

ADHD symptoms in patients with Bipolar or Drug abuse disorder

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Abstract

Background: The attention deficit and hyperactivity disorder (ADHD) is defined as a persistent state of inattention and/or hyperactivity-impulsivity. Most adult patients with ADHD symptoms are diagnosed with other mental disorders in comorbidity. Substance Use Disorders (SUD) and Bipolar Disorder (BD) are the conditions most frequently associated with a history of ADHD. Although the increasing number of studies on this topic, the relationship between SUD, BD and ADHD remains unclear.

Aim: To evaluate the prevalence of ADHD spectrum symptoms in patients with SUD, BD or SUD+BD and the clinical features associated to these phenotypes.

Methods: 147 patients were consecutively recruited for a 12 month-period of at the outpatients' service and Day Hospital of the Psychiatric Clinic of the University of Pisa, at the outpatients' service and ward of the Department of Psychiatry, Versilia Hospital, at the outpatients' clinic of the Service for Drug Addiction (Ser.T) of Viareggio. Outpatients attending the therapeutic community "Incontro" in Pistoia also entered in the study. Patients were investigated by means of the ASRS-v 1.1. (Adult ADHD Self-Report Scale) and the DCTC (Diagnostic, Clinical and Therapeutic Checklist). All patients satisfied DSM-IV-TR criteria as confirmed by the SCID-I administration.

Results: 50 patients were diagnosed with Bipolar I or II disorder (BD), 53 with Substance Use Disorder (SUD), and 44 with Dual Diagnosis (BD+SUD). 23 patients (15.6%) scored sufficiently high at the ASRS

scale and showed a history of ADHD in childhood so that to satisfy the diagnosis of adult ADHD. Other 24 patients (16.3%) achieved high scores on ASRS scale but did not show a history of ADHD in childhood. BD+SUD patients were significantly more affected by comorbid ADHD compared to BD and SUD patients [13 (29.5%) vs. 6 (12%) and 4 (7.5%), respectively]. BD+SUD patients scored highest on all ASRS scale items even if significant differences among groups resulted only in item 2, 14 and 17. These patients also referred a higher number of mixed episode in their lifetime and showed a worse global functioning.

Discussion and conclusions: Bipolar disorder comorbid with substance use disorder shows a more significant association with ADHD (in about a quarter of cases) compared with Bipolar or substance use disorder alone. The higher rate of ADHD and mixed symptoms in BD + SUD deserves clinical interest and careful attention to the treatment plan given the greater disease severity of this patient group. It is possible that the relationship between adult ADHD and SUD is mediated by the association with BD in both its full-blown and spectrum expressions.

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Introduction

Attention deficit hyperactivity disorder (ADHD) is a syndrome characterized by a persistent state of inattention and/or hyperactivity-impulsiveness, more frequent and severe than the one typically observed in peer individuals.

Originally described in a pediatric population, a growing body of clinical and research activity allowed to recognize its occurrence in adults also, supporting the hypothesis of a symptomatic continuum.

The diagnosis of adult ADHD can be difficult because hyperactive symptoms tend to decrease with age while are more frequent difficulty in driving, sexually transmitted diseases, early pregnancies, lack of social skills, study discontinuation, working and marital matters (Barkley, 2006). Furthermore, adult ADHD is often associated with a high number of psychiatric comorbidities (in more than 80% of cases), thus increasing the diagnostic challenge. It has been reported that a significant percentage of children and adults with ADHD is suffering from major depression or dysthymia (22-27%) and personality disorders (11-24%) (Barkley, 2008). According to the strict DSM-IV-TR diagnostic criteria screening ADHD assessment of 966 adults revealed a prevalence rate of 2.9% while, including patients with subthreshold symptomatology, the prevalence rate increases to 16.4%

(Faraone et al, 2005). In general, 50-70% of adolescents with ADHD continue to manifest symptoms in adulthood (Harpin, 2005; Hechtman, 2000, Mannuzza et al, 1993).

Substance use disorder (SUD) is widespread affecting 27% of the adult population (Kandel et al, 1997); of these, 15-25% show symptoms of ADHD (Wilens, 2004). ADHD is considered a risk factor for the development of a SUD. The comparison of 120 adults with ADHD versus 268 adults without ADHD (with a mean age of 40 years) showed a rate of 52% lifetime SUD in the first group compared to 27% in the second one (Biederman, 1995). Furthermore, adults with ADHD comorbid with Bipolar Disorder or Conduct Disorder have an increased risk of experiencing SUD and show an earlier onset compared to subjects with single ADHD diagnosis (Wilens, 2003). Comorbidity between SUD and ADHD is associated with an earlier onset, a longer duration of illness a more rapid progression from alcohol to other substances abuse. Finally, research on the relationship between the use of stimulants in ADHD treatment and increased risk of developing SUD led to conflicting results.

Several studies report a comorbidity between major depression and ADHD in adults of 16-31% (Barkley et al, 2006). Other studies suggest also a significant comorbidity between ADHD and Bipolar Disorder (BD). Comorbidity rates of Bipolar disorder in individuals with ADHD are highly variable

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(from 5.1% to 47.1%) as the prevalence of ADHD in individuals with Bipolar disorder (from 9.5% to 21.2%). Compared to Bipolar disorder, ADHD symptomatology is characterized by an earlier onset, by a protracted course, by the absence of a clear mood expansiveness and psychotic phenomena, by a hyperactivity and impulsivity in general smaller than those associated to mania.

In sum, the relationship between adult ADHD and substance abuse is probably mediated by the association with conduct disorder or antisocial personality disorder. The relationship between ADHD and Bipolar disorder, however, has not yet been completely well established.

The relationship between adult ADHD, Bipolar disorder (BD) and substance use disorder (SUD) is not fully understood. Moving from this point, we aimed to evaluate the prevalence of ADHD symptoms in adult patients with BD, SUD and dual diagnosis (BD+SUD) and the clinical features associated to them.

Methods

147 patients referring to the psychiatric outpatient service, Day Hospital and ward of S. Chiara (University of Pisa) and Versilia (Viareggio) Hospitals, to the outpatient units of the Service for Drug Addiction (Ser.T) (Viareggio) and the Meeting Therapeutic

Community (Pistoia) were consecutively recruited for a period of about 12 months.

DCTC (Diagnostic, Clinical and Therapeutic Checklist) and ASRS-v 1.1 (Adult ADHD Self-Report Scale) were administered. The DCTC allows clinicians to evaluate time course of psychiatric symptoms by using the CGI module and social adaptation by the GAF and the Sheehan Disability Scale; it also collects axis I comorbidity, actual and previous drug treatment and therapeutic changes proposed in the assessment phase. The ASRS-v 1.1 consists of 18 items that explore the symptoms presented during the last 6 months. The first 6 items allow to carry out a diagnostic screening for the presence of ADHD in adult subjects. The diagnosis is satisfied for scores above a 4 or more at the first 6 items and the onset of symptoms occurs before the 7 years-old of age.

Statistical analyses

Epidemiological and clinical characteristics, as well as ADHD symptoms detected by the ASRS were compared between the three groups of patients with SUD (n=53), BD (n=50) and SUD+BD (n=44). The comparative analysis for the epidemiological clinical and symptomatological characteristics of the different subgroups was conducted using the one-way ANOVA for the-dimensional variables (post-hoc comparisons were

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performed using the Bonferroni test) and the cross-tabulation for the variables categorical. We used two-tailed significance levels with a threshold of $p < 0.5$.

Results

Patient group consisted of 147 subjects (95 males (64.6%) and 52 females (43.4%)). 50 patients were diagnosed with Bipolar disorder type I or II (BD), 53 with Substance Use Disorder and 44 with Dual Diagnosis according to DSM-IV-TR criteria (APA, 2000) (table 1).

Patients with BD had a higher number of patients in the manic phase and in remission, while the BD+SUD patients showed a higher number of mixed states, even if this latter difference did not reach statistical significance. The prevalence of bipolar II depression was similar in both groups with bipolar disorder. The diagnosis of alcoholism was found to be prevalent in patients with SUD while those with dual diagnosis showed a higher number of cocaine abuse (even if both of these differences were not statistically significant). Heroin abuse was present at a similar rate in the 2 groups with SUD (30.2% vs. 36.4% respectively). The GAF scores showed a better overall functioning in patients with SUD (61.8 +20) while those with BD and BD+SUD obtained lower scores (52.4 +22.4 vs. 55.7 +12.2, respectively). The social adaptation, as measured by the Sheehan scale

in the 3 functional areas of work, family and social relations, showed no significant differences among the 3 groups, while indicating moderate levels of maladjustment in all patients. Overall clinical severity using CGI exploring different areas showed higher scores in BD and BD+ SUD patients compared to SUD subjects in relation to depression, mixed state and psychosis. BD patients compared to the other diagnostic groups showed highest scores in the scale of mania and the lowest in the scale of impulsivity (table 2).

23 patients (15.6%) achieved sufficient scores at the ASRS scale together with a history of ADHD in childhood so allowing the diagnosis of adult ADHD. Other 24 patients (16.3%) achieved ASRS high scores but did not show a history of ADHD in childhood. 13 (29.5%) patients with SUD+BD reported a history of ADHD in comparison to 4 (7.5%) with SUD and 6 (12%) with the BD. The difference among the 3 groups was statistically significant and indicated an association between SUD, BD and ADHD (figure 1).

The majority (15 of 18) of ASRS items did not differentiate significantly the 3 diagnostic groups, even if the SUD+BD subjects showed highest mean scores in all the variables explored. Only 3 items significantly differenced the 3 groups: item 2 ("difficulty in ordering items while you are performing a task that requires organization") and item 17

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("difficulty awaiting their turn") showed significantly higher scores in SUD+BD subjects than in the other 2 groups; item 14 ("difficult to relax") differed BD and BD+SUD from SUD patients. Regarding the total score of the first 6 items, the most important in terms of diagnostic specificity, SUD+BD subjects showed higher scores compared to the other 2 groups as well as in the ASRS total score (table 3).

Discussion

Adult ADHD rarely represents an isolated condition but is more often associated with other mental disorders, the most common of which are mood disorders and substance use disorders.

Our sample of 147 patients with Bipolar Disorder, Substance Use Disorder and dual diagnosis of Substance Use Disorder and Bipolar Disorder showed comorbidity with ADHD in approximately 15% of cases. A similar percentage of patients reported high scores on the ASRS scale but did not have a childhood onset as necessary for to satisfy ADHD diagnosis. The percentages of comorbidity we observed are in agreement with those reported by other authors (SUE) using different diagnostic methods of similar series (Bird et al, 1993;Kessler et al, 2006; Mc Gough et al, 2005; Nierenberg et al, 2005).

Patients with dual diagnosis SUD+BD had ADHD in about a quarter of cases, thus showing very high rates of comorbidity and higher than those of patients with only SUD and only BD.

As expected, most of our patients had at least one comorbid psychiatric disorder. In particular, patients with SUD+BD had high rates of comorbidity. Use of cocaine, stimulants and alcohol and, above all, multiple substances abuse tend to characterize most patients with dual diagnosis. This finding is in according with previous observations suggesting that the association between ADHD and mood disorder seems to characterize a particularly severe subtype of SUD, with multiple substance abuse complication and chronicity.

As far as the symptoms profile at the time of observation is concerned, BD patients were more often in manic phase and in remission, while BD+SUD subjects showed a higher number of mixed states. The overall clinical severity assessment showed a major presence of depression and psychotic and mixed symptoms in BD and BD+SUD patients. Moreover, BD subjects showed more severe manic symptoms and less impulsivity than both other diagnostic groups. The association of mixed symptoms with BD+SUD and ADHD is of great clinical interest and, probably, of great importance in the treatment plan, indicating a greater severity of this patient group, even for the

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prognosis. In this perspective, overall functioning was worse in patients with BD+SUD.

Regarding the ADHD specific symptoms, patients with dual diagnosis (SUD+BD) showed high scores in all investigated areas, particularly in the "difficulty in getting things in order when you have to do a task that requires organization" and "having problems remembering appointments or obligations". Both specific items for the diagnosis and ASRS total score were indicative of increased severity of the various domains of ADHD such as in attention, impulsivity and difficulties of organization. The "difficulty unwinding and relaxing when you have time to yourself," however, seemed to be more associated with the presence of mood disorder.

Some methodological limitations in this study deserve to be mentioned. This is retrospective study and recollecting of information may be affected by biases with regards to diagnosis and onset of symptoms. This bias, however, is shared by the 3 compared groups. As for ADHD, also, it is likely to be an underestimate assessment of frequency with which this diagnosis is reported in our country. The heterogeneity of selected cases in terms of age, sex and clinical diagnosis has to be observed. In particular, age and gender differences may influence the prevalence of ADHD. It 's likely that in our

bipolar patients who are older and mostly females, the prevalence of ADHD is less than in a paired sample for demographic characteristics. However it is also true that in young male bipolar patients drug use is very common.

Our data seemed to be in agreement with the observation that SUD in a patient with ADHD, besides having an earlier onset, is associated also to a longer life and a more rapid progression to multiple substances abuse (Wilens 1997, 2003). Additionally, when bipolar disorder is comorbid with ADHD, there is present a greater risk of experiencing a SUD.

Finally, our data suggest a significant comorbidity between ADHD and bipolar disorder. The overlapping symptomatology makes sometimes the differential diagnosis between the two conditions, especially in childhood, difficult. The protracted hypomania, especially in adolescents and young adults, is not always easily distinguishable from the hyperactivity and impulsivity typical of ADHD and in many cases there is a combination of both disorders. Obviously, this condition seems to increase exponentially the risk of developing a SUD. In conclusion, it is possible that the relationship between adult ADHD and SUD may be mediated by the association with BD in both its full-blown and spectrum expressions.

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Table 1. Differences at demographics among the diagnostic groups (Substance Use Disorder: SUD, Bipolar Disorder: BD, Dual Diagnosis: SUD+BD)

	SUD N= 53	BD N=50	SUD+BD N=44	f or χ^2	p
Age, mean (SD)	24.8 (9.6)	42.9 (15)	34.9 (6.8)	8.6	<.0001
Gender, male, n (%)	38 (71.7)	23 (46)	34 (77.3)	11.8	.003
<u>Marital status, n (%)</u>					
Single	34 (64.2)	21 (42)	35 (79.5)		
Married	9 (17)	24 (48)	4 (9.1)		
Separated or divorced	10 (18.9)	5 (10)	5 (11.4)	23.5	.0001
<u>Working status, n (%)</u>					
Student	7 (13.21)	8 (16)	5 (11.36)		
Unemployed	12 (22.64)	14 (28)	10 (22.73)		
Factory worker	23 (43.4)	18 (36)	22 (50)		
Employee	11 (20.75)	10 (20)	7 (15.91)	2.2	ns
<u>Education, n (%)</u>					
University degree	1 (1.9)	7 (14)	1 (2.3)		
High school qualification	20 (37.7)	19 (38)	11 (25)		
Primary school	32 (60.4)	24 (48)	32 (72.7)	11.6	.02

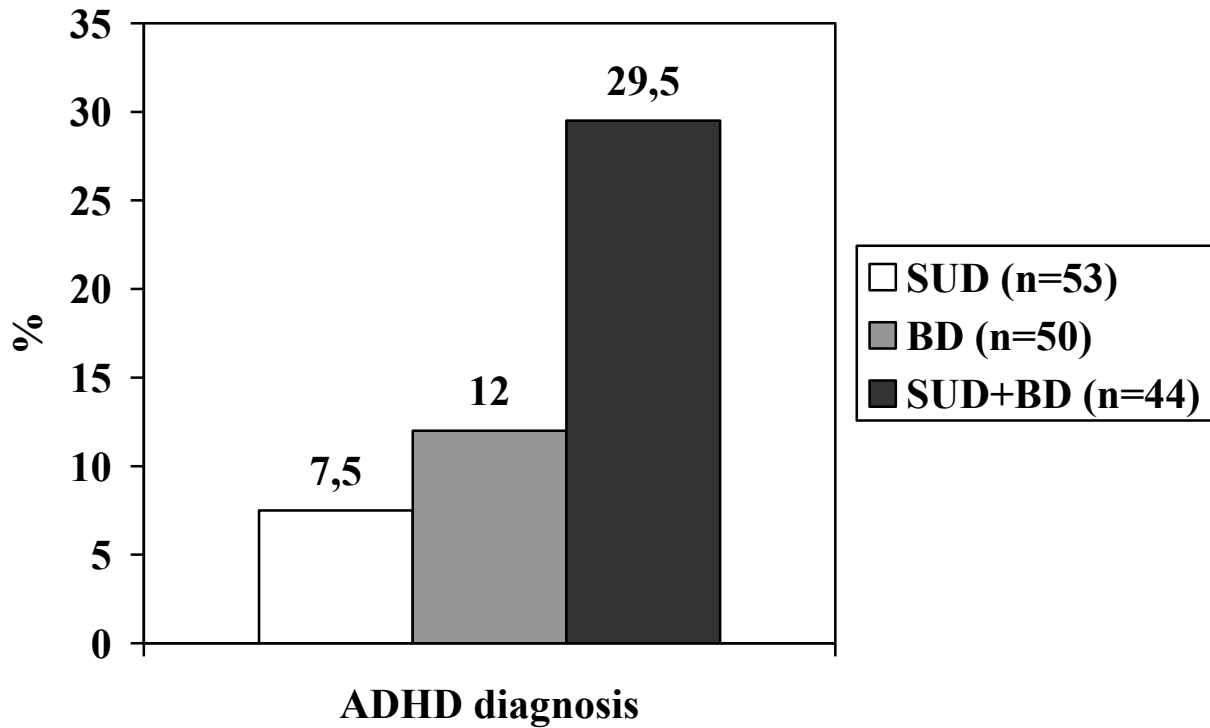
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Table 2. Differences at clinical characteristics among the diagnostic groups (Substance Use Disorder: SUD, Bipolar Disorder: BD, Dual Diagnosis: SUD+BD)

	SUD N= 53	BD N=50	SUD+BD N=44	f or χ^2 (df)	p
<u>Psychiatric diagnosis: principal, cross-sectional, n (%):</u>					
BD type I (Major Depression)	--	8 (16)	12 (27.3)	1.8(2)	ns
BD type I (Mixed State)	--	12 (24)	18 (40.9)	3.8(2)	.08
BD type I (Mania)	--	9 (18)	0 (0.0)	8.8(2)	
	.003				
BD type II (Major Depression)	--	12 (24)	13 (29.5)	0.4(2)	ns
BD (remission phase)	--	9 (18)	1 (2.3)	6.1(2)	.01
Mood-congruent psychosis	--	3 (6)	1 (2.3)	0.8(2)	ns
Mood-incongruent psychosis	2 (3.8)	5 (10)	3 (6.8)	1.0(3)	ns
Alcoholism	17 (32.1)	--	7 (15.9)	3.4(2)	.07
Cannabinoids	7 (13.2)	--	4 (9.1)	0.4(2)	ns
Cocaine and stimulants	13 (24.5)	--	17 (38.6)	2.2(2)	ns
Eroine	16 (30.2)	--	16 (36.4)	0.4(2)	ns
<u>Lifetime comorbidity, n (%)</u>					
Major Depression	2 (3.8)	--	--		
Panic Disorder	5 (9.4)	3 (6.0)	7 (15.9)	2.6(3)	ns
Panic Disorder with Agoraphobia	2 (3.8)	7 (14.0)	5 (11.4)	3.4(3)	ns
Generalized Anxiety Disorder	1 (1.9)	5 (10.0)	1 (2.3)	4.6(3)	ns
Social Phobia	1 (1.9)	1 (2.0)	1 (2.3)	0.2(3)	ns
Obsessive-Compulsive Disorder	0 (0.0)	2 (4.0)	1 (2.3)	0.8(3)	ns
Alcoholism	3 (5.7)	4 (8.0)	9 (20.5)	6.1(3)	.05
Eroine	1 (1.9)	1 (2.0)	1 (2.3)	0.2(3)	ns
Cocaine and stimulants	4 (7.8)	1 (2.0)	9 (20.5)	6.0(3)	.05
Substance abuses	7 (13.2)	0 (0.0)	18 (40.9)	9.6(3)	
	.002				
<u>GAF, mean (SD)</u>	61.8 (20)	52.4 (22.4)	55.7 (12.2)	3.3	.04
<u>Sheehan Disability Scale, mean (SD):</u>					
Working adjustment	4.6 (2.3)	4.4 (2.3)	5.2 (2.1)	1.4	ns
Family adjustment	4.4 (2.1)	3.8 (2.0)	4.6 (1.9)	2.1	ns
Social adjustment	4.4 (2.1)	4.5 (2.1)	5 (2.9)	1.1	ns
<u>CGI-Bipolar</u>					
Severity of mania	0.3 (0.7)	1.9 (1.8)	0.5 (1.0)	23.8	<.0001
Severity of depression	0.9 (1.3)	2.4 (1.6)	2.2 (1.8)	13.4	<.0001
Severity of mixed phase	0.2 (0.8)	1.2 (1.7)	1.1 (1.9)	5.7	.004
Severity of anxiety	1.8 (1.7)	1.9 (1.7)	1.5 (1.8)	0.4	ns
Severity of impulsivity	1.7 (1.8)	0.9 (1.4)	1.9 (2.1)	4.3	.01
Severity of psychosis	0.1 (0.5)	0.8 (1.6)	0.07 (0.2)	8.1	<.0001

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Figure 1. Differences at ADHD diagnosis among the diagnostic groups (Substance Use Disorder: SUD, Bipolar Disorder: BD, Dual Diagnosis: SUD+BD)



Chi-square= 9.6, p=.008

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Table 3. Differences at ASRS scores among the diagnostic groups (Substance Use Disorder: SUD, Bipolar Disorder: BD, Dual Diagnosis: SUD+BD)

	SUD N= 53	BD N=50	SUD+BD N=44	F	p
<u>Items, mean (SD)</u>					
1-How often do you have trouble wrapping up the final details of a project, once the challenging parts have been done?	0.9 (0.9)	1.2 (1.1)	1.3 (1)	1.9	ns
2-How often do you have difficulty getting things in order when you have to do a task that requires organization?	1 (1.1)	1.2 (1.2)	1.6 (1.3)	3	0.05a
3-How often do you have problems remembering appointments or obligations?	1.4 (1.2)	1.3 (1.3)	1.7 (1.3)	1.2	ns
4-When you have a task that requires a lot of thought, how often do you avoid or delay getting started?	1.5 (1.1)	1.5 (1.2)	1.9 (1.3)	2.1	ns
5-How often do you fidget or squirm with your hands or feet when you have to sit down for a long time?	1.6 (1.3)	1.5 (1.3)	1.7 (1.3)	0.4	ns
6-How often do you feel overly active and compelled to do things, like you were driven by a motor?	1.3 (1.3)	1.3 (1.3)	1.4 (1.4)	0.6	ns
7-How often do you make careless mistakes when you have to work on a boring or difficult project?	1.6 (0.9)	1.6 (1)	1.7 (0.9)	0.5	ns
8-How often do you have difficulty keeping your attention when you are doing boring or repetitive work?	1.7 (0.9)	1.8 (1.1)	1.7 (1.2)	0.2	ns
9-How often do you have difficulty concentrating on what people say to you, even when they are speaking to you directly?	1.4 (1)	1.3 (1.1)	1.5 (1.2)	0.5	ns
10-How often do you misplace or have difficulty finding things at home or at work?	1.5 (1.1)	1.6 (1.1)	1.5 (1.4)	0.2	ns
11-How often are you distracted by activity or noise around you?	1.7 (0.9)	1.6 (1)	1.8 (1.2)	0.5	ns

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12-How often do you leave your seat in meetings or other situations in which you are expected to remain seated?	1 (1)	1 (1.2)	1.3 (1.2)	1.2	ns
13-How often do you feel restless or fidgety?	1.9 (1)	2.2 (1)	2.2 (1)	1.7	ns
14-How often do you have difficulty unwinding and relaxing when you have time to yourself?	1.3 (1.2)	1.7 (1.2)	2.1 (1.3)	5.0	.008b
15-How often do you find yourself talking too much when you are in social situations?	1.4 (1)	1.7 (1.4)	1.5 (1.3)	0.5	ns
16-When you're in a conversation, how often do you find yourself finishing the sentences of the people you are talking to, before they can finish them themselves?	1.7 (1)	1.7 (1.1)	1.6 (1.2)	0.1	ns
17-How often do you have difficulty waiting your turn in situations when turn taking is required?	1.2 (1.2)	1 (1.1)	1.6 (1.1)	3.5	.03
18-How often do you interrupt others when they are busy?	1.1 (0.9)	0.9 (1)	1.2 (1.1)	1.3	ns
Score at the first 6 items, mean (SD)	7.9 (3.8)	7.9 (4.1)	9.6 (5.3)	3.7	.05a
Total score, mean (SD)	25.3 (9.0)	25.9 (9.5)	29.4 (13.2)	3.8	.05a

Bonferroni Post Hoc analysis:

a SUD+BD>BD,SUD

b SUD+BD>SUD