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First-year French medical students consume antidepressants and anxiolytics while second-years consume non-medical drugs.

Running title: mental health and addictive behavior of medical students

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Abstract

Background. First year exams are a major source of stress amongst first-year medical students.

Objective. To explore antidepressant and anxiolytic consumption and addictive behavior of medical students before and after exams.

Methods. Medical students of the 35 French medical schools were recruited through mailing lists and social networks between December 2016 and May 2017 and completed online Internet anonymized questionnaires.

Results. Overall, 4345 medical students were included (3051 first year vs. 1294 second year). In multivariate analyses, compared to those in the first year of medicine, second year students were found to have lower anxiolytic (adjusted odd ratio (aOR)=0.56, p=0.01) and antidepressant consumption (aOR=0.21, p<0.0001) but higher psychiatric follow-up (aOR=1.95, p<0.0001) after adjustment for age, gender and relationship status. Whilst second year students reported slightly higher quality of life (especially for mental health), they also reported more daily tobacco smoking (aOR=1.78, p<0.0001), more cannabis use disorders (aOR=2.37, p<0.0001), hazardous drinking (aOR=3.61, p<0.0001), and alcohol dependence (aOR=3.66, p<0.0001).

Second year medical students reported fewer difficulties relating to studying in comparison to first year students (aOR=0.60, p<0.0001) yet they reported a higher rate of recreational drugs use with a variety of reasons including self-treatment of anxiety ; disinhibition and to copy their peers (all p<0.05).

Limits. These results should be confirmed by longitudinal studies.

Conclusion. First year medical students who are faced with challenges relating to studying consume more antidepressants and anxiolytics, whilst second year students have a higher consumption of recreational drugs for a range of reasons. This suggests that the first two years at medical school are an important contributor to adverse mental health and therefore present a window of opportunity for preventative intervention.

Conflicts of interest: none declared.

Keywords: medical students, anxiety, depression, tobacco, alcohol, first year

Introduction

Around an half of medical doctors worldwide are diagnosed with burnout at some point during their career (Kansoun et al., 2019; Roberts et al., 2013). This has been reported to occur as early as foundation training medical students (Erschens et al., 2018) and during internship (Jovanović et al., 2016). Medical students are at risk of mental health and addictive issues, a phenomenon that is also observed worldwide (Erschens et al., 2018; Gignon et al., 2015; Goel et al., 2016; Kumar et al., 2017). In a small French monocentric survey carried out in Paris (N=255) published in 2015, 11% of second to sixth year medical students were identified to be alcohol dependent (Gignon et al., 2015). No data on depression rates in first year and second year medical students are available to date. Altogether, these studies suggest that targeting undergraduate students would be an effective strategy to prevent mental health and addictive behavior issues in medical students and later amongst qualified doctors of all grades, thus improving the quality of patient care.

In France, medicine is one of the longest courses available through the higher education system. French medical studies are divided into three stages. The first stage, lasting two years, is solely theory-based, with a very selective examination – the *numerus clausus* – at the end of first year (in 2014, there were 58,733 examination candidates, competing for only 7492 second year places – equaling a 12.8% success rate) (Remede.org, 2015). Previous studies have indicated that medical students experience high rates of depression and suicidal ideation(Jovanović et al., 2019). In a recent meta-analysis, only 15.7% medical students who screened positive for depression sought psychiatric input (Rotenstein et al., 2016). Depression is often associated with addictive behavior (Conner et al., 2009; Fond et al., 2013; Foulds et al., 2015). A recent study has found an increase of binge drinking in French medical students(Duroy et al., 2017). Reliable estimates of mental health and the prevalence of addictive behavior prevalence during medical training are essential to prevent, treat, and identify causes of emotional distress among medical students (Shanafelt et al., 2003) especially in light of recent work revealing a high prevalence of depression

in new qualified physicians (Mata et al., 2015). Multiple factors have been proposed to contribute to the increased burden of mental health issues amongst medical students compared to the general population including work stress; the high number of working hours; patients' and colleagues' exposure to violence; the lack of openness within the medical profession and a lack of professional support (Fond et al., 2018). Medical students also appear to be more likely to seek novel remedies in the form of new recreational drugs (Fond et al., 2016). In summary, medical students have high rates of substance use and it is unclear if this behavior is due an attempt to self-medicate (e.g. coping with stress) or other motives (including pleasure/novelty seeking).

French medical students within the first stage of medical studies appear to be in line with worldwide trends relating to burnout, mental health and addiction issues. Targeting young undergraduate students may be the best strategy to prevent later health issues. Currently, it is not clear at which point of training, preventative or interventional programs would have the most impact.

Our objectives were to determine whether first- or second-year medical students were at increased risk of antidepressant and anxiolytic consumption, psychiatric follow-up and addictive behavior. Our hypotheses were that first would be at increased risk of anxiolytic consumption, whereas second year students would have an increased risk of addictive behaviors. We also hypothesized that first-years would more frequently report motives relating to workload whilst the motives of second years would relate more frequently to pleasure.

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Population and methods

Study design

The BOURBON study was inspired by previous studies about psychostimulant use in medical students (Fond et al., 2016; Micoulaud-Franchi et al., 2014). This study was a descriptive cross-sectional observational epidemiological national study and has been named in reference to the name of the author Aliénor Bourbon, MD, who wrote the first version of the questionnaire and carried out the survey, as well as in reference to the Bourbon alcohol drink.

Study population

Medical students were recruited from the 35 medical schools in metropolitan France. The survey was distributed through faculty administration mailing lists in seventeen medical schools, with two medical schools using social networks to achieve this. Overall, 5 universities refused to send the survey to their students and 11 did not answer at all. Students of these sixteen faculties were indirectly contacted through friends, colleagues and social networks. As a result, all 35 universities are represented in the present study. Given that the total number of medical students contacted by faculty mailing lists and social networks was not available, it has not been possible to calculate an accurate response rate, which is a limit of this study, and this has also been commented upon identified in previous surveys (Bourbon et al., 2019) .

Data collection

Data was collected by a self-completed questionnaire between December 13, 2016 and May 15, 2017. All medical students who registered at a medical faculty during the year 2016-2017 were included. The medical students were interviewed through an online, anonymous questionnaire via the Google Forms software. Completion of the questionnaire took an average of 15 minutes. The questionnaire included:

- at least 23 questions for students who did not consume any substance.

- a maximum of 140 questions for students who, by their answers, opened the entire questionnaire.

The following sections were explored in the questionnaire:

- Sociodemographic data (age, sex, relationship status).

- The self-reported quality of life using the SF12-v2 quality of life score with 8 subscores (Physical Functioning, Physical well-being, Bodily Pain, General Health, Vitality, Social Functioning, Emotional Well-being, Mental Health). A higher score is indicative of a better quality of life.

- The following screening tools for addictive behavior have been used: Hazardous drinking was defined by the Alcohol Use Disorder Identification Test (AUDIT) as a score of ≥7 for men and ≥6 for women (Gache et al., 2005) and alcohol dependence by a score ≥13. Cannabis use disorder was defined by a Cannabis Abuse Screening Test (CAST) score ≥3 (Legleye et al., 2011). Current daily tobacco cigarette smoking was self-declared (binary answer). Ecstasy and cocaine consumptions during medical studies were also reported (binary answer). Opioids and other substances were not reported.

- The following psychiatric variables were requested: current psychiatric or psychological follow-up, daily antidepressant and/or anxiolytic consumption ("Do you currently consume daily antidepressants?" binary self-reported data).

- Survey questions relating to motives for psychoactive drug use permitted students to report more than one reason. The motives for consumption were detailed and reported with the following list (binary answers: During a party, pleasure seeking, novelty seeking, peer pressure (private life), peer pressure (at work), disinhibition, alleviating anxiety, stimulant effect, sedative effect, dealing with loneliness, study difficulties, stress before exam).

Ethical concerns

An email inviting potential subjects to participate was sent to medical students using the database of French medical student associations, and professional mailing lists and its content was posted on specialized internet forums and other targeted and relevant internet forums. The questionnaire described and explained the rationale of the study, as well as its goals. Potential participants were invited to self-administer a confidential web survey by clicking on a URL link: the study was entirely voluntary and students could withdraw from the survey at any time before submitting their questionnaire. Personal data was anonymized and stored on a secure server. To ensure participant confidentiality and anonymity, no identifiable data was recorded. Care was taken to delete IP addresses from the dataset. Data was stored in an offline database for later analysis. Participants were informed that by clicking the confirm button to submit their anonymous questionnaires, they gave their informed consent. Participants did not receive any financial reward. The study was carried out in accordance with ethical principles for medical research involving humans (WMA, Declaration of Helsinki).

Statistical analysis

Sociodemographic variables, addictive behavior, mental health status, desired effect for substance consumption during medical studies (categorical variables) are presented using frequency distribution and quality of life continuous data using measures of means and dispersion (standard deviation). The data was examined for normal distribution with the Shapiro-Wilk test and for homogeneity of variance with

the Levene test. Comparisons between first year and second year medical students regarding sociodemographic variables, addictive behavior, mental health status, desired effect for substance consumption and self-reported quality of life were performed using the chi-square test for categorical variables. Continuous variables were analyzed using the Student t-tests for normally distributed data and in case of normality violation, additional Mann-Whitney tests were performed to confirm the result.

Multiple logistic and linear regression analyses were then performed to confirm the association between first year of medical studies (considered as a determinant) and each characteristic or behavior (considered as outcomes), after adjusting for the following main confounding factors: age, gender and relationship status. We determined the p-value of the Hosmer-Lemeshow chi-squared for logistic regression and adjusted R-squared for linear regression. The final models provided the odd ratios (OR) or standardized beta and 95% confidence intervals (CI). The statistical analyses were performed using the SPSS version 20.0 software package. All statistical tests were two-tailed, with α level set at 0.05.

Results

Overall, 4345 medical students were included in this study (3051 first year students mean age 18.9 years [16-32] 77% females; 1294 second year students, mean age 19.8 years [17-32] 66.8% female (**Table 1**),

In multivariate analyses, compared to first year of medicine, second year students were found to be

- 78% more likely to report daily tobacco smoking, 137% more likely to have a cannabis use disorders, 261% hazardous drinking and 266% dependence (respectively aOR=1.78[1.41-2.35], p<0.0001, 2.37[1.54-3.64], p<0.0001, 3.61[2.36-5.51], p<0.0001, 3.66[3.00-4.47], p<0.0001).
- 44% less likely to report anxiolytic and 79% less likely to report antidepressant consumption (respectively aOR=0.56[0.35-0.88], p=0.01 and aOR=0.21[0.09-0.47], p<0.0001) but 95% more likely to report psychiatric or psychologic follow-up (aOR=1.95[1.31-2.91], p<0.0001) after adjustment for age, gender and being in couple.

Second year reported slightly higher rates of quality of life (Physical well-being ß=1.01[1.01-1.01], p=0.02, bodily pain ß =1.01[1.01-1.02] p<0.001, emotional well being ß =1.01[1.01-1.01], p<0.01) mental health (ß =1.02[1.01-1.03], p<0.001).

While no significant difference in illicit drug consumption has been found, second year medical students reported different motives to first years. In comparison to first year medical students, they were 40% less likely to report study difficulties (aOR=0.60[0.44-0.83], p<0.0001) and were more likely to anxiety alleviation, disinhibition, stimulation or sedation or take recreational drugs as a result of peer pressure (or to copy their peers) (all p<0.05). All adjusted p-values of the Hosmer-Lemeshow chi-squared were higher than 0.05 and the R-squared were higher than 0.2.

Discussion

In this study first-year medical students consumed antidepressants and anxiolytics more frequently than second years, who had a higher rate of psychiatric involvement and addictive behaviors. First year students were more likely to consume psychoactive drugs to help them cope with study difficulties whereas amongst second years, motives related more to sedative or stimulant effect-seeking and socializing.

The first-year students were found to consume 2 x more antidepressants and 1.5 times more anxiolytics than second years. This result may relate to study pressures priors to the first-year final exam, which result in higher rates of mood and anxiety disorders amongst this group. In contrast, second year students were almost two times more likely to be under psychiatric follow-up. It is possible that this may reflect a lack of time during first year to seek mental health review, though there is a paucity of data to explore this possibility at present.

Our results also suggest that second year students were four times more likely to report hazardous drinking, and that the risk of reporting tobacco smoking was 25% higher in second year compared to first year. Our results are consistent with those of a previous French study reporting high rates of hazardous drinking in medical students(Duroy et al., 2017). Comparing the alcohol use behavior of French medical students with the general population is difficult to date due to a lack of data in age-matched non-medical populations using a standardized scale such as the AUDIT questionnaire. In almost ten years, from 2005 to 2014, the proportion of 18-25 year old who reported becoming drunk at least once in their lifetime increased from 33% to 46% (ONDPS, 2015). In a small monocentric survey (N=255) published in 2015,

11% of second to sixth year medical students were identified as being alcohol dependent (Gignon et al., 2015), which is comparable to our reported rate of 13.8% amongst second year students.

The increases in alcohol consumption behavior observed between 2010 and 2014, however, are significant only among young women, especially female students: in 2014, 28% experienced occasional significant episodes of intoxication every month (compared to 19% in 2010) and 11% experienced at least ten episodes of intoxication during the same time frame (an increase of 7% in 2010) (Richard et al., 2015). This data represents a trend in female behavior towards that observed in young men, echoing changes in choice of drink : the share of weekly consumers of beer, a generally male drink, rose from 7% in 2005 to 16% in 2014 (Richard et al., 2015). In the BOURBON study, 31% of women reported an alcohol use disorder and 6% alcohol dependence.

Our results suggest that addressing social interactions may be a key target to reduce the onset of hazardous drinking, something which should be confirmed with further study. It may also be hypothesized that the second year of medical school is more comparable to other academic studies, whereas first year may be associated with increased anxio-depressive problems due to adaptive disorders. Second years are a subpopulation of those entering first year and therefore it may be speculated that students who require anxiolytic or antidepressant medications during first year are less likely to pass their exam and proceed to the subsequent years and are therefore absent/less represented in the second-year sample. This is yet totally speculative to date as no study has explored this point.

Moreover, the second year students reported different motives for psychoactive drug consumption. The peer pressure effect was higher in the second year, both at work (with other students) and in private life (with friends, at a party). Second years also reported more frequently seeking more frequently both sedative and stimulant effects, suggesting higher difficulties in combining their studies with social life (contrary to first-year students who spend most of their time preparing for the *numerus clausus* exam).

In France, after 6 years of relatively stable prevalence, daily tobacco smoking has decreased from 34.5% to 31.9% between 2010 and 2016 (Pasquereau A et al., 2018). A strong decrease has been found in young men (44.2% in 2016 to 35.3% in 2017) whilst the prevalence in young women remains stable (29.2% in 2016 and 28.8% in 2017) (Pasquereau A et al., 2018). The prevalence of tobacco smoking in our study

sample is much lower than national rates, with a prevalence of 15.7% amongst first year students and 19.6% amongst second years. However it is comparable to the prevalence of 18% found in a recent cross national survey carried out in German and Hungarian medical students (Balogh et al., 2018). It is also similar to the prevalence of 17.2% found in a worldwide literature review on 74,001 questionnaires from 1988 to 2013 (Roncero et al., 2015). In contrast, a higher prevalence of 31% has been reported amongst Italian medical students (La Torre et al., 2012), with lower prevalences seen amongst Spanish resident physicians (6.5%, n=634) (Ranchal Sánchez et al., 2018), and Americans medical students (6%, n= 174) (Armstrong et al., 2017) though the small sample sizes here should be taken into consideration in the interpretation of the results.

Perspectives. Recent studies have suggested that some interventions may be useful helpful for medical students experiencing stress. These include mindfulness-based stress reduction (Kuhlmann et al., 2016), omega 3 (Kiecolt-Glaser et al., 2011) and probiotics (Kato-Kataoka et al., 2016), as well as self-hypnosis, feedback on various health habits, educational discussion, changes in the length and type of curriculum, and changes in the grading system (for review see(Shiralkar et al., 2013)). These interventions combined with addiction prevention-orientated teaching could be implemented at the beginning of the second year of medical studies.

Limits. These results should be taken with caution. As our study has a cross-sectional design, no causal link can be definitely inferred. This data should be confirmed in longitudinal studies. This data was self-reported, as in all but one previous studies (Rotenstein et al., 2016). Because of the study design, it was not possible to calculate an accurate response rate. The number of second year medical students in France in 2016-2017 is evaluated to 8,205(ONDPS, 2015), which suggests a response rate around 16% in this section. The number of first-year students was 57,134 on the same period (Ministère de l'Enseignement supérieur, de la Recherche et de l'Innovation, 2017), which suggests a response rate around 5% in the first year. The response rate was therefore around 3 times higher in the second year than in the first year, which should be taken into account as a potential response bias. However, first year students had higher rates of self-reported antidepressant and anxiolytic consumptions, which is not in favor of a uniform response bias. In order to reduce any response bias, the objective of the study was not clearly declared in its title. The response rate was limited by the number of faculties who participated in the study and should therefore be calculated by the exact number of students who were contacted by

mailing and social networks: a figure which was unfortunately not available. Despite these limits, our sample is one of the largest studies assessing mental health, quality of life, psychoactive use and motives in medical students in France. Moreover, our purpose was not to estimate the exact prevalence of mental health and addictive issues but to identify which year was at higher risk of mental health/addictive behavior risk. It included around 32% of males, which is representative of the female to male ratio of medical students in France in 2015 (ONDPS, 2015). Whether or not antidepressants and anxiolytics were prescribed has not been reported in this study, nor have we examined suicidal ideations, self-reported depressive symptoms, coffee and psychostimulant consumption (Fond et al., 2016) and maladaptive perfectionism(Chand et al., 2018). Determining if antidepressants and anxiolytics were self-prescribed, delivered by a medical relative or a professional may help exploring the motives for psychotropic consumption and their potential consequences, as some of these drugs may have side effects including cognitive impairment and dependence. We hypothesized that participants were able to distinguish anxiolytics from antidepressants because they were medical students. Due to questionnaire length, no data on socio-economic-status, medical comorbidity, psychiatric family history and presence of psychiatric disorders has been reported, only psychiatric/psychotherapic follow-up. These factors may also impact on mental health and should be included in further studies. Most anxiety and depression are managed in general practice rather than psychiatry so psychiatrist input would grossly underestimate the rate of medical input for mental health issues. It was not possible to check for participants' identity, i.e. that they were actually medical students. However, the survey was broadcasted through mailing lists and medical students social networks, and each IP could be used only once to avoid multiple responses. The first page of the questionnaire mentioned the inclusion criteria (metropolitan French medical students). The AUDIT and the CAST are screening questionnaires and do not assess the severity of addictive behaviors.

Strengths. The large national multicentric sample including medical students of all French faculties may be cited as a strength of the present work. To avoid any declaration bias, the results were strictly anonymized. As previous results have suggested that medical students were not always able to identify depressive symptoms (Kuzman et al., 2014), mental health was proxy by psychiatric and/or psychological follow-up and antidepressant/anxiolytic consumption.

Conclusion

First year students consumed more antidepressants and anxiolytics while second year consumed more addictive drugs and were more frequently followed-up for their mental health. This data should be confirmed in longitudinal studies to orientate prevention programs.

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Conflicts of interest

None declared.

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