Prevalence and Correlates of Attention Deficit Hyperactivity Disorder in adults from a French Community Sample

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ABSTRACT

Validated tools are lacking in languages like French to diagnose ADHD in adults. The Adult ADHD symptoms Self-Report (ASRS) was filled out by 1,171 parents of 900 school-aged youths in the context of the Children and Parents with ADHD and Related Disorders study. Prevalence estimates based on three scoring methods are compared (6-item screener, all 18 items, or the screener followed by the 12 remaining items). Based on the recommended and more conservative scoring method, the overall prevalence of ADHD symptoms is estimated to be 2.99%, without significant group differences between genders, or between younger and older adults. Potential correlates of ADHD symptoms were also examined in their relatives (children, brothers/sisters, uncles/aunts, and parents): birth order, level of education, body mass index categories, enuresis, suicide attempts, depression, and learning disabilities. Adults can be screened for ADHD symptoms using the ASRS; negative long-term outcomes should be assessed in patients' relatives too.

Keywords: ADHD, Adult, Rating scale, Psychometrics, Prevalence

INTRODUCTION

Attention-Deficit with Hyperactivity (ADHD) is one of the most frequent disorder in children and adolescents with a worldwide mean estimated prevalence of 5.29% (Polanczyk et al, 2007). According to DSM-IV, this condition encompasses a number of pervasive and impairing symptoms including severe problems of inattention and/or hyperactivity and impulsivity (American Psychiatric Association, 1994). The World Health Organization's (WHO) ICD-10 uses the name of Hyperkinetic Disorder (HKD) and lists similar criteria (Word Health Organization, 1993), but has a more stringent diagnostic algorithm leading to a lower prevalence of HKD than ADHD (Polanczyk et al, 2007). According to DSM-IV, three types of ADHD can be distinguished according to whether the symptoms are predominantly characterized by inattention, hyperactivity-impulsivity, or both (American Psychiatric Association, 1994). Studies suggest that the Predominantly Inattentive subtype may constitute a distinct disorder (Caci et al, 2013 (Ahead of print); Capdevila-Brophy et al, 2013 (Ahead of print); Solanto, 2000).

Although it is stipulated by both diagnostic systems that ADHD symptoms are pervasive, and tend to persist into adulthood for two third of the cases (Biederman et al, 2010; Faraone et al, 2006a; Klein et al, 2012; Kooij et al, 2010), neither the DSM-IV nor the ICD-10 provide specific criteria for adults (Barkley et al, 2008). Adult prevalence rates of ADHD are estimated to be between 2.5% and 3.4% in the general population (Fayyad et al, 2007; Simon et al, 2009)[1]. This condition is associated with a broad range of negative life outcomes but is also responsive to treatment (Hodgkins et al, 2012; Shaw et al, 2012), pointing to the need for efficient screening and diagnosis procedures. Illustrative of this need, the European Network for Adult ADHD recently proposed the DIVA, a semi-structured interview for ADHD, adapted in many languages and free of charge for clinicians and researchers (DIVA Foundation, 2012). However, semi-structured interviews are costly to use in epidemiological

[1] It should be noted that the estimates reported by Fayyad et al. (2007) are based on a complex scoring algorithm whereby each of their 11,422 subjects provided retrospective assessments of childhood ADHD. For those retrospectively classified as having met ADHD criteria in childhood, a single item screener was used to asses likely current levels of ADHD. Then a random sample of 154 respondents underwent a complete one-on-one clinical reappraisal interview of current ADHD. For all the remaining participants, multiple imputation procedures were used to estimate the likely conclusions of this reappraisal based on all provided information.

research and not well suited to large scale screening procedures.

In 2000, the World Health Organization (WHO) designed a questionnaire to rigorously assess ADHD symptoms in adults (the Adult ADHD symptoms Self-Report v1.1, ASRS) that only includes 18 items rated on a 0 (*Never*) to 4 (*Very often*) scale and no item related to the age of onset, duration, and impairment criteria. It has been adapted to up to ten languages (see http://www.hcp.med.harvard.edu/ncs/asrs.php). The French adaptation was done following a classical translation-back-translation procedure. The resulting version was approved by the WHO as the official French version of the full ASRS (Caci et al, 2008). Since the initial American validation study that supported the adequacy of a reduced form of the ASRS as a screening tool for ADHD (Kessler et al, 2004a), the full ASRS has been used also in clinical samples with comorbid conditions (Adler et al, 2009), in clinical trials to monitor changes in adults, and, more recently, in adolescents (Adler et al, 2011; Adler et al, 2012). Epidemiological studies using face-to-face interviews yielded the computation of mean cross-national prevalence rates in adults that reaches 3.4% (inter-quartile range: 1.3-4.9%) (de Graaf et al, 2008; Fayyad et al, 2007; Kessler et al, 2006), and the ASRS showed strong concordance with clinician diagnoses (Kessler et al, 2005; Kessler et al, 2007). Surprisingly, one of these studies reported a point-estimate of 7.3% (s.e.=1.8%) in France (N=727), with "the lower end of the 95% confidence interval of this estimate above the prevalence estimate for the total sample" (Fayyad et al, 2007). This is a striking result for France, a country where awareness of ADHD is low given a long history of psychoanalytic dominance in psychiatric practice which excluded ADHD as a meaningful diagnosis (Gonon et al, 2010). The main objective of this paper is to report on the rates of symptoms prevalence observed among samples of French adults from the general population in order to see whether this result could be replicated. When rating a questionnaire, a symptom is often rated as present if the score on the corresponding item is greater or equal than a predetermined cut-off score, and absent otherwise (Gomez et al, 2011). Then, the symptoms deemed present by this method are typically added. This simple method is criticisable as it may lead to false positive cases and increased prevalence estimates of both symptoms of ADHD and ADHD. Furthermore, for use in epidemiological studies, it is often useful to have access to more sophisticated rating algorithms involving the use of a shorter screener to determine who really need to complete a fuller instrument, leading to a two-step procedure

such as the one proposed for the ASRS (Kessler et al., 2005). However, meeting symptom criteria on a rating scale doesn't guarantee that the person fully correspond to a clinical diagnosis of ADHD since the person would also have to meet the clinical significance or impairment criterion (criterion D). Accordingly, some authors reported that impairment is moderately related to symptoms, and clinically probably more important than symptoms (Gordon et al, 2006; Molina et al, 2009).

In both children and adults, ADHD is a condition characterized by its heterogeneity (Wahlstedt et al, 2009) and by the high frequency of comorbid diagnoses (Brown, 2009) that lead to a variety of short-term and long-term personal and familial outcomes (Hodgkins et al, 2012; Shaw et al, 2012). In this study, we also investigate the association between ADHD, demographic characteristics (e.g., gender, age, birth order) and disorders (e.g., overweight/obesity, enuresis) known to be highly comorbid with ADHD.

Among the demographic characteristics most clearly associated with ADHD, sex and age clearly come first. Indeed, the specific manifestations of ADHD are known to differ as a function of age and sex, and prevalence rates are known to decrease with age and to be higher among males than females (Barkley et al, 2008; Caci et al, 2013 (Ahead of print); Faraone et al, 2006a; Faraone et al, 2006b). Birth order is also considered to represent a very influential demographic factor in child development and, as such, was put forward as a risk for developing ADHD as well as other disorders (Birtchnell, 1971). Results of studies on ADHD are controversial (Marin et al, 2012 [Epub ahead of print]) but overall tend to show the absence of relations between ADHD and birth order (Berger et al, 2009). However, most studies focused on children and adolescents, pointing to the need to investigate if the potential effect of this factor could emerge later on in the development.

Because hyperkinesia is not only observed in ADHD but also other conditions such as anorexia nervosa (Vansteelandt et al, 2004), one representation in lay people is that hyperactivity causes thinness as it involves high levels of energy consumption. Furthermore, underweight might also result from pharmacological treatment because one the most frequent side effect of these treatments is a loss of weight through appetite decrease (Poulton et al, 2012). An epidemiological study reported that US children with ADHD had about 1.5 times the odds of being overweight before they received any pharmacological treatment for their ADHD, and 1.6 times the odds of being underweight once they

had started pharmacological treatment (Waring et al, 2008). Binge eating and bulimia behaviours are also known to be related to high levels of impulsivity (Wonderlich et al, 2004) and ADHD (de Zwaan et al, 2011; Mikami et al, 2010; Surman et al, 2006). Conversely, a recent study reported that overweight problems for adolescents with ADHD tend to persist into adulthood (McClure et al, 2012), with prevalence rates of ADHD in adults receiving treatment for obesity reported as varying between 27.4% (CI95%=[21.1; 32.9]) and 42.6% (CI95%=[36.3; 48.9]) (Altfas, 2002).

In relation to this possible association between overweight and ADHD, a recent cross-sectional study also showed that obese children presented an increased risk for enuresis and recommended that potential enuresis should be screened during the initial set-up of interventions with obese children and adolescents (Weintraub et al, 2013). This study also replicated results from previous studies (Baeyens et al, 2004; Baeyens et al, 2007), showing that enuresis tends to be comorbid with ADHD, especially in boys. Both disorders are heritable but enuresis tends to disappear with increasing age while ADHD does not (Aubert et al, 2010). A recent review of the literature report that 20% of ADHD children also had primary nocturnal enuresis and, conversely, that 10% of children with enuresis also had ADHD (Aubert et al, 2010), leading to the recommendation to systematically screen for ADHD during consultations for enuresis and vice versa. Here, we extend these studies to investigate the relations between ADHD symptoms, overweight and enuresis during adulthood.

Impulsivity, a significant characteristic of ADHD, is a well-recognized factor risk for suicide attempts (Caci et al, 2004b). For instance, follow-up studies in early adulthood of children diagnosed with ADHD yield an overall estimated suicide rate about .7% that corresponds to a relative risk ratio of 2.91 (James et al, 2004). Compared with controls, patients with ADHD are 2.4 times more likely to make a voluntary self-injury and 2.9 more likely to attempt suicide (Swensen et al, 2002). The frequent comorbidity between ADHD and depression is also suspected to play a role in the association between ADHD and suicide attempts, especially in male adolescents (James et al, 2004). Similarly, parental psychopathology and genetic predispositions are recognized risk factors for ADHD in offspring (Galéra et al, 2011; Lindblad et al, 2011) but, to our knowledge, the link between parental ADHD and suicide/suicide attempt in offspring has never been assessed.

One of the major long-term outcomes of ADHD is that affected individuals are at higher risk of

attaining a lower level of education than non-ADHD, potentially due to the comorbidity between ADHD and learning difficulties (Klein et al, 2012; Mannuzza et al, 1993) but also because impairment in functioning (foremost school and social functioning) are part of the clinical picture of ADHD. In a 33-year follow-up study (Klein et al, 2012), probands attained 13.3 (s.d.=2.1) years of education vs. 15.8 (s.d.=2.3) for controls [$t(269)=9.52$; $p<.01$; Cohen's $d=1.139$]. Controls completed a bachelor's degree (34.6%) or higher degree (29.4%) vs. 15.6% and 3.7% in probands [$\chi^2(1)=13.02$ and $\chi^2(1)=32.33$, respectively; $p<.01$].

Aims of the study

The principal aim of our study is to estimate the prevalence of ADHD symptoms in a French community sample using the full ASRS and look for an effect of sex and/or age. We predict that ADHD symptoms at adulthood will be more frequent in males, show a slight decrease as a function of age, and will be significantly associated with weight problems, enuresis, suicide attempts, depression, learning difficulties and lower educational achievement in both self and relatives.

MATERIAL AND METHODS

Study design

This paper is based on data from the Children and Adults with ADHD and Related Disorders (ChiP-ARD) study that was conducted in southern France (Caci et al, 2013 (Ahead of print); Morin et al, 2013 (Ahead of print)). This study is the largest study in France concerned with ADHD symptoms in a community sample, and one of the larger studies ever conducted in Europe. This study received the support of the Commissioner of Education and the Department of Education, complied with normative ethical prescriptions for French medical research, and the procedures used to keep paper-based and electronic data secured and anonymous were approved by the *Commission Nationale Informatique et Liberté*.

Parents of the youths participating in this study had to return a signed consent form and were asked to complete questionnaires, including the ASRS in relation to their own manifestations of ADHD. Since the participation in the study was voluntary and strictly anonymous, we have no access to the characteristics of the non-respondents. Overall, 1,171 adults mailed back completed questionnaires to the research site and form the main sample used in this study, but twelve (9 women and 3 men) did not

report their month and/or their year of birth. Women (n=651; M_{age} = 40.73; S.D. = 5.60; range = 22.00-59.17) were younger [t(1023.4)=-6.85 (p<.0001, Cohen's d=.412] than men (n=507; M_{age} = 43.16; S.D. = 6.28; range = 26.17-64.67). In order to test for the effect of age on prevalence, we divided the sample into younger (20 to 40 years old; n = 425) and older adults (40 to 65 years old; n = 733).

Participants (n=1,142, excluding participants with missing data on these variables and seven pregnant women) provided us with ratings of the height and weight, from which we computed their Body Mass Index (BMI, defined as the ratio of body weight in kilograms over squared body height in meters). Regardless of age and sex, the WHO definition for overweight is a BMI greater or equal to 25, and for obesity a BMI greater than 30 (http://who.int/mediacentre/factsheets/fs311/en/). Similarly, underweight is defined by a BMI lower than 18.50. Admittedly, BMI should be considered a rough guide because it may not correspond to the same level of body fat in different individuals.

The higher attained level of education was reported in a six-category format to match French census data of 2009 established as follows: (i) Participants who completed primary school (i.e., *Certificat d'Études Primaires*) or less were coded 0; (ii) those who completed secondary school (i.e., *BEPC, Brevet Élémentaire, Brevet des Collèges*) were coded 1; (iii) those who completed a professional certificate (i.e., *Certificat d'Aptitude Professionnel*) or diploma (i.e., *Brevet d'Études Professionnelles*) were coded 2; (iv) those who completed college (i.e., *Baccalauréat*) or obtained a professional degree (i.e., *Brevet Professionnel*) were coded 3; (v) those who completed undergraduate university studies (i.e., *premier cycle universitaire, License*), where coded 4; and (vi) those who completed graduate university studies (i.e., *deuxième ou troisième cycle universitaire, Maîtrise, Doctorat*) were coded 5.

We explored the personal and familial history using simple Yes/No questions pertaining to the participants themselves and to any of their relatives (children, brothers/sisters, and parents). We asked if they or any of their relative ever attempted or committed suicide, suffered from depression, had learning difficulties, and had enuresis. We adopted a highly conservative approach by assimilating non-responses to negative answers and, when applicable, we discarded those participants who were likely to be single children (N=145).

The ASRS

The performance of the ASRS was assessed after thorough weighting of a subsample of 154 adults included in the US National Comorbidity Survey Replication (NCS-R) (Kessler et al, 2004b) aged between 18 and 44 years-old (Kessler et al, 2005). This age limit was chosen because older participants were deemed to present too much risk of experiencing memory bias when recalling ADHD symptoms in childhood. Item scores were dichotomized: 11 items were scored 1 if the response was *Often* or *Very Often*, and the remaining 7 items were score 1 if the response was *Sometimes*, *Often* or *Very Often* (Kessler et al, 2005). The simplest scoring method of the full ASRS is to sum the dichotomized items and consider people with a count of at least 9 points as positive for ADHD (Kessler et al, 2006). Doing so, sensitivity is 56.3% and specificity is 98.3% when compared to structured diagnostic interview ratings. Six items (4 inattention and 2 hyperactivity-impulsivity symptoms) were then selected by stepwise logistic regressions as those that most accurately predicted the clinical diagnostic classification (Kessler et al, 2005). These six items present a sensitivity of 68.7%, a specificity of 99.5%, and form the ASRS-screener. A two-step procedure was suggested to further improve the performance of the ASRS: the sum of the 18 dichotomized items is computed only for those subjects who scored higher than 3 on the 6-item screener, and those who received a total score higher than 10 are considered as very likely to have ADHD. These procedures convey more information than a simple sum of item scores as the 18 items were weighted and the six items of the screener selected to improve both the sensibility and the specificity against a clinical diagnosis that included the assessment of criteria A-D. This makes the diagnosis of ADHD highly probable albeit not certain.

Analyses

Data were analysed using STATA/SE 9.2 (Stata Corp., 2007). Of the 1,175 booklets returned by parents, ASRS was empty in 4 cases; 75 other cases had at least one missing item (6.41%) and 56 cases had only one item missing item (4.78%). Given the pattern and rarity of missing values, we performed an imputation by chained equations (van Buuren et al, 1999; White et al, 2011) yielding a final sample of 1,171 complete observations.

To estimate the prevalence of ADHD symptoms, we first dichotomized the items as

recommended by the authors of the ASRS (Kessler et al, 2005). Maximum Likelihood estimates of the point-value of prevalence rates reflecting the ratio (X/n) of the number of subjects who qualify for a diagnostic (X) on the total number of subjects (n), together with a 95% Confidence Interval, will be reported for the full sample and for the sex and age specific subgroups. We will report those values based on the ASRS 6-item screener, the full ASRS and the two-stage screening process. All computations were done using an online calculator (http://www.measuringusability.com/wald.htm) (Lewis et al, 2006; Sauro et al, 2005).

RESULTS

Prevalence of ADHD symptoms, age and sex

According to the 2009 Census data, the city of Nice *intra muros* counts 191,199 inhabitants (90,791 men; 47.49%) between 20 and 64 years old. Our sample counts overall slightly less men [43.55%, $\chi^2(1)=7.218$, $p<.007$] but more men of at least 40 years old [31.17% vs. 25.78%; $\chi^2(1)=58.074$; $p<.001$] and the same proportion of women of at least 40 years old [32.12% vs. 29.39%; $\chi^2(1)=.367$; n.s.].

Table 1 presents prevalence estimates for the entire sample and for sex, age and sex-by-age subsamples. The entire sample prevalence of ADHD symptoms is 11.27% when using the 6-item screener alone, 8.37% when based on the full ASRS scale, but falls to 2.99% when using the recommended two-stage scoring algorithm. There is no significant sex and age effect on scores obtained on the 6-item screener (Fisher's exact test p=.403, and Spearman's rho=.031, n.s., respectively), on the full ASRS scale (Fisher's exact test p=.395, and Spearman's rho=.029, n.s., respectively), or on the two-stage score (Fisher's exact test p=.388, and Spearman's rho=.049, n.s., respectively). These results suggest that age and sex differences commonly reported in childhood and adolescence may fade out in adulthood (Kooij et al, 2010). Rates of prevalence were also computed on the non-imputed data and were almost identical to those reported here (these alternative rates are available from the first author).

When looking at the participants who screened positive on the 6-item screener (n=132), 61 had less than 6 positive items on the total ASRS scale, 60 had at least 6 positive items of either inattention

or hyperactivity-impulsivity (i.e., 50 were likely to correspond to the predominantly Inattentive subtype and 10 likely to correspond to the predominantly Hyperactive-Impulsive subtype), and 11 had at least 6 positive items of both inattention and hyperactivity-impulsivity (i.e., combined subtype), likely to correspond to the

When looking at the participants who screened positive in the second stage (n=35), 24 had at least 6 positive items of either inattention or hyperactivity-impulsivity (i.e., 21 likely to correspond to the predominantly Inattentive subtype and 3 likely to correspond to the predominantly Hyperactive-Impulsive subtype), and 11 had at least 6 positive items of both inattention and hyperactivity-impulsivity (i.e., likely to correspond to the combined subtype). Table 1 shows estimates of prevalence split by gender, age, and age-by-gender for ADHD subtypes.

The following regression analyses contrast the subgroup of individuals found positive using the two-stage algorithm versus the rest of the sample.

ADHD symptoms and birth order

Our sample includes 24 twins and none of them presented significant levels of ADHD symptoms. Non-twins participants who were their mother's first-born are not significantly more likely to present clinically significant levels of ADHD (OR=.196, s.e.=.200, CI95=[.027; 1.446]) than the other participants, whatever their sex (OR=1.411, s.e.=.485, CI95=[.719; 2.769]).

ADHD symptoms and BMI

Table 2 shows the prevalence of the BMI categories as defined by the WHO. Examination of these prevalence rates show that: (i) no participant presented significant levels of ADHD symptoms in the *Underweight* group, (ii) the prevalence of having a *Normal* BMI is lower for participants presenting ADHD symptoms than for those without, and (iii) the prevalence of being *Overweight* and *Obese* are about twice as high for participants with ADHD symptoms than for those without. Compared to US rates, the *Underweight* and *Obese* categories are far less prevalent in our sample (Pagoto et al, 2009).

More precisely, the results reveal a trend for participants with ADHD symptoms in presenting a higher risk of being overweight rather than normal (OR=2.052, p<.08, CI95=[.923; 4.565]) after controlling for sex (OR=3.944, p<.001, CI95=[2.918, 5.330]) and age (OR=1.039, p<.002,

CI95=[1.014; 1.065]). The results also show a similar trend for participants with ADHD symptoms in presenting of higher risk of obesity (OR=2.536, p<.08, CI95=[.889; 7.231]) after controlling for sex (OR=2.295, p<.001, CI95=[1.461; 3.605]) and age (OR=1.018, n.s., CI95=[.980; 1.058]). There is no effect of ADHD symptoms, sex and age when comparing obese to overweighed participants.

ADHD symptoms and level of education

Table 3 presents participants' levels of education split by sex and age group for the current sample and for the population of Nice in the 2009 French National census. Comparisons show a significant difference for men: our sample includes more men older than 40 years with at least a college degree [$\chi^2(1)=31.032$; p<.001)] than census data. For women, the results show an interaction effect [χ^2 (1)=4.027; p<.046)] showing that in our sample, fewer women older than 40 years have an education level lower than grade 12 and more women older than 40 years have a university degree, when compared to census data. Thus, overall, our sample tends to be more educated than the general population of Nice.

In our sample, ADHD symptoms are not associated with achieving Grade 12 or higher levels of education (OR=.657; n.s.; CI95=[.328; 1.318]) nor age (OR=1.103; n.s.; CI95=[.851; 1.428]) but that there is a significant effect of sex showing that females tend to achieve higher levels of education than males (OR=.557; p<.001; CI95=[.434; .715]). ADHD symptoms are also not associated with university completion (OR=1.113; n.s.; CI95=[.561; 2.210]) or age (OR=1.229; n.s.; CI95=[.964; 1.568]) but there is a significant effect of sex showing again that females tend to achieve higher levels of education than males (OR=.705; p<.004; CI95=[.557; .894]).

Personal and familial history of adults with ADHD symptoms

Table 4 presents the results from the associations of various comorbidities and ADHD symptoms. Adults screened positive on the ASRS strongly acknowledged that they have ADHD (OR=17.562; p<.023; CI95=[1.525; 202.196]) regardless of age and sex. These adults with likely ADHD diagnosis are almost 5 times more likely than those without to have a learning disorder regardless of age and sex, and four times more likely to report a previous episode of depression (with women presenting higher risk of depression than men). Although the odds-ratio is not significant, participants with ADHD are also two times more likely to have attempted suicide (s.e.=2.272, CI95=[.662; 13.305]) and

their siblings are 6 times more likely to have attempted or committed suicide. ADHD symptoms are also significantly related with enuresis in the informant regardless of sex, as well as in their children. Overall, lifetime enuresis is acknowledged by 4.78% of the adult informants, and by 4.87% of their children. An additional analysis even showed a significant effect of parental sex, ADHD symptoms and enuresis on child's likelihood of reporting enuresis, although these results also differed according to the gender of the parents. For instance, ADHD symptoms (OR=6.194, p<.002, CI95=[1.996; 19.221]) but not enuresis (OR=1.858, p<.306, CI95=[.568; 6.084]) in mothers was significantly associated with a higher risk of enuresis in children. Conversely, enuresis (OR=6.089, p<.004, CI95=[1.773; 20.909]) but not ADHD symptoms (OR=3.157, p<.171, CI95=[.609; 16.362]) in fathers was associated with a higher risk of enuresis in the children.

DISCUSSION

Our study is the first to report the prevalence rate of ADHD symptoms in a large community sample of French adults using all 18 items of a validated self-report questionnaire. However, given that the study design did not allow us to access characteristics of the non-respondents, it is impossible to rule out the possibility that a selection bias may have influenced the results. It may be that the non-respondents could not complete the questionnaire for insufficient mastery of the French language, did not take the study seriously enough, had more busy lifestyle, but also that they presented higher levels of ADHD, making it harder for them to sit still and concentrate on a questionnaire. For this reason, it is possible that our prevalence estimates may have been slightly inflated as a result of this design characteristic. Similarly, we cannot be fully confident that our sample is fully representative of the French population, which is not unexpected given the nature of the recruitment design. However, our sample remains large (N=1,171) and reasonably comparable to the 2009 Census data for the city of Nice, although slightly more educated. Finally, we controlled for age and sex whenever applicable to ensure that the results were not due to possible differences in this regard between our sample and the global population of Nice in 2009.

Self-rated screening tools are generally expected to yield upward biased prevalence estimates for three main reasons. First, the presence of a clinician is generally required to make the diagnoses as objective and closely related to common diagnostic criteria as possible. Second, self-report

instruments, as it is the case for the ASRS, very seldom include a comprehensive coverage of all diagnostic criteria (i.e., age at onset, duration, functional impairment, and exclusion diagnoses). Third, self-report instruments like the ASRS do not include any information about the emergence of the disorder into childhood, or about its occurrence in multiple contexts, two important facets of ADHD. To partly overcome these issues a more stringent two-step scoring method must be used. Undoubtedly, our results show that relying solely on the 6-item screener yields an unrealistic prevalence estimate of 11.27% that cannot be explained by sample bias. However, this screener was never proposed to permit valid diagnoses of ADHD, but rather to allow for a comprehensive screening of participants for more extensive evaluations procedures. Similarly, simply using the full-scale score also yield unreasonably high prevalence estimates (8.37%), although these appear to be in line with at least one previous estimate (Fayyad et al, 2007). However, the alternative two-stage scoring method using all 18 items yields a more realistic prevalence of 2.99% in adults from the community, similar to values reported in previous International studies using face-to-face clinical interviews for diagnosis (de Graaf et al, 2008; Fayyad et al, 2007; Kessler et al, 2006). These results apparently support the efficacy of this two-step procedure in identifying participants that should be targeted for more extensive evaluations (6-item screener) and then to identify those most likely to correspond to ADHD scoring criteria in a second step. Clearly, although this distinction is important in the way results from self-reports on the ASRS are computed, they have even greater relevance to web-based research or screenings protocols. Indeed, the efficacy of the two-step procedures suggest that a stem (6-item screener) and leaf (12 remaining items) protocol could be implemented so that all participants only have 6-items to answer and only a few (12%) have to complete an extended set of ADHD items. Further studies are needed to investigate the efficacy of this two-step procedure in identifying clinical levels of ADHD, as well as its rates of sensibility and specificity when compared to structured clinical interviews, such as the Diagnostic Interview for Adult ADHD (DIVA 2.0) recently developed by the European Network for ADHD in Adults (http://www.divacenter.eu).

With regard to group comparisons, they showed ratios of 1.37 for men:women, 1.39 for older: younger adults, 1.25 for older:younger women, and 1.15 for older:younger men. Overall, the ADHD symptoms prevalence estimates in our sample did not vary with sex or age, suggesting that commonly

reported age and sex differences in youths' levels of ADHD may fade out upon entry into adulthood. This observation is consistent with previous studies. It is generally acknowledged that the sex ratio is about 3:1 in youths but tends to equilibrate in adults. For instance, the World Mental Health international survey conducted in 10 countries reported a men:women sex-ratio of 1.7, close to the value reported here (de Graaf et al, 2008), and a 1.6:1 sex ratio was reported in the National Comorbidity Survey-Replication (Kessler et al, 2006).

In addition, although we found ADHD symptoms to be unrelated to educational attainment itself, the observed odds-ratio suggested a lower level for participants with ADHD. This negative result is quite unusual as ADHD into childhood is reputed to increase the risk for lower educational attainment (Hodgkins et al, 2012). Other epidemiological studies have also reported similar results: for example, the World Mental Health international surveys conducted in 10 countries reported no overall effect of ADHD symptoms on educational attainment (de Graaf et al, 2008). Outside of clinical samples this relation becomes less clear because (i) participants may present less severe symptoms (e.g. with successful adaptive behaviors, higher IQs or more effective executive functioning), and (ii) most severely affected individuals may have declined to participate in epidemiological survey, especially in a study such as this one where the main target was the child, and not the parent. Significant deficits of executive functioning affects about one-third of adults with ADHD symptoms leading to more a severe functional impairment, lower socioeconomic status and lower educational attainment in these doubly affected adults than among adults with ADHD symptoms but no deficits in executive functioning (Biederman et al, 2006). Our observation may also be related to the specific sample used in the present study, which presents slightly higher levels of education than the 2009 Census population of Nice. Another explication may be that more educated participants endorse ADHD items more frequently because of their style of life or occupation. However, although participants with ADHD symptoms did not significantly differ from those without regarding the levels of education attainments, they did report substantially higher levels of learning difficulties, clearly supporting the results from previous studies (Seidman et al, 1998), showing that at least achieving the same educational outcomes might have proven to be more challenging than for people without ADHD symptoms. This finding should be investigated in further studies in which executive functioning is

taken into consideration.

One study recently reported that first-born children were twice likely to have ADHD (Marin et al, 2012 [Epub ahead of print]) while most reports did not find relations between birth order and ADHD (Berger et al, 2009). All these studies investigated clinical samples. To our knowledge, no study examined this issue in community adults. In our sample, there was clearly no increased risk for first-borns regardless of their sex to present ADHD symptoms. Our results thus support previous findings of a lack of relation between ADHD and birth order.

We estimated the risk for overweight and obesity associated with ADHD symptoms. The prevalence for these two categories of weight related problems are very low in our sample but are nevertheless twice as high in the group with ADHD symptoms that in the group without. Due to the resulting lack of statistical power, we are only able to show a trend for a higher likelihood of overweight (OR=2.052) and obesity (OR=2.536) in the group with ADHD symptoms. No data was available regarding participants socio-economic status (SES), which may be a confounder in the relationship between ADHD symptoms and overweight/obesity. However, it should be noted that this possible confounding impact has yet only been noted, to our knowledge, in a nationally representative and community based survey of German children and adolescents (Erhart et al, 2012). A study on 6,735 U.S. residents revealed that adults with ADHD were significantly more at risk of being overweight (OR=1.58; CI95=[1.05; 2.38]) and obese (OR=1,81; CI95=[1.14; 2.64]) (Pagoto et al, 2009), albeit the odds ratio were much lower than those reported here. The possible reasons for an association between overweight/obesity and ADHD symptoms are numerous (Davis et al, 2006; Nazar et al, 2008; Nazar et al, 2012 [Epub ahead of print]). For instance, the role of low central dopamine has been suggested: this neurotransmitter is involved in both appetite regulation (Stice et al, 2011) and inhibition control (i.e. inhibition of distraction and inhibition of behaviour) (Ghahremani et al, 2012). Also, weight regulation may be challenging for individuals with ADHD symptoms who may have difficulties in planning meals ahead of time, may more frequently skip meals and may lose sight of intentions to moderate food intake due to their ADHD symptoms (Docet et al, 2012). The role of circadian rhythms may also be suspected since evening orientation is also associated with eating disorders (Natale et al, 2008), impulsivity and novelty seeking (Caci et al, 2005; Caci et al, 2004a), as well as ADHD

symptoms (Caci et al, 2009; Xu et al, 2010). A proposed relation between excessive daytime sleepiness, that is associated with ADHD symptoms, and obesity (Cortese et al, 2008) might also be incorporated within a chronobiological framework of the relations between these two disorders. Finally, sleep apnea are more likely to occur in persons suffering from obesity, and may also cause daytime sleepiness and cognitive impairment mimicking ADHD symptoms (Philipsen et al, 2006).

We also found original results regarding the associations between enuresis and ADHD symptoms in the participants themselves and their offspring. Enuresis is suspected to have a genetic origin because of familial aggregation: biological parents often report to have had enuresis as a child when their offspring are referred for enuresis (Aubert et al, 2010). Like ADHD, enuresis shows a sex ratio of about 3 boys for 1 girl. Like ADHD, enuresis also tends to persist at adulthood although the rate is about 3% much lower than the rate for ADHD. Here, participants with ADHD symptoms report higher rates of enuresis for themselves and their offspring. In both cases, the OR is greater than 5 with the upper limit of the CI95 greater than 13. This is consistent with the literature (Aubert et al, 2010; Baeyens et al, 2006; Baeyens et al, 2005; Baeyens et al, 2004). However, this relation appears to be true only for mothers. In contrast, the odds for enuresis in youths are higher if the father himself had enuresis, but not if he has ADHD. These findings support the comorbidity of ADHD and enuresis but also the idea of different pathophysiological pathways of familial transmission for these two disorders. Clearly, future research should look at the interplay between ADHD, enuresis and overweight/obesity in a developmental framework (Weintraub et al, 2013).

Finally, we observed a consistent pattern of findings regarding the associations between ADHD symptoms and depression. In a related way, although only two of 27 suicide attempters were classified as presenting ADHD symptoms, we did find that offspring and brothers/sisters of parents with possible ADHD presented a higher risk of attempting suicide. This supports the conclusion from a previous study showing that ADHD was not a direct predictor of suicide attempts in adults, where comorbid conditions seemed to play a stronger role (Agosti et al, 2011). Nevertheless, our study is the first to report that offspring of participants with ADHD symptoms presented 18 times the odds of attempting suicides than offspring of non-ADHD parents. Although this was not a main objective of the present study, this result clearly should be investigated in future studies and, if replicated, should

be used to develop targeted preventive interventions.

CONCLUSIONS

The two-stage scoring algorithm for the ASRS outperforms the other two methods in identifying probable ADHD cases. We found no significant gender effect on prevalence, and there was a trend for an association between overweight/obesity and ADHD symptoms. There are two major clinical implications of this study. First, we reported an association between ADHD symptoms in the participants themselves and enuresis in their offspring, suggesting an association between these two disorders with possibly different underlying pathways. Second, the offspring of parents likely to have ADHD presented an elevated risk of having attempted suicide. Admittedly, the comparative performance of the three scoring algorithms contrasted here and developed in US populations need to be confirmed in a French-speaking sample against a clinical assessment of ADHD (e.g. the DIVA interview). In addition, our results suggest that epidemiological identification of persons likely to present clinically significant levels of ADHD should rely on an improved scoring algorithm taking into account not only the ASRS, but also impairment and deficits in executive functions.

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