ORIGINAL ARTICLE

Self-esteem in adolescent patients with attention-deficit/ hyperactivity disorder during open-label atomoxetine treatment: psychometric evaluation of the Rosenberg Self-Esteem Scale and clinical findings

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Abstract To report on (1) psychometric properties of the Rosenberg Self-Esteem Scale (SES) studied in adolescents with ADHD, (2) correlations of SES with ADHD scale scores, and (3) change in patient-reported self-esteem with atomoxetine treatment. ADHD patients (12–17 years), treated in an open-label study for 24 weeks. Secondary analyses on ADHD symptoms (assessed with ADHD-RS, CGI, GIPD scales) and self-esteem (SES) were performed. One hundred and fifty-nine patients were treated. A dichotomous structure of the SES could be confirmed. Reliability and internal consistency were moderate to excellent. Highest coefficients were found for the correlation between SES and GIPD scores. Self-esteem significantly increased over time, accompanied by an improvement of ADHD symptoms and related perceived difficulties. The Rosenberg SES was shown to be internally consistent, reliable, and sensitive to treatment-related changes of self-esteem. According to these findings, self-esteem may be an important individual patient outcome beyond the core symptoms of ADHD.

Introduction

Attention-deficit/hyperactivity disorder (ADHD) is a disorder characterized by inattention, impulsivity, and hyperactivity that affects 3–7% of school-age children (American Psychiatric Association 2000). ADHD is associated with significant impairment of cognitive and psychosocial functioning (Barkley 2002; Biederman and Faraone 2005) and quality of life (QoL) in patients and families (Klassen et al. 2004; Matza et al. 2004; Riley et al. 2004; Sawyer et al. 2002). Additionally, there are related findings on poor self-esteem in patients with ADHD (Sawyer et al. 2002; Edbom et al. 2006; Alston and Romney 1992; Escobar et al. 2005), although research addressing this relationship has yielded conflicting results (Hoza et al. 1993). Self-esteem has been proposed to be internalized during the same developmental period in which ADHD is commonly diagnosed and treated (Bussing et al. 2000). To date, only a few studies have addressed the relationship between ADHD and self-esteem as assessed by an objective patient-reported measure (Alston and Romney 1992; Bussing et al. 2000; Hechtman et al. 1980; Serretti et al. 2005). In addition, one problem with previous self-esteem research has been that medication status has not been reported.

Generally, self-esteem has been defined as a person's positive or negative attitude toward oneself (Rosenberg 1965) and has been considered a central construct in psychological theory, with disagreement about concepts and dimensions (Tafarodi and Swann 2001). A basic dichotomy has been proposed by various authors, with,

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e.g., 'self-competence' and 'self-liking' as constitutive dimensions of global self-esteem that are not independent, however. While the former is based on skills, abilities, and talents, the latter relates to moral character, attractiveness, and other aspects of social worth (Tafarodi and Swann 1995, 2001). Genetic versus environmental determinants of self-esteem have also been investigated in order to complement research that focused on psychosocial factors (Raevuori et al. 2007; Roy et al. 1995).

Various components and factors were derived from scales/instruments that have been used to measure self-esteem. These factors may also vary for different populations or patient groups: for example, 'self-confidence' and 'self-deprecation' were described in patients with affective disorders (Serretti et al. 2005). 'Self-concept, self-perception, self-image, and (global) self-worth' appear as related terms, concepts, or dimensions in the literature (O'Dea 2006) for adolescent females. 'Academic and social self-esteem' were studied in boys with ADHD (Alston and Romney 1992). A recent study found statistically significant gender differences, with girls reporting lower self-esteem by means of the 'I think I am' scale (Ek et al. 2008).

A number of scales have been developed in order to measure self-esteem and its dimensions in various patient groups and clinical conditions, such as the 'Coopersmith Self-Esteem Inventory' (Alston and Romney 1992; Coopersmith 1967; Griffiths et al. 1999; Stern et al. 2007), 'Self-Liking/Self-Competence Scale' (Tafarodi and Swann 1995, 2001), and the 'Rosenberg Self-Esteem Scale' (SES; Griffiths et al. 1999; Rosenberg 1965; Roy et al. 1995; Tapia et al. 2007). Furthermore, there are some generic scales that assess self-esteem in subdomains, such as in the 'Child Health and Illness Profile-Child Edition' (CHIP-CE; Riley et al. 2001, 2006), KINDL (Ravens-Sieberer 2003), and 'Child Health Questionnaire' (CHQ; Landgraf 1996). Among these instruments for assessing self-esteem, the self-report version of the SES (Rosenberg 1965) remains the most widely used measure. The SES has become popular due to its long history in use, its uncomplicated language and brevity. The relative simplicity and accessibility of the SES has favored a considerable number of translations (Schmitt and Allik 2005), as well as its application in studying various mental disorders (Byrne 1996; Griffiths et al. 1999; Serretti et al. 2005). Reliability and validity of the SES have been demonstrated in several multilingual samples, including German subjects (Ferring and Filipp 1996; von Collani and Herzberg 2003). However, the SES has not been formally validated for its use in ADHD patients.

The present study was designed to primarily investigate the degree of ADHD-related difficulties, as measured by the global impression of perceived difficulties (GIPD) instrument, in adolescents with ADHD who were treated with atomoxetine. Basic results have been published elsewhere (Dittmann et al. 2006; Dittmann et al. 2009; Wehmeier et al. 2008). Patient-reported self-esteem was recorded as a secondary outcome variable that could serve as an additional parameter studied in comparison and complementary to the respective standard ADHD core symptom assessments. The patient-rated assessment of self-esteem may reflect so-called 'individual patient outcomes (IPOs)' for which there has been growing interest from ADHD experts, regulatory agencies, health insurance companies, as well as patients and parents.

The objectives of this secondary analysis were (1) to evaluate the psychometric properties of the SES (Rosenberg 1965), (2) to evaluate correlations with ADHD scales, and (3) to investigate self-esteem in adolescent patients with ADHD during atomoxetine treatment.

This self-report approach was also chosen in contrast to earlier-published parent reports on self-esteem in young ADHD patients. For availability and feasibility reasons, a modified German language version of the SES (10 items; Ferring and Filipp 1996; von Collani and Herzberg 2003) has been used in this study focusing on the 'self-competence' and 'self-liking' facets of global self-esteem in an adolescent population of ADHD patients.

Methods

Study design and procedures

This multicenter, open-label, single-arm study was designed to investigate the degree of ADHD-related difficulties, as perceived by patients, parents and physicians, in adolescents with ADHD who were treated with atomoxetine. Here we focus on the results relating to the self-esteem of adolescent patients during ADHD treatment, as assessed by self-report on the SES.

Patients were recruited at 35 investigational sites throughout Germany (office-based, board-certified child and adolescent psychiatrists, pediatricians, outpatient clinics). Boys and girls aged 12–17 years with ADHD as defined in DSM-IV-TR (American Psychiatric Association 2000), and with a minimum IQ ≥70 (investigator-estimated) were eligible for the study. The diagnosis was confirmed using the "Diagnose-Checkliste Hyperkinetische Störungen" (Diagnostic Checklist for Hyperkinetic Disorders), a structured standard instrument based on the respective DSM-IV-TR and ICD-10 criteria (Döpfner and Frölich 2000; DGKJP 2003), which is routinely used for the diagnostic assessment of ADHD in Germany. Comorbid psychiatric and somatic disorders were assessed as part of a careful clinical examination performed by the investigator. The exclusion criteria comprised abnormal laboratory findings, acute or unstable medical conditions,

cardiovascular disorder, history of seizures, pervasive developmental disorder, psychosis, bipolar disorder, suicidal ideation, any medical condition that might increase sympathetic nervous system activity, or the need for psychotropic medication other than study drug. Patients already being treated with atomoxetine were also excluded. The protocol was approved by the ethics committee of the University of Cologne, Germany, and the study was conducted in accordance with the principles of the Declaration of Helsinki.

Treatment and assessment procedures

The trial comprised three study periods: following a washout period (I), baseline assessments were carried out with all the instruments used. During the first week, the patients were treated with atomoxetine at a dose of approximately 0.5 mg/kg per day. During the following 7 weeks, the recommended atomoxetine dose was 1.2 mg/kg per day, which could be adjusted within a range of 0.5–1.4 mg/kg per day, depending on effectiveness and tolerability. Medication was given once-a-day in the morning. Assessments were carried out weekly during the first 2 weeks of treatment and every 2 weeks, thereafter.

After this 8-week treatment period (II), the physicians decided in accordance with the patients and their parents whether the patient was going to continue treatment for further 16 weeks. Patients who participated in this extension period (III) continued on the same atomoxetine dose that again could be adjusted within a range of 0.5–1.4 mg/kg per day if necessary. During the extension period, three assessments were carried out at 12, 16, and 24 weeks after baseline.

Measures

The Rosenberg Self-Esteem Scale (SES) is a widely used self-esteem scale in social science research (Rosenberg 1965) consisting of ten items, dealing with a person's general beliefs about him or herself (Table 1). A validated German language version was used (Ferring and Filipp 1996), in which the translation of one item had been revised (von Collani and Herzberg 2003) to improve consistency with the original version. Each item was rated on a four-point scale from 0 (do not agree at all) to 3 (completely agree), with high score values reflecting strong self-esteem. Five items were reversely scored from 0 (completely agree) to 3 (do not agree at all). According to a factor analysis by Serretti et al. (2005), the SES can be subdivided into two components: a 'self-confidence' subscale, including all positively worded items (1, 3, 4, 7, and 10), and a 'self-liking' subscale, consisting of all

Table 1 The Rosenberg Self-Esteem Scale (SES) and its ten items

SES item no.	SES items
1	On the whole, I am satisfied with myself
2	At times, I think I am no good at all
3	I feel that I have a number of good qualities
4	I am able to do things as well as most other people
5	I feel I do not have much to be proud of
6	I certainly feel useless at times
7	I feel that I am a person of worth, at least on an equal plane with others
8	I wish I could have more respect for myself
9	All in all, I am inclined to feel that I am a failure
10	I take a positive attitude toward myself

Rating: Each item is rated from 0 (do not agree at all) to 3 (completely agree). The items 1, 3, 4, 7, and 10 comprise the self-confidence subscale. The items 2, 5, 6, 8, and 9 (self-liking subscale) have to be reversed prior to calculating the sum score

negatively worded items (2, 5, 6, 8, and 9). For calculation of the total score, items 2, 5, 6, 8, and 9 needed to be reversed.

Additionally, ADHD core symptomatology was measured by various validated scales [Attention-Deficit/Hyperactivity Disorder Rating Scale-IV-Parent Version: Investigator-Administered and Scored (ADHD-RS-IV-Parent:Inv; DuPaul et al. 1998; Faries et al. 2001; Döpfner et al. 2006), Clinical Global Impression-Severity/Improvement-Attention-Deficit/Hyperactivity Disorder Scale (CGI-S/I-ADHD) (Guy 1976; NIMH 1985)]. Furthermore, the degree of ADHD-related difficulties was measured by the Global Impression of Perceived Difficulties (GIPD) instrument, which allows to assess ADHD-related difficulties from a patient, parent, and physician perspective. The instrument has been validated in pediatric ADHD patients (Wehmeier et al. 2007, 2008).

Tolerability assessment included monitoring of laboratory values and vital signs plus recording of spontaneously reported adverse events.

Sample size and statistical analyses

The sample size was calculated with respect to the primary objective of the study preliminarily reported elsewhere (Dittmann et al. 2006; Dittmann et al. 2009). We assumed that the true value of Kappa (Fleiss 1981) for the GIPD scale is 0.8 (between patients and parents as well as between patients and physicians). The respective two-sided 95% confidence intervals were intended to extend 0.1 from the observed value of Kappa for the estimate to be sufficiently precise. Furthermore, we assumed a true response rate of 50%. Thus, a sample size of 139 patients was considered

sufficient for the desired precision. Assuming a proportion of 5% of patients with unspecified data on the GIPD scale, a sample size of 147 patients was planned.

The data of all patients were evaluated (Full Analysis Set, FAS), using SAS version 8 or higher. The dataset for all analyses of changes from baseline to endpoint consisted of all patients with a baseline measurement and at least one post-baseline measurement during the 8-week treatment period.

Evaluation was largely descriptive. All tests of statistical significance were carried out at a nominal level of 5% using two-tailed test procedures. Two-sided confidence intervals (CIs) were computed using a 95% confidence level. All inferences regarding statistical significance were based on comparisons of the 95% CIs. This is equivalent to significance tests with p values and a two-sided α-level of 5%. To avoid correlations of imputed values, only observed cases analyses were performed. No imputation of missing values like last observation carried forward (LOCF) was applied.

Principal component analyses (PCA) and factor analysis using varimax rotation were performed in order to confirm the two subscales 'self-confidence' (items 1, 3, 4, 7, and 10) and 'self-liking' (2, 5, 6, 8, and 9). The scores for items 2, 5, 6, 8, and 9 were reversed for these analyses. The correlation structure of the items was evaluated for untreated patients using the baseline values and also for treated patients using the values observed at week 8.

The number and percentage of missing values of the SES items were computed by pooling all visits for the total scale SES, i.e., number of observations with at least one missing item divided by the number of ratings of the SES. Ceiling and floor effects for the SES score were calculated by the percentage of observations with the lowest (=0) and highest achievable scores (total score = 30, subscore = 15) for baseline and week 8 in order to evaluate patients in an untreated and a treated status. Internal consistency of the SES total score and the subscales was analyzed by using Cronbach's alpha (with 95% CI) for weeks 0 and 8. Test–retest reliability of the SES total score and the subscales was investigated by comparing weeks 6 and 8 in terms of Pearson's correlation coefficient and Cohen's Kappa (weighted version; both with 95% CI). Pearson's correlation coefficient, which is based on the original values, was used for the total scores in order to assess the linear association of the more continuous total scores. Weeks 6 and 8 were chosen because treatment (e.g., the dosing of atomoxetine) and disease severity were expected to be fairly stable during this period. Longer durations would be more prone to differences in the disease state mixing the test–retest stability of the SES with the changes in the self-esteem itself. Confidence intervals of

95% for the correlation coefficients were computed based on Fisher's z-transformation.

The correlation with other ADHD scales was evaluated using Pearson's correlation coefficients (with 95% CI)—for weeks 0 and 8 as well as for changes from week 0 to 8—between the total score and the two subscales of the SES on the one hand and (1) ADHD-RS total score and subscores, (2) CGI-Severity of ADHD, (3) CGI-Improvement of ADHD (only for changes), and (4) GIPD total score for each perspective on the other hand.

The influence of baseline covariates on the development of self-esteem was assessed by providing mixed models for repeated measurements for the total and the subscales of the SES. The models included terms for week, baseline value, gender, ADHD subtype, age at diagnosis, age at first occurrence of ADHD symptoms, comorbid oppositional defiant disorder (ODD)/conduct disorder (CD), affective disorders, age, family setting, previous methylphenidate medication, alcohol/tobacco use, and the respective interactions with week.

Results

Patient population and disposition

A total of 159 patients were enrolled in the study and started treatment with atomoxetine. 137 (86.2%) patients completed the 8-week treatment period and continued into the extension period. The extension period was completed at week 24 by 111 (69.8%) patients. The reasons for discontinuation were lack of efficacy (6.3%), protocol violation (5.7%), adverse event (4.4%), patient decision (5.0%), parent/caregiver decision (3.8%), patient lost to follow-up (1.3%) physician decision (1.3%), pre-existing condition (0.6%), and entry criteria exclusion (0.6%).

Baseline patient and disease characteristics

Table 2 shows demographics and background data with a potential impact on self-esteem. The majority of ADHD patients were boys (78.6%). The combined subtype of ADHD was diagnosed in 68 (54.4%) boys and 13 (38.2%) girls [total: 81 patients (50.9%)], and the predominantly inattentive subtype in 53 (42.4%) boys and 20 (58.8%) girls [total: 73 patients (45.9%)]. Consisting of only five subjects, the subgroup of patients with ADHD, not otherwise specified (NOS) was too small for further detailed subgroup analyses. There were no patients meeting the DSM-IV-TR criteria for the predominantly hyperactive–impulsive subtype. For the entire patient sample, the mean time span between first occurrence of symptoms (patient

Table 2 Patient characteristics (all patients, $N = 159$)

Patient characteristics	
Boys/girls, N (%)	125/34 (78.6/21.4)
Age, mean ± SD (years)	14.1 ± 1.5
Age at diagnosis	9.8 ± 2.8
Age at first occurrence of symptoms	4.3 ± 2.2
Educational status, N (%)[a]	
Secondary school: 'Hauptschule'[b]	56 (35.2)
Secondary school: 'Realschule'[b]	54 (34.0)
Secondary school: 'Gymnasium'[b]	32 (20.1)
Vocational school	4 (2.5)
Special needs school	7 (4.4)
Elementary school	3 (1.9)
Family setting, N (%)	
Nuclear family	104 (65.4)
Single mother	21 (13.2)
Step parents	18 (11.3)
Other	16 (10.1)
Never consumed alcohol, N (%)	119 (74.8)
Never smoked, N (%)	131 (82.4)
ADHD subtype, N (%)[c]	
Combined	81 (50.9)
Predominantly inattentive	73 (45.9)
ADHD, not otherwise specified	5 (3.1)
Previous medication, N (%)	137 (86.2)
Long-acting methylphenidate	92 (57.9)
Short-acting methylphenidate	119 (74.8)
Most frequent psychiatric comorbidities, N (%)[d]	
Conduct disorder	29 (18.2)
Oppositional defiant disorder	21 (13.2)
Emotional disorder	4 (2.5)
Depressed mood	2 (1.3)

ADHD attention-deficit/hyperactivity disorder; *SD* standard deviation

[a] Educational status was missing for three patients

[b] In Germany, there are three different types of secondary schools, 'Hauptschule' (lowest qualification), 'Realschule' (intermediate qualification), and 'Gymnasium' (highest qualification)

[c] According to diagnostic and statistical manual of mental disorders, fourth edition[TM]

[d] Based on investigator's clinical assessment (y/n)

report) and first professional diagnosis amounted to approximately 5.5 years.

According to the age group enrolled (12–17 years), almost all patients were in secondary education at baseline (for details see Table 2). The majority of patients (104, 65.4%) were living in a nuclear family, 21 (13.2%) with their single mother, and 18 (11.3%) with a step parent. The remaining 16 (10.1%) patients were living with their single father, foster parents, extended family, independently, in supervised accommodation, or with adoptive parents (summarized as 'Other' in Table 2).

Of the 159 patients, 137 (86.2%) had previously been treated with medication for ADHD. Compounds most frequently used had been short-acting methylphenidate ($N = 119$, 74.8%) and/or long-acting methylphenidate ($N = 92$, 57.9%). Most frequent psychiatric comorbidities were conduct disorder ($N = 29$, 18.2%) and oppositional defiant disorder ($N = 21$, 13.2%) as evaluated by the investigator.

The mean atomoxetine dose given during the first week of treatment was 0.51 mg/kg per day (SD 0.06, minimum 0.40 mg/kg per day, maximum 0.60 mg/kg per day). Thereafter, the mean doses ranged between 1.17 and 1.19 mg/kg per day (minimum 0.40, maximum 1.40 mg/kg per day).

Table 3 shows patients' baseline data for the scales used. Self-esteem, as assessed by the mean (±SD) SES total score (all patients $20.4 ± 5.1$), was lower [not significant (n.s.)] in female patients ($18.8 ± 5.8$) compared to male patients ($20.8 ± 4.9$), and in those patients with combined ADHD subtype ($19.5 ± 5.2$) compared to those with predominantly inattentive ADHD ($21.6 ± 5.0$). This pattern was also observed for the SES subscores.

Psychometric validation of the Rosenberg SES scale

Principal component analysis and factor analysis

Figure 1a and b show the correlations resulting from the principal component analyses at baseline and week 8, respectively. The items 2, 5, 6, 8, and 9 are marked with an "a" as they were reversed as stated earlier. All items correlated positively with the first component (C1). The second component (C2) distinguished between the items related to the two subscales, i.e., items 2, 5, 6, 8, and 9 were positively correlated with C2, whereas the others were negatively correlated. This structure was already observed at baseline, but it became very clear at week 8. The factor analyses at baseline and at week 8 confirmed that the scale consists of two subscales. The first two eigenvalues were larger than 1 and also most of the variance could be explained by these first two factors. The loadings onto the factors resembled the correlations with the principal components showing the same structure of the items.

Missing values

The percentage of missing values was 2.47% (31 missing, 1,222 non-missing) for the SES total score, indicating a tolerable lack of information. For the subscores, the percentages of missing values were even lower, with 2.15% (27 missing, 1,226 non-missing) for the 'self-confidence' and 1.04% (13 missing, 1,240 non-missing) for the 'self-liking' subscore.

Table 3 Baseline disease characteristics ($N = 158$)

	Gender			ADHD subtype (DSM-IV$^{\mathrm{TR}}$)	
	All patients ($N = 158$)	Male ($N = 124$)	Female ($N = 34$)	Combined ($N = 80$)	Predominantly inattentive ($N = 73$)
Self-Esteem					
SES total score	20.4 ± 5.1 [19.6; 21.2][a]	20.8 ± 4.9 [19.9; 21.7][b]	18.8 ± 5.8 [16.8; 20.9][b]	19.5 ± 5.2 [18.3; 20.6][b]	21.6 ± 5.0 [20.4; 22.8][b]
SES self-confidence subscore	9.9 ± 2.9 [9.4; 10.3]	10.0 ± 2.8 [9.5; 10.5]	9.4 ± 3.3 [8.2; 10.6]	9.5 ± 2.9 [8.9; 10.2]	10.3 ± 3.0 [9.6; 11.0]
SES self-liking subscore	10.5 ± 3.2 [10.0; 11.0]	10.8 ± 3.0 [10.3; 11.3]	9.5 ± 3.6 [8.2; 10.8]	10.0 ± 3.1 [9.3; 10.7]	11.3 ± 3.0 [10.6; 12.0]
Other instruments					
ADHD-RS	28.4 ± 10.1 [26.8; 29.9]	29.0 ± 10.0 [27.2; 30.7]	26.2 ± 10.1 [22.7; 29.7]	32.4 ± 9.8 [30.2; 34.5]	24.3 ± 8.4 [22.4; 26.3]
GIPD total score—patient	12.5 ± 5.8 [11.6; 13.5][b]	12.4 ± 5.8 [11.4; 13.5][b]	12.9 ± 5.8 [10.9; 15.0]	12.6 ± 5.2 [11.4; 13.8][d]	12.5 ± 6.4 [11.0; 14.0][d]
GIPD total score—parent	17.2 ± 6.3 [16.2; 18.2][c]	17.0 ± 5.8 [15.9; 18.0][b]	18.1 ± 7.8 [15.3; 20.9][d]	17.8 ± 6.2 [16.4; 19.2][d]	16.4 ± 6.5[b] [14.9; 17.9]
GIPD total score—physician	18.8 ± 6.0 [17.8; 19.8][c]	18.9 ± 5.9 [17.9; 20.0][c]	18.4 ± 6.7 [16.1; 20.8]	19.6 ± 6.0 [18.3; 21.0][d]	17.9 ± 6.0 [16.5; 19.3][b]
CGI-severity	4.8 ± 0.9 [4.7; 5.0]	4.8 ± 0.9 [4.7; 5.0]	4.9 ± 0.8 [4.6; 5.2]	5.0 ± 0.9 [4.8; 5.2]	4.7 ± 0.8 [4.5; 4.8]

Mean values ± SD [95% CI]

ADHD attention-deficit/hyperactivity disorder; *ADHD-RS* ADHD-rating scale; *GIPD* global impression of perceived difficulties; *GIPD* global impression of perceived difficulties (parent-rated, investigator-administered and scored); *CGI-S/I* clinical global impression-severity/improvement scale; *SES* Rosenberg Self-Esteem Scale

Missing values: [a]4, [b]2, [c]3, [d]1
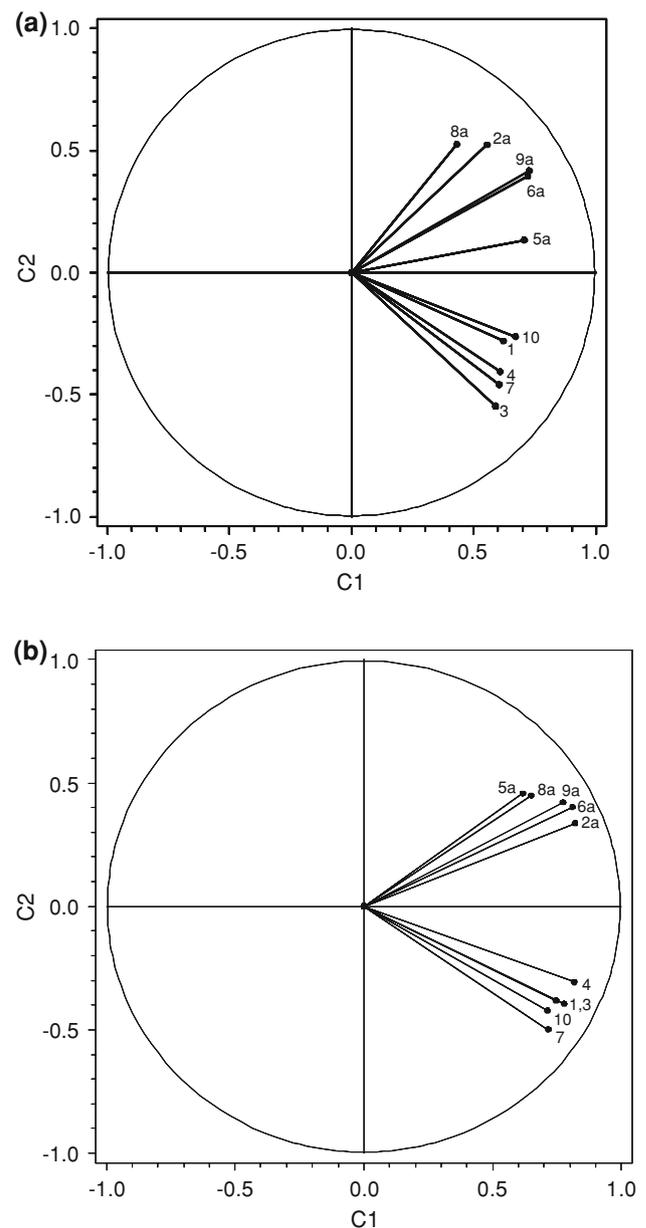
Fig. 1 Structure of the Rosenberg Self-Esteem Scale: **a** principal component analysis at week 0; **b** principal component analysis at week 8. **a** Item scores were reversed before further analysis

Floor and ceiling effects

At baseline, floor effects (SES total score = 0) were 0% for the total score, 0.63% for the subscore 'self-confidence', and 0% for the subscore 'self-liking'. The ceiling effects (SES total score = 30, subscores = 15) were 0.63% for the total score, 1.27% for the subscore 'self-confidence', and 12.03% for the subscore 'self-liking'. At week 8, floor effects remained at 0% for the total score, increased to 0.76% for the self-confidence subscore, and remained at 0% for the self-liking subscore. The ceiling

Table 4 Correlations between the Rosenberg Self-Esteem total score and the two subscores with the ADHD-RS total score, ADHD-RS hyperactivity/impulsivity subscale score, ADHD-RS inattention subscale, GIPD score (patient, parent, physician perspectives), and the CGI-Severity score at weeks 0, 8, and changes from baseline (Pearson correlation coefficients with 95% CIs)

	Week	With SES total score	With SES self-confidence	With SES self-liking
ADHD-RS total score	0	−0.14 [−0.29; 0.02]	−0.09 [−0.24; 0.07]	−0.15 [−0.3; 0.01]
	8	−0.15 [−0.31; 0.02]	−0.05 [−0.22; 0.12]	−0.22 [−0.38; −0.05]
	Changes	−0.17 [−0.33; 0]	−0.07 [−0.24; 0.1]	−0.19 [−0.35; −0.02]
ADHD-RS hyp./impuls.subscore	0	−0.09 [−0.24; 0.07]	−0.05 [−0.21; 0.11]	−0.1 [−0.25; 0.06]
	8	−0.1 [−0.27; 0.07]	−0.03 [−0.2; 0.15]	−0.16 [−0.32; 0.01]
	Changes	−0.12 [−0.29; 0.05]	−0.05 [−0.22; 0.13]	−0.14 [−0.3; −0.03]
ADHD-RS inattentive subscore	0	−0.16 [−0.31; 0]	−0.11 [−0.26; 0.05]	−0.16 [−0.31; −0.01]
	8	−0.17 [−0.33; 0]	−0.06 [−0.23; 0.11]	−0.24 [−0.4; −0.07]
	Changes	−0.18 [−0.34; −0.01]	−0.08 [−0.25; 0.09]	−0.21 [−0.37; −0.04]
GIPD score (patient perspective)	0	−0.39 [−0.51; −0.24]	−0.31 [−0.44; −0.16]	−0.34 [−0.48; −0.2]
	8	−0.49 [−0.61; −0.34]	−0.35 [−0.49; −0.18]	−0.51 [−0.63; −0.37]
	Changes	−0.06 [−0.23; 0.12]	−0.07 [−0.25; 0.11]	−0.04 [−0.21; 0.14]
GIPD score (parent perspective)	0	−0.09 [−0.25; 0.07]	−0.06 [−0.22; 0.1]	−0.1 [−0.25; 0.06]
	8	−0.31 [−0.46; −0.14]	−0.21 [−0.37; −0.04]	−0.34 [−0.48; −0.17]
	Changes	−0.1 [−0.28; 0.08]	−0.07 [−0.24; 0.11]	−0.13 [−0.29; 0.05]
GIPD score (physician perspective)	0	−0.21 [−0.35; −0.05]	−0.16 [−0.31; 0]	−0.19 [−0.33; −0.03]
	8	−0.3 [−0.45; −0.13]	−0.19 [−0.35; −0.01]	−0.35 [−0.49; −0.18]
	Changes	−0.02 [−0.2; 0.16]	0.06 [−0.12; 0.23]	−0.1 [−0.27; 0.08]
CGI-severity	0	−0.17 [−0.32; −0.01]	−0.11 [−0.26; 0.05]	−0.17 [−0.32; −0.01]
	8	−0.23 [−0.38; −0.06]	−0.16 [−0.32; 0.01]	−0.24 [−0.4; −0.08]
CGI-improvement	Changes	−0.17 [−0.34; 0]	−0.14 [−0.3; 0.04]	−0.15 [−0.31; 0.03]

ADHD attention-deficit/hyperactivity disorder; *ADHD-RS* ADHD-rating scale (parent-rated, investigator-administered and scored); *CGI-S/I* clinical global impression-severity/improvement scale; *GIPD* global impression of perceived difficulties; *SES* Rosenberg Self-Esteem Scale

effects increased to 21.97% for the total score, 24.24% for the 'self-confidence' subscore, and 43.18% for the 'self-liking' subscore.

Test–retest reliability

Pearson's correlation between ratings at weeks 6 and 8 was 0.87 [CI 0.82–0.91] for the SES total score, 0.81 [CI 0.74–0.86] for the 'self-confidence' subscore, and 0.84 [CI 0.77–0.88] for the 'self-liking' subscore. The respective Cohen's Kappas were 0.71 [CI 0.65–0.78] for the total score, 0.65 [CI 0.57–0.73] for the 'self-confidence' subscore, and 0.72 [CI 0.64–0.80] for the 'self-liking' subscore. These results indicate a moderate to good test–retest reliability within a period of 2 weeks.

Internal consistency

Cronbach's alpha indices representing internal consistency of the SES total score, the 'self-confidence' subscore, and the 'self-liking' subscore were 0.823 [CI 0.778; 0.862], 0.787 [CI 0.729; 0.836], and 0.794 [CI 0.739; 0.841] at baseline, respectively. At week 8, the Cronbach's alpha for the scores were 0.906 [CI 0.880; 0.928], 0.904 [CI 0.876; 0.928], and 0.891 [CI 0.858; 0.917], respectively. Except for the baseline rating of the subscores, all Cronbach's alpha values were above 0.80, indicating a good to excellent internal consistency of the scale.

Correlation with other scales

As shown in Table 4, the Pearson's correlations between the SES total score and the two subscale scores with the other scale scores were relatively weak at baseline, ranging from −0.05 to −0.39.

At baseline, for the SES total score, the correlation was strongest with the GIPD score representing the patient perspective (−0.39; CI −0.51 to −0.24), followed by the physician-rated GIPD score (−0.21; CI −0.35 to −0.05), while it showed a weak correlation with the parents' GIPD score (−0.09; CI −0.25 to 0.07). The correlations between the two subscales and the other scores were generally weak. Over time, the correlations increased in the total score and the self-liking subscale (n.s.). The correlation was strongest between the SES total score and the GIPD score (patient perspective: −0.49; CI −0.61 to −0.34), and

Fig. 2 Rosenberg Self-Esteem
Scale scores over time: **a** total
score; **b** scores of the subscales
'self-confidence' and
'self-liking' (means ± 95% CI)
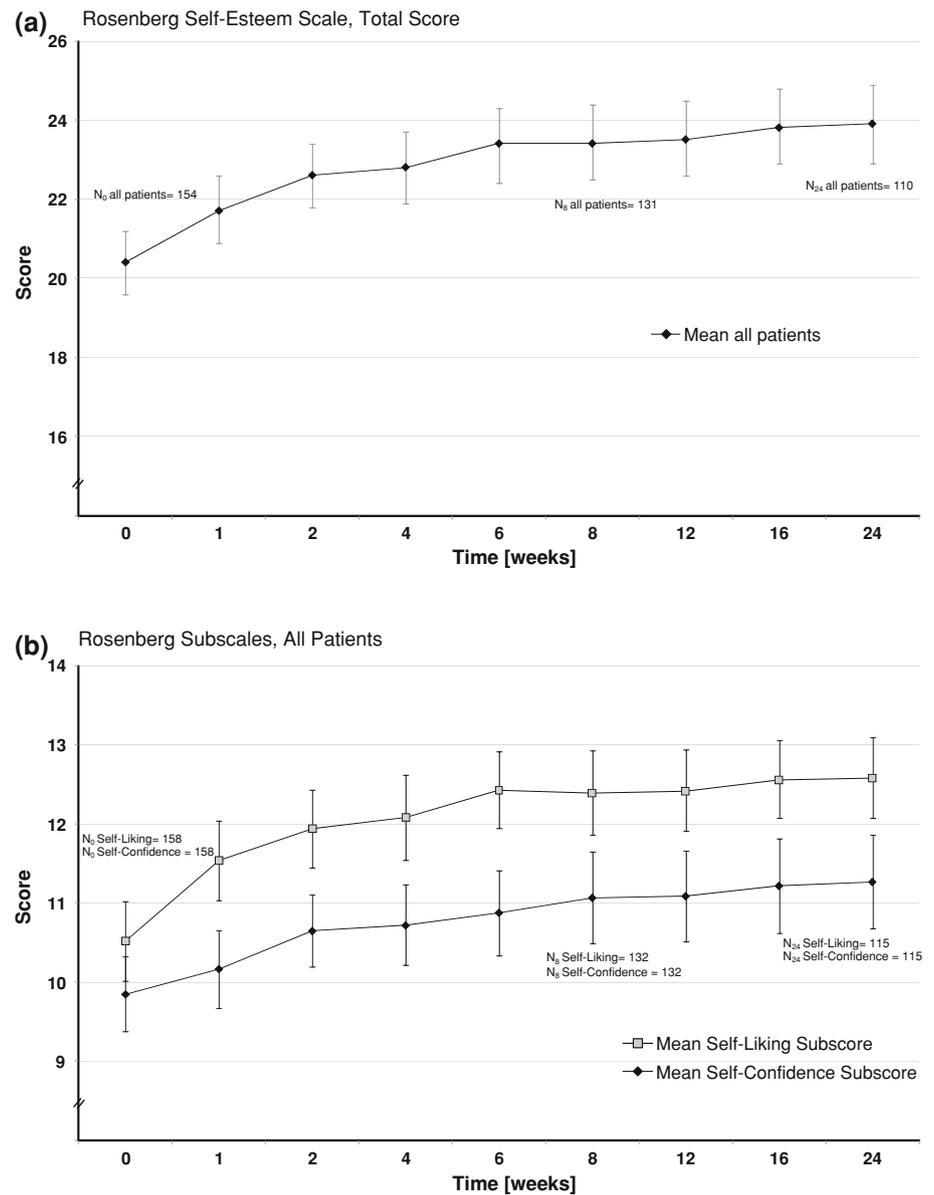
the self-liking subscore and the GIPD score (patient perspective: −0.51; CI −0.63 to −0.37).

Courses of the SES scores over time (unifactorial)

The mean SES total score statistically significantly increased in the first 2 weeks of treatment with atomoxetine, from 20.4 [95% CI 19.6; 21.2] points at baseline to 22.6 [CI 21.8; 23.4] points at week 2 (Fig. 2a). By week 8, it was reported at 23.4 [CI 22.5; 24.4] points and by the end of week 24, it was reported at 23.9 [CI 22.9; 24.9] points. Both the courses of the mean 'self-confidence' subscore and of the mean 'self-liking' subscore followed the general pattern of the mean SES total score (Fig. 2b). From week 1 onwards, the scores on the 'self-liking' subscale were

significantly higher than the scores on the 'self-confidence' subscale throughout the study.

At baseline, the mean SES total score of female patients was lower (n.s.) than the mean score of male patients (18.8 [CI 16.8; 20.9] vs. 20.8 [CI 19.9; 21.7). Over time, the difference between the gender groups decreased (Fig. 3a). At weeks 8 and 12, female patients even had slightly higher mean scores (n.s.) than male patients (female patients, week 8: 23.7 [CI 21.5; 25.9], week 24: 23.7 [CI 21.6; 25.7], male patients, week 8: 23.4 [CI 22.3; 24.5], week 24: 24.0 [CI 22.8; 25.1]).

The course of the mean SES total score was observed as largely parallel for both ADHD subtypes (Fig. 3b). Over the entire time period, patients of the combined subtype had slightly lower scores (n.s.) than patients of the

Fig. 3 Rosenberg Self-Esteem Scale: **a** total score, female and male patients, **b** total score by ADHD subtype (means ± 95% CI)

(a) Rosenberg Self-Esteem Scale by Gender

N_0 Males = 122
N_0 Females = 32

N_8 Males = 105
N_8 Females = 26

N_{24} Males = 85
N_{24} Females = 25

Mean, Male
Mean, Female

(b) Rosenberg Self-Esteem Scale by ADHD subtype

N_0 combined subtype = 78
N_0 predo. inatt. = 71

N_8 combined subtype = 68
N_8 predom. inatt. = 59

N_{24} combined subtype = 56
N_{24} predom. inatt. = 50

Mean predominantly inattentive subtype
Mean combined subtype
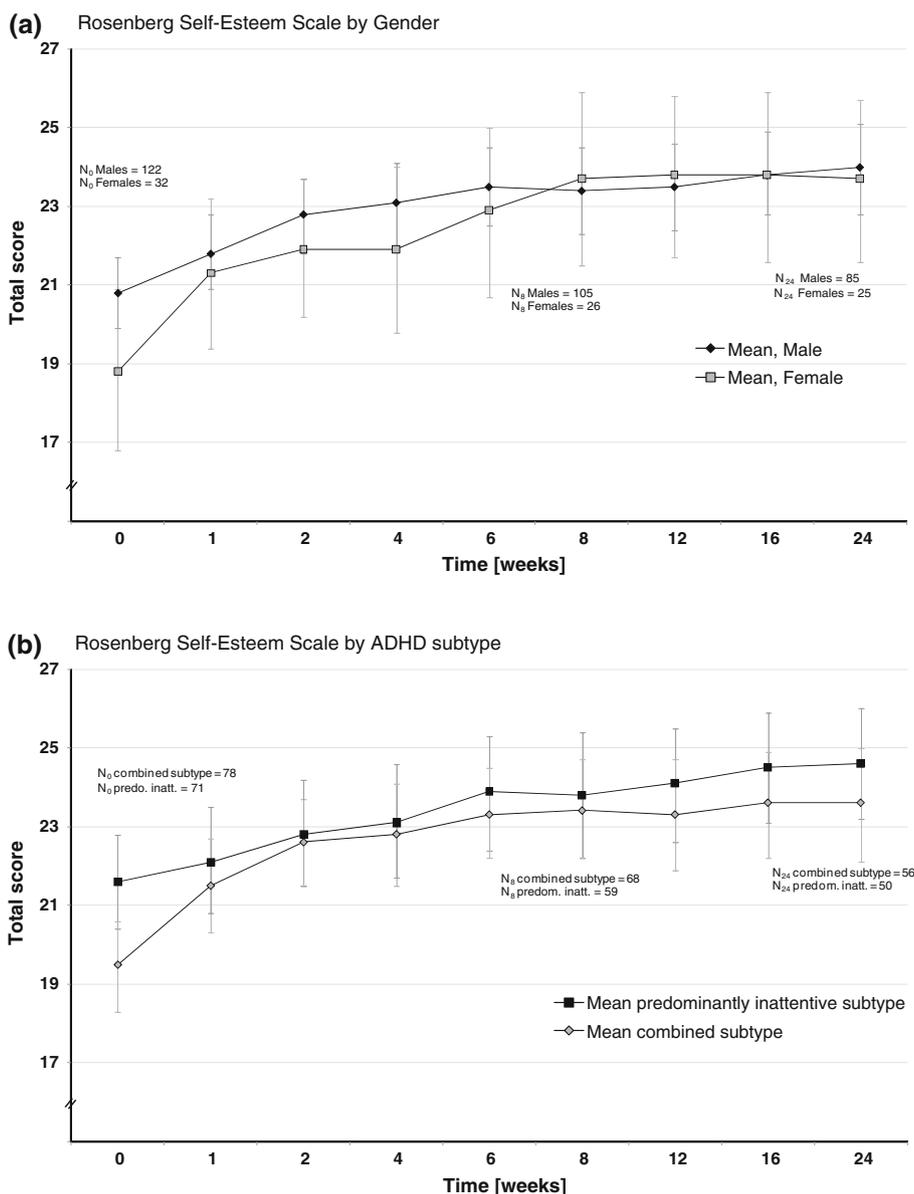
predominantly inattentive subtype. This difference did not reach statistical significance at any time.

With regard to the subscales, the female patients reported lower (n.s.) 'self-confidence' values compared to the male patients at baseline (Fig. 4a). After treatment start, this numerical proportion reversed, with higher self-confidence values for female than for male patients throughout the study. However, these differences did not reach statistical significance at any time. With regard to 'self-liking', females had slightly lower mean scores (n.s.) compared to the male patients during the study (Fig. 4b).

The patient group with the combined subtype was again associated with slightly lower mean 'self-confidence' scores than the predominantly inattentive subtype. For the

self-liking subscore, there were no relevant differences between the two subtypes (data not shown).

Influencing covariates (multifactorial)

The influence of baseline covariates on the course of self-esteem over time was analyzed by taking all covariates into one model, i.e., the influence of each of the different factors was controlled for all other factors. None of the covariates, as listed in Table 2, had a statistically significant influence on the SES total score or the self-liking subscale score. Only for two covariates, a significant influence could be found for the self-confidence subscale score (family setting; educational status): patients living in a nuclear family

Fig. 4 Rosenberg Self-Esteem
Subscales by gender:
a 'self-confidence' by gender;
b 'self-liking' by gender
(means ± 95% CI)
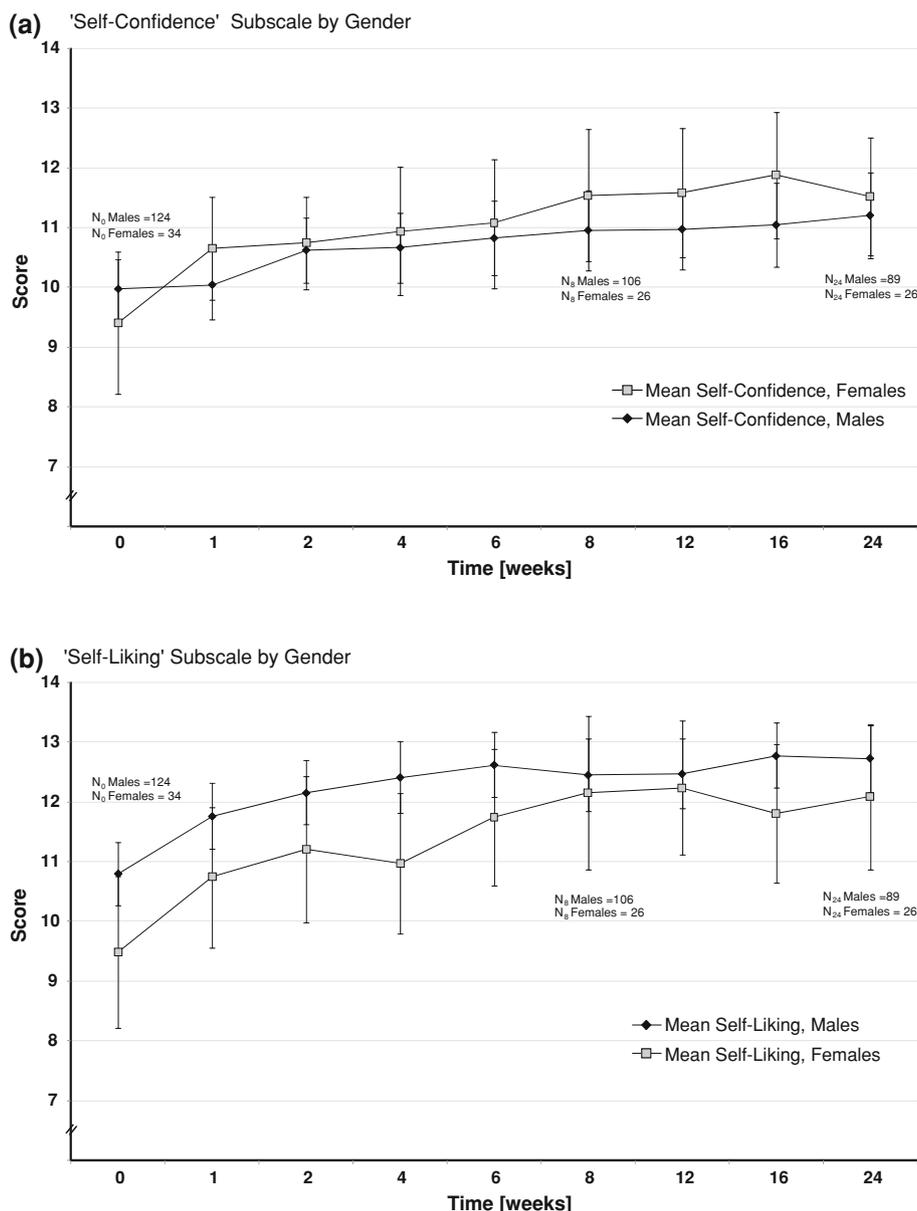
(a) 'Self-Confidence' Subscale by Gender

N_0 Males = 124
N_0 Females = 34

N_8 Males = 106
N_8 Females = 26

N_{24} Males = 89
N_{24} Females = 26

— Mean Self-Confidence, Females
— Mean Self-Confidence, Males

(b) 'Self-Liking' Subscale by Gender

N_0 Males = 124
N_0 Females = 34

N_8 Males = 106
N_8 Females = 26

N_{24} Males = 89
N_{24} Females = 26

— Mean Self-Liking, Males
— Mean Self-Liking, Females

started with baseline scores similar to patients living in other family settings, but the increase in scores over time was higher ($P = 0.0057$). Although the overall test for 'educational status of the patient' was significant (interaction with time; $P = 0.0242$), no clear pattern emerged looking at specific types of schools.

Course over time for other scales

The mean ADHD-RS-IV-Parent:Inv total score (OC) significantly decreased in the first 2 weeks of treatment with atomoxetine, from 28.4 [95% CI 26.8–29.9] points at baseline to 16.7 [CI 15.0–18.4] points at week 2. This decrease in the mean score continued during further treatment (to 11.0

[CI 9.3–12.7] points at week 24). The course of the mean ADHD-RS total scores was observed as largely parallel for both ADHD subtypes (cf. Dittmann et al. 2006; Dittmann et al. 2009). Over the entire time period, patients of the combined subtype had significantly higher scores than patients of the predominantly inattentive subtype.

With regard to the GIPD score, parents rated the ADHD-related difficulties less severe (n.s.) than physicians at baseline, but the parent and physician mean total scores converged as early as week 2 and overlapped for the remainder of the study. Compared to the parent and physician ratings, the adolescents perceived their difficulties as significantly less severe at most time points throughout the study. The mean CGI-S-ADHD score for the overall

sample significantly decreased from 4.8 [95%CI 4.7–5.0] at baseline to 3.4 [3.2–3.6] at week 8 and stayed stable, thereafter, until week 24 (3.3 [3.1 to 3.5]).

Tolerability

Investigators reported treatment-emergent adverse events in 124 (78.0%) patients over the entire study period. In 82 (51.6%) patients, the investigators considered the adverse event as possibly related to atomoxetine. Adverse events reported in more than 5% of the patients and rated as possibly related to atomoxetine were fatigue ($N = 42$, 26.2%), nausea ($N = 22$, 13.8%), headache ($N = 15$, 9.4%), upper abdominal pain ($N = 11$, 6.9%), decreased appetite ($N = 11$, 6.9%), dizziness 9 (5.7%), and vomiting 9 (5.7%). There were eight patients with serious adverse events, which were considered related to atomoxetine in two patients (1 patient with severe vomiting; 1 patient with abdominal pain, dissociation, disturbance in attention, dizziness, fatigue, and vasoconstriction). Treatment-emergent adverse events led to discontinuation in 7 (4.4%) patients: alopecia, decreased appetite, drug abuse, fatigue, vasoconstriction, vertigo, and vomiting in 1 (0.6%) patient each; except for fatigue and drug abuse, all these adverse events were rated as possibly related to treatment by the investigator. Mean laboratory parameters, including liver function tests, were found within normal ranges with only minor fluctuations over the course of the study. In vital signs, slight increases in blood pressure and heart rate were observed.

Discussion

To our knowledge, this is one of the very few studies investigating self-esteem in adolescents with ADHD. Furthermore, it is the largest single study focusing on adolescent ADHD patients treated with atomoxetine (Wilens et al. 2006a, b) for which preliminary results on efficacy and tolerability have been published elsewhere (Dittmann et al. 2006; Dittmann et al. 2009; Wehmeier et al. 2008). Atomoxetine is a non-stimulant treatment option for ADHD (Banaschewski et al. 2004; Becker et al. 2006) for which efficacy and tolerability in children and adolescents have also been demonstrated in a number of placebo-controlled randomized clinical trials (Kelsey et al. 2004; Michelson et al. 2001, 2002; Spencer et al. 2002).

The first objective of this secondary analysis was to validate the Rosenberg SES in adolescents with ADHD. We used the German language version of the Rosenberg Self-Esteem Scale (SES) to assess self-esteem (Ferring and Filipp 1996; von Collani and Herzberg 2003). Originally, it was developed as a one-dimensional scale, but some factor

analytic studies have found that self-esteem, as measured by the SES, can be decomposed into the subcomponents of 'self-competence' (i.e., feeling of having skills, abilities, and talents) and 'self-liking' (which relates to moral character, attractiveness, and other aspects of social worth; Tafarodi and Swann 2001; Schmitt and Allik 2005). This concept of dichotomy could also be supported by the results of the factor analysis in our sample of adolescent ADHD patients. Further, the scale has shown good test–retest reliability over a period of 2 weeks, and it was shown to be internally consistent (all Cronbach's alpha values were above 0.80).

Our second objective was to evaluate correlations of the SES with ADHD scale scores. The correlations between the patient-rated SES and the other scales were rather weak for each point in time as well as for change over time (Table 4). At baseline, we found weak negative correlations between the SES total and the two subscale scores with the other scale scores, with slight increases in most of them over time. The strongest correlations were found between the SES total and the patient-rated GIPD scores, both representing the patient perspective. The other scales assess different constructs of the underlying disorder (ADHD), mostly rated by another person (physician or parent), showing smaller negative correlations with SES scores.

In general, correlations with parameters such as ADHD core symptoms or related perceived difficulties were weak to modest, and thus suggest that the SES assesses an additional dimension beyond ADHD core symptoms or ADHD-related difficulties. According to our findings, self-esteem may be an important individual patient outcome in patients with ADHD.

The third objective was to investigate self-esteem in adolescent patients with ADHD during atomoxetine treatment. The relationship between self-esteem and ADHD treatment, mostly stimulant treatment, has been investigated in several studies, so far with conflicting results (Alston and Romney 1992; Bussing et al. 2000; Frankel et al. 1999; Treuting and Hinshaw 2001; Hechtman et al. 2004). In their review, Hechtman and Greenfield (2003) stated that stimulant treatment in childhood had slight benefits regarding self-esteem compared to untreated patients with ADHD in the long term. Several studies with non-stimulant treatment (atomoxetine) also reported that treatment seemed to improve self-esteem (Perwien et al. 2004, 2006; Prasad et al. 2007) but provided insufficient data to determine whether medication was responsible for the observed changes and differences in self-esteem.

In our study, mean self-esteem scores increased within the first 2 weeks of treatment with atomoxetine by week 2. The achieved level of improvement was kept, thereafter, until week 24. This increase was accompanied by the

improvement of ADHD symptoms (rated by ADHD-RS and CGI), and ADHD-related difficulties (rated by GIPD). Since there was no placebo control in this study and a cutoff value ("normal vs. "abnormal") cannot be found in the literature, the absolute mean scores and observed changes over time cannot easily be interpreted with respect to their clinical relevance. However, von Collani and Herzberg (2003), who used the same revised SES instrument as in our study, reported a mean score value of 22.7 attained in two healthy study groups ($N = 285$, 58% female, mean age 33.7 years; $N = 117$, 58% female, mean age 30.8 years). Our patients reached mean scores similar to those published for healthy subjects. Furthermore, the mean score values of the 'self-liking' subscale were reported as significantly higher than the values of the 'self-confidence' subscale throughout the study. But, the different courses of the two subscales only indicate changes over time and do not allow for a direct comparison referring to a clinical meaning (e.g., higher/better self-liking than self-confidence).

Our findings are in accordance with other atomoxetine studies: based on a combined analysis from three placebo-controlled trials of atomoxetine in children and adolescents with ADHD (mean age 10.4 years) and using the parent-rated Child Health Questionnaire (CHQ), Perwien et al. (2004) reported statistically significantly lower baseline ratings on the 'self-esteem' section for the ADHD sample compared to the normative sample (t-score 63.5 vs. 79.8, respectively). After 7–8 weeks of treatment with atomoxetine, this t-score increased to 70.3. From another open-label long-term atomoxetine trial (mean age 11.1 years) applying the same instrument, a baseline mean t-score of 39.6 was observed (Perwien et al. 2006). This t-score increased by 7.9 points after 10 weeks of treatment, which was maintained during the long-term follow-up (24 months). The short-term placebo-controlled improvements were statistically significant with a small to medium effect size of 0.32 (Perwien et al. 2004) and long-term improvements of parent-reported CHQ self-esteem in young ADHD patients in the open-label study (Perwien et al. 2006).

In children and adolescents with ADHD (mean age 10.9 years) treated with either atomoxetine or standard current therapy over 10 weeks, Prasad et al. (2007) found statistically non-significant increases on the self-reported 'global self-worth' domain of the Harter instrument (HSPP) in both groups, with no statistically significant difference between the two treatment groups.

Interestingly, the female patients in our study showed lower (n.s.) mean total SES scores compared to male patients at baseline. Over time, the difference between the gender groups decreased (Fig. 3a). At weeks 8 and 12, female patients even had higher score values (n.s.) than

male patients. With regard to the subscales ('self-confidence', 'self-liking'), our findings also suggested potential differences between male and female adolescent populations with ADHD. However, the sample size of participating female patients was too low to definitively explain the implications of the different mean scores in both groups over time, a topic that may deserve further investigation in respective controlled studies.

In order to determine possibly influencing baseline factors, such as age and gender, we analyzed the influence of covariates on the development of self-esteem in our study. Only for the 'self-confidence' subscale score, a significant influence could be found for two covariates (family setting; educational status): patients living in a nuclear family started with baseline scores similar to patients living in other family settings, but the increase in mean scores over time was significantly higher in this subgroup. Concerning the educational status of the patients, the overall test was significant (self-confidence subscale only), but with no clear pattern emerging with regard to the different specific types of schools. All other covariates (gender, age, comorbidities, concomitant medication, ADHD subtype, etc.) were found not to be the determinants of the improvement of self-esteem during atomoxetine treatment. Our results leave underlying factors of the observed increase in self-esteem in adolescent ADHD patients largely unexplained.

Limitations

The findings of this study should be interpreted with caution due to the open-label design. Most importantly, our study did not include a placebo control sample or an active comparator arm, so that the degree to which the results reflect drug-specific effects or time effects remains uncertain. Further, the proportion of patients with concomitant emotional or depressive comorbidities was low (2.5 and 1.3% only); this may in part explain why we were unable to show an impact of patients' comorbidities on self-esteem. In this study, exploratory with respect to the self-esteem outcome parameter, no other instrument assessing self-esteem or emotional problems as perceived by the patients was used.

In conclusion, the Rosenberg SES can be considered an internally consistent and reliable measure to assess changes of self-esteem experienced by adolescents with ADHD. The dichotomy of the SES (self-liking, self-confidence) observed in other psychiatric disorders was replicated in our study population. No baseline factors influencing self-esteem over the course of treatment were found. This study showed that the scale is sensitive to change as indicated by a significant improvement over time. Changes in self-esteem over the course of this open-label atomoxetine trial

were self-reported by adolescent patients with ADHD. According to these findings, self-esteem may be an important individual patient outcome beyond the core symptoms of ADHD deserving further investigation, also in controlled studies.

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