-R criteria for ADHD, 14.1\% had ‘subthreshold’ diagnoses. Two-thirds of panic patients with ADHD indicated persistence of symptoms into adulthood. Fewer had married or completed college than those with panic alone. There was no significant difference in clinical pattern and severity of panic, or comorbidity of adult Axis I and childhood anxiety disorders in both groups. Conclusion: Given its frequency and persistence, ADHD comorbidity is an important clinical consideration in all panic patients. Its co-occurrence does not influence the clinical pattern of panic, but may contribute to adverse social outcome.

Keywords: Attention deficit hyperactivity disorder (ADHD); Childhood anxiety; Comorbidity; Panic disorder

1. Introduction

Psychiatric comorbidity in panic disorder is common. Psychiatric disorders which are frequently comorbid during the lifetime course of panic patients include depression (Breier et al., 1984), other anxiety disorders, e.g. social phobia, generalized anxiety, specific phobia (Pollack et al., 1990; Goldenberg et al., 1996), and alcohol/substance abuse or dependence (Otto et al., 1992). Consideration of lifetime comorbidity should also include childhood psychopathology. Indeed, we find that during childhood, adults with panic disorder have a high prevalence of various anxiety disorders including social phobia, overanxious, avoidant and separation anxiety disorders (Otto et al., 1994; Pollack et al., 1996) as well as fearful temperaments like behavioral inhibition to the unfamiliar (Rosenbaum et al., 1991). These childhood antecedents tend to impact on the natural history of panic disorder, affecting its evolution,
clinical presentation, and outcome (Angst and Volrath, 1991; Otto et al., 1994).

The relationship between a childhood history of attention deficit hyperactivity disorder (ADHD) and panic disorder in adulthood has not, to our knowledge, been studied before, but warrants our investigation when we consider the converging lines of evidence which suggest a possible association between the two disorders.

ADHD is a heterogeneous disorder, characteristically arising in early childhood, before the age of 7 (DSM-III-R, DSM-IV). It has shown high rates of comorbidity especially with conduct, depressive and anxiety disorders (Biederman et al., 1991a). Children and adolescents with ADHD very commonly have comorbid anxiety disorder among both clinical (Last et al., 1987; Biederman et al., 1990a, 1991a; Jensen et al., 1993) and community samples (Anderson et al., 1987; Bird et al., 1988, 1993).

Reciprocally, juvenile panic disorder and/or agoraphobia patients seem to have a high rate of co-occurring ADHD as well. Bradley and Hood (1993) found that in a cohort of 28 adolescents presenting with clinically significant panic attacks, six (21.4%) had also met criteria for ADHD, while six had conduct disorder. Similarly, Biederman et al. (1997) in analysing patterns of comorbidity for children and adolescents diagnosed with panic disorder or agoraphobia, found very high rates of comorbid ADHD (58 and 81%, respectively).

In recent years, much interest has been focused on the manifestations of ADHD in adulthood. Evidence suggests that between 10 and 60% of childhood-onset ADHD show persistent features in adulthood (Gittelman et al., 1985; Mannuzza et al. 1991, 1993; Hechtman, 1992). In long-term follow-up studies of children with ADHD, a substantial number subsequently develop other psychopathology, especially mood and anxiety disorders (Biederman et al., 1996a). Adults with ADHD have a high (almost 85%) incidence of comorbid psychiatric disorder, predominantly depressive and anxiety disorders, or personality and alcohol/substance related problems (Gomez et al., 1981; Hechtman et al., 1981; Murphy and Barkley, 1996). Psychoactive substance use is increased in ADHD adults, with comorbidity of mood and anxiety disorders posing further additional risk for development of abuse/dependence (Biederman et al., 1995a,b). Alpert et al. (1996) using similar methodology and scales as employed in our study, found that adults with major depressive disorder had a high incidence of ADHD in childhood; 16% had full or partial ADHD, with 7.6% meeting full criteria.

Both ADHD (Faraone and Biederman, 1994) and anxiety disorders including panic disorder (Weissman, 1993) are likely to have significant genetic etiological contributions. Further, some family-genetic studies point to an association between the two disorders. The children of parents with anxiety disorders have higher rates of ADHD compared with children of comparison groups (Sylvester et al., 1987; McClellan et al., 1990). Biederman et al. (1991b) found a greater risk for anxiety disorders in ADHD probands and their family, than in normal subjects and their relatives. Panic and agoraphobia were more common in relatives of ADHD probands compared to relatives of controls (Biederman et al., 1992). It is likely that ADHD and anxiety share common risk factors, but patterns of familial association suggest a pattern of independent segregation in families (Perrin and Last, 1996).

In consideration of all the evidence, we hypothesized that features of ADHD, beginning in childhood, and persisting into adulthood, would be a significant co-occurrence in adults with panic disorder. The presence of ADHD comorbidity, we postulated, would also be associated with earlier onset of panic disorder, greater clinical severity and more overall dysfunction. We also studied the relationship between panic and ADHD in relation to comorbidity with other childhood or adult Axis I disorder.

2. Methods

2.1. Subjects

Subjects studied were 85 adults between the ages of 18 and 60 years, who had met criteria for DSM-III-R panic disorder, with or without agoraphobia, as determined by Structured Clinical Interview for DSM-III-R (SCID) (Spitzer et al., 1989). They had been consecutively enrolled into pharmacological treatment trials at the Anxiety Disorders Program of Massachusetts General Hospital. Patients had ex-
experienced four or more panic attacks over 4 weeks at baseline, scored at least 18 or more on the Hamilton Anxiety Scale (HAM-A) (Hamilton, 1959), and less than 17 on the 21-item Hamilton Depression Scale (HAM-D) (Hamilton, 1960). Patients with current major depression or lifetime bipolar disorder, obsessive–compulsive disorder, schizophrenia, delusional or psychotic disorders, organic brain syndrome, or substance abuse or dependence (in the last 6 months) were excluded. Those with comorbid dysthymia, other anxiety disorders or personality disorders were included only if the panic disorder was judged to be the primary diagnosis. Other exclusion criteria included active, serious medical illness, current use of psychotropic medications or presence of active suicidal risk. Patients enrolled for the study had given informed consent approved by the hospital’s Subcommittee for Human Studies.

2.2. Procedures

The presence of DSM-III-R ADHD and childhood anxiety disorders (separation anxiety, agoraphobia, social phobia, overanxious or avoidant disorder), was ascertained by administering the childhood version of the Schedule for Affective Disorders and Schizophrenia (Kiddie-SADS-E) (Orvaschel and Puig-Antich, 1987) with the companion module for ADHD. The various symptoms of the ADHD companion module were rated for their clinical significance in childhood and whether they began before the age of 7. Subjects were also asked if the ADHD symptoms continued to persist and caused substantial impairment into adulthood. Symptoms were considered significant for ADHD only if they were distinctly present at times other than during periods of anxiety or panic.

Subjects with ADHD-features comprised those who had met full ‘threshold’ criteria (eight or more symptoms before the age of 7 years), and those considered as having ‘subthreshold’ or ‘broad ADHD’ (between five and seven symptoms) (Biederman et al., 1992). Two subjects were considered ‘subthreshold’ cases despite having eight or more symptoms, as their symptoms had occurred after age 7 (9 and 10 years of age, respectively). There has, however, been increasing argument for the age of onset criteria of ADHD to be less restrictive, especially for predominantly inattentive subtypes of ADHD (Applegate et al., 1997; Barkley and Biederman, 1997). Another patient had apparently been diagnosed in childhood with ADHD and attended special schooling because of it, but was considered ‘subthreshold’ as he only endorsed six symptoms.

2.3. Statistical analyses

Categorical data were analysed using \( \chi^2 \)-tests. Two-tailed \( t \)-tests were used for other data.

3. Results

Of the 85 subjects with panic disorder included for study, comprising 42 males and 43 females, 20 subjects (23.5%) had significant ADHD-features during childhood. This included eight individuals (9.4%) who had fulfilled DSM-III-R threshold diagnoses and 12 (14.1%) who had subthreshold diagnoses. The majority of subjects (65%) endorsed persistence of ADHD-features continuing into adulthood. This included 87.5% of the threshold level subjects and 50% of the subthreshold subjects.

Table 1 summarizes the demographic profile, panic disorder clinical characteristics, and types of psychiatric comorbidity in panic disorder subjects with: (1) threshold-level ADHD; (2) ADHD features (both threshold and subthreshold ADHD); and (3) panic alone. Separate analysis was made for subjects having threshold level ADHD, and those with both full or partial criteria in comparison with patients with panic alone.

In general, panic patients with or without ADHD did not differ significantly with respect to any of the factors studied, including panic frequency, agoraphobia, generalized anxiety and anxiety sensitivity. Adult concurrent Axis I comorbidity was not significantly different, although a history of ADHD tended to give rise to more comorbid substance abuse/dependence, depression/dysthymia, and other anxiety disorders. In Table 2, similar rates of childhood anxiety disorders were noted in panic subjects with or without ADHD.

Panic patients who had a history of ADHD were, however, less likely to be married and less likely to have received higher education (fewer had com-
### Table 1
Demographic profile, clinical characteristics and adult Axis I comorbidity in panic disorder subjects: (1) with threshold-level ADHD; (2) ADHD features (both threshold or subthreshold criteria); and (3) without ADHD

<table>
<thead>
<tr>
<th></th>
<th>Panic with threshold ADHD (n = 8)</th>
<th>Panic with ADHD features (n = 20)</th>
<th>Panic disorder alone (n = 65)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Gender (male)</td>
<td>25.0%</td>
<td>55.0%</td>
<td>47.7%</td>
</tr>
<tr>
<td>Age (years)</td>
<td>32.8 (±7.5)</td>
<td>34.2 (±8.6)</td>
<td>37.0 (±10.1)</td>
</tr>
<tr>
<td>Never married</td>
<td>37.5%</td>
<td>55.0%</td>
<td>35.4%</td>
</tr>
<tr>
<td>College education and above</td>
<td>12.5%</td>
<td>26.3%</td>
<td>47.6%</td>
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#### Panic disorder characteristics

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<tr>
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<tbody>
<tr>
<td>With agoraphobia</td>
<td>75.0%</td>
<td>81.0%</td>
<td>73.4%</td>
</tr>
<tr>
<td>Anxiety Sensitivity Index</td>
<td>32.7 (±6.8)</td>
<td>31.8 (±10.8)</td>
<td>34.9 (±10.3)</td>
</tr>
</tbody>
</table>

#### Severity at baseline

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<tbody>
<tr>
<td>Full panic attacks/week</td>
<td>2.8 (±4.1)</td>
<td>2.5 (±4.1)</td>
<td>2.0 (±2.7)</td>
</tr>
<tr>
<td>HAM-A score</td>
<td>21.2 (±7.6)</td>
<td>19.7 (±6.5)</td>
<td>19.4 (±5.7)</td>
</tr>
<tr>
<td>CGI score</td>
<td>4.8 (±0.8)</td>
<td>4.7 (±0.6)</td>
<td>4.5 (±0.6)</td>
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</tbody>
</table>

#### Adult Axis I comorbidity

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</thead>
<tbody>
<tr>
<td>Generalized anxiety disorder</td>
<td>62.5%</td>
<td>45.0%</td>
<td>32.8%</td>
</tr>
<tr>
<td>Social phobia</td>
<td>50.0%</td>
<td>30.0%</td>
<td>20.3%</td>
</tr>
<tr>
<td>Specific phobia</td>
<td>18.8%</td>
<td>25.0%</td>
<td>17.2%</td>
</tr>
<tr>
<td>Obsessive–compulsive disorder</td>
<td>12.5%</td>
<td>15.0%</td>
<td>3.1%</td>
</tr>
<tr>
<td>Any comorbid anxiety disorder</td>
<td>87.5%</td>
<td>70.0%</td>
<td>56.9%</td>
</tr>
<tr>
<td>Major depressive disorder/ dysthymia</td>
<td>75.0%</td>
<td>60.0%</td>
<td>42.2%</td>
</tr>
<tr>
<td>Substance abuse/dependence</td>
<td>50.0%</td>
<td>55.0%</td>
<td>33.3%</td>
</tr>
</tbody>
</table>

* Standard deviations in parentheses.

* *P < 0.05 by χ²-test. P = NS by χ²-test or t-test for all other compared variables between comorbid ADHD groups vs. panic alone.

### Table 2
Childhood anxiety disorder comorbidity and incidence of childhood adversity in panic disorder subjects: (1) with threshold-level ADHD; (2) ADHD features (both threshold or subthreshold criteria); and (3) without ADHD

<table>
<thead>
<tr>
<th></th>
<th>Panic with threshold ADHD (n = 8)</th>
<th>Panic with ADHD features (n = 20)</th>
<th>Panic disorder alone (n = 65)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Separation anxiety</td>
<td>14.2%</td>
<td>23.5%</td>
<td>10.0%</td>
</tr>
<tr>
<td>Overanxious disorder</td>
<td>28.6%</td>
<td>37.5%</td>
<td>36.7%</td>
</tr>
<tr>
<td>Avoidant disorder</td>
<td>0</td>
<td>12.5%</td>
<td>8.3%</td>
</tr>
<tr>
<td>Social phobia</td>
<td>0</td>
<td>6.2%</td>
<td>22.4%</td>
</tr>
<tr>
<td>Agoraphobia</td>
<td>0</td>
<td>6.2%</td>
<td>11.7%</td>
</tr>
<tr>
<td>Any childhood anxiety disorder</td>
<td>28.5%</td>
<td>50.0%</td>
<td>49.1%</td>
</tr>
</tbody>
</table>

#### Childhood adversity

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<thead>
<tr>
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<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>Parents divorced</td>
<td>57.1%*</td>
<td>41.2%</td>
<td>20.0%</td>
</tr>
<tr>
<td>Physical abuse</td>
<td>42.9%*</td>
<td>29.4%</td>
<td>13.3%</td>
</tr>
<tr>
<td>Sexual abuse</td>
<td>21.4%</td>
<td>29.4%</td>
<td>15.0%</td>
</tr>
</tbody>
</table>

* *P < 0.05 by χ²-test. P = NS by χ²-test or t-test for all other compared variables between comorbid ADHD groups vs. panic alone.
pleted college) (Table 1). They also reported greater adversity in childhood, with more having divorced parents or endorsing a history of childhood physical/sexual abuse (Table 2).

4. Discussion

In a sample of adult patients presenting with DSM-III-R panic disorder, a substantial proportion experienced the onset of ADHD features during childhood, which persisted into adulthood. Almost a quarter of panic disorder patients had childhood ADHD features as ascertained by a well-validated structured diagnostic questionnaire. About two-thirds of these subjects acknowledged clinically meaningful persistence of ADHD symptoms into present adulthood. In comparison with the estimated population prevalence of ADHD of 2 to 9% of children and 1 to 3% of adults (Weiss, 1992; Spencer et al., 1994; Shaffer, 1994), the prevalence of ADHD features in our sample of panic disorder patients is significantly elevated and affirms the hypothesized relationship between the two disorders. Although the observations are made based upon a small sample size, they offer important preliminary findings which bear future replication in a larger study.

The extent to which our findings of an increased prevalence of childhood ADHD features can be generalized to all panic disorder patients is also limited by the nature of our study sample. Enrollment criteria into treatment trials excluded patients with active substance abuse, bipolar disorder and current major depression; all of which may be associated with elevated rates of ADHD (Biederman et al., 1995a, b 1996b; Alpert et al., 1996). The actual prevalence of ADHD may have been even higher if these individuals had not been excluded. On the other hand, patients referred to a tertiary specialist center for anxiety disorders may tend to be more severely or chronically ill (Berkson’s bias).

Another potential limitation is our reliance on the retrospective recall of childhood symptoms for the diagnosis of childhood psychopathology (Shaffer, 1994; Spencer et al., 1994). Such methodology may be associated with under-reporting of childhood ADHD symptoms, or difficulty in precise recall of symptom-onset (a key diagnostic criterion of ADHD). Biederman et al. (1990b) have, however, demonstrated that the retrospective diagnosis of ADHD using criterion-based structured interview is clinically valid. Even in the absence of corroborative history from parents, school or medical records, adult recall of ADHD symptoms has been shown to be accurate and provides reliable and valid diagnoses (Spencer et al., 1994). Furthermore, adults diagnosed with ADHD using similar methodology and criteria as the present study, have demonstrated good treatment response in well-designed placebo-controlled drug trials (Spencer et al., 1995; Wilens et al., 1996), establishing the delineation of a treatment-responsive clinical syndrome.

An artifactual increase of ADHD-features in panic patients might conceivably arise from symptom overlap of the two disorders; for example, inattention may be attributable to both disorders. This confound may be especially important when we consider the known preponderance of childhood anxiety disorders in adults with panic disorder (Otto et al., 1994; Pollack et al., 1996). However, we found no increased incidence of childhood anxiety disorders in the ADHD group compared with the pure panic group, which would be expected if the findings were due entirely to overlapping symptomatology. ADHD has also been distinguished from anxiety by symptom discrimination, factor analysis, patterns of association, familial aggregation and treatment response (Hazell, 1997). Milberger et al. (1995) have specifically demonstrated that the ADHD diagnosis is not an artifact of shared symptoms with other disorders, nor are comorbid conditions like anxiety or panic, an artifact of overlapping ADHD symptoms.

The approximately equal gender distribution of subjects with ADHD is notable, as boys are clearly more commonly diagnosed with ADHD than girls. However, the distinct male preponderance of ADHD in paediatric populations is often not observed in adult populations (Biederman et al., 1994; Gaub and Carlson, 1997). In addition, the sample we studied may also underestimate males with ADHD by excluding those with current comorbid alcohol/substance problems. Females do not often manifest overt expressions of ADHD such as behavioral problems and externalizing behaviors (Gaub and Carlson,
contrary to our original postulate, the presence of ADHD features during childhood did not affect the course or severity of panic disorder, although exclusion of patients with significant comorbidity may have obscured the impact of an interaction between these two conditions. Our results suggest, though, that panic patients who had ADHD features tended to have impaired educational and social function; fewer had completed college education or had ever married. This finding is consistent with previous reports of associated academic failure and social rejection in ADHD subjects (Mannuzza et al., 1993, 1997; Marshall et al., 1997). These ADHD-related cognitive, behavioral and social impairments may also increase vulnerability to development of adult psychopathology including panic disorder. We noted more reports of childhood physical in childhood and having divorced parents in the ADHD group, which is in line with observations that psychosocial adversity is a risk factor for persistence of childhood ADHD (Biederman et al., 1996c).

Overall, childhood ADHD predicts for greater psychopathology in later life (Gomez et al., 1981). Clinically, this seems to be manifested across a wide spectrum of disorders (Shekim et al., 1990), including adult ADHD, depression, substance abuse/dependence and as demonstrated in this study, panic disorder. It has been suggested, that ADHD, together with the broad range of depressive and anxiety disorders, may be conceptualized as belonging to a family of ‘affective spectrum disorders’ (Hudson and Pope, 1990), possessing shared common pathophysiology. Indeed, the various family-genetic studies support the postulated etiological relationship between ADHD and anxiety disorders.

Patterns of comorbidity may also allow the definition of specific subtypes, especially with a heterogeneous syndrome like ADHD. Some have postulated a delineation of ADHD based on comorbidity, into (1) an anxious subtype and (2) an aggressive subtype, with possibly different biological substrates (Pliszka et al., 1994), etiological factors, and treatment response (Hazell, 1997; Jensen et al., 1997). The ADHD with anxiety subtype has been characterized as having fewer hyperactivity features, corresponding closer to the DSM-III diagnosis of attention deficit disorder without hyperactivity. Studies have found that ADHD subjects with comorbid anxiety or internalizing symptoms, showed significantly poorer response to stimulant (methylphenidate) treatment than those without such symptoms (Pliszka, 1989; DuPaul et al., 1994; Tannock et al., 1995), demonstrating a clinically important utility of such a subclassification. The presence of comorbidity may significantly affect the choice of pharmacological therapy. Psychostimulants are thought to be anxiogenic, and can worsen anxiety or panic symptoms comorbid with ADHD (Spencer et al., 1996). Benzodiazepines are often used for treatment of panic, but tend to depress cortical activity and impair attention, cognition, reaction span and impulse control (Bhandary et al., 1997) and may be inappropriate for some ADHD patients.

Our findings emphasize the need for clinicians to be mindful of the frequency of ADHD features in panic patients. Routine assessment and screening for its presence is warranted as ADHD is often underdetected and undertreated even in psychiatric settings (Gomez et al., 1981). Although the co-occurrence of ADHD did not lead to earlier onset of panic, or a more adverse clinical course, there are suggestions that a poorer social outcome may result from such comorbidity. Improved detection through a heightened index of suspicion among panic disorder patients, will allow those with ADHD to receive targeted, appropriate treatment and prevent adverse sequelae. Whether these patients with panic and ADHD comorbidity respond optimally to psychostimulants, or to other therapeutic strategies, especially the use of antidepressants (alone or in combination with stimulants), remains to be further studied.

Acknowledgements

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References


