Self-reported PTSD is associated with increased use of MDMA in adolescents with substance use disorders

Lukas Andreas Basedow, Sören Kuitunen-Paul, Melina Felicitas Wiedmann, Veit Roessner and Yulia Golub

Department Of Child And Adolescent Psychiatry, Faculty Of Medicine, Technische Universität Dresden, Dresden, Germany

ABSTRACT

Background: Adolescent patients with a substance use disorder (SUD) often fulfill the criteria for a co-occurring post-traumatic stress disorder (PTSD). However, it is not clear if these dual-diagnosed adolescents present with unique levels of substance use and how their substance use relates to PTSD symptom clusters.

Objective: To investigate substance use in adolescents with co-occurring PTSD and SUD. Additionally, we explored how the use of specific substances is related to specific PTSD symptom clusters.

Method: We recruited n = 121 German adolescent SUD patients, in three groups: no history of traumatic events (TEs) (n = 35), TEs but not PTSD (n = 48), probable PTSD (n = 38). All groups were administered a trauma questionnaire and were asked to report their past-month substance use.

Results: Adolescents with probable PTSD and SUD report a higher frequency of MDMA use than adolescents with no PTSD and no TE (PTSD vs. noTE: U = 510.5, p = .016; PTSD vs. TE: U = 710.0, p = .010). The use of MDMA was more frequent in adolescents with avoidance symptoms (X² (1) = 6.0, p = .014). Participants report using substances at a younger age (PTSD vs. noTE: U = 372.0, p = .001; PTSD vs. TE: U = 635.3, p = .022) and PTSD symptom onset was on average 2.2 years earlier than first MDMA use (t (26) = -2.89, p = .008).

Conclusions: Adolescent SUD patients with probable PTSD are more likely to use MDMA than SUD patients without PTSD. The use of MDMA was associated with reported avoidance symptoms. The first age of MDMA use is initiated after PTSD onset. It is unclear whether the association of MDMA use with avoidance symptoms is due to efforts to reduce these symptoms or a result of regular MDMA use.

Auto-reporte de TEPT se asocia con un mayor uso de MDMA en adolescentes con trastornos por uso de sustancias

Antecedentes: Los pacientes adolescentes con un trastorno por uso de sustancias (TUS) a menudo cumplen los criterios para un trastorno de estrés postraumático concurrente (TEPT). Sin embargo, no está claro si estos adolescentes con diagnóstico dual presentan niveles únicos de consumo de sustancias y cómo su consumo de sustancias se relaciona con los conglomerados de síntomas del TEPT.

Objetivo: Investigar el uso de sustancias en adolescentes con concurrencia de TEPT y TUS. Además, explorar cómo el uso de sustancias específicas se relaciona con grupos específicos de síntomas de TUS.

Método: Reclutamos un n=121 pacientes adolescentes alemanes con TUS, en tres grupos: sin antecedentes de eventos traumáticos (no ETs) (n=35), ETs pero no PTSD (n=48), probable TEPT (n=38). A todos los grupos se les administró un cuestionario sobre traumas y se les pidió que informaran sobre su consumo de sustancias durante el mes anterior.

Resultados: Los adolescentes con probable TEPT y TUS informan una mayor frecuencia de uso de MDMA que los adolescentes sin TEPT y sin ETs (TEPT versus no ETs: U= 510.5, p = .016; TEPT versus ETs: U= 710.0, p = .010). El uso de MDMA fue más frecuente en adolescentes con síntomas de evitación (X² (1) = 6.0, p = .014). Los participantes informan que consumen sustancias a una edad más temprana (TEPT versus no ETs: U= 372.0, p = .001; TEPT frente a TE: U = 635.3, p = .022) y el inicio de los síntomas del TEPT fue en promedio 2.2 años antes del primer uso de MDMA (t (26) = -2.89, p = .008).

Conclusiones: Los pacientes adolescentes con TUS con probable TEPT son más propensos a usar MDMA que los pacientes con TUS sin TEPT. El uso de MDMA se asoció con el reporte de síntomas de evitación. La primera edad de uso de MDMA se inicia después del inicio del TEPT. No está claro si la asociación del uso de MDMA con los síntomas de evitación se debe a los esfuerzos por reducir estos síntomas o al resultado del uso regular de MDMA.
物质使用障碍青少年患者中自我报告的 PTSD 与MDMA的使用增加有关

背景：现有物质使用障碍(SUD)青少年患者通常符合并发病后应急障碍(PTSD)的标准。然而，尚不清楚这些双重诊断的青少年是否表现出独特的物质使用水平以及他们的物质使用与PTSD症状群的关联。

目的：我们招募了121名德国青少年SUD患者，分为三组：无创伤事件史组(TE)(n=35)、有TE但无PTSD组(n=48)、可能PTSD组(n=38)，所有组都完成了创伤问卷调查，并被要求报告他们过去一个月的物质使用情况。

方法：与无PTSD和TE组的青少年相比，可能PTSD和SUD组的青少年报告的MDMA使用频率更高(PTSD组与TE组U=510.5, p=.016; PTSD组与TE组U=710.0, p=.013)。参与者的报告在早年使用物质(PTSD组与TE组U=372.0, p=.001; PTSD组与TE组U=653.5, p=.022)并且PTSD症状的出现平均早于首次使用MDMA2.2年(t(26)=-2.89, p=.008)

结果：与无PTSD的SUD患者相比，患有可能PTSD的青少年SUD患者更可能使用MDMA。使用摇头丸与报告的回避症状有关。首次使用MDMA年龄是在PTSD发作后开始的。目前尚不清楚MDMA使用与回避症状的关联是由于努力减少这些症状还是定期使用MDMA的结果。

1. Introduction

Approximately one-third of adults who fulfil the criteria for a psychiatric disorder also fulfil diagnostic criteria for at least one co-occurring psychiatric disorder (Forman-Hoffman, Batt, Hedden, Spagnola, & Bose, 2018). Co-occurring psychiatric disorders present a challenge for mental health professionals in inpatient settings, which is reflected by the increased length of stay and medical costs observed in patients with multiple such disorders compared to patients with only one (Jansen, van Schijndel, van Waarde, & Van Busschbach, 2018).

One such pattern of co-occurring disorders is the co-occurrence of post-traumatic stress disorder (PTSD) and substance use disorders (SUDs). This co-occurrence is frequently observed in adolescents (Schulte & Hser, 2014), with 20–54% of adolescent SUD patients fulfilling PTSD criteria (Turner, Muck, Muck, Stephens, & Sukumar, 2004; Williams, Smith, An, & Hall, 2008). On the other hand, 30% of adolescent PTSD patients present with SUD (Essau, Conradt, & Petermann, 1999). The co-occurrence of PTSD and SUD in adolescents is associated with increased SUD severity (Basedow, Kuittunen-Paul, Roessner, & Golub, 2020), and often presents a situation that makes therapeutic care more challenging (Gielen, Havermans, Tekelenburg, & Jansen, 2012; Kuittunen-Paul, Roessner, Basedow, & Golub, 2020; Simmons & Suárez, 2016; Williams et al., 2008), i.e. through PTSD-associated flashbacks serving as a trigger for increased substance use.

While a number of possible explanations exist for this pattern of co-occurrence, three major hypotheses have emerged: i) SUD and PTSD may result from a common risk factor. Previous research has shown that both disorders have similar genetic and environmental factors that increase the chance of their occurrence (Xian et al., 2000). ii) Adolescents who engage in substance use may generally engage in more frequent high-risk behaviours (Baskin-Sommers & Sommers, 2006). This high-risk behavioural pattern may increase the chance of experiencing traumatic events (TEs), such as first-hand violence (Harford, Yi, & Grant, 2013), and subsequently developing PTSD (Glaesmer, Matern, Rief, Kuwert, & Braehler, 2015; Strom et al., 2012). iii) PTSD symptoms appear before a SUD is developed, and patients engage in substance use to cope with the PTSD symptoms, consequently developing a SUD (Dworkin, Wanklyn, Stasiwicz, & Coffey, 2018; Khantzian, 1997; McCauley, Killeen, Gros, Brady, & Back, 2012). This self-medication hypothesis has gained much empirical support (Chilcoat & Breslau, 1998; Sheerin et al., 2016) showing, for example, that one-fifth of PTSD patients use substances in an attempt to relieve PTSD symptoms such as hyperarousal, avoidance or intrusions (Leeies, Pagura, Sareen, & Bolton, 2010). Per definition, the self-medication hypothesis includes assumptions about the age of onset of PTSD and SUD namely, that SUD symptoms should develop following the PTSD symptoms. This pattern has been investigated and confirmed in previous studies, which showed that anxiety disorders (Slade, McEvoy, Chapman, Grove, & Teesson, 2015), conduct disorders (Guldager, Linneberg, & Hesse, 2012), and PTSD (Wu et al., 2010) predate future SUDs.

Even though the severity of adolescent SUD has been associated with a co-occurring PTSD (Basedow et al., 2020; Donbaek, Elklit, & Pedersen, 2014), little is known with regard to use of specific substances and PTSD symptomatology in adolescents. Based on the self-medication hypothesis, the specific subjective effects of different substances might be perceived as relieving symptoms, symptom neutral or leading to stronger symptoms. Accordingly, adolescents with SUD and PTSD might use different substances to achieve a subjective relief from different PTSD symptom clusters (SGs). Thus, a patient who experiences...
strong hyperarousal symptoms might show a preference for substances with a relaxing effect, e.g. benzodiazepines, while a patient with avoidance symptoms might prefer stimulating substances, e.g. amphetamine. Previous studies in adults investigating how the use of psychoactive substances relates to the presence of specific PTSD symptoms reported conflicting results (Avant, Davis, & Cranston, 2011; Dworkin et al., 2018; Khoury, Tang, Bradley, Cubells, & Ressler, 2010; Tull, Gratz, Akin, & Lejuez, 2010). For instance, the presence of avoidance symptoms has been associated with alcohol, benzodiazepine, cocaine, and cannabis use (Avant et al., 2011; Dworkin et al., 2018; Khoury et al., 2010; Tull et al., 2010). The question of specific substance use in a relation to distinct PTSD symptoms is particularly important for the development of targeted therapeutic interventions. However, no research so far could clarify these symptom-substance connections (Van Den Brink, 2015). Additionally, substance use and subsequent SUDs should have a later onset compared to the disorder that is medicated (Khantzian, 1997). This pattern has been shown previously for adult patients (Berenz et al., 2017), but not for adolescents. Furthermore, it is unclear if TEs alone might already predispose adolescents to increased substance use and SUD severity. While an association of TEs with SUD has been repeatedly suggested (Hari, 2005; Maté, 2008, 2012), previous research from our group has found similar levels of SUD severity between adolescents with TEs but not PTSD and adolescents without TEs (Basedow et al., 2020). It remains to be explored if similar differences are present concerning substance use.

We conducted this cross-sectional, exploratory study with two aims The primary goal was to investigate differences in frequency of substance use between subgroups of adolescent SUD patients (with a history of TEs and PTSD, with TEs but without PTSD, with no trauma exposure) and to explore the relationships between substance use frequency and the three PTSD SCs (intrusion, hyperarousal, avoidance). The secondary goal was to explore differences in age of first substance use and if age of first substance use differed from the onset of PTSD symptoms. Although previous research showed differences in SUD severity between those three groups (Basedow et al., 2020), the state of the literature did not support specific hypotheses regarding differences in substance use frequency.

2. Methods
2.1. Participants
Between November 2017 and November 2020, n = 234 treatment-seeking adolescents at a German outpatient clinic for adolescent substance abuse consented to participate in the study. From these participants, those who filled out the required questionnaires were selected, resulting in n = 121 (42% female) participants. These participants were divided into three groups based on whether they fulfilled PTSD criteria according to self-report (‘PTSD’), reported a TE but did not fulfill PTSD criteria (‘TE’) or did not report any TE (‘NoTE’). Detailed demographic information of the study sample can be found in Table 1.

Table 1. Sample description.

|                          | Total | NoTE | TE     | PTSD | Group comparison       |
|-------------------------|-------|------|--------|------|------------------------|
| N (female)              | 121 (51) | 35 (7) | 48 (22) | 38 (22) | Test statistic | p-value | dBonferroni-Holm | Effect size |
| Mean age in years (SD)  | 15.9 (1.3) | 15.7 (1.4) | 15.9 (1.3) | 16.2 (1.2) | X² (2) = 11.2 | .004 | .006* | V = .30 |
| ISCED level 24          | 58 (48) | 13 (37) | 24 (50) | 21 (55) | X² (10) = 10.3 | .036 | .008 | V = .21 |
| ISCED level 25          | 7 (6)      | 4 (11) | 0      | 3 (8)      | X² (10) = 9.3 | .507 | .025 | V = .20 |
| ISCED level 34          | 21 (17) | 10 (29) | 8 (17) | 3 (8)      | X² (10) = 9.3 | .507 | .025 | V = .20 |
| Number of participants divided by educational level (%) (n = 35 missing) | X² (2) = 11.2 | .004 | .006* | V = .30 |
| Number of participants divided by yearly income of parental household (%) (n = 55 missing) | X² (10) = 9.3 | .507 | .025 | V = .20 |
| Up to 10.000€           | 8 (7)      | 4 (11) | 3 (6) | 1 (3)      | X² (2) = 1.9 | .395 | .017 | V = .13 |
| Up to 20.000€           | 16 (13) | 5 (14) | 5 (10) | 6 (16) | X² (2) = 1.9 | .393 | .013 | V = .13 |
| Up to 50.000€           | 22 (18) | 7 (20) | 8 (17) | 7 (18) | X² (2) = 1.9 | .393 | .013 | V = .13 |
| Up to 45.000€           | 12 (10) | 8 (23) | 2 (4) | 2 (5)      | X² (2) = 1.1 | .565 | .05 | V = .10 |
| Number of participants fulfilling criteria for a substance use disorder (%) | X² (2) = 1.1 | .565 | .05 | V = .10 |
| Alcohol                 | 31 (26) | 6 (17) | 14 (29) | 11 (29) | X² (2) = 1.9 | .395 | .017 | V = .13 |
| Cannabis                | 49 (40) | 12 (34) | 23 (48) | 14 (37) | X² (2) = 1.9 | .393 | .013 | V = .13 |
| MDMA                    | 20 (17) | 2 (6) | 9 (19) | 9 (24) | X² (2) = 4.5 | .103 | .010 | V = .20 |
| Amphetamine             | 7 (6) | 1 (3) | 4 (8) | 2 (5) | X² (2) | 1.1 | .565 | .05 | V = .10 |
| Methamphetamine        | 16 (13) | 0 | 8 (17) | 8 (21) | X² (2) | 1.1 | .565 | .05 | V = .10 |

*Statistically significant difference; SD, standard deviation; MDMA, 3,4-methylenedioxymethamphetamine; noTE, no traumatic experience group; TE, traumatic experience but no PTSD group; PTSD, post-traumatic stress disorder group; ISCED, International Standard Classification of Education; ISCED level 24, lower secondary education – general; ISCED level 25, lower secondary education – vocational; ISCED level 34, upper secondary education – general; differences in proportions (%) were tested via chi-square tests (corrected for multiple testing by Bonferroni-Holm procedure for eight tests) and differences in means were tested via ANOVA.
2.2. Materials

2.2.1. Traumatic events and PTSD

The University of California at Los Angeles Post Traumatic Stress Disorder Reaction Index for DSM-IV (UCLA RI-IV) (Steinberg, Brymer, Decker, & Pynoos, 2004), German version by (Ruf, Schauer, & Elbert, 2011), is a self-report questionnaire that screens for TEs and PTSD symptoms in adolescents. The instrument consists of a Criterion A section, in which patients select the TE that afflicts them the most from a list and indicate the traumatizing features of the event. The next section assesses the frequency of occurrence of PTSD symptoms during the past month (rated from 0 = none of the time to 4 = most of the time) and asks for the first age these symptoms were experienced with regard to the TE. The items map directly onto the DSM-IV intrusion (Criterion B), avoidance (Criterion C), and hyperarousal (Criterion D) SCs. Since the UCLA is a self-report questionnaire and does not include clinical judgment, we considered PTSD as probable and not as established, when all four criteria (Criterion A, B, C, & D) are present (Steinberg et al., 2004). Dependent variables (DV) for this questionnaire were: age of first PTSD symptoms, probable presence of a PTSD, presence of a TE, and whether the criteria for the intrusion, avoidance, and hyperarousal SCs were fulfilled. In the current sample, internal consistency was good for criterion A and C (α = .82 and .81, respectively), and acceptable for criterion B and D (α = .77 and .76, respectively).

2.2.2. Substance use

The extent of substance use was assessed by clinical psychologists via a self-designed interview, asking specifically for the number of days each substance was used in the past month and at which age they started using the substance. DVs from this assessment were days of past-month tobacco, alcohol, cannabis, methylenedioxymethamphetamine (MDMA), and amphetamine (specifically ‘speed’, but not methamphetamine, cocaine or other stimulants) use, as well as the age of first tobacco, alcohol, cannabis, MDMA, and amphetamine use.

2.2.3. SUD diagnosis

The Mini–International Neuropsychiatric Interview for Children and Adolescents (MINI–KID) (Sheehan et al., 2010) is a diagnostic interview used to evaluate the presence of psychiatric disorders. The interview contains diagnostic questions to assess the presence of 32 psychiatric disorders according to DSM-5 criteria. The DV of interest was the presence of a SUD according to DSM-5 criteria.

2.2.4. Sociodemographic information

The caregivers of our participants answered 36 questions from a self-designed questionnaire assessing socio-demographic data. We analysed the questions indicating age in years, gender, education level of the patient as well as yearly household income (‘up to 10.000€’, ‘up to 20.000€’, ‘up to 30.000€’, ‘up to 45.000€’, ‘more than 45.000€’). Participants’ educational levels were assessed according to the International Standard Classification of Education (ISCED) (UNESCO, 2012).

2.2.5. Procedure

Data collection was embedded into the standard diagnostic procedures at our outpatient clinic. During the first appointment, the extent of past-year substance use was assessed, the questionnaires were handed out, and participants as well as legal guardians gave written informed consent to the study. The study was conducted in accordance with the Declaration of Helsinki. All procedures were approved by the Institutional Review Board of the University Hospital C. G. Carus Dresden (EK 66/022,018). Participants were not financially compensated for their contribution.

2.2.6. Statistical analysis

All analyses were conducted with IBM SPSS Statistics for Windows, version 27.0 (IBM, Corp, 2020). Since our continuous DVs (number of days of tobacco, alcohol, cannabis, MDMA, and amphetamine use during previous month, age of first substance use) were all non-normally distributed across groups according the Shapiro–Wilk test (see Supplemental Table S1) we decided to use non-parametric tests for our group comparisons.

For the assessment of differences in socio-demographic characteristics between the three groups, we performed chi-square tests on the proportion of male and female participants, educational achievement, parental income and type of SUD. Age differences were assessed via an analysis of variance.

For our main research question, we conducted chi-square tests to compare the prevalence of each substance across the three groups (noTE, TE, PTSD). Additionally, we performed a Kruskal–Wallis omnibus test to determine if our three groups differed in the five continuous DVs variables. If any of the omnibus comparisons was significant, we performed Mann–Whitney U follow-up tests between all three groups. We used three Mann–Whitney U tests, limited to the TE and PTSD groups, to analyse if the presence of the three SCs (intrusion, avoidance, hyperarousal) was associated with the use frequency of substances whose prevalence differed between the groups.

For the analyses, related to our secondary research question we conducted a Kruskal–Wallis omnibus test and Mann–Whitney U follow-up tests to investigate
group differences in age of substance use onset. Additionally, we performed six paired sample t-tests to compare age of PTSD symptom onset with age of first substance use. The level of significance was set to \( \alpha < 0.05 \). To correct for Type I error through multiple testing we used the Bonferroni-Holm procedure (Holm, 1979) to assess significance of the chi-square tests, the non-parametric tests (Kruskal–Wallis, Mann–Whitney U) and the paired samples t-tests. Wherever we report \( p \)-values, we report the adjusted Bonferroni-Holm threshold for statistical significance (\( \alpha_\text{Bonferroni-Holm} \)) as well. Effect sizes were classified according to Cohen (1988) into small effects (\( |d| \geq .20 \), \( |\bar{\eta}| \geq .01 \), \( |V| \geq .10 \)), medium effects (\( |d| \geq .50 \), \( |\bar{\eta}| \geq .06 \), \( |V| \geq .30 \)), and large effects (\( |d| \geq .80 \), \( |\bar{\eta}| \geq .14 \), \( |V| \geq .50 \)).

3. Results

3.1. Sample description

The three groups did not differ in the distribution of SUD diagnoses, level of education, or parental income. Between the three groups only the proportion of female participants differed significantly (\( \chi^2 (2) = 11.2, p = .004 \), \( \alpha_\text{Bonferroni-Holm} = .006 \)). The two gender groups did not differ in their age of first substance use (\( U = 1608.50, p = .199 \), \( \alpha_\text{Bonferroni-Holm} = .01 \)) their past-month tobacco (\( U = 1554.5, p = .101 \), \( \alpha_\text{Bonferroni-Holm} = .008 \)), alcohol (\( U = 1580.00, p = .259 \), \( \alpha_\text{Bonferroni-Holm} = .017 \)), cannabis (\( U = 1558.00 p = .215 \), \( \alpha_\text{Bonferroni-Holm} = .013 \)), MDMA (\( U = 1666.00, p = .285 \), \( \alpha_\text{Bonferroni-Holm} = .025 \)), or amphetamine (\( U = 169.00, p = .419 \), \( \alpha_\text{Bonferroni-Holm} = .05 \)) use. The types of traumas reported by our participants are displayed in Table 2. Most common were traumas related to violence (26%) and sexual abuse (22%).

3.2. Differences in substance use

We analysed differences in tobacco, alcohol, cannabis, MDMA, amphetamine use frequencies. While 13% of our sample fulfilled criteria for a methamphetamine use disorder, only \( n = 2 \) reported past-month use of methamphetamine, which is why we did not analyse methamphetamine use frequency. Furthermore, since none of our participants reported past-month use of cocaine, opioids, benzodiazepines or solvents we excluded these substances from the analyses as well.

The proportion of participants who had used MDMA in the last month differed between groups (\( \chi^2 (2) = 10.60, p = .005 \), \( \alpha_\text{Bonferroni-Holm} = .010 \), \( d = .62 \)) with the probable PTSD group reporting the highest proportion of past-month MDMA users. No difference in the use of other substances could be identified. Furthermore, across all three groups participants differed significantly in terms of the number of days of MDMA use in the last month (\( H (2) = 9.9 \), \( p = .007 \), \( \alpha_\text{Bonferroni-Holm} = .010 \), \( \eta^2 = .07 \)). The PTSD group had a higher past month frequency of MDMA use than the noTE group (\( U = 510.5, p = .016 \), \( \alpha_\text{Bonferroni-Holm} = .025 \), \( \eta^2 = .04 \)) and the TE group (\( U = 710.0, p = .010 \), \( \alpha_\text{Bonferroni-Holm} = .017 \), \( \eta^2 = .04 \)). The TE group did not differ from the noTE group in days of MDMA use in the past month (\( U = 839.5, p = .992 \), \( \alpha_\text{Bonferroni-Holm} = .050 \), \( \eta^2 < .01 \)). Both differences constitute small effects. Mean scores, proportions and complete test results are displayed in Table 3, median scores and interquartile range (IQR) can be found in Supplemental Table S2.

### 3.3. Relationship between MDMA use and specific PTSD SCs

The past month frequency of MDMA use across the TE and PTSD groups was significantly higher in the group of participants fulfilling the avoidance criterion compared to those that did not (\( U = 7.68, p = .008 \), \( \alpha_\text{Bonferroni-Holm} = .017 \), \( \eta^2 = .73 \)). For the other two SCs (intrusion, hyperarousal), no differences in frequency of MDMA use were detected, see Table 4. See Supplemental Table S3 for median and IQR values.

### 3.4. Age of onset of PTSD and substance use

Across all three groups participants differed significantly with medium-sized effects in terms of the age of their first substance use (\( H (2) = 11.3, p = .003 \), \( \alpha_\text{Bonferroni-Holm} = .008 \), \( \eta^2 = .08 \)). The PTSD group had a lower age of first substance use than the noTE group (\( U = 372.0, p = .001 \), \( \alpha_\text{Bonferroni-Holm} = .025 \), \( \eta^2 = .14 \)) and the TE group (\( U = 653.5, p = .022 \), \( \alpha_\text{Bonferroni-Holm} = .017 \), \( \eta^2 = .06 \)), with the effect being

| Trauma type               | Total (\( n = 121 \)) | TE (\( n = 48 \)) | PTSD (\( n = 38 \)) |
|---------------------------|------------------------|-------------------|---------------------|
| Natural disaster (%)      | 11 (9)                 | 10 (21)           | 1 (3)               |
| Accident (%)              | 10 (8)                 | 5 (10)            | 5 (13)              |
| War (%)                   | 3 (2)                  | 0                 | 3 (8)               |
| Domestic violence vs. patient (%) | 21 (17)         | 8 (17)            | 13 (34)             |
| Domestic violence vs. others (%) | 16 (13)            | 9 (19)            | 7 (18)              |
| Non-domestic violence (%) | 31 (26)                | 26 (54)           | 25 (66)             |
| Sexual abuse (%)          | 27 (22)                | 12 (25)           | 15 (40)             |
| Neglect (%)               | 16 (13)                | 5 (10)            | 11 (29)             |

TE, traumatic experience but no PTSD group; PTSD, post-traumatic stress disorder group.
4. Discussion

In this study, we aimed to investigate if adolescent SUD patients with co-occurring probable PTSD are more likely to use specific substances than adolescent SUD patients without PTSD, and how the use of these substances relates to PTSD symptoms. We found that adolescent SUD patients with probable PTSD start using substances at an earlier age, are more likely to use MDMA, and use it more frequently than adolescents with a SUD and a history of TEs but no PTSD, or adolescents with only a SUD. Additionally, we observed that in adolescent SUD patients with TE history, the use of MDMA is associated specifically with the presence of the avoidance SC. Finally, we report that adolescents with a history of TEs start using MDMA after the first occurrence of PTSD symptoms.

The self-medication hypothesis posits that substance use and subsequent SUDs may be the result of an attempt to self-medicate co-occurring psychiatric disorders (Dworkin et al., 2018; Khantzian, 1997; McCauley et al., 2012). This hypothesis posits that the preference for a specific substance may be the result of their ability to reduce acute symptomatology (Khantzian, 1997). In terms of co-occurring PTSD, the self-medication hypothesis implies that a co-occurring SUD occurs because the substance of choice has specific PTSD-symptom-relieving effects.

Table 3. Mean scores and group comparisons.

|                              | Total (n = 121) | NoTE (n = 35) | TE (n = 48) | PTSD (n = 38) | Group comparisons |
|------------------------------|-----------------|---------------|-------------|--------------|------------------|
|                              | Number of participants (%) having used the substance in the past month | | | | Test statistic | p-value | qBonferroni-Holm | Effect size |
| Tobacco                      | 112 (93)        | 30 (86)       | 45 (94)     | 37 (97)      | X² (2) = 3.8     | .153    | .013            | V = .18    |
| Alcohol                      | 67 (55)         | 19 (54)       | 28 (58)     | 20 (53)      | X² (2) = 0.3     | .860    | .05             | V = .05    |
| Cannabis                     | 70 (58)         | 22 (63)       | 31 (63)     | 24 (63)      | X² (2) = 2.0     | .366    | .025            | V = .13    |
| MDMA                         | 19 (16)         | 3 (9)         | 4 (8)       | 12 (32)      | X² (2) = 10.6    | .005    | .010*           | V = .30    |
| Amphetamine                  | 9 (7)           | 1 (3)         | 3 (6)       | 5 (13)       | X² (2) = 2.9     | .232    | .017            | V = .15    |
| Number of days of substance use in the past month (SD) | | | | | | | |
| Tobacco                      | 25.2 (9.7)      | 24.9 (10.6)   | 24.5 (9.9)  | 26.4 (8.8)   | H (2) = 1.5      | .468    | .025            | q² < .01   |
| Alcohol                      | 3.5 (6.4)       | 4.8 (8.2)     | 2.4 (3.9)   | 3.6 (7.1)    | H (2) = 0.2      | .890    | .050            | q² = .02   |
| Cannabis                     | 7.0 (9.7)       | 8.3 (10.6)    | 5.3 (7.9)   | 8.0 (1.6)    | H (2) = 2.4      | .297    | .017            | q² = .01   |
| MDMA                         | 0.33 (1.0)      | 0.14 (0.6)    | 0.29 (1.3)  | 0.54 (1.0)   | H (2) = 9.9      | .007    | .010*           | q² = .07   |
| Amphetamine                  | 0.49 (2.4)      | 0.23 (1.4)    | 0.7 (3.4)   | 0.47 (1.5)   | H (2) = 2.7      | .258    | .013            | q² = .01   |

* Statistically significant difference; SD, standard deviation; MDMA, 3,4-methylenedioxymethamphetamine; NoTE, no traumatic experience group; TE, traumatic experience but no PTSD group; PTSD, post-traumatic stress disorder group; differences in proportions (%) were tested via chi-square tests and differences in means were tested via the Kruskal-Wallis procedure (both analyses corrected for multiple testing by Bonferroni-Holm procedure for five tests).

Table 4. Mann-Whitney U tests assessing associations between MDMA use and PTSD symptom clusters in TE and PTSD participants.

| PTSD symptom cluster | N | Mean number of days of past month MDMA use (SD) | Group comparison |
|----------------------|---|-------------------------------------------------|------------------|
|                       |   | Mean number of days of substance use in the past month (SD) | Test statistic | p-value | qBonferroni-Holm | Effect size |
| Intrusion present     | 62 | 0.38 (0.11)                                  | U = 2.32 | .184   | .025             | q² = .59 |
| Avoidance present     | 43 | 0.52 (0.14)                                  | U = 7.68 | .008   | .017*            | q² = .73 |
| Hyperarousal present  | 67 | 0.32 (0.10)                                  | U = 0.13 | .896   | .050             | q² = .51 |

* Statistically significant difference; MDMA, 3,4-methylenedioxymethamphetamine; PTSD, post-traumatic stress disorder; differences were tested with Mann-Whitney U tests (corrected for multiple testing by Bonferroni-Holm procedure for three tests).

Table 5. Mean differences and test results for PTSD symptom onset and onset of substance use.

| Difference from age of PTSD symptom onset | N | Mean difference in years (SD) | Test statistic | p-value | qBonferroni-Holm | Effect size |
|------------------------------------------|---|-------------------------------|---------------|--------|------------------|-------------|
| First age of tobacco use                 | 31 | .07 (3.79)                    | t (30) = 0.95 | .392   | .050             | d = .02     |
| First age of alcohol use                 | 32 | -.44 (3.58)                   | t (31) = 0.69 | .494   | .025             | d = .12     |
| First age of cannabis use                | 33 | -1.10 (3.72)                  | t (32) = 0.64 | .111   | .017             | d = .29     |
| First age of MDMA use                    | 27 | -2.19 (3.93)                  | t (26) = 2.89 | .008   | .010*            | d = .36     |
| First age of amphetamine use             | 16 | -2.19 (3.25)                  | t (15) = 2.69 | .017   | .013             | d = .67     |

*Statistically significant difference; MDMA, 3,4-methylenedioxymethamphetamine; differences were tested via paired-t tests (corrected for multiple testing by Bonferroni-Holm procedure for five tests).
In fact, this pattern has been shown repeatedly in the context of alcohol use and PTSD, suggesting that after encountering TEs a common response is engaging in drinking to cope (Hawn, Cusack, & Amstadter, 2020; Wu et al., 2010).

In the context of the self-medication hypothesis, the increased use of MDMA in adolescents with co-occurring PTSD and SUD is not surprising. Since MDMA use in adolescents has been generally associated with a self-medication motive (Moonzwe, Schensul, & Kostick, 2011), and MDMA-assisted psychotherapy has recently been shown to reduce PTSD symptomatology (Thal & Lommen, 2018), adolescents in our sample with PTSD and SUD may show increased use of MDMA because it decreases their distress induced by the different PTSD SCs. Our results indeed show, that a higher prevalence of MDMA use is specifically related to the presence of the avoidance SC. Symptoms of the avoidance cluster include ‘feeling of detachment’ or ‘restricted range of affect’ which might be associated with MDMA use since MDMA has been shown to induce heightened empathy (Carlyle et al., 2019), increased pro-social behaviour (Borissova et al., 2020; Stewart et al., 2014) and is often used in social settings (McElrath & McEvoy, 2002). On the other hand, side effects of MDMA such as increased body temperature (Liechti, 2014) and increased blood pressure (Vizeli & Liechti, 2017) might explain why MDMA use is not associated with hyperarousal, since the increased activation of the sympathetic nervous system might exacerbate negative aspects of hyperarousal. Furthermore, acute detrimental effects of MDMA on memory (de Sousa Fernandes Perna et al., 2014; Kuypers & Ramaekers, 2005) could explain why the intrusion SC is not associated with its use: if memory is impaired, intrusive memories might also be suppressed. In light of the unique effects of MDMA it seems plausible that it is used by adolescents with a PTSD to reduce their avoidance-induced distress, and that this self-medication use might continue unchecked and eventually develop into a SUD.

This proposed association between MDMA use and avoidance symptoms might have clinical implications. As demonstrated by our results, a higher level of MDMA use might indicate the presence of other, untreated disorders such as PTSD. However, it is important to note that our results have little bearing on the discussion surrounding MDMA as an adjunct for PTSD therapy (Mitchell et al., 2021). Participants in our study received no psychotherapy and we have no way of assessing if their MDMA use has actually reduced PTSD symptomatology. This last point is especially important since the self-medication hypothesis is not entirely without fault. Lembke (2012) argues that the picture might be more complicated and that psychiatric symptoms not only contribute to substance use, but the reverse might also be possible: the use of psychoactive substances might lead to an increase in psychiatric symptomatology through the occurrence of withdrawal symptoms or adverse pharmacological effects.

Indeed, another explanation for our observed results could be that frequent MDMA use has negative psychopathological consequences that worsen sub-clinical PTSD symptoms, leading to a fully developed PTSD. This conclusion is supported by evidence showing that MDMA users show increased psychopathology in the Symptom Checklist-90-R compared to poly-substance users without MDMA use (Morgan, McFie, Fleetwood, & Robinson, 2002). Additionally, MDMA use has been associated with psychiatric symptoms such as depression (McGuire, 2000), prodromal psychotic symptoms (Wiedmann, Kuitunen-Paul, Basedow, Roessner, & Golub, n.d.) or depersonalization (McGuire, 2000; Thomasius, Schmolke, & Kraus, 1997) which often go hand in hand with PTSD (Aixéméry, 2018; Brady, Killeen, Brewerton, & Luberini, 2000). Moreover, regular MDMA use might impair memory (Wunderli et al., 2017), disturb sleep (Schierenbeck, Riemann, Berger, & Hornyak, 2008) or diminish interest and excitement (Parrott, 2015) which could negatively influence the developmental process of PTSD. Finally, illicit MDMA use may further increase the risk of negative consequences, because of contamination with other psychoactive substances. For example, powder or pills sold as MDMA often contain synthetic cathinones (Oliver et al., 2019) with harsher side effects than MDMA (Karch, 2015; Papasiet et al., 2016). Nevertheless, we found that adolescents use MDMA on average two years after the first onset of PTSD symptoms, which is in line with research showing that adolescent MDMA use occurs later than mental health symptoms (Falk, Carlson, Wang, & Siegal, 2006). This pattern of symptoms first – use later, can be considered further support for the self-medication hypothesis, suggesting that adolescent PTSD patients discover MDMA in their adolescence, and start using more frequently and subsequently develop a SUD in an effort to reduce their symptoms. Additionally, our findings of an earlier age of first substance use in patients with co-occurring SUD and PTSD might indicate an early exploration of self-medication options.

Our results are unusual insofar as previous research has identified other substances to be associated with co-occurring PTSD and SUD and the avoidance SC. Specifically, adult alcohol use has been repeatedly associated with co-occurring PTSD and SUD (Hawn et al., 2020) and the presence of the avoidance cluster (Dworkin et al., 2018). However, this association is the result of comparing the level of symptoms between people who drink alcohol and people who do not. We, on the other hand, might not have found this
association because our sample consisted of adolescents drinking alcohol at elevated levels already. Considering that 55% of our sample had used alcohol in the past month, which is a prevalence rate three times higher than in the general German adolescent population (Orth & Merkel, 2020), our results might actually be in line with previous findings (Dworkin et al., 2018; Hawn et al., 2020). Other studies used similar research designs as Dworkin et al (2018) and concluded that levels of avoidance symptoms are higher in participants with regular use of opioids and benzodiazepines (Avant et al., 2011), as well as cocaine, cannabis, and alcohol (Khoury et al., 2010) compared to users with lower or no use. Apart from the issue expanded upon above, these studies all consisted of adult samples. Since adolescents show different patterns of use (Chen & Kandel, 1995) and use substances in different settings (Measham, Parker, & Aldridge, 1998) than adults they might tend to use different substances for self-medications as well. Additionally, our study included participants who used various substances in the past month, and MDMA emerged as a factor nonetheless, indicating that the MDMA use might be more relevant for patients with PTSD and SUD than other substances used at the same time.

4.1. Limitations

First, this study consists of cross-sectional, retrospective data, which means we cannot investigate how the use of psychoactive substances, especially MDMA, changes during the developmental course of a SUD or PTSD. Second, we based our calculations on past-month use of different substances, which represents only a snapshot of a participant’s use history. Third, most of our measures, including our assessment of PTSD diagnosis, are based on self-report which might lead to social desirability or recall bias (Althubaiti, 2016), which could lead to an underreporting of substance use and the true proportion of substance use in this population to be larger. Additionally, this procedure might overestimate the proportion of PTSD diagnoses in our sample. Future research would be well advised to include standardized instruments and more long-term measures of use, e.g. the use over the past year, or lifetime exposure. Fourth, in assessing the age of PTSD symptom onset and substance use we could only include few participants, limiting the validity of our results regarding this topic and leading to our study having a low power to detect potential effects. Fifth, our sample consisted of a specific and limited convenience sample only including adolescent, treatment-seeking SUD patients. Therefore, we are not able to make any conclusion about the role MDMA use might play in adolescents with only a PTSD diagnosis. Sixth, because of the need to use non-parametric testing it was not possible to control for sociodemographic confounders during our main analysis. Fortunately, gender differences between the groups were not mirrored in our substance use outcomes. Finally, we conducted a large number of tests increasing our likelihood of reporting false-positive results. As a countermeasure, we only considered results to be statistically significant if they survived a correction with the Bonferroni-Holm procedure.

4.2. Conclusion

This study showed that adolescent SUD patients with co-occurring probable PTSD are more likely to have used MDMA in the past month, and use it in higher frequency, than adolescents with only a SUD, regardless of additional TE. This finding might reflect an attempt to self-medicate, specifically to deal with the SC of avoidance. On the other hand, the greater MDMA use might have facilitated the development of more severe avoidance symptoms. Independent of directionality, these results should be taken into account by clinicians encountering this highly vulnerable patient group. Particular care should be taken to comprehensively assess if substances (like MDMA) are used as a form of self-medications.

Authors’ contributions

LAB analysed the data and wrote the manuscript. SKP participated in writing the manuscript, data analysis, and contributed to the discussion. MPFW participated in writing the manuscript, and contributed to data interpretation and discussion. VR participated in writing the manuscript and contributed to discussion. YG designed the study, participated in writing the manuscript and contributed to discussion.

Data availability statement

Due to the nature of this research, participants of this study did not agree for their data to be shared publicly, so supporting data is not available.

Disclosure statement

SKP reports personal fees during the past 36 months from Mabuse Verlag, and a one-time lecture honoraria from a consortium of conference sponsors (Janssen-Cilag, Lilly Germany, Novartis Pharma, Pfizer Pharma). VR has received payment for consulting and writing activities from Lilly, Novartis, and Shire Pharmaceuticals, lecture honoraria from Lilly, Novartis, Shire Pharmaceuticals/Takeda, and Medice Pharma, and support for research from Shire Pharmaceuticals/Takeda and Novartis. He has carried out or is currently carrying out clinical trials in cooperation with the Novartis, Shire Pharmaceuticals/Takeda, Servier and Otsuka companies. The remaining authors declare that the research was conducted in the...
absence of any commercial or financial relationships that could be construed as a potential conflict of interest.

**Funding**

This work was funded by the Sächsische Aufbaubank – Förderbank [grant 100362999 to YG].

**ORCID**

Lukas Andreas Basedow  http://orcid.org/0000-0003-4866-8686

Sören Kuitunen-Paul  http://orcid.org/0000-0001-8224-6490

Melina Felicitas Wiedmann  http://orcid.org/0000-0001-7250-4329

Veit Roessner  http://orcid.org/0000-0002-1873-7081

Yulia Golub  http://orcid.org/0000-0002-9191-5884

**References**

Althubaiti, A. (2016). Information bias in health research: Definition, pitfalls, and adjustment methods. *Journal of Multidisciplinary Healthcare*, 9, 211–217. doi:10.2147/JMDH.S104807

Auxémery, Y. (2018). Post-traumatic psychiatric disorders: PTSD is not the only diagnosis. *Presse Medizin (Paris, France)*, 47(5), 423–430. doi:10.1016/j.pmed.2017.12.006

Avant, E. M., Davis, J. L., & Cranston, C. C. (2011). Posttraumatic stress symptom clusters, trauma history, and substance use among college students. *Journal of Aggression, Maltreatment & Trauma, 20*(3), 539–555. doi:10.1080/10926771.2011.588133

Basedow, L. A., Kuitunen-Paul, S., Roessner, V., & Golub, Y. (2020). Traumatic events and substance use disorders in adolescents. *Frontiers in Psychiatry*, 11. doi:10.3389/fpsyg.2020.00559

Baskin-Sommers, A., & Sommers, I. (2006). The co-occurrence of substance use and high-risk behaviors. *Journal of Adolescent Health*, 38(5), 609–611. doi:10.1016/j.jadohealth.2005.07.010

Berenz, E. C., Roberson-Nay, R., Latendresse, S., Mezuk, B., Gardner, C. O., Amstadter, A. B., & York, T. P. (2017). Posttraumatic stress disorder and alcohol dependence: Epidemiology and order of onset. "Psychological Trauma: Theory, Research, Practice and Policy," 9(4), 485–492. doi:10.1037/tra0000185

Borissova, A., Ferguson, B., Wall, M. B., Morgan, C. J., Carhart-Harris, R. L., Bolstridge, M., . . . Lawn, W. (2020). Acute effects of MDMA on trust, cooperative behaviour and empathy: A double-blind, placebo-controlled experiment. *Journal of Psychopharmacology (Oxford, England)*, 269881120926673. doi:10.1177/0269881120926673

Brady, K. T., Killeen, T. K., Brewerton, T., & Lercrini, S. (2000). Comorbidity of psychiatric disorders and posttraumatic stress disorder. *The Journal of Clinical Psychiatry, 61*(Suppl 7), 22–32. https://www.psychiatrist.com/pc/trauma/ptsd/comorbidity-psychiatric-disorders-posttraumatic-stress/

Carlyle, M., Stevens, T., Fawaz, L., Marsh, B., Kosmider, S., & Morgan, C. J. (2019). Greater empathy in MDMA users. *Journal of Psychopharmacology (Oxford, England)*, 33(3), 295–304. doi:10.1177/0269881119826594

Chen, K., & Kandel, D. B. (1995). The natural history of drug use from adolescence to the mid-thirties in a general population sample. *American Journal of Public Health*, 85(1), 41–47. doi:10.2105/AJPH.85.1.41

Chilcoat, H. D., & Breslau, N. (1998). Investigations of causal pathways between PTSD and drug use disorders. *Addictive Behaviors*, 23(6), 827–840. doi:10.1016/s0306-4603(98)00069-0

Cohen, J. (1988). *Statistical power analysis for the behavioral sciences* (2 ed.). New York, NY: Psychology Press. reprint.

de Sousa Fernandes Perna, E. B., Theunissen, E. L., Kuypers, K. P. C., Heckman, P., de la Torre, R., Farre, M., & Ramaekers, J. G. (2014). Memory and mood during MDMA intoxication, with and without memantine pretreatment. *Neuropharmacology*, 87, 198–205. doi:10.1016/j.neuropharm.2014.03.008

Donbaek, D. F., Elklit, A., & Pedersen, M. U. (2014). Post-traumatic stress disorder symptom clusters predicting substance abuse in adolescents. *Mental Health and Substance Use, 7*(4), 299–314. doi:10.1080/17523281.2013.873071

Dworkin, E. R., Wanklyn, S., Stasiewicz, P. R., & Coffey, S. F. (2018). PTSD symptom presentation among people with alcohol and drug use disorders: Comparisons by substance of abuse. *Addictive Behaviors*, 76, 188–194. doi:10.1016/j.addbeh.2017.08.019

Essau, C. A., Conradt, J., & Petermann, F. (1999). Häufigkeit der Posttraumatischen Belastungsstörung bei Jugendlichen: Ergebnisse der Bremer Jugendstudie. *Zeitschrift Für Kinder- Und Jugendspsychiatrie Und Psychotherapie*, 27(1), 37–45. doi:10.1007/s10398-010-0242-4

Falck, R. S., Carlson, R. G., Wang, J., & Siegal, H. A. (2006). Psychiatric disorders and their correlates among young adult MDMA users in Ohio. *Journal of Psychoactive Drugs*, 38(1), 19–29. doi:10.1080/02791072.2006.10399824

Forman-Hoffman, V. L., Batts, K. R., Hedden, S. L., Spagnola, K., & Bose, J. (2018). Comorbid mental disorders among adults in the mental health surveillance survey. *Annals of Epidemiology*, 28(7), 468–474. doi:10.1016/j.annepidem.2018.03.002

Gielen, N., Havermans, R., Tekelenburg, M., & Jansen, A. (2012). Prevalence of post-traumatic stress disorder among patients with substance use disorder: It is higher than clinicians think it is. *European Journal of Psychotraumatology*, 3(1), 17734. doi:10.3402/ejpt.v3i0.17734

Glaesmer, H., Matern, B., Rief, W., Kuwert, P., & Brachler, E. (2015). Traumatisierung und posttraumatische Belastungsstörungen. *Der Nervenarzt*, 86(7), 800–806. doi:10.1007/s00115-014-4235-z

Guldager, S., Linneberg, I. H., & Hesse, M. (2012). Order of age at onset for substance use, substance use disorder, conduct disorder and psychiatric illness. *Mental Health and Substance Use*, 5(2), 73–84. doi:10.1080/17523281.2011.616178

Harford, T. C., Yi, H., & Grant, B. F. (2013). Other- and self-directed forms of violence and their relationships to DSM-IV substance use and other psychiatric disorders in a national survey of adults. *Comprehensive Psychiatry*, 54(7), 731–739. doi:10.1016/j.comppsych.2013.02.003

Hari, J. (2005, July 19). Childhood trauma & addiction: The 4600% risk factor. *OpenDemocracy*. https://www.opendemocracy.net/en/childhood-trauma-addiction-4600-risk-factor/
Maté, S. (2020). A systematic review of the self-medication hypothesis in the context of posttraumatic stress disorder and comorbid problematic alcohol use. Journal of Traumatic Stress, 33(5), 699–708. doi:10.1002/jts.22521.

Holm, S. (1979). A simple sequentially rejective multiple test procedure. Scandinavian Journal of Statistics, 6(2), 65–70. Retrieved from https://www.jstor.org/stable/4615733

IBM, Corp. (2020). IBM SPSS statistics for windows (27.0) [Computer software]. Armonk, NY: IBM Corp.

Jansen, L., van Schijndel, M., van Waarde, J., & Van Busschbach, J. (2018). Health-economic outcomes in hospital patients with medical-psychiatric comorbidity: A systematic review and meta-analysis. PLoS ONE, 13(3), e0194029. doi:10.1371/journal.pone.0194029.

Karch, S. B. (2015). Cathinone neurotoxicity ("the ‘3Ms’). Current Neuropharmacology, 13(1), 21–25. doi:10.2174/1570159X1366614210225009.

Khantzian, E. J. (1997). The self-medication hypothesis of substance use disorders: A reconsideration and recent applications. Harvard Review of Psychiatry, 4(5), 231–244. doi:10.3109/1067322970930550.

Khoury, L., Tang, Y. L., Bradley, B., Cubells, J. F., & Ressler, K. J. (2010). Substance use, childhood traumatic experience, and Posttraumatic Stress Disorder in an urban civilian population. Depression and Anxiety, 27 (12), 1077–1086. doi:10.1002/dan.20751.

Kuitunen-Paul, S., Roessner, V., Basedow, L. A., & Golub, Y. (2020). Beyond the tip of the iceberg: A narrative review to identify research gaps on comorbid psychiatric disorders in adolescents with methamphetamine use disorder or chronic methamphetamine use. Substance Abuse, 1–20. doi:10.1080/08987077.2020.1806183.

Kuyppers, K. P. C., & Ramaekers, J. G. (2005). Transient memory impairment after acute dose of 75mg 3,4-Methylenedioxyamphetamine. Journal of Psychopharmacology (Oxford, England), 19(6), 633–639. doi:10.1177/0269881105056670.

Leeies, M., Pagura, J., Sareen, J., & Bolton, J. M. (2010). The use of alcohol and drugs to self-medicate symptoms of posttraumatic stress disorder. Depression and Anxiety, 27 (8), 731–736. doi:10.1002/dan.20677.

Lembke, A. (2012). Time to abandon the self-medication hypothesis in patients with psychiatric disorders. The American Journal of Drug and Alcohol Abuse, 38(6), 524–529. doi:10.3109/00952990.2012.694532.

Liechti, M. E. (2014). Effects of MDMA on body temperature in humans. Temperature: Multidisciplinary Biomedical Journal, 1(3), 192–200. doi:10.4161/23328940.2014.955433.

Maté, G. (2008). In the Realm of hungry ghosts: Close encounters with addiction by gabor mate M.D. (Vol. 1). Toronto, CA: Knopf Canada.

Maté, G. (2012). Addiction: Childhood trauma, stress and the biology of addiction. Journal of Restorative Medicine, 1(1), 56–63. doi:10.14200/jrm.2012.1.1005.

McCauley, J. L., Killeen, T., Gros, D. F., Brady, K. T., & Back, S. E. (2012). Posttraumatic stress disorder and co-occurring substance use disorders: Advances in assessment and treatment. Clinical Psychology: A Publication of the Division of Clinical Psychology of the American Psychological Association, 19(3). doi:10.1111/cpsp.12006.

McElrath, K., & McEvoy, K. (2002). Negative experiences on ecstasy: The role of drug, set, and setting. Journal of Psychoactive Drugs, 34(2), 199–208. doi:10.1080/02791072.2002.10399954.

McGuire, P. (2000). Long term psychiatric and cognitive effects of MDMA use. Toxcology Letters, 112–113, 153–156. doi:10.1016/S0378-4274(99)00219-2.

Measham, F., Parker, H., & Aldridge, J. (1998). The teenage transition: From adolescent recreational drug use to the young adult dance culture in britain in the MID-1990s. Journal of Drug Issues, 28(1), 9–32. doi:10.1177/00202469802800102.

Mitchell, J. M., Bogenschutz, M., Lilenstein, A., Harrison, C., Kleinman, S., Parker-Guilbert, K.,…Doblin, R. (2021). MDMA-assisted therapy for severe PTSD: A randomized, double-blind, placebo-controlled phase 3 study. Nature Medicine, 27(6), G. M. O., 1025–1033. doi:10.1038/s41591-021-01336-3.

Moonzwe, L. S., Schensul, J. J., & Kostick, K. M. (2011). The role of MDMA (Ecstasy) in Coping with negative life situations among urban young adults. Journal of Psychoactive Drugs, 43(3), 199–210. doi:10.1080/02791072.2011.605671.

Morgan, M., McFie, L., Fleetwood, L., & Robinson, J. (2002). Ecstasy (MDMA): Are the psychological problems associated with its use reversed by prolonged abstinence? Psychopharmacology, 159(3), 294–303. doi:10.1007/s002130100907.

Oliver, C. F., Palamar, J. J., Salomone, A., Simmons, S. J., Philogene-Khalid, H., Stokes-McCloskey, N., & Rawls, S. M. (2019). Synthetic cathinone adulteration of illegal drugs. Psychopharmacology, 236(3), 869–879. doi:10.1007/s00213-018-5066-6.

Orth, B., & Merkel, C. (2020). Die Drogenaffinität Jugendlicher in der Bundesrepublik Deutschland 2019. Rauchen, Alkoholkonsum und Konsum illegaler Drogen: Aktuelle Verbreitung und Trends. Bundeszentrale für gesundheitliche Aufklärung.

Papaseit, E., Pérez-Mañá, C., Mateus, J.-A., Pujadas, M., Fonseca, F., Torrens, M.,…Farré, M. (2016). Human pharmacology of mephedrone in comparison with MDMA. Neuropsychopharmacology, 41(11), 2704–2713. doi:10.1038/npp.2016.75.

Parrott, A. C. (2015). Why all stimulant drugs are damaging to recreational users: An empirical overview and psychological explanation. Human Psychopharmacology: Clinical and Experimental, 30(4), 213–224. doi:10.1002/hup.2468.

Ruf, M., Schauer, M., & Elbert, T. (2011). UPID: UCLA PTSD Index for DSM IV (Child version, revision 1, deutsche Fassung). Retrieved from https://kops.uni-konstanz.de/handle/12345678/18103

Schierenbeck, T., Riemann, D., Berger, M., & Hornyk, M. (2008). Effect of illicit recreational drugs upon sleep: Cocaine, ecstasy and marijuana. Sleep Medicine Reviews, 12(5), 381–389. doi:10.1016/j.smrv.2007.12.004.

Schulte, M. T., & Hser, Y.-I. (2014). Substance use and associated health conditions throughout the lifespan. Public Health Reviews, 35(2). Retrieved from https://www.ncbi.nlm.nih.gov/pmc/articles/PMC3537082/

Sheehan, D. V., Sheehan, K. H., Shytie, R. D., Janavs, J., Bannon, Y., Rogers, J. E., Milo, K. M., Stock, S. L., & Wilkinson, B. (2010). Reliability and validity of the Mini International Neuropsychiatric Interview for Children and Adolescents (MINI-KID). The Journal of Clinical Psychiatry, 71(3), 313–326. https://doi.org/10.4088/JCP.09m05305whi
Sheerin, C., Berenz, E. C., Knudsen, G. P., Reichborn-Kjennerud, T., Kendler, K. S., Aggen, S. H., & Amstader, A. B. (2016). A population-based study of help seeking and self-medication among trauma-exposed individuals. Psychology of Addictive Behaviors, 30(7), 771–777. doi:10.1037/adb0000185.

Simmons, S., & Suárez, L. (2016). Substance abuse and Trauma. Child and Adolescent Psychiatric Clinics of North America, 25(4), 723–734. doi:10.1016/j.chc.2016.05.006.

Slade, T., McEvoy, P. M., Chapman, C., Grove, R., & Teesson, M. (2015). Onset and temporal sequencing of lifetime anxiety, mood and substance use disorders in the general population. Epидemiology and Psychiatric Sciences, 24(1), 45–53. doi:10.1017/S2045796013000577.

Steinberg, A. M., Brymer, M. J., Decker, K. B., & Pynoos, R. S. (2004). The University of California at Los Angeles Post-traumatic stress disorder reaction index. Current Psychiatry Reports, 6(2), 96–100. doi:10.1007/s11920-004-0048-2.

Stewart, L. H., Ferguson, B., Morgan, C. J. A., Swaboda, N., Jones, L., Fenton, R.,…Curran, H. V. (2014). Effects of ecstasy on cooperative behaviour and perception of trustworthiness: A naturalistic study. Journal of Psychopharmacology (Oxford, England), 28(11), 1001–1008. doi:10.1177/0269881114544775.

Strom, T. Q., Leskela, J., James, L. M., Thuras, P. D., Voller, E., Weigel, R.,…Holz, K. B. (2012). An exploratory examination of risk-taking behavior and PTSD symptom severity in a veteran sample. Military Medicine, 177(4), 390–396. doi:10.7205/MILMED-D-11-00133.

Thal, S. B., & Lommen, M. J. J. (2018). Current perspective on MDMA-assisted psychotherapy for posttraumatic stress disorder. Journal of Contemporary Psychotherapy, 48(2), 99–108. doi:10.1007/s10879-017-9379-2.

Thomasius, R., Schmolke, M., & Kraus, D. (1997). MDMA (*Ecstasy*)-Konsum—Ein Überblick zu psychiatrischen und medizinischen Folgen. Fortschritte der Neurologie - Psychiatrie, 65(2), 49–61. doi:10.1055/s-2007-996309.

Tull, M. T., Gratz, K. L., Aklín, W. M., & Lejuez, C. W. (2010). A preliminary examination of the relationships between posttrauma stress symptoms and Crack/Cocaine, Heroin, and Alcohol Dependence. Journal of Anxiety Disorders, 24(1), 55–62. doi:10.1016/j.janxdis.2009.08.006.

Turner, W. C., Muck, R. D., Muck, R. J., Stephens, R. L., & Sukumar, B. (2004). Co-occurring disorders in the adolescent mental health and substance abuse treatment systems. Journal of Psychoactive Drugs, 36(4), 455–462. doi:10.1080/02791072.2004.10524428.

UNESCO (2012). International standard classification of education ISCED 2011. UNESCO Institute for Statistics. http://www.uis.unesco.org/Education/Pages/international-standard-classification-of-education.aspx

Van den Brink, W. (2015). Substance use disorders, trauma, and PTSD. European Journal of Psychotraumatology, 6(1), 27632. doi:10.3402/ejpt.v6.27632.

Vizeli, P., & Liechti, M. E. (2017). Safety pharmacology of acute MDMA administration in healthy subjects. Journal of Psychopharmacology, 31(5), 576–588. doi:10.1177/0269881117691569.

Wiedmann, M. F., Kuitunen-Paul, S., Basedow, L. A., Roessner, V., & Golub, Y. (n.d.) Attenuated psychotic symptoms in adolescents with chronic cannabis and MDMA use. Frontiers in Psychiatry.

Williams, J. K., Smith, D. C., An, H., & Hall, J. A. (2008). Clinical outcomes of traumatized youth in adolescent substance abuse treatment: A longitudinal multisite study. Journal of Psychoactive Drugs, 40(1), 77–84. doi:10.1080/02791072.2008.10399763.

Wu, P., Bird, H. R., Liu, X., Duarte, C. S., Fuller, C., Fan, B.,…Canino, G. J. (2010). Trauma, posttraumatic stress symptoms, and alcohol-use initiation in children. Journal of Studies on Alcohol and Drugs, 71(3), 326–334. doi:10.15288/jsad.2010.71.326.

Wunderli, M. D., Vonnmoos, M., Fürst, M., Schädelin, K., Kraemer, T., Baumgartner, M. R.,…Quednow, B. B. (2017). Discrete memory impairments in largely pure chronic users of MDMA. European Neuropsychopharmacology: The Journal of the European College of Neuropsychopharmacology, 27(10), 987–999. doi:10.1016/j.euroneuro.2017.08.042.

Xian, H., Chantarujkapon, S. I., Scherrrer, J. F., Eisen, S. A., Lyons, M. J., Goldberg, J.,…True, W. R. (2000). Genetic and environmental influences on posttraumatic stress disorder, alcohol and drug dependence in twin pairs. Drug and Alcohol Dependence, 61(1), 95–102. doi:10.1016/S0376-8716(00)00127-7.