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Stress, attention deficit hyperactivity disorder (ADHD) symptoms and tobacco smoking: The i-Share study

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ABSTRACT

Background: The contribution of mental health to the risk of smoking is increasingly acknowledged but still insufficiently studied during the key period of student life. In particular, the simultaneous action of stress and Attention Deficit Hyperactivity Disorder (ADHD) symptoms on the risk of smoking remains poorly understood.

Aims: To assess the effects of stress and ADHD symptoms on tobacco smoking.

Method: Multivariate modeling was conducted on the French i-Share study (n = 8110, median age 20.3 years, 74.8% females, 32.9% regular/occasional smokers) to evaluate the associations between stress, ADHD symptoms and tobacco smoking, adjusting for potential family/socio-demographic confounders. *Results:* Students with high levels of stress were more likely to smoke > 10 cigarettes/day (adjusted odds ratio (aOR): 1.48, 95% CI: 1.12–1.96) than those with low levels of stress. Students with high levels of ADHD symptoms were more likely to smoke > 10 cigarettes/day (aOR: 2.08, 95% CI: 1.58–2.75) than those with low levels of ADHD symptoms.

Conclusions: Stress and ADHD contribute independently to the risk of smoking. Interventions targeting each condition are likely to reduce the burden of tobacco use in students.

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1. Introduction

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With more than 1 billion smokers worldwide and 6 million deaths per year, the tobacco epidemic is a major factor threatening human health and economic development [1]. Despite massive public health policies targeting its use, tobacco still remains unduly consumed, notably in western countries. France does not escape this pattern since 34.3% of adults are daily smokers [2]. While tobacco smoking is intrinsically a modifiable behavior, the highly addictive power of nicotine makes smoking cessation a daunting task. Tobacco initiation and addiction, like numerous health risk behaviors, settle down mostly during adolescence and young adulthood [3]. Student life is consequently a critical period when interventions may efficiently modify the onset of problematic behaviors and subsequently improve future outcomes. In this

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http://dx.doi.org/10.1016/j.eurpsy.2017.07.007 0924-9338/© 2017 Published by Elsevier Masson SAS. line, the Center for Disease Control has recently expended the age 26 range for initiation prevention to college/university young adults 27 [4]. Beyond the classical social risk factors for tobacco use (e.g. 28 poverty, low education, cigarette availability, peer influences), 29 individual mental health factors may play a crucial role [5]. In 30 particular, stress and Attention Deficit Hyperactivity Disorder 31 (ADHD) symptoms are two potentially important contributors that 32 represent identifiable targets for interventions. 33

Stress has been shown to be associated with tobacco use (e.g. 34 initiation, continuation and difficulties to quit) in both human and 35 animal studies [6–8]. Epidemiological studies have shown that 36 individuals exposed to high levels of stress report rates of cigarette 37 smoking between two and three times higher than their non-38 39 stressed counterparts [8-10]. Engagement in smoking is often attributed to stress by individuals themselves. Indeed smoking is 40 reported to be a means to alleviate stress and anxiety symptoms 41 [11]. This is biologically plausible since acute nicotine modifies 42 cerebrocortical neuroactive steroids and plasma corticosterone 43 concentrations [12]. Stress and smoking may also have common 44 genetic and environmental vulnerabilities. Interestingly, females 45

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may be more prone to smoking than men when exposed to stress [13,14]. Some authors even suggest that stress plays a key role in the emergence of tobacco use in women [14].

49 ADHD symptoms also represent significant independent risk 50 factors for smoking. Epidemiological and clinical studies have repeatedly shown a consistent association between childhood/ adult ADHD and tobacco use with a twofold risk of onset and dependence in ADHD individuals [15–17]. Although still to be elucidated, the underlying etiology of this association may be subsumed by several hypothesized mechanisms. In particular, 56 shared genetic/environmental vulnerability and clinical/neurocognitive characteristics could make people with ADHD more likely 58 to consume tobacco [18]. Of note, the gender effect in the 59 relationship between ADHD and tobacco use remains unclear owing to scarce data and contradictory results [19,20].

61 Limitations in the literature regarding the links between tobacco 62 smoking, stress and ADHD are manifold. First, stress and ADHD have 63 hardly been studied simultaneously. Although these two psychopathological dimensions are likely related, there is scant data 64 65 regarding their association, especially in university students 66 [21,22]. Consequently, whether they confound each other, interact 67 or represent different pathways leading to smoking is still unknown. 68 Second, there may be gender differences with regard to the effect of 69 both stress and ADHD symptoms on tobacco smoking. Although 70 postulated, this potentially gender-specific vulnerability remains 71 insufficiently studied in the available data. Third, the concurrent 72 effects of stress and ADHD symptoms on tobacco smoking have 73 hardly been investigated during late adolescence and young 74 adulthood, yet this period is crucial in the crystallization of long-75 lasting risky behaviors. Clarifying the respective contributions of 76 stress and ADHD symptoms to smoking in students is essential since 77 it may yield levers for innovative interventions.

78 The i-Share cohort, which is one of the largest epidemiological 79 studies conducted in European students, offers a unique possibility 80 to test whether stress and ADHD symptoms contribute indepen-81 dently to the risk of smoking and if the association varies according 82 to the sex. Addressing the key research question of the interplay 83 between stress, ADHD and tobacco use could open new avenues for 84 designing preventive and smoking cessation interventions early 85 on. The aim of the present study was to assess the effects of stress 86 and ADHD symptoms on tobacco smoking in the at-risk population 87 of students.

88 2. Material and methods

2.1. Study population 89

90 Study subjects were participants in the Internet-based Students 91 Health Research Enterprise (i-Share, www.i-share.fr) project, a 92 prospective population-based cohort study of students in higher 93 education institutions in France. The objectives of i-Share are to 94 evaluate important health aspects among university students over 95 the course of 10 years, including mental health, risk behaviors, 96 addictions, accidents, infections and migraine. Eligible participants 97 had to be officially registered at a university or higher education 98 institute (within the Universities of Bordeaux, Versailles and Nice), 99 be at least 18 years of age, able to read and understand French and 100 provide informed consent for participation. Participants were 101 invited to participate thanks to a recruitment campaign started in 102 February 2013. Students were informed about the objectives of the 103 study through promotion campaigns (via information stands at 104 registration, lectures, flyers, social media and newsletters). 105 Specifically, a group of trained students informed their peers 106 about the study and collected information to initiate the online 107 recruitment process. Registration was conducted in two steps:

108 firstly, an online portal pre-registration was required; secondly, each student completed a self-administered online questionnaire. 109 The baseline inquiry collected information on students' health, 110 personal and family medical histories, socio-demographic cha-111 racteristics, and lifestyle habits. The i-Share cohort is still ongoing. 112 For this specific study, we used data available as of April 29th, 113 2016. Only students aged between 18 and 30 years old were 114 included. The i-Share project on which this study was based was 115 approved by the Commission nationale de l'informatique et des 116 libertés (CNIL) [DR-2013-019]. 117

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2.2. Measures

2.2.1. Main variables of interest: stress and ADHD symptoms

Stress: perceived stress was assessed by using the short version 120 of the Perceived Stress Scale (PSS-4) [23]. This self-reported 121 questionnaire measures the degree to which situations in one's life 122 over the past month are appraised as stressful (i.e. how overloaded, 123 124 uncontrollable and unpredictable respondents find their lives). The 125 PSS-4 consists of four items with possible responses rated on a 0 (never) to 4 (very often) scale. The global score was obtained by 126 summing the items with reverse coding to score items 2 and 127 3. Higher scores corresponded to higher perceived stress. As the 128 129 PSS-4 is not a diagnostic instrument, no cutoff was available to determine stressed individuals. Consequently, scores were divided 130 into tertiles within each gender, the lowest tertile of the score 131 distribution being the reference. The PSS has demonstrated good 132 reliability and validity in university student samples [23]. 133

2.2.2. ADHD symptoms

Students were asked to complete questions about their 135 behavior during the past 6 months based on the 6-item version 136 of the Adult ADHD Self-Report Scale (ASRS-v1.1, available in 137 various languages at http://www.hcp.med.harvard.edu/ncs/asrs. 138 php) [24]. The ASRS-v1.1 is a screening tool and not a diagnostic 139 instrument. This scale lists the 6 questions found to be the most 140 predictive of symptoms consistent with ADHD. Each of the six 141 items was coded using a 5-point Likert scale ranging from never (0)142 to very often (4). We calculated three different scores by summing 143 the items: 1: a global score (6 items); 2: an inattention symptoms 144 score (4 items); 3: a hyperactivity symptoms score (2 items). 145 Scores were then dichotomized according to the 90th centile of the 146 score distribution within each gender. This cutoff was chosen in 147 order to identify a subgroup with a high level of ADHD symptoms 148 in the absence of a validated cutoff in French university students. 149

2.2.3. Covariates

Using the self-administered online questionnaire we built the following variables: age (continuous), sex (male/female), student variables (including current place of living [at parents' home/other place], job activity [yes/no], alcohol consumption [no/rare/ occasional/regular/very regular]), and family variables (including family financial help [yes/no], parents' marital status [separated/ not separated], parents' educational level [no postgraduate studies/postgraduate studies], family economic condition in childhood [comfortable/satisfactory/difficult], family support during childhood [high/moderate/low], parents' alcohol or depression problem [at least one parent has/had alcohol and/or depression problem: yes/no]).

2.2.4. Outcomes tobacco smoking variable

If students were smokers (i.e. answered yes to the question "do 164 you smoke tobacco regularly or occasionally?"), the number of 165 cigarettes smoked per day was quantified (i.e. students answered 166 the question "how many cigarettes on average do you smoke 167 per day/week/month?"). A count number of cigarettes smoked 168

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169per day was generated which allowed a tobacco smoking170categorical variable to be constructed (none, ≤ 10 cigarette/day,171> 10 cigarette/day).

172 2.3. Statistical method

173 We first described the study sample. Then we compared the 174 characteristics of students with respect to their level of cigarette smoking (i.e. none, < 10 cigarette/day, > 10 cigarette/day). In order 175 176 to ascertain whether students' behaviors were associated with 177 smoking, we conducted multinomial regression model analyses. In 178 the modeling process, variables were introduced sequentially. 179 At step 1, we entered stress and ADHD symptoms. At step 2, we 180 added all covariates linked to the categorical tobacco-smoking 181 variable with a P < 0.05 (except student alcohol consumption 182 which was not introduced into the main regression analyses but 183 further considered in sensitivity analyses). We then estimated 184 the following two-way interactions: stress \times ADHD, sex \times stress, 185 $sex \times ADHD$. Results were presented for the whole sample. In 186 secondary analyses we decided to present the results stratified on 187 gender, independently from the presence or absence of statistical 188 interaction with sex. Indeed, owing to the assumptions about 189 possible divergent outcomes in females and males and because the 190 sample was gender-imbalanced (significantly more females than 191 males), it seemed relevant to present the results separately by 192 gender. Finally we conducted sensitivity analyses to test the 193 robustness of the findings: (1) adjusting on youth alcohol 194 consumption; (2) conducting the analyses according to the age at 195 onset of tobacco smoking (i.e. age > 16 years and < 16 years); (3) 196 conducting the analyses by considering separately the inattention and the hyperactivity dimensions of the ASRS-v1.1; (4) conducting 197 Hurdle modeling. The latter approach is a multivariate model that 198 199 estimates jointly a two-part model with two sets of coefficients for: 200 (1) being or not a smoker (the estimates being equal to those 201 resulting from a logistic model); (2) the cigarette count/day for 202 those who smoke (this part of the model is fitted with a negative 203 binomial link). Therefore, the Hurdle model can be used to verify

whether the independent variables predict severity (as assessed by
the cigarette count) beyond predicting the fact of being a smoker.205All P-values were two-tailed and we considered P < 0.05 to be
statistically significant. We performed all analyses using the SAS
statistical software (SAS version 9.3; SAS Institute Inc, Cary, NC).208

3. Results

The total sample comprised 8110 participants. Fig. 1 shows the 210 flow chart of the study population. Of the 11,186 individuals who 211 pre-registered on the i-Share study homepage, 9051 fully regis-212 tered by changing their password and customizing their identifi-213 cation number. For this study, we included the 8110 participants 214 who met the inclusion criteria and fully completed the baseline 215 questionnaire. Table 1 summarizes the characteristics of the 216 sample by levels of tobacco smoking. The mean age of the 217 participants was 21.0 years (SD = 2.3) and 74.8% were females. In 218 total, 32.8% of the students reported being smokers. Students with 219 high levels of stress (high tertile) were more likely to smoke than 220 students with low levels of stress (low tertile) (P < 0.0001). 221 Students with high levels of ADHD symptoms were also more 222 likely to smoke than those with low levels of ADHD symptoms 223 224 (P < 0.0001). All the student and family variables were statistically significantly related to smoking (all P < 0.05). Table 2 shows the 225 associations between stress, ADHD symptoms and levels of 226 tobacco smoking in the total, female and male samples (multino-227 mial regression models). All models were significant with Wald 228 Chi-squares showing *P*-values < 0.001. Full models were adjusted 229 on age, sex (only for the total sample), current place of living, job 230 activity, family financial help, parents' marital status, parents' 231 educational level, family economic condition in childhood, family 232 support during childhood, parents' alcohol or depression problem. 233 Students with high levels of stress were more likely to smoke more 234 than 10 cigarettes/day (fully adjusted odds ratio (aOR): 1.48, 95% 235 CI: 1.12–1.96) than those with low levels of stress. Students with 236 high levels of ADHD symptoms were more likely to smoke more 237 than 10 cigarettes/day (fully aOR: 2.08, 95% CI: 1.58-2.75) than 238





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Table 1

Characteristics of i-Share total sample according to levels of tobacco consumption (n=8110).

	% (<i>n</i>) or mean (SD)	Tobacco smoki	P-value		
		No smoker (<i>n</i> =5446)	\leq 10 cigarettes/day (<i>n</i> =2310)	> 10 cigarettes/day (n=354)	
Student variables					
Age (years)	21.0 (2.3)	20.7 (2.3)	20.7 (2.2)	21.6 (2.3)	< 0.0001
Female sex	74.8 (6067)	75.2 (4094)	75.6 (1746)	64.1 (227)	< 0.0001
Current place of living (parent's home)	31.9 (2589)	33.2 (1806)	30.1 (695)	24.9 (88)	0.0004
Job activity (yes)	41.0 (3324)	38.5 (2097)	45.4 (1049)	50.3 (178)	< 0.0001
Family financial help (yes)	81.9 (6642)	82.3 (4484)	81.8 (1889)	76.0 (269)	0.011
Alcohol consumption					< 0.0001
No, rare, occasional	27.4 (2220)	35.8 (1947)	10.2 (235)	10.7 (38)	
Regular	50.3 (4076)	50.2 (2735)	52.1 (1204)	38.7 (137)	
Very regular	22.4 (1814)	14.0 (764)	37.7 (871)	50.6 (179)	
Stress					< 0.0001
High tertile	30.9 (2502)	28.4 (1549)	34.7 (802)	42.7 (151)	
Medium tertile	34.6 (2809)	35.3 (1922)	34.2 (791)	27.1 (96)	
Low tertile	34.5 (2799)	36.3 (1975)	31.0 (717)	30.2 (107)	
ADHD symptoms					< 0.0001
High	12.2 (993)	10.3 (561)	15.3 (353)	22.3 (79)	
Low	87.8 (7117)	89.7 (4885)	84.7 (1957)	77.7 (275)	
Family variables					
Parents' marital status (separated)	31.2 (2531)	28.3 (1542)	35.8 (828)	45.5 (161)	< 0.001
Parents' educational level (postgraduate and more)	65.5 (5309)	64.5 (3513)	67.8 (1567)	64.7 (229)	0.018
Economic condition in childhood (difficult)	9.1 (736)	8.5 (465)	9.6 (222)	13.8 (49)	0.010
Support during childhood (moderate or little)	27.5 (2227)	25.6 (1395)	29.9 (691)	39.8 (141)	< 0.0001
Parents' alcohol or depression problem (yes)	45.0 (3646)	41.6 (2266)	49.7 (1149)	58.5 (207)	< 0.0001

P-values from one-way analysis of variance (non-parametric) and Chi-square tests.

239 those with low levels of ADHD symptoms. The same pattern of results was observed in both genders. There were no significant 240 241 interactions with respect to tobacco smoking (high level of stress \times ADHD, *P* = 0.50; sex \times high level of stress, *P* = 0.48; 242 sex \times ADHD symptoms, P = 0.60). The Spearman test showed a 243 significant correlation between continuous stress and ADHD 244 245 variables (rho = 0.34, P < 0.001). Sensitivity analyses showed 246 the same pattern of results: (1) adjusting on student alcohol 247 consumption (high vs. low stress: > 10 cigarettes: aOR: 1.70 [1.28-248 2.26]; high vs. low ADHD: > 10 cigarettes/day: aOR: 1.84 [1.392.46]); (2) conducting the analyses on the earlier-onset tobacco 249 smoking subsample (< 16 years of age) (high vs. low stress: 250 > 10 cigarettes/day: aOR: 1.44 [1.04–2.03]: high vs. low ADHD: 251 > 10 cigarettes/day: aOR: 2.20 [1.60–3.02]) and on the later-onset 252 tobacco smoking subsample (> 16 years of age) (high vs. low 253 stress: > 10 cigarettes/day: aOR: 1.56 [0.94–2.61]; high vs. low 254 ADHD: > 10 cigarettes/day: aOR: 1.76 [1.05–2.95]); (3) conducting 255 the analyses by considering separately the inattention (high vs. 256 low inattention: > 10 cigarettes/day: aOR: 2.34 [1.78–3.08]) and 257 the hyperactivity (high vs. low hyperactivity: > 10 cigarettes/day: 258

Associations between stress, ADHD symptoms and tobacco smoking in university students (multinomial regression models): i-Share study (n=8110).

	\leq 10 cigarettes/day			> 10 cigarettes/day			
	Unadjusted OR (95% CI)	Stress and ADHD adjusted OR (95% CI)	Fully adjusted OR (95% CI)	Unadjusted OR (95% CI)	Stress and ADHD adjusted OR (95% CI)	Fully adjusted OR (95% CI)	
Total sample							
Stress							
High tertile	1.43 (1.26-1.61)	1.34 (1.19–1.52)	1.30 (1.14-1.48)	1.78 (1.39-2.33)	1.55 (1.19-2.02)	1.48 (1.12-1.96)	
Medium tertile	1.13 (1.01-1.28)	1.11 (0.99–1.25)	1.11 (0.98-1.26)	0.92 (0.70-1.22)	0.87 (0.66-1.16)	0.91 (0.68-1.21)	
Low tertile	Reference	Reference	Reference	Reference	Reference	Reference	
ADHD symptoms							
High	1.57 (1.36-1.81)	1.46 (1.26-1.69)	1.43 (1.23-1.66)	2.50 (1.92-3.26)	2.21 (1.68-2.91)	2.08 (1.58-2.75)	
Low	Reference	Reference	Reference	Reference	Reference	Reference	
Female sample							
Stress							
High tertile	1.43 (1.24-1.65)	1.34 (1.16-1.55)	1.28 (1.10-1.48)	2.12 (1.51-2.97)	1.82 (1.29-2.58)	1.45 (1.01-2.07)	
Medium tertile	1.18 (1.03-1.36)	1.16 (1.01-1.33)	1.14 (0.99-1.32)	1.14 (0.79-1.65)	1.08 (0.74-1.56)	1.01 (0.70-1.48)	
Low tertile	Reference	Reference	Reference	Reference	Reference	Reference	
ADHD symptoms							
High	1.62 (1.37-1.91)	1.51 (1.28-1.79)	1.49 (1.25–1.77)	2.63 (1.89-3.65)	2.24 (1.60-3.14)	2.26 (1.60-3.19)	
Low	Reference	Reference	Reference	Reference	Reference	Reference	
Male sample							
Stress							
High tertile	1.68 (1.31-2.15)	1.61 (1.25-2.07)	1.62 (1.25-2.10)	2.06 (1.30-3.26)	1.80 (1.13-2.89)	1.67 (1.02-2.72)	
Medium tertile	1.10 (0.87-1.40)	1.09 (0.86-1.39)	1.08 (0.85-1.38)	1.25 (0.79-1.99)	1.20 (0.76-1.92)	1.19 (0.74–1.91)	
Low tertile	Reference	Reference	Reference	Reference	Reference	Reference	
ADHD symptoms							
High	1.44 (1.09–1.91)	1.27 (0.95-1.69)	1.21 (0.90-1.63)	2.20 (1.40-3.46)	1.89 (1.19-3.02)	1.80 (1.12-2.91)	
Low	Reference	Reference	Reference	Reference	Reference	Reference	

OR: odds ratio; CI: confidence interval. Full models adjusted on age, sex (only for total sample), current place of living, job activity, family financial help, parents' marital status, parents' educational level, family economic condition in childhood, family support during childhood, parents' alcohol or depression problem.

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Table 3

Associations between stress, ADHD symptoms and tobacco smoking in university students (Hurdle models): i-Share study (n=8110).

	Liability to be a smoker: logit part			Smoking severity: positive part			
	Unadjusted OR (95% CI)	Stress and ADHD adjusted OR (95% CI)	Fully adjusted OR (95% CI)	Unadjusted RR (95% CI)	Stress and ADHD adjusted RR (95% CI)	Fully adjusted RR (95% CI)	
Total sample							
Stress							
High tertile	1.48 (1.32-1.66)	1.37 (1.22-1.54)	1.31 (1.16-1.48)	1.17 (1.06-1.29)	1.13 (1.02–1.24)	1.11 (1.01-1.23)	
Medium tertile	1.11 (0.99-1.24)	1.08 (0.96-1.21)	1.08 (0.96-1.21)	1.02 (0.92-1.12)	1.00 (0.91-1.11)	1.03 (0.93-1.13)	
Low tertile	Reference	Reference	Reference	Reference	Reference	Reference	
ADHD symptoms							
High	1.69 (1.47-1.93)	1.56 (1.36-1.79)	1.52 (1.32-1.75)	1.29 (1.16–1.44)	1.26 (1.13-1.40)	1.24 (1.12-1.38)	
Low	Reference	Reference	Reference	Reference	Reference	Reference	

OR: odds ratio; RR: rate ratio; CI: confidence interval. Full models adjusted on age, sex, current place of living, job activity, family financial help, parents' marital status, parents' educational level, family economic condition in childhood, family support during childhood, parents' alcohol or depression problem. The logit part of the Hurdle model explores the liability to be a smoker. The positive part of the Hurdle model explores smoking severity (modeling of number of cigarettes per day in smokers only).

aOR: 1.95 [1.48–2.57]) dimensions; (4) conducting Hurdle
modeling (see Table 3). The fact that the associations were
significant when considering tobacco smoking as a count number
(positive part of the Hurdle model) reflected a linear increase in the
risk of smoking.

264 **4. Discussion**

265 4.1. Principal findings of study

266 In this large sample of university students, high levels of stress 267 and ADHD were independently associated with tobacco smoking. 268 The pattern of associations was true in both genders. The relationships between stress, ADHD symptoms and the risk of 269 270 smoking appear to reflect distinct pathways since: (1) stress and 271 ADHD symptoms were independent contributors to tobacco 272 smoking; (2) there was no significant interaction between high 273 levels of stress and ADHD symptoms. All the associations described 274 were adjusted for a range of potential confounders including student 275 and family variables. This is a relevant result owing to the scarcity of 276 data regarding the interplay between stress, ADHD and tobacco use.

277 4.2. Comparison with other studies and interpretation

278 Despite the relatedness of ADHD and stress, the current data do 279 not support the hypothesis that they act in combination to heighten 280 the risk of tobacco smoking. The presence of elevated ADHD 281 symptoms does not create a specific vulnerability in highly stressed 282 individuals and does not put them at greater risk of smoking, and 283 reciprocally. The unique contributions of stress and ADHD towards 284 tobacco smoking suggest that each relationship could rely on 285 different underlying pathophysiological mechanisms.

286 Stress was linked to tobacco smoking, which is consistent with 287 animal and human data. Self-medication may apply since nicotine is 288 used to lessen stress and anxiety symptoms. The effects of nicotine 289 on stress are mixed: acute nicotine administration mitigates stress 290 by increasing plasma corticosterone levels whereas chronic nicotine 291 administration alters the adaptive response to chronic stress [8]. In 292 turn, chronic stress may reduce nicotine responsiveness through 293 interactions between persistent elevated plasma corticosterone 294 levels and the dopaminergic system. All these mechanisms are 295 likely to promote nicotine addiction. Nevertheless, the mechanisms 296 linking stress to smoking are complex and possibly bidirectional. 297 Beyond the immediate stress reduction provided by smoking, stress 298 itself may result from nicotine craving and withdrawal symptoms. 299 Stress may also result from early exposure to tobacco [8]. However, 300 when conducting the analyses in the subsamples of early and later 301 tobacco users (under or over 16 years of age), we found the same 302 pattern of associations, which is not in favor of a reverse causation mechanism in this sample. Even so, the interplay still needs to be303disentangled so epidemiological longitudinal human data integrat-304ing biological variables are required.305

In line with the large body of literature focusing on the ADHD-306 tobacco link, students with high levels of ADHD symptoms smoked 307 308 at significantly higher rates and at heavier levels than those with low levels of ADHD symptoms. Here again the self-medication 309 hypothesis may explain this pattern since individuals with ADHD 310 smoke to improve their attention and executive functioning 311 [25]. Alternatively this association may be due to common 312 environmental/genetic vulnerabilities between ADHD and tobacco 313 smoking [18]. Both the nicotinic-acetylcholinergic circuits and the 314 dopamine reward processing mechanism possibly underlie the 315 association mechanistically [18,26]. Of note, we found no specific 316 gender effect in this sample. 317

4.3. Strengths and limitations 318

The strengths of the study are the large number of participants, 319 the high rate of females, the standardized assessment tools, the 320 concurrent evaluation of stress and ADHD, the detailed informa-321 tion on potential confounders and the age group considered (i.e. 322 late adolescence, young adulthood). A set of limitations should 323 however be considered to properly interpret the findings. First, 324 325 the cross-sectional design makes temporal sequences not strictly evaluable, which limits causal inferences. Second, biases on 326 measures are possible owing to the use of self-reports. Reassur-327 ingly, both perceived stress and current ADHD symptoms were 328 shown to be reliable in college students [23,27]. Third, the 329 Perceived Stress Scale is not a clinical instrument. Yet it remains 330 relevant in the context of the present epidemiological study since it 331 is one of the most widely used psychological tool for assessing 332 nonspecific perceived stress. Fourth, The ASRS-v1.1 could show 333 elevated scores in the presence of comorbid substance use or 334 anxiety-depression. However the ASRS-v1.1 has shown a good 335 validity with ADHD diagnostic [24] including for patients 336 presenting with substance use disorders [28]. Fifth, a sampling 337 bias could have arisen since participants were volunteers in the i-338 Share project and extrapolation to other student populations may 339 be limited. Last, potential confounding factors were unmeasured 340 (e.g. current psychiatric diagnosis, biological variables). 341

4.4. Implications, unanswered questions and future research

From the public health perspective of reducing the harm caused 343 by tobacco, mental health contributors such as stress and ADHD 344 symptoms are key targets to address in the student population in 345 order to prevent enduring tobacco consumption and its related 346 negative outcomes. Beyond universal programs directed towards 347 the whole student population (e.g. educating students about 348

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349 tobacco risks), preventive interventions should include both 350 specific selective and indicated programs. Selective interventions 351 could be set up to target students presenting with high levels of 352 stress and ADHD symptoms. This involves the following: screening 353 stress and ADHD; being able to refer to mental health professionals 354 those with high levels in order to diagnose and treat when 355 appropriate (e.g. ideally through university health services, when 356 available): providing information on tobacco risks to those with 357 high levels of stress and ADHD symptoms. Finally, indicated 358 programs targeting students already engaged in tobacco smoking 359 should take into account stress and ADHD dimensions. After 360 screening tobacco smoking and mental health problems, smoking 361 cessation interventions should be run in parallel with treatment 362 for stress and ADHD. Since weaning from chronic nicotine 363 consumption is accompanied by higher levels of stress, effective 364 stress management programs need to be developed to encourage 365 students to quit smoking durably. Importantly, the constructs we 366 tapped were not direct diagnoses. Rather they corresponded to the 367 higher levels of psychological dimensions. Aside from suggesting a 368 possible clinical diagnosis, taking into account subsyndromal 369 levels of stress and attention difficulties in a non-clinical 370 population may guide interventions. Instead of merely providing 371 therapeutic interventions focusing on people displaying an already 372 identified disorder, the current findings point to the need to 373 promote positive psychological interventions.

374 From a mechanistic perspective, this study underlines the 375 importance of individual cognitive and emotional dimensions in 376 the genesis of the risk of smoking. Nevertheless, it is still unclear 377 whether stress and ADHD symptoms trigger tobacco use, promote 378 its maintenance and are consequences of a similar vulnerability or 379 whether all these mechanisms function concomitantly to some 380 extent. Further studies will likely unravel the complexity of the 381 associations by exploring causality through understanding of the 382 temporal sequences and integration of experimental variables (e.g. 383 biological and neuro-imaging variables).

384 5. Conclusions

385 High levels of perceived stress and attention problems are two 386 mental health features that may independently promote tobacco 387 consumption in young adults. The student population, which is at 388 high risk of adopting a long-term pattern of smoking but which is 389 also potentially more reachable in terms of public health 390 interventions, may benefit from specific actions focusing on stress 391 and ADHD symptoms. Both pragmatic and mechanistic research 392 including randomized controlled trials is needed to better 393 understand these associations and determine which interventions 394 are successful in getting individuals to reduce their smoking.

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405 Disclosure of interest

In the last 3 years M.-P.B. has received financial support for theorganization and participation to scientific meetings.

The other authors have not supplied their declaration of Q3 408 competing interest. 409

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