Ther Adv Psychopharmacol
2017, Vol. 7(11) 241–247
DOI: 10.1177/2045125317714193



# Extended-release methylphenidate monotherapy in patients with comorbid social anxiety disorder and adult attention-deficit/hyperactivity disorder: retrospective case series

**Ahmet Koyuncu, Fahri Çelebi, Erhan Ertekin, Burcu Ece Kök and Raşit Tükel**

Correspondence to:
**Ahmet Koyuncu**
Academy Social Phobia Center, Atatürk Mah. İkitelli Cad. No:126 A/Daire:6 Küçükçekmece, Istanbul, Turkey
**ahmet_koyu@hotmail.com**

**Fahri Çelebi**
**Burcu Ece Kök**
Department of Child and Adolescent Psychiatry, Istanbul Medical School, Istanbul University, Istanbul, Turkey

**Erhan Ertekin**
**Raşit Tükel**
Department of Psychiatry, Istanbul Medical School, Istanbul University, Istanbul, Turkey

***Abstract***

**Background:** The relationship between social anxiety disorder (SAD) and attention-deficit/hyperactivity disorder (ADHD) is a subject which has recently become a topic of interest for research.

**Methods:** In this study, 20 patients with comorbid SAD and adult ADHD who were treated with extended-release methylphenidate monotherapy were evaluated retrospectively.

**Results:** Clinical response for both ADHD and SAD symptoms was observed in 17 of 20 patients. Overall, one patient did not respond to treatment and two patients dropped out of treatment at the beginning due to adverse effects.

**Conclusion:** Extended-release methylphenidate improved both SAD and ADHD symptoms and was generally well tolerated. Further studies are required to investigate the relationship between SAD and ADHD.

***Keywords:*** attention-deficit/hyperactivity disorder, comorbidity, extended-release methylphenidate, social anxiety disorder, treatment

Received: 28 October 2015; revised manuscript accepted: 24 February 2017

## Introduction

Although both social anxiety disorder (SAD) and attention-deficit/hyperactivity disorder (ADHD) are common disorders in the community, comorbidity of these two disorders have not been adequately investigated in psychopharmacological trials. The reason may be the long-time predominant view of ADHD as a childhood disorder. The lack of ADHD-related components in screening tools like the Fourth Edition of the Diagnostic and Statistical Manual of Mental Disorders (DSM-IV) and the Structured Clinical Interview for DSM-IV Axis I Disorders (SCID-I)[1] also may have contributed further to the overlooking of this diagnosis by clinicians. However, prospective studies have shown that ADHD frequently persists into adulthood and has an ongoing impact on patients.[2–8] Epidemiological studies in adults in the general population have found a prevalence of 4.4%,[9] and a 6-month prevalence of 1.1%.[10]

There are few specific studies investigating ADHD comorbidity in patients with SAD and little is known on this subject. Our research group had previously conducted a study with 130 patients with SAD and found the rate of comorbid childhood ADHD as high as 72%. Lower levels of functionality and higher scores in fear/anxiety and avoidance subscales and total scores of the Liebowitz Social Anxiety Scale (LSAS) were found in the group with comorbid ADHD, when compared with those without ADHD.[11] A total of two other studies were conducted among small numbers of patients; one group had 33 patients with SAD and found the rate of childhood ADHD to be 3%,[12] whereas in the other

study, among patients with SAD, approximately 8% reported childhood symptoms of ADHD.[13] In addition, an association between the generalized type of SAD and ADHD was suggested by a childhood study.[14]

However, in studies of ADHD, SAD is reported to have a high prevalence as a comorbid anxiety disorder. Studies of communities have found a relationship between adult ADHD and comorbid anxiety disorders.[9,10,15,16] There are also child and adolescent studies that emphasize this relationship.[17–19] Moreover, the rates of developing an anxiety disorder were 17.7% for patients with ADHD and 1.9% for the control group without ADHD; ADHD was reported to be a predictor for the development of an anxiety disorder in a 11-year follow-up study.[20] Several studies assessed SAD comorbidity in ADHD; a study in adult ADHD patients revealed a rate of approximately 30% of SAD comorbidity.[9] Another study suggested an association between adult ADHD and comorbid SAD (odds ratio = 7.50).[10] In two other studies with adult ADHD patients, researchers looked for criteria for SAD and found rates of 40% in 73,[21] and 18.6% in 70 patients.[22] Biederman and colleagues[23] found that 32% of adult ADHD patients had SAD and that the SAD comorbidity rate was higher than in the control group.

Lately, treatment studies have been conducted with patients who have comorbid SAD and ADHD. Adult patients were grouped as atomoxetine-treated ($n = 224$) and placebo-treated ($n = 218$), and atomoxetine was found to improve symptoms of both ADHD and comorbid SAD.[24] In another study, patients who had SAD without comorbid ADHD were treated with atomoxetine and no significant difference was found compared with placebo.[25] In another study in patients with ADHD and comorbid SAD, 21 children and adolescents received methylphenidate treatment, and a significant improvement was found in both ADHD and SAD scores.[26] The improvement of ADHD and SAD scores were correlated. Methylphenidate treatment was shown to be safe and effective in children with ADHD/SAD.[26]

We have previously reported two cases of comorbid SAD and ADHD. The patients showed improvement in both ADHD and SAD symptoms concurrently with extended-release methylphenidate monotherapy, and the stimulant was well tolerated.[27] After these two cases were reported, 18 more cases with comorbid diagnoses of SAD and ADHD were treated with extended-release methylphenidate monotherapy between September 2014 to May 2015 and the patients were assessed retrospectively to comprise this article.

## Materials and method

A total of 20 patients who were referred to a private social phobia center and Incirli Ethica Hospital, Istanbul, Turkey between 1 February 2014 and 15 April 2015, and received diagnoses of generalized-type SAD and current adult ADHD, and received extended-release methylphenidate monotherapy were included in this study. Extended-release methylphenidate treatment is a routine treatment for patients who have generalized-type SAD and comorbid ADHD in our clinic. We have retrospectively evaluated the case files of the patients who have already used methylphenidate as part of their routine treatment. Retrospective studies in Turkey do not require ethics committee approval. This is in accordance with the Turkish Ministry of Health's policy where ethics committee approvals are only mandatory by regulations for prospective clinical trials. Written informed consent was obtained from all participants for inclusion in this study and all patients were informed that a de-identification process will be used to protect their personal and health-related information.

All patients were administered the SCID-I Clinician Version in the first appointment.[1] None of the patients received any diagnosis for a current mood disorder or another Axis I disorder for the last 6 months. The adult ADHD diagnosis was assessed with clinical interviews according to DSM-IV criteria.[28] For assessment of childhood ADHD, each patient was administered the Turkish version of the Schedule for Affective Disorders and Schizophrenia for School Age Children, Present and Lifetime Version (K-SADS PL), ADHD module.[29] The Turkish version of K-SADS-PL has been proved to be a valid and reliable instrument.[30] The K-SADS-PL is a semi-structured diagnostic interview constructed for assessing current and past episodes of psychopathology during childhood and adolescence according to DSM-III-R and DSM-IV criteria.[29]

According to the DSM-IV criteria; 12 of the patients had an inattention type of childhood ADHD, and 8 had combined-type of childhood ADHD. Present ADHD was evaluated by clinical interview in accordance with DSM-IV criteria

**Table 1.** Comparison of the rating scale scores before and after treatment.

| | *N* | Mean rank | Sum of rank | *Z* | *p*-value |
|---|---|---|---|---|---|
| LSAS - fear/anxiety | 18 | 9.5 | 171.0 | –3.725 | <**0.001** |
| LSAS - avoidance | 18 | 9.5 | 171.0 | –3.724 | <**0.001** |
| LSAS - total | 18 | 9.5 | 171.0 | –3.724 | <**0.001** |
| ASRS | 18 | 9.5 | 171.0 | –3.726 | <**0.001** |

ADHD, attention-deficit/hyperactivity disorder; ASRS, Adult ADHD Self-Report Scale; LSAS, Liebowitz Social Anxiety Scale.

and we found that diagnosis of ADHD persisted at a clinically significant level in all patients. The patients were asked to fill out Adult ADHD Self-Report Scale (ASRS)[31] and LSAS.[32] The clinical follow up of the patients were carried out with these two scales.

LSAS[32] was developed in order to evaluate the social and performance-related situations in which the individuals with SAD demonstrate fear or avoidance. The items are rated by the clinician considering the severity of the fear and avoidance of the patient in the last week on a 4-level Likert scale. The total score is acquired by the sum of fear and avoidance scores.

The ASRS[31] is a rating scale developed by the World Health Organization for adult ADHD and it is designed to evaluate current ADHD symptoms. It consists of 18 items based on DSM-IV criteria adapted for adults with ADHD and measured on a five-level Likert scale (0 = never/seldom and 4 = very often). The items one to nine cover the symptoms of inattention, and the remaining nine items evaluate the hyperactivity/impulsivity component of ADHD.[33] Since our patients did not have any other comorbid disorders for the last 6 months, ASRS was accepted as the ADHD score for the last 6 months.

None of the patients had a history of epilepsy and all the patients had healthy results from cardiological examinations. A total of 20 patients were initiated on extended-release methylphenidate monotherapy. Overall, two of the patients dropped out due to adverse effects. A total of 18 patients were treated with 18–54 mg/day [mean dose 27.5 mg, standard deviation (SD): 10.45]. The patients were followed up between 4–8 weeks (mean 6.66, SD: 1.94). An improvement higher than 50% of LSAS and ASRS was accepted as a response.

Since the distribution of the variables was not fit for normal distribution and there was a small number of patients ($n = 20$), we used the Wilcoxon test to compare means. $p$-values $<0.05$ were considered to be statistically significant. Statistical analysis was performed by using the Statistical Package for Social Sciences (SPSS) version 15.0.

## Results

A total of 9 of the 20 patients were female (45.0%) and 18 were single (90.0%). The mean age of patients was 26.60 years (SD: 5.9), the average educational years was 14.00 years (SD: 2.3), the mean age of onset of SAD was 12.40 years (SD: 5.1), and the mean duration of the disorder was 14.20 years (SD: 7.5). Overall, 13 of the patients were working on a wage (65.0%), whereas 7 patients were students (35.0%). There were previous psychiatric referral history and antidepressant treatment in 5 of the patients (25.0%), and 15 patients (75.0%) had their first contact with psychiatry before enrollment.

A total of 18 of the 20 patients used extended-release methylphenidate on a mean duration of 6.66 weeks (SD: 1.94) and a mean dose of 27.5 mg/day (SD: 10.45). The two patients discontinued the drug in the beginning of treatment, due to headaches and loss of appetite, and anxiety, discomfort, palpitations and tremor, respectively. A total of 17 patients responded. One patient did not respond with 1 month of treatment for either ADHD or SAD.

Mean scale scores of baseline and post-treatment LSAS and ASRS measurements of 18 patients are given in Table 1.

Appetite loss was transient in 8 of the 17 patients who benefited from treatment and only 1 patient

had severe loss of appetite. Overall, two patients suffered from insomnia, seven had transient dryness of mouth, and two patients had transient headaches.

## Discussion

In our study, 17 patients showed response for both ADHD and SAD concurrently with extended-release methylphenidate when retrospectively evaluated. Methylphenidate was generally well tolerated except for a patient who showed no response and two patients who discontinued the medication due to adverse effects.

These are compatible with another study in children and adolescents with comorbid SAD and ADHD.[26] The researchers proposed that findings of their study might also be valid for adult population, as our findings suggest. Also, atomoxetine monotherapy was found to be more efficient than placebo in SAD/ADHD group, in line with our findings showing that in case of this comorbidity ADHD medications may be also efficacious for SAD symptoms.[24]

Anxiety and ADHD were perceived as disorders that excluded each other previously. It was hypothesized that anxiety would decrease impulsivity, daring behaviour and novelty-seeking.[34] Earlier studies even reported that anxiety decreased response to stimulants,[35–37] though further investigations failed to support this hypothesis.[38] Recent studies reported ADHD treatments to concurrently improve anxiety.[24,26,27,39,40]

There are both childhood and adulthood studies that report an association between ADHD and anxiety.[9,10,15–19] Anxiety may become more prominent in ADHD patients with the increase of residual cognition and attention problems as the patient gets older.[34] In line with these results, it was reported that attention-deficit is anxiogenic,[41] and a follow-up study reported ADHD as a risk factor for the development of an anxiety disorder.[20] Considering these findings, the observation that ADHD treatments also improve comorbid SAD symptoms in our cases may be a result of a psychopathological and etiological relationship between the two disorders.

Moreover, there are studies that showed dopaminergic abnormalities in SAD. Schneier and colleagues[42] reported that a generalized type of SAD may be associated with low binding to striatal dopamine 2 (D2) receptors. Tiihonen and colleagues[43] also reported that SAD may be associated with a dysfunction of the striatal dopaminergic system. Abnormal striatal function in SAD has also been reported during cognitive tasks.[44] There are pharmacological studies on this issue. Monoamine oxidase inhibitors, which act on dopamine, are efficacious in the treatment of SAD. A total of two studies reported that phenelzine was significantly superior to placebo in patients with a generalized type of SAD.[45,46] D2 receptor antagonist drugs have been reported to precipitate SAD symptoms in patients with psychotic disorders and Tourette's disorder.[47,48] There has also been some interesting evidence of SAD in dopamine-related disorders such as Parkinson's disease. The prevalence of SAD is increased in patients with Parkinson's disease.[49] In our study, methylphenidate was associated with a high rate of response in SAD patients who have comorbid ADHD. This may also indicate the relationship with SAD and dopamine since methylphenidate inhibits dopamine reuptake. Further studies are required on this topic.

In addition, in our study group 12 patients with inattention type of childhood ADHD, had their ADHD persist into adulthood with same severity. But all 8 patients with the combined-type ADHD received diagnoses of inattention-type ADHD at the time of their referral to us. The hyperactive/impulsive component of these patients had remitted. This finding is in line with studies that report that inattention persists despite the remission of hyperactive component during the development of children with ADHD.[50,51]

Our study has several limitations. We evaluated the treatment outcomes retrospectively in an unblinded fashion and therefore our study lacks a placebo arm. All patients were told that they would be treated with an ADHD medication that might also benefit them for their social anxiety symptoms. Thus, we could not totally exclude a potential bias that might be resulted from possible positive expectations in both patients and the assessor. These limitations indicate the need for a randomized controlled trial which will evaluate the effectiveness of methylphenidate in patients with comorbid SAD and ADHD. Another limitation is that our study sample ($n = 20$) was small. Those limitations make it difficult to generalize our results. In addition, five patients (25%) have a history of previous psychiatric treatment and we did not assess the possible effect of previous

treatment on the current treatment outcomes of the patients. Some of the information (e.g. age of onset of SAD) are based on retrospective recall and this may also cause a limitation. Also, patients were not followed up for longer periods.

## Conclusion

In our study, 17 of 20 patients with comorbid SAD and ADHD showed response with methylphenidate for both SAD and ADHD symptoms. Overall, one patient did not respond and two patients discontinued the medication due to adverse effects. Extended-release methylphenidate monotherapy was generally well tolerated. Further studies are required to comprehensively investigate the relationship between ADHD and SAD and the treatment approaches in the presence of their comorbidity.

## Funding

This research received no specific grant from any funding agency in the public, commercial, or not-for-profit sectors.

## Conflict of interest statement

The authors declare that there is no conflict of interest.

## References

1. First M, Spitzer R, Gibbon M, *et al. Structured clinical interview for DSM-IV axis-I disorders (SCID-I)*. Washington, DC: American Psychiatric Press, 1997.
2. Mannuzza S, Klein RG, Besler A, *et al*. Adult outcome of hyperactive boys. Educational achievement, occupational rank, and psychiatric status. *Arch Gen Psychiatry* 1993; 50: 565–576.
3. Mancini C, Van Ameringen M, Oakman JM, *et al*. Childhood attention deficit/hyperactivity disorder in adults with anxiety disorders. *Psychol Med* 1999; 29: 515–525.
4. Rasmussen P and Gillberg C. Natural outcome of ADHD with developmental coordination disorder at age 22 years: a controlled, longitudinal, community-based study. *J Am Acad Child Adolesc Psychiatry* 2000; 39: 1424–1431.
5. Biederman J, Faraone S, Milberger S, *et al*. A prospective 4-year follow-up study of attention-deficit hyperactivity and related disorders. *Arch Gen Psychiatry* 1996; 53: 437–446.
6. Biederman J, Petty CR, Evans M, *et al*. How persistent is ADHD? a controlled 10-year follow-up study of boys with ADHD. *Psychiatry Res* 2010; 177: 299–304.
7. Biederman J, Petty CR, Clarke A, *et al*. Predictors of persistent ADHD: an 11-year follow-up study. *J Psychiatr Res* 2011; 45: 150–155.
8. Lara C, Fayyad J, de Graaf R, *et al*. Childhood predictors of adult attention-deficit/hyperactivity disorder: results from the World Health Organization World Mental Health Survey Initiative. *Biol Psychiatry* 2009; 65: 46–54.
9. Kessler RC, Adler L, Barkley R, *et al*. The prevalence and correlates of adult ADHD in the United States: results from the National Comorbidity Survey Replication. *Am J Psychiatry* 2006; 163: 716–723.
10. Park S, Cho MJ, Chang SM, *et al*. Prevalence, correlates, and comorbidities of adult ADHD symptoms in Korea: results of the Korean epidemiologic catchment area study. *Psychiatry Res* 2011; 186: 378–383.
11. Koyuncu A, Ertekin E and Yüksel C. Predominantly inattentive type of ADHD is associated with social anxiety disorder. *J Atten Disord* 2015; 19: 856–864.
12. Safren SA, Lanka GD, Otto MW, *et al*. Prevalence of childhood ADHD among patients with generalized anxiety disorder and a comparison condition, social phobia. *Depress Anxiety* 2001; 13: 190–191.
13. Mortberg E, Tilfors K and Bejerot S. Screening for ADHD in an adult social phobia sample. *J Atten Disord* 2012; 16: 645–649.
14. Chavira DA, Stein MB, Bailey K, *et al*. Comorbidity of generalized social anxiety disorder anddepression in a pediatric primary care sample. *J Affect Disord* 2004; 80: 163–171.
15. Smalley SL, McGough JJ, Moilanen IK, *et al*. Prevalence and psychiatric comorbidity of attention-deficit/hyperactivity disorder in an adolescent Finnish population. *J Am Acad Child Adolesc Psychiatry* 2007; 46: 1575–1583.
16. Piñeiro-Dieguez B, Balanzá-Martínez V, García-García P, *et al*. Psychiatric comorbidity at the time of diagnosis in adults with ADHD: the CAT study. *J Atten Disord* 2016; 20: 1066–1075.
17. The MTA Cooperative Group. Multimodal Treatment Study of Children with ADHD. A 14- month randomized clinical trial of treatment strategies for attention-deficit/hyperactivity disorder. *Arch Gen Psychiatry* 1999; 56: 1073–1086.

18. de la Barra FE, Vicente B, Saldivia S, *et al*. Epidemiology of ADHD in Chilean children and adolescents. *Atten Defic Hyperact Disord* 2013; 5: 1–8.

19. Yüce M, Zoroglu SS, Ceylan MF, *et al*. Psychiatric comorbidity distribution and diversities in children and adolescents with attention deficit/hyperactivity disorder: a study from Turkey. *Neuropsychiatr Dis Treat* 2013; 9: 1791–1799.

20. Tai YM, Gau CS, Gau SS, *et al*. Prediction of ADHD to anxiety disorders: an 11-year national insurance data analysis in Taiwan. *J Atten Disord* 2013; 17: 660–669.

21. Edel MA, Rudel A, Hubert C, *et al*. Alexithymia, emotion processing and social anxiety in adults with ADHD. *Eur J Med Res* 2010; 15: 403–409.

22. Sobanski E, Bruggemann D, Alm B, *et al*. Psychiatric comorbidity and functional impairment in a clinically referred sample of adults with attention-deficit/hyperactivity disorder (ADHD). *Eur Arch Psychiatry Clin Neurosci* 2007; 257: 371–377.

23. Biederman J, Faraone SV, Spencer T, *et al*. Patterns of psychiatric comorbidity, cognition, and psychosocial functioning in adults with attention deficit hyperactivity disorder. *Am J Psychiatry* 1993; 150: 1792–1798.

24. Adler LA, Liebowitz MR, Kronenberger W, *et al*. Atomoxetine treatment in adults with attention-deficit/hyperactivity disorder and comorbid social anxiety disorder. *Depress Anxiety* 2009; 26: 212–221.

25. Ravindran LN, Kim DS, Letamendi AM, *et al*. A randomized controlled trial of atomoxetine in generalized social anxiety disorder. *J Clin Psychopharmacol* 2009; 29: 561–564.

26. Golubchik P, Sever J and Weizman A. Methylphenidate treatment in children with attention deficit hyperactivity disorder and comorbid social phobia. *Int Clin Psychopharmacol* 2014; 29: 212–215.

27. Koyuncu A, Çelebi F, Ertekin E, *et al*. Extended-release methylphenidate treatment and outcomes in comorbid social anxiety disorder and ADHD: 2 case reports. *J Psychiatr Pract* 2015; 21: 225–231.

28. American Psychiatric Association. *Diagnostic and statistical manual of mental disorders*. 4th ed. Washington, DC: American Psychiatric Association, 1994.

29. Kaufman J, Birmaher B, Brent D, *et al*. Schedule for affective disorders and schizophrenia for school-age children-present and lifetime version (K-SADS-PL): initial reliability and validity data. *J Am Acad Child Adolesc Psychiatry* 1997; 36: 980–988.

30. Gokler B, Unal F, Pehlivanturk B, *et al*. Reliability and validity of schedule for affective disorders and schizophrenia for school age children-present and lifetime version-Turkish version (K-SADS-PL-T). *Turk J Child Adolesc Ment Health* 2004; 11: 109–116.

31. Kessler RC, Adler L, Ames M, *et al*. The World Health Organization Adult ADHD Self-Report Scale (ASRS): a short screening scale for use in the general population. *Psychol Med* 2005; 35: 245–256.

32. Liebowitz MR. Social phobia. *Mod Probl Pharmacopsychiatry* 1987; 22: 141–173.

33. Haavik J, Halmøy A, Lundervold AJ, *et al*. Clinical assessment and diagnosis of adults with attention-deficit/hyperactivity disorder. *Expert Rev Neurother* 2010; 10: 1569–1580.

34. Weiss M, Gibbins C and Hunter JD. Attention-deficit hyperactivity disorder and anxiety disorder in adults. In: Buitelaar JK, Kan CC and Asherson P (eds) *ADHD in adults*, Chapter 11. Cambridge, UK: Cambridge University Press, 2011, pp.130–137.

35. Pliszka SR. Effect of anxiety on cognition, behavior, and stimulant response in ADHD. *J Am Acad Child Adolesc Psychiatry* 1989; 28: 882–887.

36. Pliszka SR. Comorbidity of attention-deficit hyperactivity disorder and overanxious disorder. *J Clin Psychiatry* 1998; 59(Suppl. 7): 50–58.

37. Tannock R, Ickowicz A and Schachar R. Differential effects of methylphenidate on working memory in ADHD children with and without comorbid anxiety. *J Am Acad Child Adolesc Psychiatry* 1995; 34: 886–896.

38. Diamond IR, Tannock R and Schachar RJ. Response to methylphenidate in children with ADHD and comorbid anxiety. *J Am Acad Child Adolesc Psychiatry* 1999; 38: 402–409.

39. Sumner C, Sher L, Suttun V, *et al*. *Atomoxetine treatment for pediatric patients with ADHD and comorbid anxiety*. Paper presented at the Annual Meeting of the American Academy of Child and Adolescent Psychiatry (AACAP), 23 October 2005, Toronto, ON.

40. Geller D, Donnelly C, Lopez F, *et al*. Atomoxetine treatment for pediatric patients with attention-deficit/hyperactivity disorder with comorbid anxiety disorder. *J Am Acad Child Adolesc Psychiatry* 2007; 46: 1119–1127.

41. Roth RM, Wishart HA, Flashman LA, *et al*. Contribution of organizational strategy to verbal

learning and memory in adults with attention-deficit/hyperactivity disorder. *Neuropsychology* 2004; 18: 78–84.

42. Schneier FR, Liebowitz MR, Abi-Dargham A, *et al*. Low dopamine $D_2$ receptor binding potential in social phobia. *Am J Psychiatry* 2000; 157: 457–459.
43. Tiihonen J, Kuikka J, Bergstrom K, *et al*. Dopamine reuptake site densities in patients with social phobia. *Am J Psychiatry* 1997; 154: 239–242.
44. Sareen J, Campbell DW, Leslie WD, *et al*. Striatal function in generalized social phobia: a functional magnetic resonance imaging study. *Biol Psychiatry* 2007; 61: 396–404.
45. Liebowitz MR, Schneier F, Campeas R, *et al*. Phenelzine and atenolol in social phobia. *Psychopharmacol Bull* 1990; 26: 123–125.
46. Liebowitz MR, Schneier F, Campeas R, *et al*. Phenelzine vs. atenolol in social phobia: a placebo controlled comparison. *Arch Gen Psychiatry* 1992; 49: 290–300.
47. Mikkelsen EJ, Detlor J and Cohen D. School avoidance and social phobia triggered by haloperidol in patients with Tourette's disorder. *Am J Psychiatry* 1981; 138: 1572–1576.
48. Scahill L, Leckman JF, Schultz RT, *et al*. A placebo-controlled trial of risperidone in Tourette syndrome. *Neurology* 2003; 60: 1130–1135.
49. Stein MB, Heuser IJ, Juncos JL, *et al*. Anxiety disorders in patients with Parkinson's disease. *Am J Psychiatry* 1990; 147: 217–220.
50. Biederman J, Mick E and Faraone SV. Age-dependent decline of symptom of ;attention deficit hyperactivity disorder: impact of remission definition and symptom type. *Am J Psychiatry* 2000; 157: 816–818.
51. Faraone SV, Biederman J and Mick E. The age-dependent decline of attention deficit hyperactivity disorder: a meta-analysis of follow-up studies. *Psychol Med* 2006; 36: 159–165.