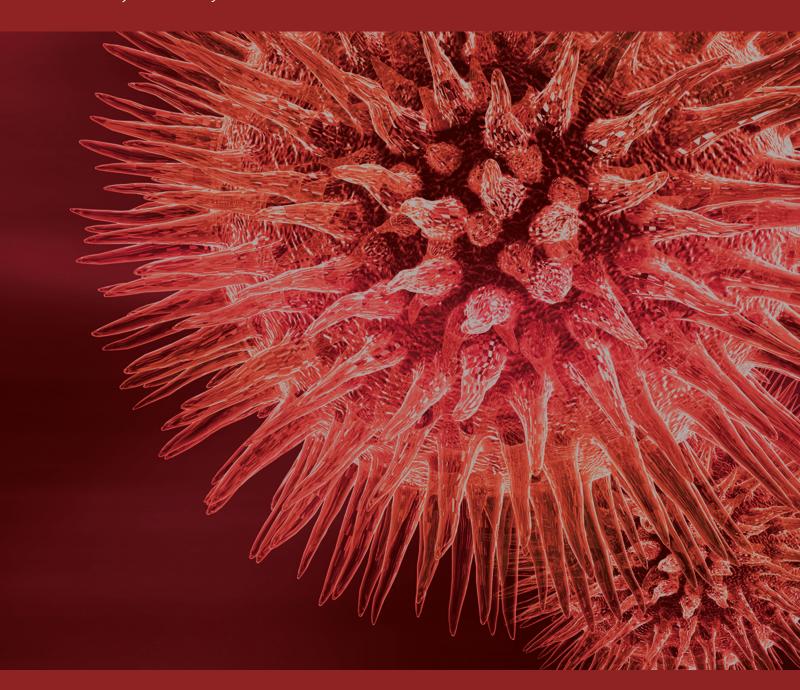
Substance Use and Dual Diagnosis Disorders: Future Epidemiology, Determinants, and Policies

Guest Editors: Sahoo Saddichha, Christian G. Schütz, Baxi Neeraj Prasad Sinha, and Narayana Manjunatha



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Editorial

Substance Use and Dual Diagnosis Disorders: Future Epidemiology, Determinants, and Policies

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Dual diagnosis or dual disorders are terms used to define the presence of an addictive disorder and another mental health disorder in an individual. With a high prevalence of dual diagnosis (above 50%) being well documented in clinical and epidemiological studies, clinicians, researchers, and policy makers have increasingly been paying attention to the challenges of identifying and implementing adequate management of cooccurring disorders/dual pathology, especially since they have been frequently associated with relapses, poor treatment engagement, and overall unsatisfactory treatment outcomes. The papers selected for this special issue represent a good panel for addressing this challenge. It is however quite certain that the subject is extremely vast and, hence, the selected topic and the papers are not an exhaustive representation of this area of dual diagnostic disorders. Nonetheless, they represent the rich and complex web of interactions which underplay dual diagnosis, which we have the pleasure of sharing with the readers.

The special issue contains five papers, from different geographical regions of the world, each dealing with a different subject within this vast area. A paper from Germany titled "Reflections on Addiction in Students Using Stimulants for Neuroenhancement: A Preliminary Interview Study" uses face to face interviews with university students to explore determinants of nonmedicinal uses of methylphenidate and amphetamines for pharmacological

neuroenhancement. While highlighting the need for long term empirical research, on the basis of some quite interesting results, the authors conclude that the beliefs and behavior of their sample population appear to be risky in terms of development of addiction. Such findings can help in understanding the underpinnings of addictions in student population and may have the potential to ultimately improve targeted interventions for this important group.

In a paper from Malaysia titled "The Effect of Nicotine Dependence on Psychopathology in Patients with Schizophrenia," A. Yee et al. study the prevalence of nicotine dependence in a cross-sectional study and investigate the effects of nicotine dependence on psychopathology among 180 outpatients with schizophrenia at a general hospital in Malaysia. They have observed a higher prevalence of nicotine dependence among patients with schizophrenia when compared to the general population in Malaysia. They have also observed a significant association between negative symptoms of schizophrenia and nicotine use, which supported the notion of self-medication hypothesis of schizophrenia.

In another paper from Brazil titled "Revictimization of Violence Suffered by Those Diagnosed with Alcohol Dependence in the General Population," F. G. Moreira et al. studied the vicious association of violence and alcohol dependence syndrome in a general population. Although they observed that urban and familial violence in the general population and

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alcohol dependence had a complex interplay, they felt that a policy of reducing familial and domestic violence may be necessary to reduce alcohol dependence. This is an interesting conclusion and calls for further validation in well-designed longitudinal studies.

In a paper from Australia titled "Khat Use: What Is the Problem and What Can Be Done?" which was unique in being a qualitative research study as well as studying a minority population, Y. S. Omar et al. used the techniques of focused group discussions and thematic analysis to address khat use and evolve strategies to deal with this rapidly progressing problem.

In a paper from Canada, titled "Attention Deficit Hyperactivity Disorder Symptoms, Comorbidities, Substance Use, and Social Outcomes among Men and Women in a Canadian Sample," E. Vingilis et al. screened for ADHD symptoms and its correlates including substance use. They observed a higher lifetime cocaine use and comorbid anxiety and depression, which points to the difficulties of being able to manage this complex group of patients.

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Research Article

Khat Use: What Is the Problem and What Can Be Done?

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The chewing of khat leaves is an established tradition in East Africa but is much less prevalent in other areas of the world and is mostly limited to Somali communities. However, our understanding of what constitutes problematic khat use in the Somali community in Victoria, Australia, is limited. The objectives of this study were to better understand the views of Somali community representatives and primary care practitioners regarding problematic khat use, to consider relevant harm minimisation strategies, and to develop resources to assist individuals with problematic khat use and their families. Qualitative research methods were used to investigate the experiences and perceptions of khat use among Somalis and mainstream primary care practitioners. Six focus groups were conducted with 37 members of the Somali community and 11 primary care practitioners. Thematic analysis was used to analyse transcripts. Various indicators of the problematic use of khat were identified, including adverse physical and mental health effects, social isolation, family breakdown, and neglect of social responsibilities. Potential harm minimisation strategies were identified including the adoption of health promotion through education, outreach to the community, and the use of universal harm minimisation strategies specifically tailored to khat use.

1. Introduction

Khat (*Catha edulis*) is a leaf cultivated in Kenya, Yemen, and Ethiopia [1, 2]. Khat contains the alkaloids cathine and cathinone which have amphetamine-like properties and has been used for centuries in many African countries for its euphoric effect and as a sanctioned cultural practice [2–4].

Frequent khat use in the long-term has been associated with various health effects, including oesophagitis, gastritis, duodenal ulcer, hepatic cirrhosis, autoimmune hepatitis, migraine, cerebral haemorrhage, pulmonary oedema, and myocardial infarction [5, 6]. With regard to psychotropic effects, khat may produce euphoria, increased confidence, and enhanced alertness [5, 7]. In terms of adverse psychological effects, khat can contribute to such conditions as depression, anxiety, mood instability, and mania. There have also been some case reports of drug-induced psychosis, and, in individuals with established psychotic disorders, khat use

may lead to an increased risk of relapse [5, 8, 9]. Furthermore, the use of khat by individuals with a prior history of exposure to trauma has been associated with an increased risk of developing psychotic symptoms [3, 10–12].

In Somalia, khat is typically chewed by groups of men in culturally sanctioned gatherings [2, 3, 13]. Traditionally, khat consumption by women is considered socially unacceptable and is rarely used [14].

However, gender differences particularly in the Western countries have become less evident, with more women using it openly [3, 15]. In Australia, it has been reported that some Western teenagers also chew khat [16]. Globally, the use of khat has increased over the past few decades and the demographics of users are changing, with an increase in the proportion of younger users and also female users [17, 18].

With regard to the Somali community in Australia, 9,589 people identified as being of Somali ancestry according to

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the 2011 Australian Census data, with 54.8% of those living in the state of Victoria and 98.8% of individuals who identified as being born in Somalia live in the state capital city of Melbourne. The largest groups of Somalis in Melbourne are in the local government areas of Banyule, Moonee Valley, and Melbourne [19]. In Australia, awareness of the use of khat and its associated problems has been increasing, although the definition of problematic use, particularly when compared with other drugs, remains controversial [8, 20, 21].

In recent years there has been a significant increase in the amount of khat that is being imported into Australia where it is not locally cultivated on a large scale [8]. Although khat is categorised by the WHO as a drug of abuse [8, 19], it is not controlled at the UN level [22]. In the UK, a report by the UK Advisory Council on the Misuse of Drugs in 2005 recommended that khat use should be discouraged although it is not a prohibited substance [8]. In Australia, khat use has varying legal status across the different states and territories [16]. In Victoria, New South Wales, and Tasmania individuals with a licence may legally obtain up to five kilograms of khat per month for personal consumption [4, 16, 23]. In other states and territories, the possession, trade, and cultivation of khat are not legal [16].

Furthermore, indicators of problematic khat use are poorly defined. The culture of khat use in Western countries including Australia has been associated with adverse social conditions related to experiences of displacement and marginalisation of immigrant East African communities [4, 11, 21]. In the UK, it has been noted that disadvantaged and unemployed young Somalis are particularly vulnerable to problematic khat use in addition to other substances' abuse [23]. In Australia, an increased prevalence of cigarette smoking among khat users has been reported [16].

While knowledge and understanding of the problems associated with khat use has been increasing, there is a need to further understand how problematic khat use is defined and what strategies may minimise the potential harms associated with khat use, particularly in the Australian context.

2. Objectives

The objectives of this study were to

- (1) understand the views of the Australian Somali community representatives and primary care practitioners regarding the definition of problematic khat use;
- (2) identify harm minimisation strategies that have particular relevance to individuals who use khat and their families;
- (3) use these findings to develop resources that may assist individuals with problematic khat use and their families.

3. Method

This study used qualitative research methods to investigate the views and experiences of the Somali community and primary care practitioners. Banyule Community Health Centre (BCHC) was chosen as a location for this study as there is a significant Somali population in the centre's catchment area, the City of Banyule in Melbourne, Australia. Approval for the study was granted by St Vincent's Hospital Human Research and Ethics Committee (Reference: LRR Protocol 033/12).

Community participants were purposively selected through key members of the Somali Australian Friendship Association, as well as informal community networks that were identified as being impartial regarding the debate about khat use within the Somali community. Primary care practitioner participants were recruited through BCHC.

Six focus group interviews each lasting about three hours, comprising a total of 48 participants, were conducted representing Somali youth (n=7), Somali elder men (n=10), Somali elder women (n=11), Somali community representatives (n=9), and two primary care practitioners' focus groups from BCHC in West Heidelberg (n=11). Data saturation was reached and hence no additional focus group interviews were required.

The participant focus groups of this study were culturally and linguistically homogeneous. Age differences were considered; youth were grouped separately from the community elders in order to avoid people feeling unable to comfortably express their views in the presence of community elders. The youth focus group consisted of 4 young men and 3 young women. Similarly, the community representative focus group consisted of 5 men and 4 women. For community elders, men and women were interviewed separately in Somali language. In Somali culture, women (particularly elder women) may not feel comfortable expressing their views in the presence of elder men.

Khat users were not specifically identified from nonkhat users. This is because the use of khat is contentious amongst members of the Somali community, and hence the researchers did not intend to marginalise identified khat users in the study.

Interviews with primary care practitioners, youth, and community representatives were conducted in English by the bilingual primary researcher, and the focus groups with community elders were conducted in Somali language. Participant information sheets (in English) were distributed among participants prior to conducting the interviews. The primary researcher explained this information in Somali language for the community focus groups whose English was limited. The primary researcher was present in all focus groups and was accompanied by other members of the group acting as comoderators. Group interaction was encouraged in order to explore common and contrasting perspectives [24].

Three focus groups were held in Banyule Community Health Centre: one focus group was held in the Neighbourhood Renewal Community hub, one was held in a church used as a community centre, and one was held at a community centre in Coburg.

Participants were verbally informed that the results from the study may be shared in future for presentations at academic and community meetings, and could be published in the peer-reviewed literature. Participants were also assured that all data would be deidentified, the anonymity of each participant would be maintained, and all information would remain confidential.

Signed consent and completed surveys related to participants' demographic characteristics were obtained during focus group interviews. Interviews were recorded and transcribed verbatim. These data are stored at Victorian Transcultural Mental Health accessible only by researchers involved in this project.

The participants were coded in the following way according to the focus groups they were part of:

- (i) EMFGP (elder male focus group participant);
- (ii) EFFGP (elder female focus group participant);
- (iii) Y (youth focus group participant):
 - (a) YFGMP (youth focus group male participant),
 - (b) YFGFP (youth focus group female participant);
- (iv) CR (community representative focus group participant):
 - (a) CRFGMP (community representative focus group male participant),
 - (b) CRFGFP (community representative focus group female participant);
- (v) PPFGP (primary care practitioner focus group participant).

The transcripts from the focus group interviews were analysed using content analysis [25]. The domains identified in the semistructured interview with the focus groups were used as a guide for the initial grouping of key themes. In order to ascertain the views of participants, an "emic" perspective was adopted. Transcripts were analysed to group and refine common as well as contrasting themes. The themes identified were reviewed independently by the coauthors for verification.

4. Results

4.1. Health and Social Problems Associated with Khat Use. A full project report is available from Victorian Transcultural Mental Health (formerly Victorian Transcultural Psychiatry Unit) [26]. As summarised in Table 1, a variety of factors were identified as being associated with problematic khat use. An elderly participant in the EM focus group stated that the meaning of the term "khat" is "bahalkuqaaday" (be taken and eaten by a predator). Physical and mental health problems linked to khat use were prominent concerns articulated, particularly, by the elder female focus group participants.

"Many khat users were dealt with by psychiatrists... many developed sense of fear, they see something that doesn't exist... Therefore, I think khat harms people mentally particularly for those who add to other substances when they use khat." (EFFGP7)

"... When people use it [khat] they have something called "thubab" which means when people chew [continuously] at least two or three

TABLE 1: Problems associated with khat use.

Theme	Frequency response*
Social problems (including family breakdown and family violence, poor social integration, social isolation, and withdrawal)	All 48 out of 48: 100%
Adverse physical health effects (including gastrointestinal problems and dental problems)	Majority 36 out of 48: 75%
Adverse mental health effects (including mood instability, disturbed behaviour, and psychotic symptoms)	Majority 35 out of 48: 73%
Perpetuation of unemployment	Majority 28 out of 48: 58%
Neglect of social roles and responsibilities	Half 24 out of 48: 50%
Negative impact on level of functioning	Few 15 out of 48: 31%
Neglect of meaningful activities	Few 6 out of 48: 13%

^{*}Few: less than half of the participants, Half: half of the participants, Majority: more than half of the participants, and All: all of the participants.

days and they stop and they don't chew, they experience... hallucinations and they see things which obviously is not a normal thing." (CRFGMP3)

All groups identified social problems associated with khat use, although the EF focus group provided most elaboration, emphasising family breakdown and problems created by khat users' loss of occupational and social role. Some participants argued that the problem is not khat itself but rather how Somali Australians use khat. Thus, the frequent use of khat in significant amounts was identified as being problematic.

The majority of participants in this study identify that "marfishes," where khat is consumed, are unhygienic:

"Large institutionalized places of khat usages mainly restaurants...are not hygienically in the best shape..." (CRFGMP10)

Interestingly, some participants from EF claimed that places where women could go for khat use are cleaner and in better condition than men's places.

4.2. The Association of Khat Use with Other Legal or Illegal Substances. Most participants, with the exception of the youth focus group participants, underscored the association between khat use and cigarette use. CRFGMP9 stated, "Khatchewing and cigarette go together. There is not a khat chewer who does not smoke or if there are, they are very few." A former khat user from EM focus group explained how he and his associates used other substances like ginger and clove in order to enhance the flavour of khat.

Anecdotal associations of khat use with alcohol and marijuana were mentioned. EFFGP2 recounted, "Khat, drug, and alcohol are the same... [and] they lead to the same way of thinking and the same attitudes. Users of these substances attract each other."

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However, two male participants from community representatives rejected the view that khat is similar to alcohol and other drugs, suggesting that khat is a better alternative:

"I think they use khat as an alternative to other substances like marijuana or whatever so, in that sense it is actually good...there is no evidence or anecdotal evidence or lived experience where people combine illegal drugs with khat..." (CRFGMP10)

4.3. Khat Use and Social Integration. Many participants, mainly from the EM and EF focus groups, believed that khat use is a barrier to social integration and khat users are marginalised. As a result, they develop their own subculture and do not engage actively with non-khat user Somalis and the wider Australian community:

"It is impossible to chew khat and at the same time to mix and interact with other Somalis who do not chew even those from your own village let alone to interact with non-Somalis." (EMFGP8)

Their poor engagement with others is also attributed to their altered sleep-wake cycle, the degree of use, and the isolating nature of locations where khat is chewed. CRFGMP7 expressed that khat users appear "to be hiding somewhere..."

- 4.4. Getting Help for Problematic Khat Use. Respondents provided diverse views regarding places where someone affected with khat use may get help. Some argued that Somalis do not identify khat use as a problem and subsequently do not seek help, while some acknowledged that stigma may also adversely influence help-seeking behaviour:
 - "...if a person is not identifying it as a problem, then they're not going to see it as needing help. Within the Somali community, I don't think we believe... in something called addiction." (YFGFP6)

Some participants expressed the belief that khat users seek financial help from their extended families or social security benefits in order to purchase khat. A few, mostly young people, underlined that the community does not openly talk about problems associated with khat use and hence about how to help individuals and their families.

A number of participants acknowledged that some people with problematic khat use seek help from mosques and Islamic religious centres as an alternative to drug and alcohol counselling services:

"I've seen people who want to get clean then they turn to religion ... and they start going to the mosque and you know when you start turning to

Table 2: Harm minimisation strategies for individuals with problematic khat use.

Theme	Frequency response*
Adopting a health promotion strategy through education	Majority 46 out of 48: 96%
Developing awareness of when khat use becomes problematic	Majority 41 out of 48: 85%
Focusing on established users, who are generally mature older men, and younger men who are at risk of problematic khat use as well as other substances' use	Majority 36 out of 48: 75%
Support through religious activities	Majority 34 out of 48: 71%
Increasing public awareness of potential harms associated with khat use through the use of written information and other various oral means	Half 24 out of 48: 50%
Development of community centres and social programs through which people who are at risk of khat use may be assisted to expand their social activities	Half 24 out of 48: 50%
Developing culturally sensitive intervention strategies using an outreach approach	Half 24 out of 48: 50%
Adopting universal harm minimization strategies specifically tailored to khat use	Few 9 out of 48: 19%
Encouraging mainstream drug and alcohol counselling services to provide assistance	Few 7 out of 48: 15%
Further discussion and debate regarding the legal status of khat	Few 4 out of 48: 8%

^{*}Few: less than half of the participants, Half: half of the participants, Majority: more than half of the participants, and All: all of the participants.

religion, you know Islam it cleanses you so pretty much they give up their bad hobbies and you know what they do so that kind of becomes like an alternative kind of like a rehab for them..." (YFGFP5)

4.5. Suggested Strategies for Helping Individuals and Families Affected by Khat Use. A range of strategies to help individuals and families affected by khat use were identified by participants as noted in Table 2.

A few participants suggested that public awareness of khat could be modelled on the public awareness education programs for cigarette and alcohol. Some argued that because Somalis in general do not place as much value on the written word, education through word of mouth, verbal, and visual education via community radio and television may be worthwhile:

"...we are an oral society...so by educating people not with pamphlets and graphics and stuff like that but by Somali way; the certain way we communicate in our society..." (CRFGMP2)

Resolving the legal status of khat was also suggested by some participants as an important issue. However, some argued that illegalisation of khat could criminalize an entire generation of older men who use khat and that this step may increase the risk of marginalizing men who are already vulnerable. Hence harm minimisation was identified as a meaningful approach:

"We could also actually make a lot of men criminals, which is something I'm also against in that sense." (YFGMP1)

"I think there should be a shift from the discussion of criminalisation to the harm-minimisation... if you remove that without a dialogue and discussion with the community, then it shifts to more an illicit drug."

- 4.6. Perspectives of Primary Care Practitioners. A key theme that emerged from health care practitioners was the lack of experience and understanding in general, regarding khat. Only the single Somali participant (PPFGP5) identified that they had worked with a client who they were aware used khat. There was an identified need to further understand khat's relative impact and potential for dependence in order to better understand the nature of problematic khat use. As identified by the Somali participant, as a result of the "silent" nature of khat use in the community, problems associated with its use are not widely known:
 - "...it's a silent drug that's in use. And because it's silent the harms of it are probably also silent." (PPFGP1)
- 4.7. Understanding When Khat Use Becomes Problematic. Despite their lack of specific knowledge, some PP mainstream participants suggested that khat could be compared to other substances of abuse and that it may become problematic when it is associated with impairment in people's level of functioning:
 - "...Being a stimulant I guess people are staying awake and then crashing out and sleeping so that's obviously affecting their family life..." (PPFGP2)
- 4.8. Care for Individuals with Problematic Khat Use. Despite the limited understanding of the specific issues related to khat use overall, one of the key themes that emerged was the need for mainstream drug and alcohol counselling services to be in a position to provide necessary assistance. Additionally, harm minimisation strategies used for other addictive substances were suggested to be helpful and could be applied effectively:
 - "...I'm not saying it's a perfect system...but that's the system that exists...what there is in these services is specialised knowledge about treatment of addiction...and treatment of problematic drug use..." (PPFGP1)

Mirroring the views of community members, a significant theme emerged relating to the potential risks of criminalizing culturally sanctioned practices, particularly without the involvement of the community:

- "...if we made use of this drug illegal we'll be essentially turning all users of this drug into criminals straight away and you'd put them into a new system..." (PPFGP1)
- 4.9. Harm Minimisation. With respect to specific harm minimisation strategies, one of the key themes to emerge was the potential application of universal strategies with adaptation to khat use. A theme emerged that guidance may be found from considering strategies that have been successful in reducing the harms associated with tobacco, alcohol, cannabis, marijuana, amphetamine, and heroin use:
 - "...basic strategies like maybe reducing the amount that they're chewing, maybe reducing the frequency, if they're attending these group meetings every day for instance I don't know if that's feasible really or realistic that they could attend every second day..." (PPFGP7)

It was noted that there is potential for role models within the community to act as advocates for change and that there is the potential for one group member's behaviour to provide a catalyst to change in other members of the group:

"...sometimes there are a group of users and one of them will be having a lot of problems in their life but want to do something about it and will go and do something about it and then everyone else in that group will start to see that person making changes in their life, so it's kind of a bit of a snowball effect." (PPFGP11)

Culturally sensitive intervention strategies were also suggested. In particular, it was noted that interventions may be more useful in a group format, rather than through individual therapy. Both community and PP participants acknowledged the need for more information and research, in order to understand the impact of khat use and to understand what specific strategies may effectively meet the needs of individuals with problematic khat use and their families.

5. Discussion

This study explored perceptions of khat and its perceived level of harm in the urban Australian context. It examined the complexities regarding possible interventions that may assist individuals with problematic khat use and their families. The qualitative methodology used allowed an elaboration of diverse views of the Somali community members.

Some respondents believed that khat use in Australia is an accepted cultural practice while others argued that it helps users escape from problems posed by the new environment and resettlement. A relationship between khat use and maintenance of Somali cultural identity amongst migrants

in Australia has been identified in earlier studies [21]. The vast majority of interviewees from the Somali community in this study correlated khat use with many adversities including physical and mental health problems. Additionally, negative social impacts linked to problematic khat use, including family breakdown, poor social integration, and unemployment, were identified.

Furthermore, khat use was seen to be associated with use of other substances, although some respondents considered khat as less harmful than alcohol and other drugs. The vast majority agreed that Somalis do not identify khat use as problematic. However, khat users were identified as being marginalised, hence reinforcing the silent nature of the problem. The reservations noted regarding the potential implications of illegalising khat use and the marginalisation of users are consistent with findings by Feigin et al. [4].

PP participants noted the important role of mainstream services as for individuals with alcohol and other substance use disorders. This highlights the importance of education and training of primary care practitioners. As noted by Fitzgerald, there is an unmet need for education campaigns to reduce patterns of harmful consumption of khat among members of the African communities in Australia [8].

Integrating the perspectives of the Somali community participants and primary care practitioners, a range of strategies to help individuals and families affected by khat use were identified. These strategies include establishing culturally appropriate and sensitive services and using social resources, such as families, community networks, community services, education through the media, and employing other culturally relevant ways of transmitting knowledge and information such as word of mouth and visual strategies. Universal harm minimisation goals, such as reducing the amount of khat used and the time spent using khat, were recommended.

There are a number of limitations of this study. First, a group of problematic khat users was not specifically identified. Rather, the aim of this study was to seek the perspectives of a broad range of community members, including users and nonusers. Second, participants were drawn from a defined geographical region. Third, PP participants included drug and alcohol workers but did not include a broader range of primary care practitioners such as general practitioners or community nurses. Fourth, whilst saturation of perspectives was reached, a wider range of views may have been evident with a larger number of focus groups. Fifth, the data may have been enhanced if the focus groups were supplemented by face-to-face interviews with participants; this was not possible due to time constraints.

Notwithstanding limitations, the findings emphasise the need for a culturally informed and broader understanding of what constitutes problematic substance use. In this case, the study has facilitated development of information resources for individuals and their families and for primary care practitioners in the local community. In a broader context, the findings potentially have relevance to Somali communities living in other Western countries, as well as, more generally, to the use of lesser known substances favoured by specific cultural groups.

6. Conclusions

In conclusion, there is a need for a greater level of awareness of khat use in immigrant Somali communities and its associated problems including health effects, impairment in functioning, family disharmony, and marginalisation from society. Primary care practitioners are well placed to provide assistance to individuals with problematic khat use, employing harm minimisation strategies. A culturally sensitive approach is warranted and outreach primary care services have an important role in attempting to engage with members of the Somali community around this issue. Further training of primary care practitioners including drug and alcohol service practitioners is necessary to improve awareness of khat and its effects. Universal strategies of motivational interviewing and harm minimisation adapted to suit the cultural context, such as by involving members of the Somali community and family members, are warranted.

Conflict of Interests

The authors declare that there is no conflict of interests regarding the publication of this paper.

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Research Article

Attention Deficit Hyperactivity Disorder Symptoms, Comorbidities, Substance Use, and Social Outcomes among Men and Women in a Canadian Sample

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Background. Attention deficit hyperactivity disorder (ADHD) is a neurodevelopmental disorder that can persist in adolescence and adulthood. Aim. To examine prevalence of ADHD symptoms and correlates in a representative sample of adults 18 years and older living in Ontario, Canada. Method. We used the Centre for Addiction and Mental Health Monitor, an ongoing cross-sectional telephone survey, to examine the relationships between ADHD positive symptoms and comorbidities, substance use, medication use, social outcomes, and sociodemographics. Results. Of 4014 residents sampled in 2011-2012, 3.30% (2.75%–3.85%) screened positively for ADHD symptoms (women = 3.6%; men = 3.0%). For men, distress, antisocial symptoms, cocaine use, antianxiety medication use, antidepressant medication use, and criminal offence arrest were associated with positive ADHD screen. For women, distress, cocaine use, antianxiety medication use, antidepressant medication use, pain medication use, and motor vehicle collision in the past year were associated with positive ADHD screen. Conclusions. ADHD symptoms are associated with adverse medical and social outcomes that are in some cases gender specific.

1. Introduction

Attention deficit hyperactivity disorder (ADHD) is a neuro-developmental disorder with symptoms of inattention, hyperactivity, and impulsivity that present in multiple settings [1]. Initially ADHD was viewed as a disease of childhood that declined or disappeared in adulthood. Research over the past 30 years has found ADHD to persist in adolescence and adulthood for 50% to 60% of childhood ADHD cases [2]; though ranges as extreme as 4% to 80% have also been reported [1–6].

Although symptoms of ADHD have been extended developmentally upward to adults and the diagnostic criteria of ADHD have been revised in the DSM-5 to reflect more accurately the experience of affected adults, adult ADHD research is in an early stage [1, 7, 8]. Most ADHD research has focused on homogeneous samples of clinically referred, young Caucasian males [9]. These samples have the advantage of extensive assessment but lack representation from non-clinical groups exhibiting ADHD symptoms [10, 11]. Clinical samples are found to show more symptoms and impairment [11]. Moreover, many of these studies suffer from major

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methodological shortcomings, including small sample sizes, referral biases, high loss to follow-up, inadequate matching of groups, and lack of gender inclusion and analysis [9, 10, 12]. On the other hand, population-based, representative samples overcome many of these methodological weaknesses, while their findings allow inferences to be made to the general population [11, 13].

Data on prevalence of adult ADHD are limited, but estimates based on international studies using multistage household probability samples range from 1.2 to 7.3% with an average of 3.4% [14]. No population-based adult ADHD prevalence estimates are available for Canada.

Current research suggests that gender differences in the prevalence of adult ADHD may differ from prevalence patterns reported in children. Studies of ADHD in children find that boys are much more affected than girls, with clinically referred studies having gender differences closer to 9:1 and epidemiological studies closer to 3:1 [15]. Among adults, results are mixed. Kessler et al. [16] found that diagnosis of ADHD in their survey of 18-44-year olds was 5.4% for men and 3.2% for women, while Faraone and Biederman [6] found no differences (men = 3.0%; women = 2.8%). Information on ADHD and age is very limited, despite the historical controversy on whether ADHD stays the same, declines, changes, or disappears in adulthood. A recent meta-analysis on adult ADHD found that only two studies included participants over 60 years of age; the mean ages of most studies were upper teens to mid-30s [9]. The meta-analysis of these age-limited studies showed a gender by age interaction with symptoms declining as men but not women reached their 40s.

Clinical studies of adolescents and adults with ADHD have found higher rates of psychopathology, such as mood, anxiety, childhood disruptive, antisocial personality, and substance use disorders compared with control groups [4, 5, 15, 17]. A recent meta-analytic study examining the association of childhood ADHD and substance use and abuse/ dependence found that children with ADHD were significantly more likely as young adults to have ever used nicotine, cannabis, and cocaine but not alcohol and were significantly more likely to develop substance use disorders than controls [18].

Those with ADHD are also less likely to enter college and to graduate and generally have 2 years less schooling [19]. They are less likely to be employed and have lower SES and income and higher crash and criminal offence rates, although in some studies direct relationships between ADHD and various delinquencies disappear when comorbid conditions are included [2, 5, 20]. However, Weiss and Hechtman [3] found in their 15-year follow-up that although 50–60% of young adults initially diagnosed with ADHD continue to exhibit symptoms, their adult ADHD patients had lower risk of antisocial or criminal behaviours, despite slightly elevated rates in adolescence. Thus, there is a need for sound epidemiological data to understand the manifestations of ADHD symptoms in adulthood by gender, psychiatric comorbidity, and social outcomes.

The purpose of this study was to examine prevalence of ADHD symptoms and their relationship with comorbidities

and social outcomes and to explore differences by gender, in a large population-based survey of adults in Ontario, Canada.

2. Methods

- 2.1. Sample. The data are based on telephone interviews (landlines and cell phones) with 4,014 Ontario adults (ages 18 or older) over 24 months between January 2011 and December 2012. The data are from the Centre for Addiction and Mental Health (CAMH) Monitor, an ongoing cross-sectional, computer-assisted telephone survey administered by the Institute for Social Research at York University, Canada (see [21] for details). Each monthly cycle uses a two-stage probability sampling procedure. In the first stage, a random sample of telephone numbers was selected with equal probability from within each regional stratum. In the second stage, one respondent aged 18 or older who was able to complete the interview in English was then selected from within each household according to the most recent birthday of all household members. Response rates based on estimated eligible sample averaged 52.89%.
- 2.2. Measures. All scales were based on well-validated measures and demonstrated good internal consistency.
- 2.2.1. ADHD Measures. (1) Adult ADHD Self-Report Scale-V1.1 (ASRS-V1.1) was developed by Kessler et al. [22] as part of the WHO Composite Diagnostic Interview. Psychometric validation against DSM-IV based psychiatric diagnoses by experienced clinicians demonstrated that the 6-item, 5-point Likert scale screener was superior to the 18-item version on specificity (99.5% versus 98.3%), sensitivity (68.7% versus 56.3%), total classification accuracy (97.9% versus 96.2%), and Cohen's kappa (0.76 versus 0.58) [23–25]. Positive ADHD symptoms screen is a total score greater than 13 [25]. (2) Previous ADHD diagnosis was assessed by the item "have you ever been diagnosed with Attention Deficit Disorder (ADD) or Attention Deficit Hyperactivity Disorder (ADHD) by a doctor or health care professional?" (3) ADHD medication use was assessed by items querying if, when and how long, they had been treated with medication for ADHD or ADD by a doctor or health care professional, and whether they are currently taking it (adapted from Ontario Student Drug Use and Health Survey) [26].
- 2.2.2. Psychiatric Distress and Medication Use Measures. (1) General Health Questionnaire (GHQ12) is a 12-item, 4-point widely used screening instrument for current psychiatric distress that captures depression/anxiety and problems with social functioning [27–29] with a score of three and higher as a positive screen; (2) depression/anxiety/pain medication use: in the past 12 months have you taken any prescription medication: to reduce depression? to reduce anxiety or panic attacks? for pain?
- 2.2.3. Antisocial Behaviour Measure. (1) Antisocial Personality Disorder Scale from the Mini-International Neuropsychiatric Interview (MINI-APD), a 12-item, dichotomous scale,

was designed to provide a short clinical screening tool to assess delinquencies (truancy, cheating/lying/stealing, bullying, and hurting animals/people) before and after age 15. We excluded one item of the MINI-APD (forced someone to have sex before age 15), as required by the ethics review board. A score of three or more on the latter six MINI-APD questions indicated a positive APD screen [30].

2.2.4. Substance Use and Abuse Measures. (1) Lifetime cannabis and cocaine use (never used = 0, ever used = 1); (2) Alcohol Use Disorders Identification Test (AUDIT) is a validated screening instrument developed by the WHO, to detect individuals at the less severe end of the spectrum of alcohol problems, with a score greater than seven indicating hazardous alcohol use [31-33]. The AUDIT has been extensively used in both national and Ontario surveys which demonstrate the validity of the instrument in Canadian populations and the utility of the 8+ cutoff [34-36]. (3) The cannabis subscale of the Alcohol, Smoking and Substance Involvement Screening Test (ASSIST) is a 6-item screening instrument to assess risk of experiencing health and other problems (social, financial, legal, and relationship) from their current pattern of cannabis use, with scores of four or more indicating moderate or high risk of problems [37].

2.2.5. Social Problems. These were self-report items: (1) vehicle crash involvement in past year and (2) ever in lifetime arrested for a criminal offence.

2.2.6. Sociodemographics. (1) Gender, (2) age, (3) marital status, (4) educational status, (5) employment status, and (6) income were included.

2.3. Statistical Analysis. All analyses used linearized methods based on sample design and weighted by probability of selection. The percentages reported are considered representative for the population surveyed. We used logistic regression analysis to estimate odds ratios for ADHD positive symptoms associated with sociodemographics, previous ADHD diagnosis, medication use, comorbidities, substance use and abuse, and social problems. We conducted separate regression analyses for men and women. We adjusted for age, marital status, education, and employment. Results are based on "valid" responses; responses such as "do not know" and refusals were considered missing data and excluded from analyses.

3. Results

Overall, 3.30% (C.I.2.75%, 3.85%) of the sample screened above the cutoff for positive ADHD symptoms. Table 1 indicates significant differences between those who screened positively and negatively for ADHD symptoms. A greater percent of those who screened positively were younger, less likely to be married, had lower education, and were part-time employed or other, compared to those who screened negatively. A higher percentage of those who screened positively for ADHD symptoms reported previous ADHD diagnosis,

TABLE 1: Characteristics of CAMH Monitor survey respondents who screened positively and negatively for symptoms on the Adult ADHD Self-Report Scale-V1.1 January 2011–December 2012.

	AD	HD+	ADF	ID –	_
	Sc	reen	Scr	een	P
	N	%	N	%	
Age					
18-24	26	5.4	458	94.6	
25-44	54	3.9	1346	96.1	< 0.001
45-64	49	3.6	1326	96.4	\0.001
≥65	4	0.6	666	99.4	
Gender					
Female	76	3.6	2023	96.4	0.254
Male	57	3.0	1847	97.0	0.234
Marital status					
Married/partner	70	2.6	2584	97.4	
Widowed/sep./div.	18	4.1	421	95.9	0.002
Never married	44	5.0	831	95.0	
Education					
High school	20	5.2	366	94.8	
Completed HS	20	2.5	791	97.5	0.015
Some after sec.	56	3.9	1377	96.1	0.013
Univ. deg.	33	2.5	1304	97.5	
Employment status					
Full time	54	2.8	1903	97.2	
Part time	22	5.5	380	94.5	0.018
Other	56	3.4	1586	96.6	
Household income					
<20,000	11	8.3	121	91.7	
20-49,999	31	15.4	579	94.9	< 0.001
50-100,000	39	19.0	1042	96.4	10.001
>100,000	31	2.6	1152	97.4	
ADHD previously diagnosed					
Yes	22	22.7	75	77.3	< 0.001
No	111	2.9	3783	97.1	10.001
ASPD screen (≥4)					
ASPD	10	25.6	29	74.4	< 0.001
Non-ASPD	121	3.1	3791	96.9	10.001
Psychiatric distress (GHQ-12)					
Yes (+3)	67	11.8	502	88.2	< 0.001
No (0-2)	66	1.9	3368	98.1	
Ever treated with ADHD meds					
Yes	6	15.0	34	85.0	< 0.001
No	62	3.3	1802	96.7	.0.001
Antidepressant meds use					
Yes	48	17.5	227	82.5	< 0.001
No	85	2.3	3633	97.7	

TABLE 1: Continued.

	ADI	HD+	ADF	HD –	
	Sci	reen	Scr	een	P
	N	%	N	%	
Anti-anxiety Meds Use					
Yes	27	19.6	111	80.4	< 0.001
No	42	2.4	1725	97.6	<0.001
Pain Meds Use (with and without pres.)					
Yes	47	5.3	843	94.7	< 0.001
No	85	2.8	2996	97.2	<0.001
AUDIT					
Yes (8+)	25	5.0	477	95.0	0.039
No (0-7)	106	3.1	3295	96.9	0.039
ASSIST					
Mod/High (4+)	15	7.7	180	92.3	< 0.001
Low (0-3)	116	3.1	3678	96.9	<0.001
Lifetime used cannabis					
Yes	94	5.8	1520	94.2	< 0.001
No	38	1.6	2329	98.4	<0.001
Past 12 mths cannabis use					
Yes	38	7.3	486	92.9	0.008
No	94	2.7	3352	97.3	0.008
Lifetime used cocaine					
Yes	32	11.3	251	88.7	< 0.001
No	100	2.7	3606	97.3	<0.001
Ever arrested for a crime?					
Yes	23	7.5	284	92.5	< 0.001
No	110	3.0	3573	97.0	\0.001
Crash in past year					
Yes	13	6.0	202	94.0	0.03
No	120	3.0	3868	97.0	0.03

psychiatric, substance use, and social problems compared to those who screened negatively.

Examination of sociodemographics by gender indicates (Table 2) that for men and women the odds of screening positively for ADHD symptoms were significantly lower for the 25–44-year-old age group compared to the 18–24-year-old group. However, women aged 45–64 had significantly lower rates than those aged 25–44, and those aged 65 and older showed lower rates than those aged 45–64. For marital status, no differences were found by gender.

Different patterns emerged between men and women on education and employment. Among men, those who reported not completing postsecondary education showed higher odds of screening positively for ADHD symptoms than those with only a high school education. For women, those who reported achieving a postsecondary diploma or degree showed significantly lower odds of screening positively for ADHD symptoms than those who did not complete a postsecondary degree. For employment no significant differences were observed among men between those who reported being unemployed and those who reported working either full or part time. Among women, however, those who reported being employed full time showed significantly lower odds of screening positively for ADHD symptoms.

The adjusted logistic regression (Table 3) shows variables with significant odds ratios. Those who reported previous diagnosis for ADHD and ADHD medication use showed significantly higher odds of screening positively for ADHD symptoms. Gender differences were also found: women showed much higher odds of screening positively for ADHD symptoms when they had been diagnosed (adjusted odds ratio [OR] 15.04, 95% confidence interval [CI] 6.40-35.25) or treated for ADHD (OR 19.25, CI 7.47–49.61) compared to men who reported being diagnosed (OR 6.14, CI 2.65-14.24) or treated (OR 9.00, CI 3.73-21.70). The results also indicated that psychiatric symptoms and medications were comorbid with ADHD positive symptoms. Those who screened positively on the GHQ for distress and reported antidepressant and antianxiety medication use had higher odds of screening for ADHD symptoms. Women also showed significantly higher odds of screening for ADHD symptoms when they reported using prescription pain killers in the last year, while men showed no significant relationship. Both men and women who reported past year cannabis use and cocaine use ever showed significantly higher odds of screening positively for ADHD symptoms.

Gender differences also emerged for social problems. While women who reported a collision in the last year showed significantly higher odds of screening positively for ADHD symptoms, no significant relationship was found between arrest for criminal offence and ADHD symptoms. However, the findings were reversed for men.

4. Discussion

This first population-based Canadian study of adult ADHD symptoms found prevalence of 3.3% screening positively for ADHD symptoms and no differences between men and women. This is congruent with M. D. Weiss and J. R. Weiss's [37] suggestion that the higher clinical prevalence of boys to girls could reflect differential referral patterns between children and adults. This finding is also consistent with the average prevalence of 3.4% found in a review of other countries using similar epidemiological sampling methodology [13]. Kessler et al. [25], using the same ADHD screening instrument, found 4.4% screened positively for ADHD, but their sample was limited to American adults 18-44 years of age. Our study is among the few that included elderly persons. We found reported ADHD symptoms highest among the 18-24year olds, consistent with other studies [38], although for women the odds of ADHD positive symptoms decreased across all age groups whereas for men ADHD positive symptoms stabilized from young adulthood. Nonetheless, our

Table 2: Odds ratios (ORs) and confidence intervals (CIs) for positive ADHD symptoms by sociodemographic variables for men and women.

Variables		Men			Women	
variables	OR	95% CI	P	OR	95% CI	P
Age						
18-24 (ref.)						
25-44	0.18	0.06-0.53	**	0.13	0.02-0.64	*
45-64	0.86	0.36-2.03	NS	0.12	0.03-0.40	* * *
≥65	0.83	0.47 - 1.47	NS	0.51	0.28-0.95	*
Marital status						
Married (ref.)						
Wid./div./sep.	2.20	0.84-5.77	NS	1.91	0.96-3.79	NS
Never married	1.12	0.44 - 2.80	NS	1.41	0.73-2.74	NS
Education						
<high (ref.)<="" school="" td=""><td></td><td></td><td></td><td></td><td></td><td></td></high>						
High school compl.	0.59	0.33-1.04	NS	0.55	0.28-1.06	NS
Some after sec.	2.1	1.15-3.65	*	0.93	0.52-1.66	NS
University degree	0.88	0.48-1.59	NS	0.51	0.31-0.83	**
Employment						
Unemployed (ref.)						
Full time	0.82	0.41-1.67	NS	0.57	0.33-0.98	*
Part time	2.17	0.94-4.99	NS	0.91	0.46-1.78	NS

NS: not significant, ${}^*P < 0.05$, ${}^{**}P < 0.01$, and ${}^{***}P < 0.001$.

TABLE 3: Adjusted odds ratios (ORs) and confidence intervals (CIs) associated with positive ADHD symptoms for men and women by ADHD diagnosis, medication use, comorbidity screeners, and social problems as relevant in overall regression analyses.

Variables		Men			Women	
variables	OR_{adj}	95% CI	P	OR_{adj}	95% CI	P
ADHD diagnosis	6.14	2.65-14.24	* * *	15.04	6.40-35.35	* * *
ADHD meds	9.00	3.73-21.70	* * *	19.25	7.47-49.61	* * *
Presc. pain meds	1.28	0.68-2.39	NS	2.02	1.24-3.28	**
Antianxiety meds	4.88	2.38-10.02	* * *	9.07	5.47-15.06	* * *
Antidepressant meds	6.59	3.13-13.89	* * *	8.75	5.17-14.79	* * *
Distress—GHQ	6.48	3.59-11.70	* * *	5.31	3.26-8.66	* * *
Antisocial screen (≥4 symptoms)	11.61	4.01-33.63	* * *		No cases	
Cannabis use Past yr	2.24	1.20-4.20	*	2.20	1.18-4.08	*
Cocaine use Lifetime	3.40	1.73-6.64	* * *	4.51	2.32-8.75	* * *
Collision Past yr	0.36	0.05-2.46	NS	2.97	1.43-6.19	**
Arrested criminal offence lifetime	2.62	1.33-5.16	**	1.25	0.42-3.67	NS

 OR_{adj} : odds ratio adjusted for age, marital status, education, and employment status, NS: not significant, *P < 0.05, **P < 0.01, and ****P < 0.001.

results confirm that ADHD symptoms persist for some adults across the adult lifespan among both men and women and are associated with adverse psychiatric, substance use, and social outcomes that were in some cases gender specific. Accordingly, these results suggest the importance of screening for ADHD among adult patients presenting with internalizing or externalizing psychiatric symptoms and/or substance use.

Our study found few differences in the clinical phenotypes of men and women who screened positively for ADHD symptoms. Although diagnosis of ADHD among those who screened positively was low at 22.7%, women reporting ADHD diagnosis and medication treatment had more than two times higher adjusted odds of screening positively for ADHD symptoms compared to men. Given that girls with ADHD tend to be underidentified because of their less disruptive behaviours [37], it may be that those who have been diagnosed have more severe symptoms and hence are more likely to have been treated. Additionally, it may be that women are more willing to respond positively to screening items compared to men.

Psychiatric comorbidities are commonly found among adult ADHD patients, in particular, mood, anxiety, substance use, and antisocial personality disorders [5, 37]. The higher adjusted odds of positive ADHD symptoms for those who reported distress and antidepressant and antianxiety medication use could reflect the higher comorbidities found with ADHD. A portion could also be due to misdiagnosis of ADHD symptoms or possibly treatment with SSRIs for ADHD. Or ADHD symptoms can also be part of the symptom cluster for mood and anxiety disorders.

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ADHD patients are also at significant risk for substance use, particularly for cannabis and cocaine, with 40% prevalence of lifetime diagnosis of substance use disorders [39]. A recent meta-analysis found that young adults diagnosed with ADHD as children were significantly more likely to use cannabis and cocaine but not alcohol [18]. Our study found that for those screening positively for ADHD symptoms, adjusted odds for cannabis use in past year and lifetime cocaine use were significantly higher, but not for the AUDIT or the ASSIST suggesting greater use but not necessarily abuse. The gender differences found for prescription pain medication, antisocial screen, and collisions in past year and lifetime arrest for criminal offence may reflect differences in externalizing and internalizing outcomes for men and women associated with ADHD symptoms.

The results of this study are subject to important limitations. These data are based on self-report screeners and do not reflect the breadth of information needed for clinical diagnoses. This is a key issue because the current study only reflects self-reported symptoms and does not examine impaired functioning and other issues related to specific diagnoses. Indeed, Gambino [40] cautions on the use of screening tests in prevalence estimation because screening tests tend to have relatively high false positive rates which result in overestimation of true prevalence in a population study. Thus, this population based sample may represent functioning persons with some ADHD and/or other comorbid symptoms but not actual diagnoses, although the screening tool (ASRS-V1.1) was validated against DSM-IV based psychiatric diagnoses by experienced clinicians and demonstrated good psychometrics. Additionally, although the response rate over 50% is very good for a telephone survey and data were weighted to reflect a representative sample of Ontario residents, the sample could potentially be biased. Moreover, although the total sample size is over 4000, cell sizes can be very small because psychiatric problems, such as ADHD, substance use, and collisions have low prevalence; small cell sizes and large CIs suggest a low level of precision, as indicated in some of the variables in Table 3. Nevertheless, these observations are of substantial interest in providing prevalence estimates by gender and by age, particularly for older age groups.

There are several clinical implications. Higher reports of ADHD symptoms are associated with more difficulties, further validating the ADHD self-report construct in a community sample. The relationships between the variables in this study also provide insights into better operationalizing self-reported adult ADHD symptoms. ADHD is typically regarded as an externalizing condition, but it has been acknowledged in the literature that internalizing symptoms

are comorbid in adolescence and adulthood [6]. It is unclear why these internalizing symptoms emerge, whether they emerge biologically after adolescence or whether adults with ADHD have become depressed because of their chronic behavioural difficulties that may have persisted since childhood. The nature of the comorbidities is important to understand for treatment directions. A final notable finding is the proportion of symptoms reported in the 18–24-year olds that is higher than that in the older participants. This will be an important finding to follow to determine whether this is the result of more public awareness of ADHD, or whether this reflects some cohort effect in increased reported ADHD symptoms in our young people.

Ethical Approval

The study received ethical approval from the CAMH, York University, and University of Western Ontario research ethics boards

Conflict of Interests

The authors declare that there is no conflict of interests regarding the publication of this paper.

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Research Article

Reflections on Addiction in Students Using Stimulants for Neuroenhancement: A Preliminary Interview Study

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The use of stimulants for the purpose of pharmacological neuroenhancement (NE) among students is a subject of increasing public awareness. The risk of addiction development by stimulant use for NE is still unanswered. Therefore, face-to-face interviews were carried out among 18 university students experienced in the nonmedical use of methylphenidate and amphetamines for NE assessing aspects of addiction. Interviews were tape-recorded, verbatim-transcribed, and analyzed using a qualitative approach. The interviews showed that participants—the majority had current or lifetime diagnoses of misuse or addiction to alcohol or cannabis—reported an awareness of the risk of addiction development associated with stimulant use and reported various effects which may increase their likelihood of future stimulant use, for example, euphoric effects, increase of self-confidence, and motivation. They also cited measures to counteract the development of addiction as well as measures taken to normalize again after stimulant use. Students were convinced of having control over their stimulant use and of not becoming addicted to stimulants used for NE. We can conclude that behavior and beliefs of the students in our sample appear to be risky in terms of addiction development. However, long-term empirical research is needed to estimate the true risk of addiction.

1. Introduction

The use of "smart drugs" containing over-the-counter-(OTC-) drugs as well as prescription drugs and illicit drugs for the purpose of pharmacological neuroenhancement (NE) by healthy people has attracted an increasing amount of attention [1–4]. In particular, (psycho-) stimulants such as methylphenidate (MPH) and amphetamines (AMPH) such as prescription amphetamines (e.g., Adderall, attention) as well as illicit amphetamines (e.g., ecstasy, speed) seem to be the most prevalent substances used for the purpose of enhancing mental performance as previous quantitative surveys prove: Among university students, prevalence rates range broadly from 1 to 38% [5–9].

In interdisciplinary debates on medical, social, and ethical implications of NE, aspects relating to addiction

play a considerable role [10–14]. The common mode of action of AMPH and MPH is an interaction with synaptic norepinephrine and dopamine transporters. In contrast to MPH, AMPH additionally leads to vesicular release (exocytosis) of dopamine, which means an increase of action-independent dopaminergic activity [15–17].

Based on theoretical reflections on the mechanisms of action of NE drugs, Heinz and colleagues (2012) argue that any current or future NE drug will have the potential to induce dependence; given this risk of addiction, for ethical reasons they argue against clinical research into NE [10]. This position is rejected by Shaw [12] who argues that safety and research in the area of NE do not pose unique difficulties.

Smith and Farah point out that, according to an estimate by Kroutil and colleagues (2006), 5% of the nonmedical users of prescription stimulants meet the criteria for abuse or

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dependence. However, the immediate and long-term risk of abuse or addiction among stimulant users for NE is unclear [14, 18].

Although no data is available on the percentage of addicted subjects among stimulant users for NE, the addiction risk of stimulants is well known among students: An interview study by Partridge and colleagues among healthy university students without experiences of stimulant use for NE revealed that they identified psychological dependence as a potential negative consequence [19]. In our own interview study of 18 student users of MPH and AMPH, we also demonstrated students' concerns about the risk of addiction regarding stimulants compared to caffeine [20] and found that users of stimulants for NE showed significantly higher rates of misuse of alcohol and cannabis compared to healthy controls [21].

In view of the medical data indicating that stimulants used for NE come with the risk of dependence and given the fact that many who have heard about NE believe that it might induce dependence, the aim of this study was to describe students' behaviour with respect to stimulant use and dependence with the help of semistructured interviews with students who have taken stimulants for NE.

2. Methods

By posting placards on public bulletin boards throughout the campus of the University of Mainz from 2009 to 2010 we searched for healthy participants (without any psychiatric disorders leading to the necessity of being prescribed stimulants such as MPH or AMPH) who had already used prescription or illicit stimulants (AMPH, MPH, ecstasy, and cocaine) for the explicit purpose of NE. Of the thirty students who contacted us via telephone or e-mail, only twenty-two responded to our e-mail requests for an appointment and agreed to participate. Twenty-two interviews were carried out. Two students had to be excluded because of having current physicians' prescriptions for stimulants (e.g., Ritalin); two interviews failed for technical reasons (the recorder did not work appropriately). Finally, eighteen interviews entered further analysis.

In previous studies we already analyzed the interview transcripts of these 18 users regarding moral differences between illicit stimulants and caffeine (legal stimulant drug) and regarding life context of pharmacological academic performance enhancement [20, 22]. In addition, data about a general overview of knowledge about stimulants for CE, patterns of use, and diagnoses of abuse and addiction compared to twenty healthy controls have already been published [21].

Each interview was divided into two parts. First, a trained psychologist conducted a structured clinical interview (SKID). This interview is a diagnostic instrument to indicate major mental disorders and personality disorders. The SKID and questions on psychoactive medication as a result of having a psychiatric disorder with the need of psychoactive medication ensured that potential participants with psychiatric disorders and having psychoactive medication with a physician's prescription for medical reasons could be

TABLE 1: Characteristics of participants.

Characteristics	Percentage/number 100%, <i>n</i> = 18
Gender	66.7% male $(n = 12)$
Gender	33.3% female $(n = 6)$
Age (mean \pm SD)	$25.8 \text{ years} \pm 2.88$
Completed semesters (mean \pm SD)	7.35 semester ± 3.79
Department of	
Humanities	44.4% (n = 8)
Natural sciences	33.3% (n = 6)
Economics	22.2% (n = 4)

Data are given as mean \pm standard deviation (SD) according to Franke et al. [20].

excluded from the analysis. Addiction was no reason for study exclusion. Second, based on a semistructured interview guideline, two interviewers asked open and closed questions regarding the nonmedical use of substances for CE. Beyond sociodemographic data such as age, area of study, and grades, we asked: "Do you think that the/your use of illicit stimulants may lead to addiction?", "Which effects of the stimulant you used did you experience?", and "Have you experienced a need to increase dosage in order to achieve the same level of effects?" In addition, interviewees had the opportunity to tell us about further aspects important to them.

Prior to the interview, participants gave written informed consent for being interviewed and for tape-recording. Each participant received thirty Euros for compensation after he/she had been interviewed. The local Ethics Committee (Landesärztekammer Rheinland-Pfalz, Medical Association, Rheinland-Pfalz) approved this interview study.

One independent person transcribed the contents of the tape-recorded interviews. Afterwards, transcriptions were analysed by two raters with a qualitative approach based on inductive category development [23, 24]. The two raters analyzed the transcripts independently. Rater 1 came up with 6 initial categories and rater 2 with 5 initial categories (cf. Figure 1). The raters discussed the initial categories and developed a joint set of 5 categories. Some of the categories directly resulted from the respective interview questions. Because of a high level of agreement during the category discussions, no third rater was needed.

3. Results

Among all eighteen participants (100% who met the inclusion criteria and whose interviews were correctly tape-recorded and analysed), fourteen had used illicit AMPH and eight prescription MPH. Four student participants (22.2%) used both prescription and illicit stimulants for academic NE.

For participants' characteristics see Table 1 and one of our previous publications [20]. As described in our previous study on these subjects, SKID interviews revealed that the vast majority (88.9%, 16 of 18 participants) of the participants had current or lifetime diagnoses of misuse or addiction of alcohol, cannabis, or AMPH (see Table 2) [21].

Table 2: Diagnoses of misuse and dependence among all interviewed student participants with the use of a structured clinical interview (SCID-I).

Diagnoses of substance misuse and dependence (total number of users: $n = 20$)	Lifetime (pa	st) diagnoses	Current d	liagnoses
Alcohol misuse	<i>n</i> = 9	45%	n = 7	35%
Alcohol dependence	n = 3	15%	n = 2	10%
Cannabis misuse	n = 5	25%	n = 1	5%
Cannabis dependence	n = 4	20%	n = 1	5%
Amphetamine misuse	n = 2	10%	n = 1	5%
Amphetamine dependence	n = 2	10%	n = 0	0%

Originally 20 student participants had been surveyed by interview questionnaires [21]. 18 were tape-recorded and verbatim-transcribed for further analysis with a qualitative approach based on inductive category development [23]. Table 2 contains all diagnoses regarding substance misuse and dependence; there were no diagnoses of misuse or dependence of further substances.

Category development

Initial categories: rater 1

- Effects
- Modifications in stimulant dosage
- Explicit reference to addiction
- Reflections on how to adequately handle stimulants
- Side effects
- Intake of additional substances with addictive potential

Initial categories: rater 2

- Subjective effects
- Dosage modifications
- Reflections concerning addiction development
- Measures taken to counteract addiction development
- Substances used to fight overdose or hangover



Final joint categories

- Effects
- Modifications in stimulant dosage
- Addiction
- Self-control
- Measures taken to normalize again after stimulant intake

FIGURE 1: Category development.

We analysed contents of the interviews associated with addiction-related issues. In order to present the answers we obtained in more detail, we grouped the answers as follows: (1) effects, (2) modifications in stimulant dosage, (3) participants' evaluation of aspects of addiction, (4) self-control, and (5) measures taken to counteract stimulants' effects and to "normalize" again after stimulant use.

3.1. Effects. All student participants had used stimulants with the intention of NE. Each participant described the subjective effects of stimulant use in a slightly different way. The answers included rather general descriptions of positive cognitive, motivational, and emotional effects such as having increased alertness, being fitter, being in a better mood, experiencing an increase in self-confidence, being more communicative, being better focused, having better concentrated attention, being better motivated, being more vigilant, being more cheerful, being more energetic, experiencing euphoria or euphoric episodes, feeling strengthened, or feeling ready to take on anything. Others said that stimulant use would lead to being less able to respond to criticism, being less sensitive

but more automatic, feeling closer to oneself, being a little bit hysterical or hyped up, being more aggressive, being more distressed, experiencing an increased tendency to do one's own thing, feeling detached, or experiencing an increase in appetite.

In sum, the effects recognized after the use of stimulants for NE described by the participants are interwoven with aspects which favor—at least in parts—the development of addiction.

3.2. Modifications in Stimulant Dosage. In the interviews, we asked the participants whether during the time period when they used stimulants for NE there had been a need to increase the dosage of stimulants in order to maintain the effects. Three participants said yes, whereas twelve answered that there was no need to increase dosage; three were ambivalent regarding dosage.

One of those students who increased dosage said: "At least I felt as if the effect reduced. [...] But I don't know if that actually happened."

According to the answers obtained, the need to increase dosage depends on the method and duration of stimulant intake. Whereas one student stressed that in view of the short duration of intake there was no need for dosage increase, another participant said with regard to AMPH use: "If you take it several days in a row, then you have to increase the dose in order to reach the same effect. Otherwise if there are more than two weeks in between, it's always the same dose." Another student stated that he knew from others about the perceived need to increase dosage and that in view of this he carefully paid attention not to increase dosage: "I really keep an eye on not having to increase the dose, also because I don't want to do so."

3.3. Addiction. When asked whether they believe that the use of stimulants for NE may lead to addiction eleven participants responded "quite likely."

For several participants, the risk of addiction played a considerable role. One student said that the experience of stimulants providing support in one's daily routine might facilitate addiction: "A certain addiction can definitely come up very quickly because it helps someone in their everyday life and with all these pressures to perform an addiction can be expected."

Some of the interviewees distinguished between physical and mental addiction. For most participants, physical aspects of addiction do not seem to be of primary relevance. In contrast, several participants stressed mental aspects of addiction.

One student talked about his impression that high expectations concerning stimulant effects that are not totally fulfilled by subsequent uses may facilitate dependency.

"When I take something for the first time it works perfectly, the second time the effect is actually the same but you already expect it to work as well. But if you already approach it like that, I feel as if the effect was very good the second time, but subjectively a tiny little bit worse than the first time."

3.4. Self-Control. In spite of the fact that a great number of the participants believed that NE substances have some addictive potential, most of them felt that they have things under control. In order to underline this, some interviewees reported having taken measures to counteract the risk of addiction. Several students said that for them it is important to have nonconsumption intervals in between in order to prevent the development of addiction. For example: "Because I wanted to maintain the feeling that I only take the substances when I want to and not because I have to [due to an addiction], I've been taking an abstinence break for almost three months."

Another one said that he introduced nonconsumption intervals "in order to avoid enjoying it too much."

One interviewee stressed reasonableness and pointed out that he is using stimulants very deliberately:

"I do all that very carefully and not because of any addiction. I never got addicted to anything. [...] I always watch out where I get the stuff from."

Another student explicitly mentioned individual responsibility in this context. He said:

"I think it's an important aspect that you can learn how to handle it. And that you can do it in a responsible way. That's why you should only do it occasionally. To me that's one main aspect."

3.5. Measures Taken to Normalize Again after Stimulant Intake. Several participants reported negative effects and problems that occurred following the duration of stimulating effects after stimulant intake. These after-effects include sleeplessness and heightened alertness, but also feelings of depression, lack of energy, and sleep problems.

Some of the interviewees said that, in order to avoid problems related to sleeplessness and heightened alertness that may arise afterwards, they took special measures.

One of them said: "I was a serious chain smoker and drank loads of alcohol in order to calm myself down a little bit"

Other interviewees also talked about illegal drugs and prescription drugs:

"After the last consumption you have to stay awake quite a while until you're tired enough to fall asleep. There is the opposite consumption, you can drink loads of alcohol that works against it, or some smoke weed in order to calm down to then fall asleep."

Another example is: "When I took a really high dose during the day, I took [Zoplicone, Tetrazepam, or Melatonin] to fall asleep. That's pretty strong, which is actually the reason why I don't take it every day."

Another interviewee reported "I always have diazepam at home, which is an antidote for most drugs."

4. Discussion

In the present study, we focused on aspects of addiction among students who used stimulants for NE purposes. Students talked about several aspects of misuse and addiction including desirable effects, dosage of the stimulants used, self-control, and means taken to counteract stimulant effects and to "normalize" again after stimulant use. It is important to stress that the data obtained in this preliminary qualitative study is in no way representative and that, based on the spontaneous answers of the interviewees, we are not able to draw any definitive conclusion on the effects of stimulants for NE in healthy individuals.

Furthermore, the student participants are a self-selected group. In order to avoid attracting students with an urgent need of money, we choose to offer a low to moderate remuneration of thirty Euros. Thus, we do not think that the recruitment process favoured participants with current drug addictions.

The average age of the interviewees of 25.8 years is very high, and two-thirds are male. Possible reasons for this may be that older students experience an increase in pressure to graduate soon or that those who take longer time to finish their studies may tend to seek additional distractions and experiences. It may also be speculated that male students are more prone to experiment. The results obtained are in accordance with data collected by DeSantis and Hane [25], who reported a higher percentage of male students using stimulants for enhancement and a higher incidence in older students. The number of students interviewed is too low to draw any conclusion on whether in certain fields of study a higher percentage of students misuse stimulants than in others. During the period of study recruitment (2009-2010), there have not been any major changes in the university setting that impacted the students' use of stimulants.

In the International Classification of Diseases version 10 (ICD-10) stimulant dependence is described in the ICD-10 F 15.2. Symptoms to diagnose stimulant dependence include the presence of physical and psychological damage, craving, reduced ability to control stimulant use, development of stimulant tolerance with increased dosage for stable stimulant effects, withdrawal symptoms in case of abstinence, and mentally focusing on stimulant use and continued use despite detrimental consequences of stimulant use. In the Diagnostic and Statistical Manual of Mental Disorders (version DSM-IV-TR), AMPH dependence can be found in chapter 304.40 and is diagnosed when an individual persists in AMPH use despite problems related to use of the AMPH; compulsive and repetitive use may result in tolerance to the effect of AMPH and withdrawal symptoms when AMPH use is reduced or stopped. The results of this study have to be considered in view of these diagnostic criteria.

All stimulant-using participants of this study aimed at NE. Beyond that, most of the described types of effects show "pleasant" states that increase the likelihood of using the stimulant again. Among the most significant ones are an increase in self-confidence, euphoric episodes, being more communicative, being fitter, being in a better mood, being better motivated, more cheerful, more energetic, feeling strengthened, and feeling ready to take on anything.

A very important aspect for the diagnosis of addiction according to the ICD-10 and DSM-IV-TR is an increase of dosage because of tolerance development and the perceived need to increase dosage in order to maintain the desired level of stimulating effects. At least in some consumers, stimulant use went along with some adaptation process. Three out of 18 participants said that, during the overall time span of stimulant consumption, there was a need to increase the dosage, and three were ambivalent. It is important to stress that, for those who used stimulants during a longer period of time, the answer to this question might be indicative of some addictive tendency. In contrast, the question concerning dosage increase does not apply to those who used stimulants only once or a few times. The users were well aware of this context. In several interviews, the wish to avoid an increase in dosage was picked out as a central theme.

The majority of the users believed that stimulant use for NE quite likely or definitely may lead to addiction. This is

in accordance with the results obtained in our quantitative survey among high school students and university students [26], according to which more than 90% of the participants believed that NE drugs could lead to addiction.

With regard to the perceived risk of addiction, for the interviewees frequency of use clearly played a role which is in line with the reflections by Compton and Volkow [13]: The perceived risk of addiction was one of the reasons why several users reported on having introduced longer intervals in stimulant administration. Others said that they assume that the risk of addiction would be higher the longer a person uses stimulants for NE.

Concerning the risk of addiction, the students stressed mental aspects of addiction, whereas they did not consider the risk of physical addiction to be considerable. Strikingly, with regard to a perceived risk of addiction, several students confidently talked about having control over the situation. They reported intentionally having introduced intervals in which they did not take stimulants in order to avoid becoming addicted, or they cited other measures taken to avoid having to increase the dosage. Several users asserted that they control the situation and that the substance does not control them, be it by some addictive potential or by the perceived need to use it. The underlying ideas seem to be as follows: I am strong enough to withstand becoming addicted and I want to autonomously decide on whether or not to take the drug.

Apart from the participants' subjective beliefs regarding their self-control of the use of MPH and AMPH for NE, objective diagnoses using SKID interviews show very high rates of current or lifetime misuse and addiction with regard to alcohol, cannabis, and AMPH on the one hand. On the other hand, there were only one participant diagnosed with current AMPH misuse and no participant diagnosed with current AMPH dependence. It is important to stress, however, that we do not know whether the reason for current lack of AMPH dependence and scarce diagnoses of current AMPH misuse is due to the fact of efficient self-control or the fact that the participants currently do not use any stimulants for NE. Therefore, more research is needed to analyze the risk of developing stimulant misuse and/or dependence in the context of using stimulants for NE.

In the interdisciplinary debate on NE, ethical issues concerning risks and benefits, fairness, justice, cognitive liberty, autonomy, authenticity, and personal identity are intensively discussed [27]. Individual autonomy is one of the key concerns; such concerns imply that it is up to the individual person to decide freely on whether or not to modify one's brain chemistry [28, 29]. NE drugs' addictive potential may curtail individual autonomy in a highly problematic way, for addiction clearly undermines a person's capacity to autonomously decide on whether or not to use NE drugs [30, 31]. The users in our study clearly experience this threat to autonomy.

Heinz et al. (2012) suggest that any risk of addiction associated with the use of stimulants for NE will result in a very unfavourable risk-benefit ratio for these kinds of NE and will be a central ethical argument against running clinical trials on NE [10]. Despite their acknowledgement of

the risk of addiction, a considerable part of the interviewees nevertheless continued using these substances. One reason for their continued use may be the self-reassuring strategies described above and their impression of having control over the situation. The putative subjective benefits of NE, which may lead participants to accept the risk-benefit ratio, serve as another explanation.

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In any case, in spite of the risks involved, the users voluntarily enroll in some kind of self-experiment on the effects and side effects of NE. Some users stressed individual responsibility and argued that they use stimulants for NE in a responsible way as long as they have control over the situation and avoid getting addicted or having unforeseen side effects. These attitudes lead us to the question: Is pharmacological NE something that can be done in a responsible way? It seems that at least some NE consumers do assume this.

In sum, the risk of addiction and the need to find an adequate strategy in order to prevent addiction matter considerably to the interviewees. This is in accordance with Hall and Lucke who noted that MPH is under "legal control because of the high rates of dependence and adverse effects experienced by regular users" [32]. According to Forlini and Racine, as well as Partridge and colleagues, beneficial effects of stimulants for NE are widely portrayed in the media while the risk of dependence is underreported [33, 34]. The results obtained in this study give a clear hint to the need to pay more attention to the addictive potential of stimulants used for NE.

In addition, the after-effects of stimulant intake have to be taken into consideration. Here, the users reported on a broad spectrum of effects from heightened alertness and sleeplessness to depressive periods and lack of energy. Some users reported on having taken measures after stimulant intake to "normalize," which include drinking alcohol, smoking cannabis, or taking benzodiazepines. Such consumption carries the potential for further individual and health problems, such as polytoxicomania. Furthermore, these extra measures to normalize point to the negative influence that coingestion of other drugs may have the risk of developing dependence. Taken together, in order to adequately consider the effects of drug use for NE on the individual persons involved, it is important to take into account the pharmacological aftereffects as well as additional drugs used in order to normalize again.

5. Conclusion

In the present interview study, the student participants used stimulants with the aim of NE. The risk of addiction by stimulant use played a considerable role in the answers obtained. Taken together, the subjects reported on a broad spectrum of aspects of addiction related to stimulants used for NE, including an awareness of the fact that stimulants imply a potential risk of addiction. Even if the participants are well aware of this fact, they evaluate the risk as being considerably low for themselves. Furthermore, several interviewees talked about strategies that serve as a means to control stimulant use and to counteract stimulant dependence. Behavior and beliefs of the students in our sample appear to be risky

in terms of addiction development. However, long-term empirical research is needed to estimate the true addiction risk of stimulant use for NE and to characterize factors associated with a high risk of becoming addicted.

Conflict of Interests

All authors declare to have no competing interests.

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Research Article

The Effect of Nicotine Dependence on Psychopathology in Patients with Schizophrenia

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Introduction. Our study aims to determine the prevalence of nicotine dependence and investigate the effect of nicotine dependence on psychopathology among schizophrenia patients. *Methods*. A cross-sectional study was carried out in an outpatient psychiatric clinic at a general hospital in Malaysia. 180 recruited subjects were administered the Malay version of Mini International Neuropsychiatric Interview (MINI), the Positive and Negative Symptom Scale (PANSS), and the Malay version of Fagerstrom Test for Nicotine Dependence (FTND-M) questionnaires. *Results*. The prevalence of nicotine dependence among the subjects was 38.1% (n = 69) and they were mainly composed of male gender, Malay ethnicity, being treated with atypical antipsychotics, and taking other illicit drugs or alcohol. Subjects with severe nicotine dependence scored less in the negative subscale of PANSS compared with the nonsmokers (P = 0.011). On performing the hierarchy multiple regressions, dependence status still significantly predicted negative scores after adjusting the confounders (t = -2.87, P = 0.005). *Conclusion*. The rate of nicotine use disorder among schizophrenia patients in this study is higher than that of the general population in Malaysia. The significant association between nicotine dependence and negative psychopathology symptoms will help the healthcare practitioners in their management of nicotine dependence among schizophrenia patients.

1. Introduction

Schizophrenia is a severe and disabling mental illness [1]. Persons with schizophrenia are at high risk of shorter life expectancy [2–4], due to the increased mortality related to circulatory and respiratory diseases, with chronic cigarette smoking being a major contributory factor [5, 6].

Worldwide statistics have shown that smoking contributes significantly to mortality [7, 8], with nicotine being more addictive than alcohol, marijuana, or cocaine [9]. Compared to the general healthy population, the prevalence of smoking is found to be much higher among people with psychotic disorders [10–12] and, among those suffering from schizophrenia, the occurrence of smoking and nicotine dependence is higher than that of both the general population and those with other mental illnesses [13–17]. Schizophrenic

patients who smoke tend to have higher frequency of heavy smoking [8, 12], with rates ranging from 60% [16] to as high as 80% [18]. In addition, they are less likely to quit smoking [12, 19–22]. Hence, it is not surprising that smokers with psychiatric disorders suffer higher rates of morbidity and mortality secondary to smoking related illnesses [22, 23].

Smoking is the leading preventable cause of morbidity and premature mortality [24–26]. In Malaysia, one out of every five deaths is related to smoking. This is significant as smoking is the most important modifiable cause of premature death, responsible annually for an estimated 120,000 years of potential life loss [27]. The objective of this study is therefore to assess the prevalence of smoking and nicotine dependence among schizophrenic patients in a general hospital and to determine its associated factors, including the severity of illness.

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2. Methods

180 patients were recruited from the outpatient psychiatric clinic in a general hospital from August to November, 2011, via purposive sampling method. The clinic had two follow-up sessions each week, with an average of 100-160 patients, and it covered a wide spectrum of psychiatric cases. It was estimated that 50-60% of the attendees met the diagnosis of schizophrenia. Inclusion criteria were patients who (a) met DSM-IV-TR [28] criteria for schizophrenia, (b) were at least 18 years of age, (c) provided informed consent, and (d) were able to understand and communicate in English or Bahasa Malaysia in order to complete the study measurements. Exclusion criteria were those who (a) had Axis I diagnosis other than schizophrenia or substance use disorder, (b) had an organic mental disorder, (c) had a diagnosis of mental retardation, (d) were experiencing unstable general medical conditions, and (e) were grossly psychotic and unable to cooperate with the interviewer. All patients who were identified as having schizophrenia in the clinic were approached. Written informed consent was obtained from patients who chose to participate in the study, after the discussion of study details with the researcher. 19 patients were excluded due to various reasons. The study was conducted in accordance with the Declaration of Helsinki and the National Medical Research Registry of the Ministry of Health and The Ministry of Health Medical Research Ethical Committee, which approved and monitored the study (Ethical committee reference no. NMRR-11-697-9166).

The study was conducted by a single interviewer who was trained in the use of the study instruments. A demographic and clinical data sheet was used to aid in the collection of the variables addressed in the study which, among others, included gender, ethnicity, medication use (typical or atypical antipsychotic), and history of substance use (lifetime use of alcohol, opioid, metamphetamine, cannabis, and ecstasy). This information was gathered via direct interview and/or review of patient's clinical records. The subjects were administered the Malay version of Mini International Neuropsychiatric Interview (MINI), the Positive and Negative Symptom Scale (PANSS) to rate the symptoms of schizophrenia [29], and the Malay version of Fagerstrom Test for Nicotine Dependence (FTND-M) [30]. The interview was completed with the subjects performing a breath test to measure the levels of carbon monoxide in their exhaled air, by using the simple handheld breath analyzer (piCO+ Smokerlyzer). This instrument provided a direct measure of the carbon monoxide in parts per million (CO ppm). The MINI is a short structured diagnostic interview for researchers to accurately determine the presence of any psychiatric disorders according to DSM-IV or ICD-10 [31, 32]. It was administered in either English or in the Malay language, according to the patient's preference and main spoken language. Previous research has shown that 39.4% of smokers failed to meet the DSM-IV-TR criteria for nicotine dependence [33]. Hence, the FTND-M was used to assess the nicotine dependence among schizophrenia patients in this study. This easy-to-use self-report questionnaire is noninvasive, low-cost, and easy to score and has good validity and reliability for determining

nicotine dependence among the smokers [30]. In our study, the patients were categorized as nicotine dependent if they had a score of more than two of that on the FTND-M [30]. Furthermore, all the nicotine-dependent patients were further classified as having high/severe dependence (FTND-M > 6) or mild-moderate dependence (FTND-M \leq 6), as defined in previous studies [34, 35].

2.1. Statistical Analysis. Analyses of data were performed using the Statistical Package for Social Studies (SPSS) to generate the relevant descriptive epidemiological statistics. Differences between nicotine dependence and nonnicotine dependence on categorical variables were tested using either the chi-squared test or Fisher's exact test. To examine the relationship between nicotine dependence and psychopathology (PANSS), multivariate general linear model approach was used, with covaried gender, ethnicity, use of atypical antipsychotic medication, and comorbid use of illicit drug or alcohol, with familywise error multiple testing corrections where appropriate. A bootstrap analysis was conducted, using Preacher and Hayes' indirect macro for SPSS, to examine the indirect effect of nicotine dependence (independent variable) and psychopathology (dependent variable). For each analysis, 1000 random samples of the original size were taken from the obtained data, replacing each value as it was sampled. Statistical significance was evaluated at the <0.05 level using two-sided test.

3. Results

The study group comprised predominantly males (64.1%, n=116) with the mean age of 41.5 years old (SD = 11.41). The current prevalence of nicotine dependence in the study subjects was found to be 38.1% (n=69). The exhaled carbon monoxide in parts per million was correlated positively with FTND-M scores (Pearson's rho = 0.739, P<0.01). The mean number of cigarettes smoked in the sample was 17 sticks per day. Among the subjects who were smoking, they have been smoking for a mean of 19.94 years and they have started smoking at the mean age of 19.7 years (SD 6.25). In 37% of the subjects, there was a positive family history of smoking. Sociodemographic characteristics and clinical details, according to smoking status, are shown in Table 1.

Multivariate analysis of covariance was used to examine the relationship between nonsmokers (n=112, 61.9%), smokers with severe nicotine dependence (n=21, 11.6%), mild-moderate nicotine dependence (n=48, 26.5%), and PANSS scores, while controlling the gender, ethnicity, use of atypical antipsychotic medication, income, and comorbid using illicit drug or alcohol (Table 2). The nicotine dependence status was significantly associated with the PANSS scores (Wilk's lambda 0.898; F(2.37)=2.78; P=0.017). We conducted pairwise comparisons of the total and subscale PANSS scores between nonsmokers, those with mild dependence and those with severe dependence, using Bonferroni familywise error multiple testing corrections. Those with severe nicotine dependence scored less in the negative subscale compared to that of the nonsmokers

TABLE 1: Sociodemographic characteristics and clinical features according to nicotine dependence.

Characteristics	Nicotine dependence	Nonnicotine dependence	Statistic	P	OR/mean difference (95% CI)
	n = 69	n = 112			(95% C1)
Age, years: mean (s.d.)	39.6 (10.8)	42.6 (11.6)		0.087	
Male, <i>n</i> (%)	68 (98.6)	48 (42.9)	$\chi^2 = 57.5$	**<0.001	90.6 (12.1-676)
Ethnicity, n (%)					
Malay	41 (49.4)	42 (37.5)			
Chinese	20 (29)	50 (44.6)	$\chi^2 = 8.3$	**<0.001	
Indian	8 (11.6)	20 (17.90)			
Duration of illness, years: mean (s.d.)	13.9 (10.4)	15.6 (9.8)		0.287	
Atypical antipsychotic, n (%)	46 (66.7)	53 (53.5)	$\chi^2 = 6.4$	**0.014	2.23 (1.19-4.15)
Chlorpromazine equivalents (mg), mean (s.d.)	276.8 (190.6)	291.1 (487.0)		0.816	
Taking illicit drugs/alcohol, n (%)	19 (27.5)	2 (1.8)	$\chi^2 = 27.6$	**<0.01	0.05 (0.01-0.21)
Fagerstrom Test for Nicotine Dependencescore, mean (s.d.)	4.16 (2.36)	_			
CO ppm (s.d)	13.91 (7.16)	2.22 (0.65)		**<0.01	11.69 (9.97–13.42)
Marital status, n (%)					
Single	50 (72.5)	72 (64.3)		0.22	
Divorced	2 (2.9)	1 (0.9)			
Married	17 (24.6)	39 (34.8)			
Employment, n (%)					
Employed	41 (59.4)	55 (49.1)		0.22	
Unemployed	28 (40.6)	57 (50.9)			
Total income, n (%)					
≤RM500	43 (62.3)	92 (82.1)		*0.014	11.35 (0.011-0.017)
RM501-1000	15 (21.7)	15 (13.4)			
RM1001-2000	6 (8.7)	2 (1.8)			
RM2001-3000	4 (4.8)	3 (2.7)			
>RM3000	1 (1.4)	0			
Education level, <i>n</i> (%)					
Primary	10 (14.5)	15 (13.4)			
Secondary	53 (76.8)	75 (67)		0.22	
College/university	6 (8.7)	21 (18.8)			
No education	0	1 (0.9)			

^{*}P < 0.05, **P < 0.01, s.d. = standard deviation, OR = odds ratio, CI = confidence interval, and CO ppm = carbon monoxide in parts per million.

(P = 0.015). On performing the hierarchy multiple regressions, dependence status still significantly predicted negative scores after adjusting the confounders (t = -2.87, P = 0.005).

4. Discussion

Based on all the literature reviewed, prevalence of smoking is found to be high among people with schizophrenia and our current study found a similar pattern. The prevalence of nicotine dependence found in this study was 38.1% (n=69) with the subjects being more likely to be male and from the Malay ethnic group. They were also more likely to be taking illicit drugs or alcohol and were on atypical antipsychotic

treatment. The findings of this study showed that subjects with severe nicotine dependence had less severity in negative symptoms compared to the nonnicotine dependent subjects.

The smoking rate of this study was much lower than it was reported in some studies done in the west [8, 16, 36] and among schizophrenic patients in a Chinese population [37]. The possible reason for the lower prevalence of nicotine use disorder in this study could be related to the lower prevalence of nicotine use among the Malaysian general population, estimated to be 23.1%, compared to other countries, which ranged from 27% to 43.3% [38].

There has been no study on ethnicity, though the National Health and Morbidity Survey 1996 found that Malay men were more likely to smoke [39]. Other studies have shown

	Nonsmoker	Mild-moderate nicotine dependence	Severe nicotine dependence	N – M Mean difference	N – S Mean difference	M – S Mean difference
	n = 112	n = 48	n = 21			
Total PANSS score, mean, amean	49.13	51.56	51.43	0.62	1.16	0.54
(s.d)	50.33 ^a (10.28)	49.71 ^a (12.21)	49.17 ^a (9.22)	(P = 0.98)	(P = 0.95)	(P = 0.97)
Positive subscale score, mean,	8.54	9.65	9.76	-0.09	-0.04	0.05
amean (s.d)	8.94 ^a (2.64)	9.04° (3.09)	8.99 ^a (3.93)	(P = 0.88)	(P = 0.95)	(P = 0.98)
Negative subscale score, mean,	18.01	17.13	14.67	1.89	4.54	2.64
amean (s.d)	18.41 ^a (5.67)	16.52 ^a (6.45)	13.87 ^a (4.48)	(P = 0.26)	$(^*P = 0.011)$	(P = 0.06)
General psychopathology	22.70	24.02	24.14	0.50	0.65	0.14
subscale score, mean, amean (s.d)	23.42 ^a (4.13)	22.92 ^a (6.27)	22.77 ^a (7.07)	(P = 1)	(P = 1)	(P = 1)

TABLE 2: Hierarchical multiple regression between smoking severity and PANSS scores.

N, nonsmoker; M, mild-moderate nicotine dependence; S, severe nicotine dependence; and PANSS = Positive and Negative Syndrome Scale. $^*P < 0.05, ^{**}P < 0.01, s.d = standard deviation.$

similar male preponderance [10, 37], concurrent hazardous use of alcohol and other illicit drugs [8, 11, 15], with studies suggesting that smoking is a reliable clue for other substance use and abuse [8] including alcohol [40, 41].

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Smoking alters the level and effectiveness of medications in the blood, as it is hypothesized that nicotine interacts with many of the same central pathways thought to be abnormal in persons with schizophrenia [8, 36, 42]. Smoking also increases the metabolism of neuroleptics [43-45], with studies showing that individuals with schizophrenia and smoking tend to receive consistently higher doses of antipsychotics compared to nonsmokers [14, 46, 47]. The choice of pharmacological treatment is likely to have influence on smoking behavior [48], as earlier studies found that typical antipsychotics were associated with increased smoking in some individuals [49, 50] and they had greater difficulty to quit smoking [36]. Several reports have suggested that atypical antipsychotics, namely, clozapine, have helped in the reduction of smoking among schizophrenic smokers who have switched to this medication [51, 52]. In a small group of patients with schizophrenia or schizoaffective disorder, who were treated with transdermal nicotine patches and atypical or typical antipsychotic medications, George et al. [36] found a more favorable cessation rates among smokers who had received risperidone and olanzapine, compared to those on typical antipsychotics.

The literature is divided into smoking and symptoms of schizophrenia [10, 53]. In this present study, subjects who were severely nicotine dependent scored less in the PANSS negative symptoms. This finding seemed to be in agreement with other previous studies which showed that smokers had lower negative symptoms [6, 54–56]. A preclinical trial came up with evidence that nicotine affected several neurotransmitter systems, including dopamine, glutamate, and γ -aminobutyric acid (GABA), and certain neurocognitive deficits associated with these neurotransmitters

improved after nicotine was administered in patients with schizophrenia. However, dopamine has been found to be the most implicated when the relationship between nicotine use and negative symptoms was studied [57]. By stimulating the release of dopamine in the nucleus accumbens and prefrontal cortex, nicotine reduces the negative symptoms of schizophrenia, explaining its use as a form of self-medication [58]. These positive effects could be an important mechanism that explains the comorbidity of schizophrenia and nicotine dependence [59].

Our study has several limitations that need to be high-lighted. Firstly, as the information collection was done via self-reporting, it raised the possibility of underestimating the other substances. Secondly, it was not possible to identify a causal relation between the association of smoking and nicotine dependence and other variables because of the cross-sectional design of this study. Thirdly, there was no comparison made with a control group. Nevertheless, our study was able to prove that smoking is not only prevalent among the study subjects but reflects the severity of patients' illness.

5. Conclusion

The rate of nicotine use disorder among schizophrenia patients in this study is higher than that of the general population in Malaysia. Although causal links cannot be inferred, our study found a significant association between nicotine dependence and negative psychopathology symptoms, which will be an added value for the healthcare practitioners in their management of nicotine dependence among schizophrenic patients.

Conflict of Interests

The authors declare no conflict of interests in this paper.

^aMultivariate analysis of covariance with PANSS total score and subscale scores as dependent variables; covariates appearing in the model are evaluated at the following values: gender = 1.36, ethnicity = 1.70, drug and alcohol abuse = 1.12, income = 1.25, and atypical antipsychotic = 1.55. These tests are based on the linearly independent pairwise comparisons among the estimated marginal means and adjusted for multiple comparisons using Bonferroni familywise error correction.

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Research Article

Revictimization of Violence Suffered by Those Diagnosed with Alcohol Dependence in the General Population

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Objective. To verify the association between violence and alcohol dependence syndrome in sample populations. Method. Population-wide survey with multistage probabilistic sample. 3,744 individuals of both genders, aged from 15 to 75 years, were interviewed from the cities of São Paulo and Rio de Janeiro using the Composite International Diagnostic Interview (CIDI 2.1). Results. In both cities, alcohol dependence was associated with the male gender, having suffered violence related to criminality, and having suffered familial violence. In both cities, urban violence, in more than 50% of cases, and familial violence, in more than 90% of cases, preceded alcohol dependence. The reoccurrence of traumatic events occurred in more than half of individuals dependent on alcohol. In São Paulo, having been diagnosed with PTSD is associated with violence revictimization (P = 0.014; Odds = 3.33). Conclusion. Alcohol dependence syndrome is complexly related to urban and familial violence in the general population. Violence frequently precedes alcoholism, but this relationship is dependent on residence and traumatic events. This vicious cycle contributes to perpetuating the high rates of alcoholism and violence in the cities. Politicians ordering the reduction of violence in the large metropolises can, potentially, reduce alcoholism and contribute to the break of this cycle.

1. Introduction

Disorders related to alcohol are included in the ten most important issues in public health worldwide; alcohol dependence syndrome is the fifth most incapacitating disease in the Americas and Europe [1]. Within those factors that can be highlighted that make this disease so incapacitating is the relationship between alcoholism and the occurrence of accidents and violence [2].

The association between alcohol use and accidents occurs frequently, especially in traffic [3, 4]. Among individuals involved in traffic accidents, 61% tested positive for alcohol, of which 56% were run over and 70% were victims of shock and vehicle rollover [5]. In the city of Recife, during the popular party Carnival, 88% of victims who died in traffic accidents tested positive for alcohol [6].

On the other hand, having been a victim of a traumatic situation and the development of pathological use of alcohol

have also been found to be related [7]. Experiencing violence during childhood [8] and witnessing violence during childhood [9] have been identified as precursors to alcoholism in adults. The relationship between alcohol use, violence, and diverse psychiatric disorders, including Posttraumatic Stress Disorder (PTSD), has been shown in population-wide studies [3].

Although it is clear that some traumatic events, such as accidents, are associated with a rise in the improper use of alcohol, the relationship between alcohol use and violent traumas is not so clear. The discussion of whether violent traumas precede or are triggers of alcohol dependence syndrome and predispose individuals to revictimization has been the focus of several studies [8, 10, 11]. In this sense, the focus of the present study was to investigate these relationships using data collected from the "Epidemiological Study of Violence and Post Traumatic Stress in the Cities of São Paulo and Rio de Janeiro" [12].

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2. Methods

With 11,244,369 and 6,323,037 habitants, respectively, São Paulo and Rio de Janeiro are the two most populated metropolises in Brazil and are also among the most violent cities in the country [13]. In 2003, the average rate of homicides in these cities was 47.13 and 44.3 per 100,000 habitants, respectively, while the rate in the country was 28.6. Like the social indicators, the homicide rates vary considerably within the cities; for example, in 2003, the rates varied between 2.90 and 88.20 within the 96 administrative districts of São Paulo and between 0 and 91.77 within the 33 administrative regions of Rio de Janeiro [14–16].

Between June 2007 and July 2008, a cross-sectional, epidemiological study was conducted in one phase in these two cities, with the multistage probabilistic sample representative of the population aged 15 to 75 years. A company specialized in household surveys, the Brazilian Institute of Public Opinion and Statistics (IBOPE), was hired to carry out the fieldwork, under supervision of the authors, members of the CIDI Training Center WHO/Brazil/UNIFESP. The authors had open access to the team of raters engaged in the project and were responsible for the training. The training course comprised a 30-hour theoretical and practical module [12].

To select the sample, different areas of the cities were classified according to homicide rates and later divided into seven groups (1 = less than 10 homicides per 100,000 habitants; 2 = 10.01 to 20; 3 = 20.01 to 30; 4 = 30.01 to 40; 5 = 40.01 to 50; 6 = 50.01 to 60; 7 = more than 60 homicides per 100,000 habitants). Then, all of the census-based sectors within each group were mapped and randomly drawn. The number of census-based sectors within each group varied between 4 and 18, according to the size of the population in each group. In each census-based sector, 43 cases (São Paulo) and 30 cases (Rio de Janeiro) were randomly selected. In each residence selected, all of the residents aged between 15 and 75 were identified and later chosen using the Kish method. In São Paulo, the three most violent groups were oversampled [16].

The study from the Millennium Institute included a protocol containing 13 instruments [12]. For the present paper, the following instruments were used: (1) sociodemographic questionnaire and (2) Composite International Diagnostic Interview, CIDI 2.1 (OMS), the validated version in Brazil [17, 18].

The psychiatric diagnoses rated in the present study were as follows: (a) alcohol dependence syndrome and (b) Posttraumatic Stress Disorder (PTSD). The rating was done with version 2.1 of the Composite International Diagnostic Interview (CIDI 2.1), lifetime version, which is a structured interview that generates psychiatric diagnoses using the diagnostic criteria of the International Classification of Diseases (ICD-10) and of the Diagnostic Statistical Manual (DSM-IV). The Brazilian version of the CIDI 2.1 was translated and validated by Quintana et al. [17], with sensitivity and specificity for disorders secondary to alcohol use (79.5% e 97.3%). When compared with the Structured Clinical Interview (SCID), the PTSD section of the CIDI 2.1 presented a sensitivity of 82.4% and a specificity of 84.8%, using the criteria from the ICD-10 and sensitivity of 51.5% and specificity of 94.1% for the criteria

of the DSM-IV [18]. The diagnoses were generated with a diagnostic algorithm from CIDI 2.1 using the diagnostic criteria from the DSM-IV. The list of traumatic events on the CIDI 2.1 was revised and adapted and 18 new events were added to the original 11 events, adding an evaluation on the intensity of the event, number of times, and ages of the first and last occurrences for each of the 29 events. The standardization, reliability, and validating of the included events were published by Quintana et al. [19]. The events were considered severely traumatic if the interviewee rated the level of intensity of the event as 5 on a scale from 1 to 5.

To group the traumatic events, the authors modified Breslau's classification [20]. The class "assaultive violence" was divided in family violence, sexual crime, spousal violence, criminal violence, and new forms of crime-related violence, which includes the events related to the criminal organization PCC and to being threatened via telephone.

The statistical procedures were executed with Statistical Package for Social Sciences (SPSS, 19th version) for Windows and STATA version 10.0. Due to the multistage, stratified design and the oversampling of the most violent areas, all of the analyses were weighted to control for the effect of the different probabilities of selection in each stage, via a calculation for complex samples done on STATA.

The statistical analyses, both exploratory and inferential, were completed with a sample divided by location of the interview. Through contingency tables, the association between alcohol dependence syndrome and sociodemographic data, severe traumatic events (indicated by a rating of 5), and PSTD was verified. To further evaluate the temporal relationship of the association between alcohol dependence syndrome and traumatic events, variables were generated based on the age of onset of alcohol dependence syndrome and the age of the first and most recent traumatic events.

Severe traumatic events that were found to be significantly associated with alcohol dependence syndrome were grouped based on the temporal relationship between the traumatic event and the onset of the syndrome, respecting the coherence of the nature of the events, resulting in the grouping displayed in Table 1.

From the results described above, two models of logistic regression were elaborated on using alcohol dependence syndrome as the dependent variable. The first model was carried out with the entire sample, including traumatic events and sociodemographic data. The second model included PTSD and was carried out with only those interviewees who suffered a severe traumatic event.

To evaluate the temporal relationship between the occurrence of traumatic events and the establishment of alcohol dependence syndrome, variables considering the age of onset of alcohol dependence syndrome and the age of the first and most recent traumatic event were used to create the groups described above. Finally, another variable was generated, based on the age of onset for alcohol dependence syndrome and the age of the first and most recent traumatic event, grouping all of the traumatic events significantly associated with alcohol dependence syndrome. This variable was compared with sociodemographic data and PTSD through contingency tables and later a logistic regression.

TABLE 1: Grouping of traumatic events related to alcohol dependence syndrome.

- (1) Accidents
 - (a) Suffering a life-threatening car or motorcycle accident
 - (b) Suffering another type of life-threatening accident
- (2) Violence and criminality
 - (a) Physically assaulted or attacked without weapon
 - (b) Surrendered, assaulted, or threatened with a weapon
 - (c) Maintained in captivity or kidnapped
 - (d) Tortured or being victim of terrorism
 - (e) Threatened with death
 - (f) Being victim of gang wars or drug traffickers
 - (g) Being home when an intruder attempted to invade your home
 - (h) Witnessing someone suffer a severe, life-threatening injury or witnessing someone being killed
 - (i) Witnessing gunfire
 - (j) An intruder attempted to invade your home when you were not at home
 - (k) Seeing a corpse, except at funerals, or had to touch a corpse for any reason
 - (l) Seeing atrocities or carnages, such as mutilated corpses or killings
- (3) New forms of crime-related violence
 - (a) Witnessing or suffering consequences from attacks of the First Capital Command, PCC^{1,2};
 - (b) Becoming stressed with the attacks of PCC
 - (c) Being threatened via telephone
- (4) Sexual crime
 - (a) Rape, which is when someone has had a sexual relationship with you that you did not want or threatened you or used force
 - (b) Being abused sexually, which is when someone touches you or feels your genitals when you did not want this
- (5) Family violence
 - (a) A family member beat you with enough force to cause injuries
 - (b) Witnessing during childhood a severe fight with physical aggression at home
- (6) Illness or death of a person close to you
 - (a) Nonviolent sudden death of a person close to you
 - (b) Relative or close friend had a life-threatening illness or injury
- (7) Spousal violence: physically assaulted by a spouse
- (8) Getting beaten by someone else (except spouse or family)

3. Results

The final sample included 2,536 interviews in São Paulo and 1,208 in Rio de Janeiro, with corresponding rates of response of 84.5% and 80.5%, respectively.

Among the interviewees in both cities, the predominant gender was female (57.7%, IC = 55.7–59.6) as well as individuals who were married or cohabitating (55.5%, IC = 53.5–57.4). In regard to age, 21.4% (19.8–23.1) of the interviewees were in the third decade of life, and 22.7% (21.0–24.3) were in the fourth decade of life. With regard to education, 39.5% (37.6–41.5) of the interviewees had between nine and twelve years of study. Almost half (44.8%, IC = 42.9–46.8) of the interviewees

reported histories of migration, the majority of interviewees (59.2%, IC = 57.2-61.1) were employed, and less than one-third (23.4%, IC = 21.8-25.1) reported a family history of mental illness (Table 2).

In São Paulo, 9.3% (7.1–11.5) of men were diagnosed with alcohol dependence syndrome, and 3.3% (2.2–4.4) of women were diagnosed, totalling 5.8% (4.7–6.9) across genders. In Rio de Janeiro, 8.8% (6.0–11.5) of the men were diagnosed, and 4.2% (2.6–5.9) of the women were diagnosed, totaling 6.2% (4.7–7.7) across both genders. When considering disorders related to alcoholism and the occurrence of alcohol dependence syndrome and/or alcohol abuse, the lifetime prevalence was as follows: in São Paulo, 22.2% (18.3–26.1) in

¹This question and the following question refer to the wave of violence against security forces and some civil targets organized by the criminal organization "First Capital Command" (PCC), originating in the city of São Paulo on May 12, 2006, which subsequently spread through the state of São Paulo and other states in Brazil. For two days, the city of São Paulo became immersed in an intense climate of terror which caused the closing of commercial establishments and the emptying of the streets even during business hours.

²For interviews conducted in Rio de Janeiro, the question was modified to include an active criminal organization equivalent to PCC that, during the sequence of events in São Paulo, perpetrated violent acts against the population, such as assaults on mass transit, followed by lighting a bus on fire with passengers aboard.

Table 2: Sample distribution sociodemographic characteristics (n = 3,744).

	São Paulo	Rio de Janeiro	Total
	% (95% IC)	% (95% IC)	% (95% IC)
Gender			
Masculine	41.9 (39.5-44.3)	43.4 (40.3–46.5)	42.3 (40.4-44.3)
Feminine	58.1 (55.7–60.5)	56.6 (53.5–59.7)	57.7 (55.7–59.6)
Age (years)			
15–19	8.5 (7.2-9.7)	8.4 (6.7–10.1)	8.4 (7.4-9.5)
20-29	22.9 (20.8–24.9)	17.9 (15.5–20.2)	21.4 (19.8-23.1)
30-39	23.9 (21.8–25.9)	19.6 (17.2–22.0)	22.7 (21.0-24.3)
40-49	17.1 (15.3–19.0)	19.9 (17.4–22.4)	17.9 (16.4–19.4)
50-59	15.7 (13.8–17.5)	16.4 (14.1–18.7)	15.9 (14.4-17.4)
60-69	8.1 (6.8–9.5)	11.6 (9.6–13.6)	9.1 (8.0-10.3)
70–75	3.9 (2.9-4.9)	6.3 (4.7–7.8)	4.6 (3.7-5.4)
Average (standard deviation)	39.5 (38.7-40.3)	42.4 (41.3-43.4)	40.3 (39.7–40.9)
Marital status			
Single	28.3 (26.1–30.5)	31.4 (28.4–34.3)	29.2 (27.4-31.0)
Married/cohabitating	56.9 (54.5–59.3)	51.9 (48.9-55.0)	55.5 (53.5-57.4)
Separated/divorced	9.0 (7.6–10.4)	10.7 (8.8–12.7)	9.5 (8.3-10.6)
Widowed	5.8 (4.6-7.0)	6.0 (4.5–7.5)	5.9 (4.9-6.8)
Education			
0 to 4 years	20.0 (18.1–21.9)	14.6 (12.4–16.8)	18.5 (17.0-20.0)
5 to 8 years	25.5 (23.4–27.6)	23.1 (20.4–25.7)	24.8 (23.2–26.5)
9 to 12 years	38.9 (36.5–41.3)	41.1 (38.1–44.2)	39.5 (37.6-41.5)
13 years and older	15.6 (13.7–17.5)	21.2 (18.7–23.7)	17.2 (15.6–18.7)
Employment status			
Currently employed	60.3 (57.3–62.7)	56.4 (53.3–59.6)	59.2 (57.2-61.1)
With income	59.0 (56.5–61.5)	55.5 (52.0-58.3)	57.9 (55.9–59.9)
Migration history			
Migrant	50.0 (47.6-52.5)	31.7 (28.8–34.6)	44.8 (42.9-46.8)
Family history of psychiatric disorder			
Yes	22.1 (20.1–24.2)	26.7 (23.9–29.4)	23.4 (21.8-25.1)

men, 4.9% (3.9–5.9) in women, and 14.2% (12.1–16.3) in both genders; in Rio de Janeiro, 24.3% (19.7–28.9), 9.6% (6.6–12.7), and 17.4% (14.2–20.5), respectively. These prevalence rates were similar in both cities, predominantly in males (P=0.000), except when examining alcoholism in women, which was almost twice as high in Rio de Janeiro compared to São Paulo (P=0.005). However, when considering just alcohol dependence syndrome, there is no significant difference between women in Rio de Janeiro and São Paulo.

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In general, 86.4% of interviewees reposted the occurrence of at least one traumatic event in their lifetime. When considering traumatic events self-reported as severe (rated as 5 on a 1–5 scale), 64.9% (62.2–67.3) of interviewees in São Paulo reported a severe traumatic event, 60.8% (57.1–64.4) of men and 67.9% (64.9–71) of women. In Rio de Janeiro, 66.9% (64–69.9) of interviewees reported a severe traumatic event, 61.1% (56.5–65.7) of men and 71.4% (67.6–75.2) of women. There was no significant difference between the two cities (Table 3).

In the logistic regression model carried out in the total sample, including traumatic events and sociodemographic data, alcohol dependence syndrome was associated with males, younger age, less education, having suffered a severe, life-threatening accident, having suffered criminal violence and familiar violence, and having been beaten by a person outside the family in São Paulo. In Rio de Janeiro, alcohol dependence syndrome was associated with males, being single, having suffered criminal violence, having suffered violence associated with new types of crime, and having suffered familial violence. See Table 4.

In the second model, which included PTSD and was carried out with only those interviewees who reported having suffered a severe traumatic event, similar associations were found in both cities, and PTSD was found to be related to alcohol dependence syndrome in São Paulo (P=0.016; Odds = 1.885; IC = 1.128–3.15).

In the analysis of the temporal relationship between the occurrence of traumatic events associated with alcohol dependence syndrome and the onset of this syndrome, it was found that a large portion of traumatic events occurred before the onset of alcohol dependence syndrome in both cities. The exception was found with events grouped as "new

Table 3: Prevalence of traumatic events (n = 3,744).

		São Paulo			Rio de Janeiro	
	Males	Females	Total	Males	Females	Total
	% (95% IC)					
Accidents	16.06 (13.28–18.85)	11.98 (9.87–14.09)	13.69 (11.99–15.39)	15.92 (12.49–19.36)	14.11 (11.16–17.06)	14.90 (12.66–17.14)
Criminal violence	46.18 (42.44-49.92)	44.85 (41.62–48.09)	45.41 (42.96–47.85)	47.45 (42.71–52.19)	52.62 (48.45–56.79)	50.38 (47.24–53.51)
New forms of criminal violence	9.15 (6.94–11.37)	18.99 (16.42–21.57)	14.87 (13.09–16.65)	12.29 (9.25–15.34)	22.14 (18.66–25.63)	17.87 (15.47–20.27)
Sexual violence	0.20(0.00-0.39)	4.01 (2.83–5.18)	2.41 (1.72–3.10)	1.31 (0.24–2.38)	6.79 (4.68 - 8.90)	4.41 (3.12–5.70)
Family violence	6.79 (4.90–8.67)	14.91 (12.68–17.14)	11.51 (9.98–13.03)	10.00 (7.08–12.91)	17.88 (14.71–21.05)	14.46 (12.26–16.67)
Death or severe illness of relative or close friend	29.62 (26.16–33.08)	39.44 (36.27-42.62)	35.33 (32.97–37.68)	33.20 (28.68–37.73)	42.65 (38.51–46.78)	38.55 (35.48-41.62)
Getting beaten by a person (except relatives or torture)	1.57 (0.64–2.49)	2.96 (1.80–4.12)	2.37 (1.60–3.15)	3.10 (1.64–4.57)	2.21 (1.11–3.32)	2.60 (1.71–3.49)
Spousal violence	0.44(0.15-0.73)	6.57 (5.03–8.11)	4.00 (3.09-4.91)	1.01 (-0.09 - 2.10)	7.30 (5.18–9.41)	4.57 (3.27–5.87)

Table 4: Logistic regression conducted by interview location, including traumatic events and sociodemographic data (SP = 2,536; RJ = 1,208).

Location		P	Odds ratio	IC (95%)	
Location		Ρ		Minimum	Maximum
	Male	3.67	0.00	2.42	5.58
	Age (years)	0.98	0.01	0.96	1.00
	Education (years)	0.93	0.00	0.89	0.97
	Civil state				
	Married	Reference			
	Widowed	0.55	0.36	0.15	1.98
	Separated/divorced	1.62	0.14	0.85	3.06
	Single	0.92	0.70	0.59	1.43
São Paulo	Traumatic event				
Sao I auto	No	Reference			
	Severe accident	1.92	0.00	1.25	2.95
	Violence and criminality	1.78	0.01	1.18	2.67
	New forms of criminal violence	1.38	0.24	0.80	2.36
	Sexual violence	2.02	0.09	0.88	4.60
	Family violence	1.86	0.02	1.13	3.09
	Death of a close friend	1.18	0.39	0.81	1.70
	Spousal violence	1.92	0.09	0.90	4.08
	Being beaten by another person (except torture)	4.93	0.00	2.45	9.93
	Male	3.25	0.00	1.90	5.56
	Age (years)	1.01	0.36	0.99	1.02
	Education (years)	0.98	0.47	0.91	1.04
	Civil state				
	Married	Reference			
	Widowed	2.04	0.19	0.70	5.99
	Separated/divorced	1.51	0.31	0.67	3.38
	Single	2.43	0.00	1.37	4.30
Rio de Janeiro	Traumatic event				
Kio de janeno	No	Reference			
	Severe accident	1.10	0.74	0.63	1.91
	Violence and criminality	2.23	0.01	1.17	4.25
	New forms of criminal violence	2.18	0.00	1.29	3.66
	Sexual violence	1.85	0.16	0.78	4.38
	Family violence	2.93	0.01	1.30	6.60
	Death of a close friend	1.31	0.24	0.83	2.05
	Spousal violence	1.02	0.97	0.34	3.04
	Being beaten by another person (except torture)	1.26	0.59	0.54	2.96

types of violence and criminality," namely, events related to FCC and threats by phone. More than one-fifth of the individuals dependent on alcohol who reported violent and criminal events in both cities suffered violence before and after becoming dependent on alcohol, which characterizes revictimization.

In São Paulo, 20.5% of individuals dependent on alcohol also suffered accidents before and after becoming dependent on alcohol. Adding together all of the traumatic events associated with alcohol dependence syndrome, 55% of the interviewees in São Paulo who were dependent on alcohol also suffered a severe traumatic event, and 68.8% of interviewees in Rio de Janeiro reported severe traumatic events before

and after becoming dependent on alcohol, characterizing revictimization. In the city of São Paulo, having PTSD was associated with revictimization (P=0.014; Odds = 3.33) (Tables 5, 6, and 7).

4. Discussion

Brazilian studies show an elevated consumption of alcohol, and the age of initial use has been 12.5 years, with lifetime frequency at 65.2% in young students from 12 to 17 years [21]. In a household survey conducted in the Brazilian adult population, Laranjeira and colleagues [22] found that 48% of the sample reported not having drunk alcohol in the past year.

Table 5: Proportion of individuals who suffered traumatic events related to alcohol before, after, or before and after the onset of alcohol dependence syndrome (SP = 2,536; RJ = 1,208).

	São Paulo		Rio	Rio de Janeiro	
	N	%	N	%	
"Accident after alcohol"	8	18.2	7	38.9	
"Accident before alcohol"	27	61.4	10	55.6	
Accident before and after alcohol	9	20.5	1	5.6	
Total	44	100	18	100	
"Violence and criminality after alcohol"	26	26.3	12	22.6	
"Violence and criminality before alcohol"	45	45.5	27	50.9	
Violence and criminality before and after alcohol	28	28.3	14	26.4	
Total	99	100	53	100	
"New violence after alcohol"	28	84.8	25	92.6	
"New violence before alcohol"	5	15.2	2	7.4	
Total	33	100	27	100	
"Familiar violence after alcohol"	1	2.6	1	4.2	
"Familiar violence before alcohol"	36	94.7	22	91.7	
Familiar violence before and after alcohol	1	2.6	1	4.2	
Total	38	100	24	100	
Alcohol dependence syndrome before being beaten by strangers	1	6.2	1	14.3	
Being beaten by strangers before alcohol dependence syndrome	15	93.8	6	85.7	
Total	16	100	7	100	

Table 6: Proportion of individuals with a traumatic event related to alcohol and dependence syndrome, including proportion of individuals who suffered events before, after, or before and after the onset of alcohol dependence syndrome (SP = 2,536; RJ = 1,208).

Location		N	%	% of individuals with trauma and alcohol dependence syndrome
	No severe traumatic event and no alcohol	845	33.4	
	Severe traumatic event and no alcohol	1542	60.9	
	Trauma and alcohol			
	"Trauma after alcohol"	19	0.8	15.8
São Paulo	"Trauma before alcohol"	35	1.4	29.2
	Trauma before and after alcohol	66	2.6	55.0
	Total trauma + Alcohol dependence syndrome	120	4.8	100.0
	Alcohol and no traumatic event	26	1	
	Total	2533	100	
	No severe traumatic event and no alcohol	374	31	
	Severe traumatic event and no alcohol	760	63	
	Trauma and alcohol			
	"Trauma after alcohol"	12	1	18.8
Rio de Janeiro	"Trauma before alcohol"	8	0.7	12.5
	Trauma before and after alcohol	44	3.6	68.8
	Total trauma + alcohol dependence syndrome	64	5.3	100.0
	Alcohol and no severe traumatic event	8	0.7	
	Total	1206	100	

Table 7: Logistic regression conducted with only those who suffered serious traumatic events and also presented with a diagnosis of alcohol dependence syndrome, by location of interview, including PTSD and sociodemographic data compared with trauma suffered before and after alcohol dependence syndrome.

Location of interview		P	Odds ratio	IC (9	IC (95.0%)	
Location of interview		Ρ	Odds ratio	Minimum	Maximum	
	Male	0.68	0.84	0.36	1.94	
	Age (years)	0.20	1.02	0.99	1.05	
	Education (years)	0.88	1.01	0.91	1.12	
	Civil state					
São Paulo	Married	Reference				
	Widowed	0.50	0.35	0.02	7.18	
	Separated/divorced	0.39	0.62	0.21	1.86	
	Single	0.53	1.36	0.52	3.53	
	PTSD	0.01	3.33	1.28	8.67	
	Masculine	0.20	2.17	0.65	7.22	
	Age (years)	0.65	0.99	0.94	1.04	
	Education (years)	0.88	0.99	0.85	1.14	
	Civil state					
Rio de Janeiro	Married	Reference				
	Widowed	0.04	0.05	0.00	0.88	
	Separated/divorced	0.54	2.10	0.19	23.14	
	Single	0.13	0.34	0.08	1.39	
	PTSD	0.27	2.36	0.51	10.84	

However, within those who drank, 29% usually consumed 5 or more drinks per occasion (38% of men). In the total sample, including those who do not drink, 3% met criteria for alcohol abuse, and 9% met criteria for alcohol dependence.

Intoxication, by drugs and more importantly by alcohol [23], was found in 3.1% of interviewees (IC = 1.4–4.8), 5.8% of men (IC = 3.5–8.1), and 1.2% of women (IC = 0.1–2.3), who also have already hurt themselves when intoxicated with alcohol or drugs, and 0.7% of interviewees, of which 1.4% of men (IC = 0.2–2.5) and 0.3% of women have already hurt someone else while intoxicated with drugs or alcohol. Looking at assaultive violence in this same study, 2.3% (IC = 0.8–3.8) of interviewees, of which 4.1% of men (IC = 2.1–6.1) 11 and 1% of women (IC = 0–2.0), have already assaulted someone when intoxicated with alcohol or other drugs; this study did not differentiate between intoxicating substances.

If population-wide studies have demonstrated a strong relationship between the exposure to violence and the development of various mental disorders, including PTSD and disorders related to alcohol use [3], alcohol use as self-medication by people already exposed to tragic events would further expose these people to new traumatic situations, setting the vicious cycle. This chaining of events can occur independently of the emergence of PTSD; alcohol use predisposes trauma that increases alcohol use in the hope of trying to deal with this pain. Repeated exposure to traumatic events has been associated with disorders related to alcohol use, and this association has been more strongly observed in women and adolescents [8, 10, 11].

Brazilian surveys on alcohol misuse consider the prevalence of the abuse and dependence on alcohol, not only on dependence syndrome. Laranjeira and colleagues [22] found a prevalence rate of 19% in men, 4% in women, when considering the Brazilian average. The prevalence found in the present study is similar to the city of São Paulo, 22.2% in men and 4.9% in women. However, in Rio de Janeiro, a larger prevalence of abuse and/or alcohol dependence was found in women, at 9.6%. Even so, this prevalence is still much lower than that of men, which is 24.3%. Coherent with the findings in the present study, all of the national surveys have found prevalence 3 to 4 times greater in men than in women [21, 22, 24]. In a similar form to the present study, Andrade et al. [24] found the association between alcohol dependence syndrome and younger adults and less education.

The finding of the prevalence of exposure to traumatic events throughout the lifespan was high in both cities, 89.5% in Rio de Janeiro and 86% in São Paulo. Compared to other studies in Brazil and in other Latin American countries, the general levels of exposure to traumatic events were higher in the present study, even when considering only the events self-reported as severe, with an intensity level of 5 [24–26]. Differences like these can be explained by a broader list of traumatic events used in the present study. When comparing the same traumatic events, Brazilians are discretely more exposed to urban violence, as domestic and sexual violence is more prevalent in Mexico [25] and in Chile [26]. Compared to the literature, the present study found lower rates of domestic violence. This difference is most likely due to the method, as many of the previous studies were designed to measure violence [12, 27-31] in specific populations, such as children and adolescents [27-29] and women [30, 31], using more comprehensive instruments.

The associations found between alcohol dependence syndrome and traumatic events, including violence and criminality, are strongly established in the literature, as was demonstrated in the Introduction [4, 32]. The mediation of this association by PTSD is also well studied [3, 7]. Breslau's study [7] found that the development of alcoholism is related to PTSD but not to the occurrence of traumatic events without the development of this mental disorder. In the present study, an association was found between PTSD and alcohol dependence syndrome in São Paulo and not Rio de Janeiro. Similar to the larger prevalence of alcohol abuse in women in Rio de Janeiro, cultural differences can collaborate to get these results. This divergence shows the importance of moderation when comparing data from studies from one population to another, reinforcing the importance of the production of regional data.

When conducting the logistic regression, sexual and conjugal violence did not have a significant relationship to alcohol dependence syndrome. With regard to sexual violence, a possible explanation for this result is the low prevalence of these types of events reported by men: 0.2% in São Paulo and 1.3% in Rio de Janeiro, probably due to underreporting of these events in this sample. The literature reports this difficulty, due to the feelings of guilt and shame of the victim, especially strong in today's male population [33]. Since alcohol dependence syndrome is more prevalent in men, underreporting may have skewed these results.

Similarly, the prevalence rates found of conjugal violence suffered by men are equally low: 0.4% in São Paulo and 1% in Rio de Janeiro. Here, the reason for this finding is most likely the method. In a study examining dynamics of violence in couples, Carvalho et al. [34] propose that, regardless of prevalence, female aggression against men occurs with less severity of violence. When considering only physical violence of great intensity, this occurs basically against women, presenting lower prevalence in alcohol dependence syndrome. Studies that compare alcohol use and domestic violence do not discuss alcohol dependence exclusively [4, 21]. Acute alcohol intoxication, which often is used to measure this category of violence, was not measured in the present study.

As was presented in the above introduction, traumatic events of diverse types and Posttraumatic Stress Disorder are complexly related with the existence or development of alcohol dependence syndrome. An important aspect of this complexity is the temporal relationships between the events. Despite being a cross-sectional, epidemiological study, when considering the age at which traumatic events occurred and the development of alcohol dependence syndrome, this discussion can be advanced. Among the individuals dependent on alcohol who have suffered severe accidents, 61.4% in São Paulo and 55.6% in Rio de Janeiro suffered accidents in the onset of alcohol dependence. Among the individuals dependent on alcohol who reported violent and criminal events, 45.5% in São Paulo and 50.9% in Rio de Janeiro suffered traumatic events before the development of alcohol dependence. The exception is found in the cases of threats by telephone and attacks by PCC (the wave of violence against security forces and some civil targets organized by the criminal organization "First Capital Command" (PCC),

originating in the city of São Paulo on May 12, 2006, which subsequently spread through the state of São Paulo and other states in Brazil. For two days, the city of São Paulo became immersed in an intense climate of terror which caused the closing of commercial establishments and the emptying of the streets even during business hours); in Rio, 92.6% of individuals were already dependent on alcohol by the time of the violent events. This is possibly due, because they were recent events, to not having enough time to develop alcohol dependence syndrome. Alcohol intoxication, independent of alcohol dependence syndrome, predisposes an individual to accidents of various types [2], as it can facilitate the occurrence of violent events related to criminality, like theft, assaults, and kidnapping [2]. While being intoxicated by alcohol, the individual's vigilance, reflexes, and capacity for reaction are reduced, becoming more vulnerable. Alcohol dependence syndrome is insidious, taking years to be established, and is often preceded by improper use of alcohol [2]. In this way, even if the alcohol dependence has been previously established, this does not mean that alcohol use was not previously related to violent accidents and events, but this cannot be measured in the present study. On the other hand, the literature corroborates the present finding that traumatic experiences of a violent accident or situation lead to the onset of alcohol dependence syndrome, especially when mediated by PTSD [35]. This hypothesis is based on the notion that alcohol use is a form of self-medication, observed in clinical populations [36]. Some authors have observed that a decrease in PTSD symptoms would concomitantly cause a decrease or improvement in alcohol dependence [37]. In a study conducted with women who have suffered violence, Kaysen et al. [38] found that the intensity with which alcohol was ingested proportionally increased the intensity of traumatic symptoms, reinforcing the thesis of self-medication.

"Taking a beating" from someone who is not a member of the family was reported by 2.4% of the interviewees in São Paulo and 2.6% of the interviewees in Rio de Janeiro, with a traumatic experience rated at the most severe intensity level. This event is associated with alcohol dependence syndrome in São Paulo and preceded the syndrome in 93.8% of cases in São Paulo and 85.7% in Rio de Janeiro. There were no cases of recidivism (a traumatic event before and after the alcohol dependence) in either city. According to common sense, an individual dependent on alcohol who reports a history of being beaten by a stranger is often interpreted as someone who involved themselves in a fight while intoxicated. The data does not corroborate this hypothesis, because this type of event does not repeat itself after the onset of the alcohol dependence. In this case, the self-medication hypothesis, or the increase in alcohol use to deal with symptoms resulting from a traumatic experience, is again more strongly suggested [35]. The prevalence rate of interviewees who reported physical violence perpetrated by a family member is 11.5% in São Paulo and 14.5% in Rio de Janeiro. In more than 90% of cases, the violence preceded the alcohol dependence. This temporal relationship is expected, because this form of violence generally occurs during infancy. In the Bordin et al. study [27], experiencing severe physical punishment was associated with emotional problems and behavioural issues

in children and adolescents. Paula et al. [28] showed that adolescents exposed to violence within the family had twice as many problems with mental health as those who were not exposed to intrafamiliar violence and were three times more likely to present with mental health issues than those exposed to only urban violence (P = 0.04; IC 95% = 1.03; 7.55). The explanation for this relationship between violence suffered during infancy and the development of mental disorders involves many factors, among which is the alteration of reactions to stress, measured by the hypothalamus-pituitary-adrenal axis (HPA). Studies with animal models and brain imaging studies in adults who have suffered severe traumas during early childhood show that early trauma can determine alterations of the HPA axis or structural modifications of the nervous system, with permanent damage [39].

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Other factors associated with the examination of child-hood domestic violence are sociocultural. In a national survey examining the consumption of psychiatric drugs by elementary and secondary school students carried out in the public education system in the 27 Brazilian state capitals [5], the negative parent-child relationship of the students and negative relationships between parents of the students were found to be associated with heavy alcohol use by students, and the moderation by the parents in the treatment of their children was found to be associated with students not using alcohol heavily.

Other studies show the relationship between having suffered violence during childhood or witnessing domestic violence during childhood and violent behaviour during adulthood [40]. Braga [41] explains that parents as well as social environment have a direct impact on children, who are learning cultural norms of behaviour. In other words, an individual raised with corporal and violent punishments can comprehend these practices as a form of education and not as violence. Here, the vicious cycle of violence, alcohol, and violence perpetuates itself over generations.

The relationship between suffering violence and development of alcohol dependence may not be causal but may be due to underlying factors. Epidemiological studies show that an individual who lives in violence finds himself more vulnerable to mental illness and especially the development of alcoholism [24]. The phenomenon of the banality of violence, the idea that a culture of violence exists in certain environments, does not diminish the damaging effects of this violent behaviour. On the contrary, chronic exposure to trauma, whether continuous or intermittent, is capable of altering the HPA axis, leading to functional losses in the body and mental illness [42]. This pathological modulation of the HPA axis can predispose PTSD, which in turn predisposes alcohol dependence syndrome and new traumatic events [7, 39].

On the other hand, the literature shows the influence of alcohol use on the genesis of violent behaviour [23]. The question of the vicious cycle returns, which is demonstrated in the present study. Adding together all of the severe traumatic events related with alcohol dependence, 55% of individuals dependent on alcohol in São Paulo and 68.8% in Rio de Janeiro report events occurring both before and after the development of alcohol dependence. Suffering trauma predisposes alcohol dependence, which in turn predisposes

new traumas and violent events, in the same individual and also within families, for generations, collaborating with the perpetuation of a violent society.

Finally, various discrepancies were found in the results of these two cities, within the relationships of the prevalence rates as well as the correlations of alcohol dependence syndrome. These discrepancies were minimized with the creations of the groups. Cultural and sociological factors possibly implicated in these differences fall out of the scope of this project.

New studies with other designs, including a qualitative approach, are necessary to clarify these points. Longitudinal studies as well as regional studies are also necessary to enlarge and deepen the comprehension of these findings.

5. Conclusion

Alcohol dependence syndrome is complexly related to urban and familiar violence in the cities of São Paulo and Rio de Janeiro. Urban violence, in more than 50% of cases, and family violence, in more than 90% of cases, precede alcohol dependence syndrome.

In both cities, the reoccurrence of traumatic events occurs in more than half of individuals with alcohol dependence, characterizing a vicious cycle that contributes to the perpetuation of high rates of alcoholism as well as a violence society. Politicians ordering the reduction of violence in large metropolises are necessary to break this cycle, potentially reducing, as a result, alcoholism in this population.

Conflict of Interests

The authors declare that there is no conflict of interests regarding the publication of this paper.

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