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Recreational Drug Use and Distress From Hallucinations in the General Dutch Population

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***Background and Hypothesis*: Distress associated with auditory (AH) and visual (VH) hallucinations in the general population was found to be predictive of later need for mental healthcare. It is, therefore, important to understand factors relating to the distress individuals experience from their hallucinations. Hallucinations can easily occur under substance-induced states, but recreational drug use is also known as a self-medication strategy. The current study, therefore, investigated whether recreational drug use by individuals from the general population is associated with the degree of distress experienced from AH and/or VH. *Study Design*: Drug use and distress severity associated with AH (*N* = 3.041) and/or VH (*N* = 2.218) were assessed by means of an online survey in the general Dutch population (>14 years of age). *Study Results*: Multiple linear regression revealed that while past month consumption of alcohol was associated with less AH- and VH-related distress, past month cannabis use was associated with more AH- and VH-related distress. Furthermore, past month use of nitrous oxide was associated with more severe VH-related distress. *Conclusion*: Recreational use of alcohol, cannabis, and nitrous oxide may play important differential roles in the degree of distress associated with AH and VH in individuals from the general population. The consumption of these substances could form a potential risk factor for the development of distressing hallucinations or function as a signal marker for their occurrence. Due to the cross-sectional design of the current study, the causal relation between recreational drug use and distressing hallucinations remains to be elucidated.**

Key words: schizophrenia/hallucinatory distress/recreational drug use/alcohol/cannabis/nitrous oxide

Introduction

Schizophrenia and related psychotic disorders are typically characterized by delusions, hallucinations, and cognitive deficiencies. According to the psychosis continuum hypothesis, however, symptoms observed in individuals with psychotic disorders also occur in non-clinical populations.[1] In 2009, Van Os et al. estimated the prevalence of psychotic experiences in the general population to be higher than 8% and found that the majority of these were not related to clinical impairment. Interestingly, factors associated with the occurrence of psychotic experiences in clinical populations were demonstrated to be also predictive of psychotic experiences in the general population.[2]

For a long time, hallucinatory experiences were conceptualized as characteristic symptoms of schizophrenia.[3] More recently, however, hallucinations were recognized not exclusively to be a hallmark of schizophrenia spectrum disorders,[4] as they are frequently reported by individuals from the general populations as well. The prevalence of hallucinatory experiences among these populations was estimated to vary between 4% and 21%.[5] However, phenomenological aspects of hallucinations experienced by patients with psychotic disorders differ from those occurring in individuals from the general population.[6–9] Hallucinations among healthy individuals often occur only under certain circumstances, such as during stressful periods or as a result of sleep deprivation or substance use and occur less frequently compared to those in patient populations.[9]

Even though the occurrence of hallucinations among individuals from the clinical and individuals from the general populations is well-known, factors relating to the development of distress experienced from

hallucinations by the individual are less well-known.[9] Among the strongest discriminating features reported are the intensity, frequency as well as controllability of hallucinations.[10] Indeed, frequent and intense hallucinations which are perceived as not being controllable, result in substantial hallucinatory distress for the individual.[4] While it is well-known that for the greater majority of patients with psychotic disorders auditory (AH) and visual (VH) hallucinations are often accompanied by severe distress,[11] Waters et al. reported that hallucinations among individuals from the general population are often only temporary and generally experienced as harmless by the individual.[4] These findings are in sharp contrast to those from Daalman et al. and to those from the recent study by Linszen et al., both emphasizing the role of distress associated with hallucinations also in nonpsychotic individuals.[8,12] Notably, AH-related distress in nonpsychotic individuals was found to be predictive of later need for mental healthcare in these voice-hearers.[13] The experienced distress associated with the hallucination may form one of the key aspects differentiating transient hallucinations from severe and intrusive hallucinations.[9]

Uncovering traits or behaviors that are indicative of the individual trying to cope with hallucinatory-related distress could enable better identification of those who might be at risk of developing severe distress related to their hallucinations. One such candidate feature may be recreational drug use, as this is known to lead to substance-induced states in which hallucinations can occur easily.[14] However, the relation between hallucinatory experiences and recreational drug usage in the general population has been poorly investigated, and results are not unequivocal. On the one hand, there are reports highlighting that the usage of alcohol, cannabis, and other psychoactive drugs forms risk factors for experiencing psychotic symptoms.[2,15,16] On the other hand, the usage of drugs may also serve as means for self-medication to alleviate stress or anxiety levels.[17] Importantly, as different types of recreational drugs have distinct working mechanisms, their effects on hallucinatory distress may vary.

With the current study, we aim to investigate the potential of different types of recreational drugs in forming predictive features for distress from AH or VH hallucinations in the general Dutch population (≥14 years of age). We investigated 12 types of recreational drugs and grouped these into the following categories: dopaminergic, serotonergic, sedative, cannabinoid, and dissociative drug category. The associations of the different types of recreational drugs and drug categories with the degree of AH- and VH-related distress were assessed. The outcomes may help further elucidate the role of different types of recreational drugs in the development of distressing hallucinations, which is a crucial step in the development of psychosis.

Methods

Participants

Data used for the present investigation originate from the larger cross-sectional online study called "Zie ik spoken" (in English: "Do I see ghosts?"). Recruitment of participants took place via national media channels as well as several events (eg, Lowland's festival). Data collection took place between September 2016 and May 2017 via a website.

Measures

To quantify the presence and phenomenology of AH and VH, we used the Questionnaire for Psychotic Experiences (QPE).[18] Data on recreational drug use were collected by asking participants to specify which of a number of recreational drugs they had used in the past month. Finally, questions on demographic information (sex, age, and years of education) were included in the survey as well.

Questionnaire for Psychotic Experiences

The QPE consists of 50 items that aim to quantify the presence and phenomenology of psychotic experiences. Psychometric properties of the QPE in terms of reliability and validity were recently confirmed to be satisfactory.[18] In addition to the examination of 9 delusion subtypes, the occurrence, content, and phenomenology of hallucinations across all sensory modalities are assessed. For the present investigation, the hallucination items from the QPE were of specific interest. For each hallucinatory modality, an introductory screening question on the lifetime experience in that modality was asked. Affirmative responses were followed by questions on the occurrence of the hallucination during the past week, and, if not, within the past month. Participants that reported a hallucinatory experience during the past week or month received subsequently questions about the phenomenology of their hallucinations. Questions of main interest for the present study were those addressing the degree of distress associated with AH and/or VH. Hallucinatory distress was measured on a 6-point Likert scale (ranging from "no distress" to "severe distress") for both AH and VH. The current study did not collect information on the simultaneous occurrence of AH and VH, nor on distress related to such multimodal hallucinations. The questionnaire was described in further detail by Rossell et al. and more recently by Linszen et al.[12,18]

Questions on Drug Usage

Screening questions about drug usage addressed whether or not the individual consumed certain drugs (ie, alcohol, cannabis, ecstasy, cocaine, amphetamine/speed, Gamma-Hydroxybutyric acid [GHB], nitrous oxide gas,

4-FA/4-FMP, 2C-B, Ketamine, psilocybin, LSD) at least once in the past week, in the past month or at another time during their lifetime. Week and month items were merged into a binary variable per drug type, indicating whether or not the specific type of drug was used in the past month. The following drug categories were distinguished: the *dopaminergic* category included amphetamine as well as cocaine; the *sedative* category included alcohol and GHB; the *serotonergic* category included ecstasy, LSD, psilocybin, 4-FA, and 2-CB; the *cannabinoid* category included cannabis; and the *dissociative* category included nitrous oxide. The present study did not collect information on the frequency or dosage of drugs consumed.

Data

Current analyses were restricted to AH and VH given the comparably smaller sample sizes of participants who reported having experienced tactile and/or olfactory hallucinations in the past month. The degree of distress associated with AH in the past month and the amount of AH-associated distress in the past week were merged into one single variable, indicating the associated hallucinatory distress in the past month or week. The same procedure was used for week and month items on the degree of distress associated with VH in the past month and week as well as for phenomenological items.

Only valid entries from participants aged 14 years or older were included (figure 1). For analyses on the distress related to AH, only participants who reported the experience of an AH at least once in the past month were included (N = 3.041). Likewise, only participants who reported the experience of a VH in the past month were included for analyses concerning VH-associated distress (N = 2.218). Finally, whereas "drug users" are defined as individuals who consumed at least one of the recreational drug types under study (including alcohol) in the past month, "non-drug users" are individuals who reported to not have consumed any of the investigated drugs in the past month.

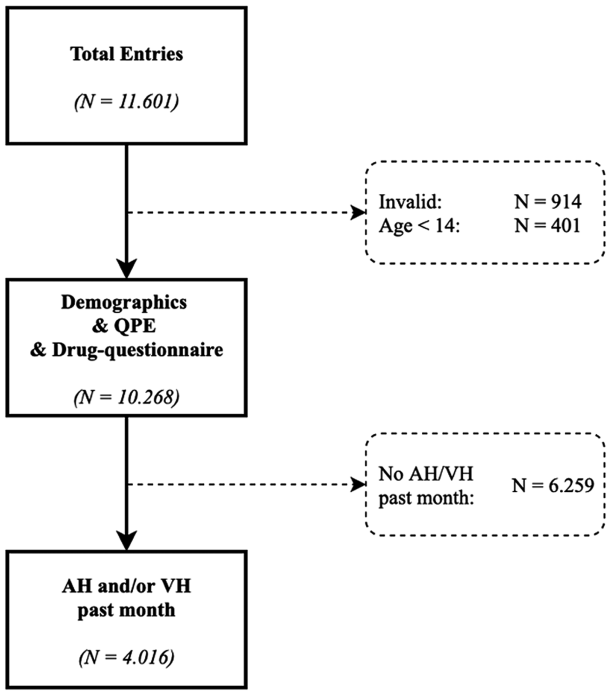

Fig. 1. Exclusion flow chart of the current study. QPE, Questionnaire for Psychotic Experiences; AH, auditory hallucinations; VH, visual hallucinations.

Statistical Analyses

Statistical analyses were performed in RStudio version 2021.09.2.[19] T tests and chi-square tests were used to assess possible differences between the drug-user and nondrug user groups in terms of demographic variables. Multiple regression analyses were performed with the amount of distress experienced from AH or VH in the past month as outcome variables, and drug categories (ie, dopaminergic, serotonergic, sedative, cannabinoid, and dissociative drugs) as predictor variables. Next, the association between the specific types of drugs and AH- or VH-related distress was investigated. Furthermore, the association between the number of different types of drugs used and AH- and VH-related distress was assessed. For all multiple regression analyses, years of education and sex were included as covariates and a backward elimination method was used to select the best-fitting model. Finally, reported P-values are those after correction by False Discovery Rate (FDR).

Results

Demographics

About two-thirds (69.6%) of the full sample reported the use of at least one of the investigated drugs in the past month (table 1). Although the sample at large had a larger proportion of women (68.9%) than men, this imbalance was even larger in the nondrug user group (79.5% women) than in the drug-user group (64.3% women) ($X^2(1) = 235$, $P < .001$). On average, participants in the drug-user group had received slightly more years of education than participants in the nondrug user group ($t(10266) = -19$, $P < .001$). There was no age difference between drug users and nondrug users ($t(10266) = 1$, $P = .3$). Finally, the median AH-related distress for participants who experienced an AH in the past month was 0 (IQR = 1) and the median VH-related distress for participants who experienced a VH in the past month was 1 (IQR = 2).

Distress From AH

Multiple linear regression analyses demonstrated that the past month use of sedative drugs was associated with

Table 1. Demographic Characteristics of the Study Sample

			Drug Group		
		Total Sample	Nondrug User	Drug-User	
		(*N* = 10.268)	(*N* = 3.118)	(*N* = 7.150)	Statistics
Age (in years)	Mean (SD)	35.5 (15.2)	35.7 (15.7)	35.4 (15)	$t(10266)=1$, $P = .3$
Sex	Female, *N* (%)	7076 (68.9%)	2479 (79.5%)	4597 (64.3%)	$X^2(1)\ 0 = 235$, $P < .001$
	Male, *N* (%)	3192 (31.1%)	639 (20.5%)	2553 (35.7%)	
Education (in years)	Mean (SD)	13.9 (2.1)	13.3 (2.34)	14.2 (1.99)	$t(10266) = -19$, $P < .001$

Note: SD, standard deviation; N, sample sizes.

a lesser degree of AH-related distress ($R^2 = 0.0214$, $\beta = -0.19$, $P < .001$). Conversely, past month use of cannabinoid drugs was associated with a more severe degree of AH-associated distress ($R^2 = 0.0214$, $\beta = 0.13$, $P = .016$). Other drug categories were not significantly associated with the degree of distress perceived from AH (all *P*'s > .783). Further analyses on the specific type of recreational drug revealed that the consumption of alcohol was associated with less AH-related distress ($R^2 = 0.0213$, $\beta = -0.19$, $P < .001$), while other sedative drugs were not associated with AH-related distress (all *P*'s > .536). As the only cannabinoid drug investigated in the current study was cannabis, it was this drug's use that was associated with more distress as experienced from AH ($R^2 = 0.0213$, $\beta = 0.13$, $P = .017$). Figure 2A depicts the degree of AH-related distress separately for nondrug users, alcohol, and cannabis users. Finally, there was no significant association between the number of different types of drugs used and AH-related distress ($R^2 = 0.0141$, $\beta = -0.02$, $P = .156$).

Distress From VH

Similar to results on AH-related distress, multiple linear regression analyses revealed that the past month use of sedative drugs was associated with a lesser degree of VH-related distress ($R^2 = 0.0225$, $\beta = -0.11$, $P = .038$), while past month use of cannabis was associated with a more severe degree of VH-related distress ($R^2 = 0.0227$, $\beta = 0.16$, $P = .044$). Other drug categories were not significantly associated with the degree of distress perceived from VH (all *P*'s > .411). With respect to sedative drugs, the use of alcohol turned out to be associated with less VH-related distress ($R^2 = 0.0227$, $\beta = -0.12$, $P = .031$). In addition, past month use of nitrous oxide was associated with a more severe degree of VH-associated distress ($R^2 = 0.0227$, $\beta = 0.46$, $P = .014$). Figure 2B depicts the degree of VH-related distress separately for nondrug users, alcohol, cannabis, and nitrous oxide users. Finally, there was no significant association between the number of different types of drugs used and VH-related distress ($R^2 = 0.0164$, $\beta = 0.01$, $P = .630$).

Discussion

The present investigation aimed to identify whether recreational use of dopaminergic, serotonergic, sedative, cannabinoid, and dissociative drugs, is associated with the degree of distress perceived from AH and VH in the general population. We showed that while the consumption of alcohol was associated with a lesser degree of distress related to AH, the usage of cannabis was related to a more severe degree of AH-associated distress. Similar results were found with respect to the degree of distress associated with VH. That is, whereas the usage of alcohol was associated with a smaller degree of perceived distress related to VH, the consumption of cannabis was associated with more VH-related distress. Furthermore, the usage of nitrous oxide was also associated with a more severe degree of perceived distress related to VH.

In explaining these differential findings for alcohol, cannabis, and nitrous oxide on the experienced distress from AH and VH, it is necessary to review some of their known working mechanisms as possibly relating to hallucination distress. First, the use of alcohol was found to alleviate stress levels and anxiety by increasing inhibitory GABAergic activity and reducing excitatory glutamatergic levels in the brain.[17] Alcohol was reported to be used more frequently as self-medication to cope with emotional distress, anxiety, and pain than, for example, cannabis.[20] This effect of alcohol might explain the present results with respect to the associations found between past month alcohol use and less distress experienced from AH and VH. Although possibly providing temporary relief from distressing hallucinations, given the highly toxic effect of alcohol on brain cells,[21,22] this strategy for self-medication is expected to have more detrimental results on the long run. When excessive alcohol consumption is observed in people who suffer from hallucinations, clinicians may take this as a warning signal and are encouraged to offer alternative coping strategies to alleviate hallucinatory distress.

Second, among recreational drugs, the effect of cannabis on psychotic experiences belongs to the most well-documented ones. Several studies and reviews on the prevalence and association of psychotic experiences

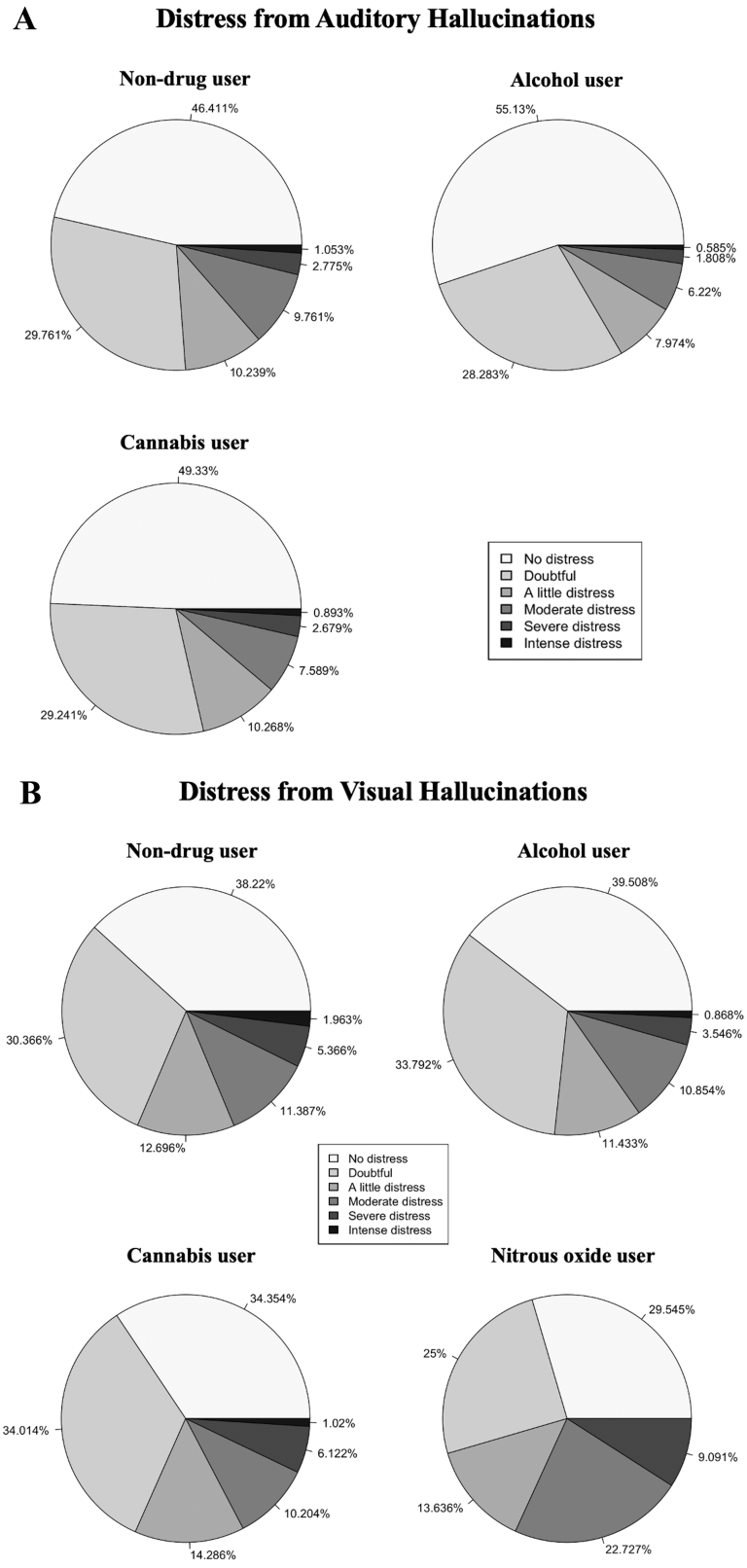

Fig. 2. (A) Pie chart of the degree of distress associated with AH separately for nondrug users, alcohol, and cannabis users. (B) Pie chart of the degree of distress associated with VH separately for nondrug users, alcohol, cannabis, and nitrous oxide users. AH, auditory hallucinations; VH, visual hallucinations.

reported significant associations between cannabis use and general psychotic experiences,[2,15,16,23] and more specific AH.[24] Moreover, cannabis use was found to result in subjective feelings of anxiety and physiological distress.[25] Even though these findings suggest cannabis usage as an important risk factor for the later emergence of psychosis, the crucial roles of genetic interactions are undeniable. Specifically, findings from the largest genome-wide association study meta-analysis to date demonstrate an association between the genetic vulnerability for schizophrenia and the genetic liability for cannabis use as indicated by overlap of the specific genetic loci.[26] This suggests that cannabis use is not a causal factor in the development of schizophrenia, but an association that results from shared vulnerability. As the current study is cross-sectional, we cannot differentiate between a causal effect and shared vulnerability, but possibly both routes will play a role. In a general student population sample, cannabis use was furthermore found to be positively related to hallucination proneness and the degree of believe in the reality an individual held about their hallucinations.[27] Given that the extent of belief concerning the reality of hallucinations in psychotic individuals was found to be related to the amount of hallucinatory distress experienced by the individual,[11] our finding strengthens the notion of cannabis use as being a potential risk factor for the development of distress experienced from hallucinations.

Finally, the same rationale for the association between cannabis and hallucinatory distress might be applicable to our finding concerning the association between nitrous oxide and the higher severity of distress associated with VH. Similar to cannabis use, nitrous oxide was reported to be associated with the induction of acute psychosis. In particular, the consumption of nitrous oxide was reported to result in feelings of depression and hypomania and may induce AH as well as VH.[28] As nitrous oxide has become an increasingly popular recreational drug, but as of yet little is known about its possible negative impact on mental health, these results should be taken as an incentive for further studies.

Limitations

The collection of data by means of an online survey provided a notably large sample size, however, the current investigation also has some limitations. First, due to the cross-sectional design of this study, we cannot infer information on the sequence or timing/proximity of hallucinatory distress in relation to drug use, and, thus, on causality. Based on studies examining the relationship between psychotic symptoms and drug use, it appears likely that drug use may be the result as well as the inducer of distress related to hallucinations, depending on the certain type of drug used, among others. For instance, whereas alcohol might be used as self-medication to alleviate the experienced distress from psychotic symptoms, the use of cannabis may induce and/or worsen psychotic symptoms.[29]

Information on frequency or dosage of the consumed recreational drugs was not collected as part of the current study, preventing the examination of these factors on the distress related to the experience of AH and VH. Furthermore, no clinical data or data on the distress related to the simultaneous experience of AH and VH were collected. Therefore, an important limitation of the current study is the fact that it remains uncertain how many participants in this general population sample may have been part of a clinical population. Other general limitations of this study were described by Linszen et al.[12]

Future research aimed at further elucidating the relationship between recreational drug use and distress related to hallucinations should employ a longitudinal design. For example, a design employing ecological momentary assessment could be used to examine dynamic and causal relations between recreational drug use and the occurrence of distressing hallucinations.

Conclusion

The current investigation found that the recreational use of alcohol, cannabis, and nitrous oxide is associated with the degree of distress related to AH and/or VH in the general Dutch population. First, the use of alcohol was found to be associated with less severe distress experienced from both AH and VH. This finding may be related to the frequently reported use of alcohol for self-medication purposes to alleviate emotional discomfort or anxiety. Next, supporting findings on the well-documented relationship between cannabis use and general psychotic experiences, the consumption of cannabis was found to be associated with more severe distress perceived by AH and VH. Results concerning the positive association between nitrous oxide and the degree of distress related to VH is novel and in need of replication. Although the cross-sectional design of the current study prevents conclusions to be drawn concerning causality, the differential associations between recreational use of alcohol, cannabis, and nitrous oxide and hallucinatory distress indicate there to be an intricate relation that warrants further examination. Increasing our understanding of this relation may inform early interventions for individuals who might be at risk of developing severely distressing hallucinations.

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Data Availability

The data that support the findings of the current study are available on request from the corresponding author M. van der Weijden-Germann.

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