

COGNITIVE FUNCTIONING, CLINICAL PROFILE AND LIFE EVENTS IN YOUNG ADULTS ADDICTED TO DRUGS. DOES BEING A GIRL MAKE A DIFFERENCE?

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Abstract

Objective: Gender features play a fundamental role as risk factors in drug addiction, entailing differences in vulnerability, onset, drug use and clinical trajectories. Even if increasing empirical evidence has attested that drug abuse in emerging adulthood is associated with cognitive impairments, personality disorders and psychological distress, limited research has analyzed these aspects from a gender perspective. The present research focuses on gender differences in youths (18–24 years of age) diagnosed with substance use disorders (SUDs), in order to detect possible differences between females and males as regards their neuropsychological functioning, clinical profiles and past life experiences.

Method: Neuropsychological functioning (neuropsychological battery Esame Neuropsicologico Breve-2), the severity of the symptomatology (Symptom Checklist-90-Revised), personality profile and disorders (Shedler Westen Assessment Procedure-200) and life history were assessed in two groups of young adults with SUDs, 20 males and 20 females (mean age = 21 years, SD = 2.2). Participants were recruited in a therapeutic community in Venice, Italy.

Results: Girls showed less cognitive impairment but higher psychological distress with respect to boys; between the two groups, no differences emerged regarding the personality profiles. The girls' life histories presented more experiences of abuse and maltreatment; they also moved more quickly from substance use to dependence. Boys, instead, were more involved in criminal activity.

Conclusions: Given our results, it seems that gender differences manifest early, at emerging adulthood. Consequently, a gender-oriented treatment for drug addiction should be offered even at an early age, focusing on early adverse experiences and their potential traumatic effect on girls. By contrast, young men seem to rely on compromised cognitive functions, which require a specific treatment approach, since they constitute a crucial factor for individual adjustment and treatment outcomes. Results should be interpreted relative to some limitations (such as the small sample size and the preliminary and cross-sectional nature of the research), and future studies are required.

Key words: drug addiction, gender, emerging adulthood, personality disorder, neuropsychological functioning

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Introduction

Substance use disorders (SUDs) are highly prevalent psychiatric clinical conditions with lifetime prevalence in community samples of about 2–3% in the United States (SAMHSA 2014) and 30–75% in clinical samples worldwide (Verheul et al. 2000). In Italy, about 1% of the general population is diagnosed with SUDs, whereas 16% of youths aged 15–24 years use drugs in Europe (Di Blasi et al. 2015). Substance use disorders in youth have become an increasingly worrying issue; drug users younger than 25 years of age are estimated to represent 27% of the whole addicted population (EMCDDA 2013). Although in adulthood, males still

seem to be more likely to use and abuse drugs (Di Pierro et al. 2015), recent studies have demonstrated that in adolescence, this gender gap is eventually filled (Keyes et al. 2008). This is true both for the use of drugs such as cocaine, cannabis and heroin and for the abuse of new synthetic nonprescribed psychoactive drugs, which girls may use for their anorectic effect (Cranford et al. 2013, Swendsen et al. 2012, UNODC 2014).

Several studies have shown that drug abuse has a neurotoxic effect on brain circuitries, leading to structural and functional modifications, particularly in the dopaminergic mesolimbic system of reward (Cadet et al. 2014). A cascade of neuroadaptations has also been demonstrated (Robison and Nestler 2011).

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These structural and functional changes are consequent to continued substance abuse and mediate severe neuropsychological deficits, even in adolescence. It must be said that this altered functioning could be, at the same time, a cause and an effect of drug abuse and addiction (Keshavan et al. 2014). On one hand, the malfunctioning of specific cortical regions may foster risky behaviors, impulsivity, a misperception of possible damage and emotional dysregulation, eventually resulting in drug use; on the other hand, this maladaptive functioning could be directly facilitated by the chemical action of the substance, altering both functionally and structurally the above brain regions (Wetherill and Tapert 2013).

Even if the prevalence of drug abuse in adolescence is currently similar among males and females, gender seems to have an effect on the severity and typology of the negative effects drugs have on boys and girls, also impacting the effectiveness of treatment plans (Becker and Curry 2008, Fox and Sinha 2009). In fact, drug consumption and abuse seem to affect, both negatively and predominately, males' cognitive capacities, whereas they appear to be more powerfully connected with emotional dysregulation in females (Bonn-Miller et al. 2011). Studies addressing gender-specific differences in neurocognitive abilities resulting from severe drug exposure are still scarce and have reached mixed results. For instance, Lisdahl and Price (2012) have found better outcomes in females, whereas Shrestha and colleagues (2014) have demonstrated worse consequences in girls.

Drug addiction in adolescence

It has been proven that due to a period of specific vulnerability, the pervasiveness of SUD disorders in adolescence and young adulthood is higher than in other developmental phases, and it is associated with a number of comorbid conditions and impaired psychological functioning (Chambers and Potenza 2003). From a psychological standpoint, this vulnerability has been connected with the specific developmental tasks that youths must face, encompassing the onset of puberty (resulting in significant physical changes) and the substantial interpersonal and psychosocial transitions (Blos 1989) while shifting from a parent- to a peer-referenced functioning. More recently, this view has been integrated by neuroimaging research that has suggested that this phenomenon could be linked to the general immaturity of the cerebral cortex and to an imbalance between the maturation of different regions, leading to affective dysregulation (Ismail et al. 2017). In fact, the affective node represented by the orbitofrontal cortex limbic system is hyperactivated by adolescents' drive towards an exploration of the environment and new complex relationships, but this activation is not adequately counterbalanced by the maturation of the dorsolateral prefrontal cortex, which supervises high cognitive functions and develops later in life (Giedd et al. 2008, Paus et al. 2008, Poletti 2009). This imbalance is thought to be at the basis of adolescents' difficulty in modulating their reactions to social stimuli and to complex social relationships, resulting in disappointment, frustration, anxiety, depression or externalizing symptoms, such as aggression or substance abuse (Beattie et al. 2015).

Gender-specific differences

The studies in this field have also verified gender-specific differences in the development and functioning of brain structures, paths and rhythms of maturation,

myelination and pruning of cerebral circuits in adolescence and young adulthood (Gogtay et al. 2004, Sowell et al. 2004). For instance, frontal lobes reach their peak of grey matter at 12 years of age in males and at 11 in females, whereas in parietal lobes, grey matter is highly present at 12 years of age in boys and at 10 in girls. Other regions are not affected by gender in their maturation (e.g., the temporal lobes, which reach their peak of grey matter at 17 years of age in either males or in females) (Mills et al. 2014). Developmental changes occur in the structure of the social brain in late childhood and adolescence. It is unclear how (and if) these nonhomogeneities have an effect on the possible onset of psychopathologies or on SUDs in particular. Nevertheless, it has been demonstrated that gender affects SUD vulnerability rates (Lezak et al. 2012), pathways to addiction (with the *telescoping effect* described by Palmer et al. 2009) and the intervention process and its outcomes (Becker and Curry 2008, Fox and Sinha 2009). An important issue related to the gender-based rhythms of maturation of brain regions is that the early development of the prefrontal cortex in females (responsible for high cognitive functions) may protect girls (to a certain extent) from severe negative impairments in cognition. This positive effect could be due to drug abuse and generally has its onset in late adolescence (usually from 14 years of age), when the prefrontal cortex in females has reached a greater maturation compared to that of their male peers. On the other hand, boys' brain areas deputed to emotion regulation develop earlier than those of their female peers do. Thus, girls could show higher impairment in emotion regulation. If, instead, drug use is initiated in pre-, early or mid-adolescence, it is possible that males will be more vulnerable to neurobehavioral and cognitive disturbances (Lisdahl and Price 2012, Price et al. 2014).

Of course, the path to psychopathology is much more complex than a direct link between the neurobiological substratum and psychiatric disorders. Thus, the etiopathogenetic model of developmental psychopathology has considered the role of the environment and of early primary relationships (Lenroot and Giedd 2006, Alvarez and Emory 2006). In fact, it has been demonstrated that offspring of substance-abuser parents face a two-fold risk for developing SUDs themselves, given the well-established intergenerational nature of the disorder (EMCDDA 2012). Prenatal substance exposure is also a direct predictor of SUDs in adolescence and young adulthood, with rates of 29% and 46%, respectively (Baer et al. 2003, Alati et al. 2006, Glantz and Chambers 2006, O'Brien and Hill 2014). Traumatic experiences in the first years of life have also been associated with alcohol or drug abuse in later life (Craparo et al. 2014). As a whole, girls seem to have some robust protective factors against the onset of SUDs, as they show higher levels of education, less criminal activity and earlier contact with SUD treatment, compared with boys, but also manifest more social problems (e.g., unemployment), more traumatic experiences and more problems in close relationships.

Psychological and psychopathological functioning in drug-addicted adolescents

Very few studies have addressed the personality traits of young adult patients suffering from substance use disorders and co-occurring personality disorders, and even less attention has been given to the topic in adolescent drug users. Nevertheless, some research

Table 1. Demographics of male and female participants

	Males	Females
	% (N) or M (\pm SD)	% (N) or M (\pm SD)
Age	21.05 (2.31)	20.90 (\pm 2.25)
High school degree	30.0 (6)	35.0 (7)
School drop-out	65.0 (13)	80.0 (16)
Years of education	9.8 (\pm 2.19)	10.15 (\pm 1.23)
Unemployment	70.0 (14)	55.0 (11)
Poly-drug use	80.0 (16)	85.0 (17)
Use of synthetic drugs	85.0 (17)	80.0 (16)
Primary drug of abuse: heroin	76.0 (15)	76.0 (15)
Age of drug use onset	13.3 (1.95)	13.7 (1.48)
Years from use to dependence	2.75 (1.52)	1.76 (1.41)
Age of first contact with SUDs services	18.3 (2.49)	17.7 (1.99)
SUDs-related diseases (HIV, HPC)	35.0 (7)	15.0 (3)
Pharmacotherapy	80.0 (16)	80.0 (16)
Replacement therapy	60.0 (12)	70.0 (14)
Parental substance abuse/dependence	38.9 (7)	50.0 (10)
Past experiences of abuse/maltreatment	40.0 (8)	85.0 (17)
Criminal activity	70.0 (14)	30.0 (6)

has focused on this issue, showing a pervasiveness of Cluster B diagnosis in these individuals (Di Pierro et al. 2014, Kokkevi et al. 1998, Langås et al. 2012, Parolin et al. 2016), with women more likely to receive a diagnosis of paranoid, borderline, histrionic personality disorder (Trull et al. 2010). As for emotional-behavioral functioning, SUDs at a young age are associated with high symptoms of anxiety and depression (Fergusson et al. 2011). These symptomatic manifestations are more evident in girls than in boys (Greenfield et al. 2010).

Objectives

The present study focuses on gender differences in emerging adults diagnosed with severe substance use disorders to the extent of being referred to residential treatment; specifically, participants were currently in treatment in a therapeutic community in Venice, Italy. In particular, the study intends to provide some results on neuropsychological functioning and clinical profiles in this population, in terms of personality disorders and the severity of symptomatology. Finally, it aims to investigate the role of past life experiences, specifically in childhood and adolescence, on the cognitive and clinical functioning of these subjects. In order to explore these issues, a group of young women with SUDs was compared to a group of men of a similar age, also diagnosed with SUDs. Based on previous literature, we expect that drug addicted young women, with respect to young men, might show a better cognitive profile and a higher severity of symptomatology. We also postulate a different distribution between boys and girls regarding the personality profile and the presence of personality disorders. Finally, it can be hypothesized that girls experienced more adverse life events in their developmental age.

Materials and Methods

The present study adopted a descriptive, cross-sectional and correlational perspective to examine the

neuropsychological, personality and symptomatological features of the two groups of young adults with SUDs.

Participants

Participants were recruited from the therapeutic community “Villa Renata” in Venice, Italy, and data collection occurred as part of a broader research project (Psychological Assessment and Treatment With Addicted Youth; P.A.T.W.A.Y.),¹ which took place from 2013 to 2016. The following inclusion criteria were adopted: (a) meeting DSM-IV-TR (APA 2000) criteria for substance use disorder; (b) having spent less than three months in the treatment facility and (c) age ranging from 18 to 24 years. The administration of the assessment protocol was part of the standard procedure applied upon admission to the therapeutic community; thus, all inpatients who met the inclusion criteria participated in the study, and none refused to take part in it. The sample included 40 inpatients (M = 21 years, SD = \pm 2.2). The assessment took place, on average, 1.6 months after patients’ admission to the inpatient treatment facility. At the time of recruitment, participants had been abstinent from drugs for, on average, 3.2 months. None of them presented other relevant medical conditions. Two different groups of 20 female and 20 male inpatients were obtained. As reported in **table 1**, in both groups, most individuals had completed on average less than 10 years of school (reaching a low level of education), and most of them were not engaged in employment or education (70% of boys and 55% of girls). The majority of subjects (76%) indicated heroin as the primary substance of

¹ The authors confirm that the submitted study was conducted according to the WMA Declaration of Helsinki – Ethical Principles for Medical Research Involving Human Subjects. This study does not require ethics committee approval, because it was carried out according to a non-interventional protocol. All patients gave their informed consent to the anonymous use of their clinical data for this independent study.

abuse in both groups. However, both female and male inpatients were mainly poly-drug users (85% and 80%, respectively), having used different synthetic drugs besides cocaine and alcohol. The onset of drug-related problems occurred during early adolescence for both girls and boys, on average at 13–14 years of age. The first contact with SUD treatment services occurred between ages 17 and 18. At the time of recruitment, 80% of individuals in both groups were prescribed with pharmacotherapy, and 60% of males and 70% of females had methadone replacement therapy; 35% of the boys and 15% of the girls were diagnosed with health diseases related to SUD. As regards adverse experiences in the developmental age, 38.9% of boys and 50% of girls reported that at least one of their parents had SUDs.

Instruments

Sociodemographic data. The collection of sociodemographic data occurred according the standard protocol adopted by the therapeutic community at admission, using an ad hoc interview format. If necessary, data were integrated and/or confirmed by information reported by outpatient mental health services that referred the patient to the facility.

Brief Neuropsychological Examination-2 [Esame Neuropsicologico Breve-2] (ENB-2; Mondini et al. 2011). This is a comprehensive neuropsychological battery ideated and standardized for the Italian population. It includes 16 subtests (Digit span, Immediate and Delayed recall prose memory, Interference memory at 10 and 30 seconds, a Trial making test parts A and B, Token test, Word phonemic fluency test, Abstract reasoning test, Cognitive estimation test, Test of overlapping figures, Spontaneous drawing, Copy drawing, Clock drawing, and Ideative and ideomotor praxis test). The ENB-2 allows the investigation of several cognitive domains: attention, executive functioning, perception, praxis abilities and comprehension. The battery provides both an assessment of the single cognitive tasks and a total score (global cognitive index) indicating the overall cognitive profile. Age (15–20, 21–30 years) and education (lower than 9 years and higher) are the two criteria used to identify subgroups of individuals and their respective normative scores. The fifth percentile was used to determine cut-off scores for each subgroup; according to the cut-off score, the performance is classified into three categories: below average (impaired), at the limit and average (normative). The battery shows good psychometric characteristics, revealing good differential validity in discriminating normative and clinical groups and sufficient test-retest reliability (range from 0.57 to 0.97) (Mondini et al. 2003, Mondini et al. 2011).

The Shedler Westen Assessment Procedure (SWAP-200; Westen and Shedler 1999a, 1999b) is a set of 200 descriptive statements (items) regarding adult personality aspects. It is based on the Q-Sort method, with a fixed score distribution, and it requires the clinician to sort the items into eight categories based on their applicability to the patient, from 7 (*highly descriptive*) to 0 (*not descriptive*). The major advantage of the present assessment is that it relies on an external observer's judgment instead of self-reporting, which is subject to a number of biases. The SWAP-200 assessment provides (a) a personality diagnosis expressed as the matching of the patient's description

with 10 prototypical descriptions of *DSM-IV* personality disorders (standardized score named PD-T); according to DSM, the 10 personality disorders are grouped into three clusters (A,B,C); (b) a personality diagnosis based on the matching of the patient with 11 Q-factors of personality derived empirically (standardized scores named Q-T); and (c) a dimensional profile of healthy and adaptive functioning. The presence of one or more personality disorders is determined when the patient's PD-T and/or Q-T are ≥ 60 and the adaptive functioning scale is ≤ 60 ; if the score ranges from 55 to 60, then subclinical traits of that personality disorder or style are present. In sum, the SWAP-200 provides both categorical and dimensional diagnoses. The reliability of SWAP-200 personality descriptions ranges from 0.75 to 0.89 (Shedler and Westen 1998, Westen and Muderrisoglu 2003, Marin-Avellan et al. 2005), and scores correlate with several external criterion measures (e.g., Westen and Shedler 1999a, Westen and Muderrisoglu 2003, Westen and Weinberger 2004). The study by Blagov and colleagues (2012), after reviewing empirical evidence on the SWAP-200, attests its validity and reports new test-retest reliability data (median coefficient >0.85). To our knowledge, an Italian translation of the SWAP-200 is currently available (Lingiardi et al. 2006; Shedler et al. 2014). Given the need for a clinician's judgment to complete the SWAP-200, this assessment was not administered to the comparison group.

The Symptom Checklist-90-Revised (SCL-90-R; Derogatis 1994). This is a self-report measure assessing 90 clinical symptoms on a 5-point Likert scale, ranging from 0 (*not at all*) to 4 (*extremely*). The symptoms are factored into nine psychiatric dimensions (depression, anxiety, somatization, obsessive-compulsive behavior, interpersonal sensitivity, hostility, phobic anxiety, psychoticism and paranoid ideation), plus altered appetite and disturbed sleep. The instrument provides three global scores: the Global Stress Index (GSI) indicating the general psychological distress of the individual; the Positive Symptom Total (PST), revealing the number of symptoms the respondent has endorsed to any degree, and the Positive Symptom Distress Index (PSDI), a measure of distress intensity. The psychometric properties of the original version of the checklist show acceptable levels of internal consistency (ranging from 0.77 to 0.90), test-retest reliability (ranging from 0.68 to 0.90) and convergent and discriminant validity (Derogatis 2011). However, despite the extensive and widespread application of the instrument, some studies have questioned its factorial invariance across different samples (Cyr et al. 1985, Prunas et al. 2012). The Italian translation and adaptation of the SCL-90-R (Sarno et al. 2011) show adequate results for principal component analysis (a single factor explains 65.22% of the variance) and internal consistency with Cronbach's alpha (from 0.68 to 0.87 for the nine dimensions and = 0.97 for the GSI score).

Strategies of data analysis

Data were analyzed using the IBM Statistical Package for the Social Sciences (SPSS) 23.0. Descriptive statistics (frequencies, mean scores and percentages) and nonparametric tests (the Mann-Whitney U test, Pearson's Chi-Square test and Spearman's Rho correlation) were applied, due to the limited number of subjects.

Results

Neuropsychological performances in young women and men

To fulfill our first aim, the sociodemographical variables capable of influencing performance on the neuropsychological battery (Mondini et al. 2011) were analyzed, and the two groups were compared for age and years of education. The use of the Mann–Whitney test confirmed that the two groups were similar for both age ($z = -.468, p = .647$) and years of education ($z = -.514, p = .620$).

Table 2 illustrates the descriptive results of the ENB-2 performance in the two groups. Results showed that 35% of female and 80% of male inpatients presented an altered global cognitive profile, considering both those whose global cognitive index reached the limits of the normative performance and those who had fully impaired neuropsychological functioning. When compared by the Chi-squared analysis, girls showed a global cognitive profile significantly more adequate than that of the boys ($X^2 = 7.501, p = .006$) (**table 2**).

With respect to the performance on the single tests of the ENB-2 battery, we can observe that boys had a worse performance on the Copy drawing test ($X^2 = 8.069, p = .005$), a task assessing visual perception and constructional skills, even though this result did not

remain significant, using Bonferroni's correction ($p = .05/16 = .003$). Interesting differences between genders can also be detected in those tasks tapping into the domain of executive functions, even though the results did not reach statistical significance. Male-female differences in the executive domain can be detected in the Abstract Reasoning test, Phonemic fluency test, Clock drawing test and the Overlapping figures test; on all these tests, a higher percentage of boys than girls had an altered performance.

As regards memory abilities, descriptive data indicate that a higher rate of boys scored above the normative scores on the Delayed recall prose memory test (35%) and on the Interference memory test at 30 seconds (30.0%), while girls reached lower scores on the Interference memory test at 10 seconds and on the Digit span test.

However, both groups presented elevated rates of altered performance in two tasks assessing executive functions: the Tmt-B, a test of attention and task switching, providing information about visual search speed, mental flexibility and executive function (60% boys, 50% girls), and the Cognitive Estimation test, assessing the capacity of answering a question for which relevant knowledge, but not the specific answer, is available (40% in both groups). Girls and boys also showed similar high percentages of impairment on the Delayed recall prose memory test (40%).

Table 2. Percentages of patients with neuropsychological deficits

Cognitive domain Test	Males			Females			Chi-squared test	
	Limit %(N)	Impaired %(N)	Altered %(N)	Limit %(N)	Impaired %(N)	Altered %(N)	X ²	p
Attention								
TMT-A	-	25.0 (5)	25.0 (5)	-	20.0 (4)	20.0 (4)		
TMT-B	5.0 (1)	55.0 (11)	60.0 (12)	-	50.0 (10)	50.0 (10)		
Memory								
Digit span	-	-	-	-	10.0 (2)	10.0 (2)		
Immediate recall	5.0 (1)	40.0 (8)	45.0 (9)	15.0 (3)	35.0 (7)	50.0 (10)		
Delayed recall	-	35.0 (7)	35.0 (7)	5.0 (1)	20.0 (4)	25.0 (5)		
Interference memory 10s	5.0 (1)	20.0 (4)	25.0 (5)	35.0 (7)	5.0 (1)	40.0 (8)		
Interference memory 30s	15.0 (3)	15.0 (3)	30.0 (6)	10.0 (2)	10.0 (2)	20.0 (4)		
Comprehension								
Token test	-	15.0 (3)	15.0 (3)	-	-	-		
Executive Function								
TMT-B	5.0 (1)	55.0 (11)	60.0 (12)	-	50.0 (10)	50.0 (10)		
Cognitive estimation	25.0 (5)	15.0 (3)	40.0 (8)	15.0 (3)	25.0 (5)	40.0 (8)		
Abstract reasoning	15.0 (3)	15.0 (3)	30.0 (6)	10.0 (2)	5.0 (1)	15.0 (3)		
Phonemic fluency test	15.0 (3)	15.0 (3)	30.0 (6)	5.0 (1)	15.0 (3)	20.0 (4)		
Clock Drawing test	5.0 (1)	45.0 (9)	50.0 (10)	10.0 (2)	15.0 (3)	25.0 (5)		
Overlapping figures	10.0 (2)	10.0 (2)	20.0 (4)	-	10.0 (2)	10.0 (2)		
Perception								
Spontaneous drawing	-	-	-	-	-	-		
Copy drawing	5.0 (1)	40.0 (8)	45.0 (9)	-	5.0 (1)	5.0 (1)	8.069	.005
Praxis Ability								
Ideomotor praxis	-	5 (1)	5.0 (1)	-	-	-		
Global Index	15.0 (3)	65.0 (13)	80.0 (16)	5.0 (1)	30.0 (6)	35.0 (7)	7.501	.006

Note: "altered" comprehend limit and impaired performance

In sum, girls showed significantly better cognitive abilities in terms of global profile than boys did, and this result was statistically significant; from a descriptive point of view, females had a better performance on tests involving visuospatial skills and executive function, although it was not statistically significant. However, young patients with SUDs from both groups showed high rates of impairment on two tests assessing executive function, delineating a cognitive domain of particular concern.

Clinical profiles: personality and symptoms in the two groups

In regard to the second aim of the study, investigating sex differences in personality functioning and symptomatology, we performed nonparametric statistics to compare males and females. Descriptive data on the SWAP-200 procedure indicated that personality disorders (PDs) were frequent among young inpatients of both groups. As a matter of fact, with respect to the DSM classification, in both groups, high rates of individuals were diagnosed with at least one personality disorder: 70% of drug-addicted boys and 80% of girls (table 3). However, significant differences in terms of personality profile did not emerge between boys and girls, neither running Chi-squared analysis nor the Mann-Whitney's U test. The primary diagnosis referred more frequently to Cluster B

in both groups; specifically, 50% of boys and 56.3% of girls were diagnosed with a Cluster B disorder. Cluster A disorders were identified for 28.6% of boys and 13.5% of girls, while 21.4% of subjects in the male group and 31.3% in the female group received a Cluster C primary diagnosis. Histrionic personality disorder was the most common primary diagnosis in boys (21.4%), followed by paranoid, antisocial and narcissistic disorders (each reaching rates of 14.3%). When both subclinical and clinical traits were taken into account, the histrionic profile remained the most reported, but borderline and dependent features emerged more clearly (while the presence of antisocial characteristics was reduced). As regards females, the most frequent diagnoses were histrionic (31.3%) and borderline (25%) disorders, but the dependent personality diagnosis was also identified (18.8%). The same abovementioned personality styles were the most reported among girls when both traits and disorders were considered.

In sum, according to the DSM categorization, personality disorders were frequently diagnosed in both males and females; Cluster B disorders were the most common, especially the histrionic disorder, irrespective of gender.

In relation to the Q-factor categorization, a PD diagnosis was detected in 80% of male subjects and in 85% of their female counterparts, similar to data reported by the DSM classification. The primary diagnosis was dependent personality for both young men (37.5%) and young women (29.4%). Histrionic

Table 3. Personality Disorders and traits assessed with the SWAP

Classi- fication	Personality	Males						Females					
		min	max	M	SD	Traits or Disorder % (N)	Primary % (N)	min	max	M	SD	Traits or Disorder % (N)	Primary % (N)
PD-T	PD						70.0 (14)						80.0 (16)
	Cluster A						28.6 (4)						12.5 (2)
	Paranoid	35	72	50.60	9.68	30.0 (6)	14.3 (2)	34	59	45.55	5.60	5.0 (1)	-
	Schizoid	38	60	47.15	6.51	15.0 (3)	7.1 (1)	33	61	46.90	8.83	20.0 (4)	-
	Schizotypal	41	59	50.00	5.47	25.0 (5)	-	32	61	48.65	7.94	25.0 (5)	14.3 (2)
	Cluster B						50.0 (8)						56.3 (9)
	Antisocial	41	68	52.95	8.50	40.0 (8)	14.3 (2)	44	64	50.20	4.74	10.0 (2)	-
	Borderline	48	65	56.25	5.70	50.0 (10)	7.1 (1)	40	67	56.60	7.39	60.0 (12)	25.0 (4)
	Histrionic	43	66	54.55	6.14	55.0 (11)	21.4 (3)	40	69	54.95	7.94	45.0 (9)	31.3 (5)
	Narcissistic	40	65	52.15	8.51	50.0 (8)	14.3 (2)	41	59	48.75	4.88	15.0 (3)	-
	Cluster C						21.4(3)						31.3 (5)
	Avoidant	36	60	46.85	6.21	10.0 (2)	-	36	59	47.65	6.33	15.0 (3)	-
	Dependent	38	64	51.65	6.99	40.0 (8)	14.3 (2)	46	64	53.70	5.56	35.0 (7)	18.8 (3)
Obsessive	32	60	44.35	6.37	5.0 (1)	7.1 (1)	34	63	45.55	8.10	15.0 (3)	14.3 (2)	
Q-T	PD						80.0 (16)						85.0 (17)
	Antisocial	41	70	53.50	8.59	45.0 (9)	18.8 (3)	43	64	50.80	4.98	20.0 (4)	-
	Schizoid	36	59	47.25	6.40	15.0 (3)	-	31	61	46.30	8.90	15.0 (3)	-
	Paranoid	35	69	49.30	9.84	35.0 (7)	12.5 (2)	39	64	45.95	5.97	10.0 (2)	-
	Obsessive	39	59	47.10	5.23	10.0 (2)	-	33	64	47.25	7.61	15.0 (3)	-
	Histrionic	42	65	53.65	6.83	35.0 (7)	-	35	67	55.60	8.06	55.0 (11)	17.6 (3)
	Narcissistic	32	58	48.10	6.95	15.0 (3)	-	37	66	45.47	6.45	5.0 (1)	-
	Avoidant	36	61	46.75	7.59	15.0 (3)	-	37	59	47.75	6.74	15.0 (3)	-
	Depressive	38	58	49.25	5.98	25.0 (5)	-	39	71	51.25	8.12	25.0 (5)	11.8 (2)
	Dysregulated	41	65	51.50	6.93	35.0 (7)	12.5 (2)	37	70	51.85	8.05	35.0 (5)	11.8 (2)
	Dependent	45	70	56.05	6.63	45.0 (9)	37.5 (6)	44	69	57.50	7.80	12.0 (60)	29.4 (5)
Hostile	31	63	49.15	8.66	30.0 (6)	-	31	62	46.40	7.80	15.0 (3)	-	
Adaptive functioning	38	56	47.45	5.47	73.0 (11)		38	72	49.25	8.06	93.0 (14)		

disorders were frequent in the female group (17.6%), while boys showed high rates of antisocial functioning (18.8%), delineating a slight difference between groups, at least from a descriptive point of view. When both subclinical traits and clinical disorders were considered, a similar scenario emerged for boys, among whom high rates of dependent and antisocial characteristics (45% each) were detected. For girls, instead, histrionic features were confirmed as highly frequent (55%), while a dysregulated personality profile result was more common (35%) than the dependent profile (as reported when only full-blown disorders were considered).

Thus, both groups showed high rates of dependent personality functioning, but they differed from each other, since boys presented higher rates of antisocial subclinical and clinical features, while girls presented more histrionic subclinical and clinical traits.

The adaptive functioning result was inadequate for the totality of males and for 90% of girls.

Taken together, the results indicated that high rates of young adults with SUDs, of both genders, were diagnosed with at least one personality disorder; boys and girls could not be distinguished by the presence of specific characteristics regarding the personality functioning. According to DSM classification, Cluster B disorders were diagnosed most frequently in both groups, especially histrionic and borderline profiles. With regard to the SWAP classification, dependent personality disorder was the most common diagnosis in both groups, which slightly differed from each other in terms of antisocial functioning in boys and histrionic features in girls.

Results regarding the psychological distress, as assessed by the self-report SCL-90-R, displayed that both female and male young inpatients showed a clinically significant global symptomatological profile, with GSI scores above the clinical cut-off for 60% and 75% of individuals, respectively, as shown in **table 4**. The majority of subjects in both groups reached the clinical range in the two other global indices, the Positive Symptom Total index (indicating the number of symptoms complained of) and the Positive Symptom Distress index (reporting the overall intensity of

distress). Comparing the two groups from a descriptive point of view, young female inpatients seemed to reach higher scores in all dimensions (scales and global indices) of the questionnaire. Statistically significant results were detected for some of them, attesting higher psychological distress in girls than in boys. The Mann–Whitney's U test revealed a significant difference between the two groups for the Positive Symptom Distress Index ($z = -2.196$, $p = 0.028$) and for two psychiatric dimensions: phobic anxiety ($z = -2.533$, $p = .011$) and paranoid ideation ($z = -2.048$, $p = .040$). Results were confirmed by the Chi-squared test for the PSDI ($X^2 = 7.025$, $p = .020$) and for the two psychiatric dimensions, phobic anxiety ($X^2 = 5.584$, $p = .041$) and paranoid ideation ($X^2 = 5.584$, $p = .018$), even if the results did not remain significant according to Bonferroni's correction ($p = .05/12 = .004$).

Both girls and boys reported overall high psychological distress, but the former group of inpatients showed higher levels of symptoms in two scales and as regards the global index assessing the perceived symptoms' intensity.

Adverse past experiences

Comparing females and males on adverse past experiences, a significant difference emerged regarding the time between the first experiences with drugs and the onset of drug dependence: 2.75 years for boys and only 1.75 for girls, indicating that girls became addicted to drugs more quickly ($z = 8.485$, $p = .008$). A significantly higher rate of girls (85%) also experienced past events of abuse and/or maltreatment during childhood and/or adolescence than boys (40%) ($X^2 = 8.640$, $p = .008$). Conversely, boys were more involved in criminal activities ($X^2 = 6.400$, $p = .026$) (**table 1**).

In order to explore the third aim of the present study, Spearman's Rho correlations were also applied to test for any associations between those variables that were most relevant for the purposes of the research, including the global neuropsychological profile, the three global indices of the SCL-90-R (GSI, PST, PSDI), the SWAP-200 classifications and the sociodemographical

Table 4. Symptomatological profile at SCL-90-R

Scales	Males					Females					Chi-squared test or Mann Whitney's U	
	min	max	M	SD	Clinical % (N)	min	max	M	SD	Clinical % (N)	X ² or z	p
Somatization	39	76	54.05	13.34	40.0 (8)	37	76	60.05	13.31	60.0 (12)		
Obsessionality	37	71	53.55	11.01	40.0 (8)	36	75	56.20	12.16	65.0 (13)		
Interpersonal sensitivity	38	75	53.30	11.40	45.0 (9)	38	76	61.50	12.93	70.0 (14)		
Depression	43	76	60.75	12.03	65.0 (13)	40	76	64.00	10.75	75.0 (15)		
Anxiety	40	76	58.00	11.80	55.0 (11)	40	76	63.15	12.77	70.0 (14)		
Hostility	39	76	57.10	11.41	50.0 (10)	42	76	60.95	12.43	60.0 (12)		
Phobic anxiety	43	75	49.45	9.02	15.0 (3)	44	76	58.20	13.19	50.0 (10)	$z = -2.533$ $X^2 = 5.584$.011 .041
Paranoid ideation	36	76	55.50	14.07	50.0 (10)	44	76	64.30	10.79	85.0 (17)	$z = -2.048$ $X^2 = 5.584$.040 .018
Psychoticism	42	76	57.95	11.88	55.0 (11)	44	76	64.05	12.23	65.0 (13)		
GSI	39	76	57.95	11.84	60.0 (12)	41	76	63.65	11.59	75.0 (15)		
PST	35	75	55.35	11.48	55.0 (11)	36	73	58.80	9.86	75.0 (15)		
PSDI	42	76	58.25	11.57	60.0 (12)	43	76	66.60	9.03	95.0 (19)	$z = -2.196$ $X^2 = 7.025$.028 .020

variables that differentiated the two groups (namely past experiences of abuse and maltreatment, criminal activity and the time from the first drug experiences to drug dependence). The two groups were considered separately according to the purpose of identifying potential clusters or profiles that characterized young female and male inpatients.

As illustrated in **table 5**, an inverse association was detected between cognitive abilities and criminal activity in boys; in this group, higher psychological distress also positively correlated with higher scores on the borderline, dependent and dysregulated personality profiles. These latter results resemble those detected in the female group; girls showed a similar positive association between psychological symptoms and borderline, dependent and dysregulated personality characteristics. Girls showed a negative correlation between global cognitive profile and past experiences of abuse and/or maltreatment, indicating that having experienced this kind of adverse event in the developmental age is associated with lower cognitive abilities. This association was examined more in depth (beyond the global cognitive functioning), assessing a correlation between the number of tasks assessing executive functions that showed an impaired performance and the abuse/maltreatment variable; the results reported a significant correlation ($r = .605, p = .006$), confirming the inverse association.

Discussion

The present study aimed to contribute to previous literature on gender differences in substance use disorders, focusing on a specific group of individuals:

patients admitted to residential treatment (given the severity of their drug use disorder) and aged 18-24 (i.e., in their emerging adulthood, which has been proposed as a specific developmental stage facilitative of addictions) (Sussman and Arnett 2014). The investigation focused on clinical aspects that are considered highly relevant in terms of treatment outcome and individual adjustment, namely neuropsychological functioning, which plays an important role in individual adjustment and emotional competences (Blair and Ursache 2011, McClelland et al. 2007), personality disorders, severity of symptomatology and adverse life experiences.

Our first aim was to investigate sex differences in neuropsychological functioning. Previous research reports gender-based rhythms of prefrontal brain maturation, sex differences among healthy subjects and a possible higher vulnerability to neurobehavioral and cognitive impairments related to drug abuse in boys (Crane et al. 2013b, Lisdahl and Price 2012, Price et al. 2014). Based on this data, we postulated that females would score better on neuropsychological tests, and the results confirmed this hypothesis. A statistically significantly higher proportion of males (80%) showed an altered global profile compared to girls (35%). No statistically significant data were obtained for the single tasks included in the assessment battery; thus, the present study could not identify sex differences in specific neuropsychological domains but rather, only such differences in the broader cognitive profile. From a descriptive point of view, young men performed worse in the domains of visual perception and executive function; girls, instead, scored lower in two tests assessing memory abilities. These results are in line with those studies on gender differences in drugs'

Table 5. Correlations between global cognitive profile, personality profiles and socio-demographic variables

Variables	Males		Variables	Females		Variables
	Rho	p		Rho	p	
<i>ENB-2</i>			<i>DEMOGRAPHICS</i>	<i>ENB-2</i>		<i>DEMOGRAPHICS</i>
Global cognitive profile	-.512*	.021	Criminal Activity	Global cognitive profile	-.477*	Abuse/Maltreatment
<i>SWAP-200</i>			<i>SLC-90-R</i>	<i>SWAP-200</i>		<i>SLC-90-R</i>
PD-T Borderline	.492*	.028	GSI	PD-T Borderline	.464*	GSI
	.481*	.032	PST		.454*	PST
PD-T Dependent	.537*	.015	GSI	PD-T Dependent	.524*	GSI
Q-T Dysregulated	.675**	.001		Q-T Dysregulated	.678**	GSI
	.622**	.003	PST		.633**	PST
	.693**	.001	PSDI		.691**	PSDI
				<i>SWAP-200</i>		<i>DEMOGRAPHICS</i>
				PD-T Borderline	.554*	Abuse/Maltreatment
				PD-T Histrionic	.664**	
				PD-T Obsessive-compulsive	-.591**	
				Q-T Histrionic	.609**	
				Q-T Dependent	.664**	
				Q-T Obsessive-compulsive	-.573**	
				PD-T Antisocial	.502*	Criminal Activity
				PD-T Narcisistic	.492*	
				Q-T Antisocial	.568**	

Note: * .05, ** 0.01.

effects on neurocognition, highlighting poorer memory performance in females and poorer decision-making in males (Crane et al. 2013a, Crane et al. 2013b, Lisdahl and Price 2012, Price et al. 2014). It is important to acknowledge that currently available results are still scarce and partly inconsistent, with studies reporting in contrast more executive impairments in adolescent girls (Medina et al. 2009); however, nascent and current evidence points out sex differences in the impact of drugs on neurocognitive functioning and ascribes to males a higher vulnerability.

In respect to the second aim of the study, we expected that women would be more likely to receive a diagnosis of paranoid, borderline, histrionic personality disorders (Trull et al. 2010). But contrary to expectations, young males and females diagnosed with SUDs could not be distinguished in terms of personality profiles and disorders, according to either DSM or SWAP-200 classifications. Descriptive data indicate that with respect to DSM, in both groups, a considerably high rate of subjects were diagnosed with at least one personality disorder (70–80%). Cluster B disorders, in particular histrionic PD, were the most frequent primary diagnoses; however, adopting a dimensional approach, borderline and dependent features were also quite common. According to SWAP-200, among those subjects diagnosed with a PD (80–85%), dependent personality disorder was detected as the most common diagnosis; from a dimensional point of view, a slight sex difference emerged, with boys presenting higher antisocial features and girls showing more histrionic traits. Overall, the results depicted a clinical condition of high concern in young adults admitted to inpatient treatment for SUDs, regardless of gender. The high rates of PDs, especially Cluster B disorders, are consistent with the available research specifically targeting this clinical population in this developmental stage (Kokkevi et al. 1998, Langås et al. 2012) and also with studies including older individuals (Di Pierro et al. 2014, Mackesy-Amiti et al. 2012). However, dependent personality disorders and features were also frequently detected, as previously also reported (Langås et al. 2012) by research using the SWAP-200 procedure (Parolin et al. 2016). Concerning the symptomatological profile assessed by the SCL-90-R, young women's clinical condition was characterized by higher psychological distress; they reported higher levels of phobic anxiety and paranoid ideation. Moreover, they reported experiencing psychological distress of higher intensity (PTSD) than males, as previously attested by other research (Fergusson et al. 2011, Greenfield et al. 2010).

Past life experiences seemed to differentiate the two groups, and the results reached statistical significance; girls were more likely to have been exposed to abuse and maltreatment during their developmental age, while males had been more involved in criminal activity. Studies have consistently shown that being a victim of physical or sexual abuse increases the risk of using drugs in adolescence by two to four times (Whitesell et al. 2013). Past traumatic experiences, such as abuse and maltreatment, are part of a broader constellation of risk factors that characterize women who develop SUDs, including low employment and dysfunctional romantic and family relationships (Du et al. 2013, ESPAD 2013, Lewis et al. 2014). These factors tend to exceed the protective contribution offered by potential positive characteristics such as lower criminal activity and higher education (Du et al. 2013), delineating a clinical condition of particular vulnerability. Girls also moved more quickly from substance use to dependence; other research on gender differences in drug addiction

recognizes strong distinctions with regard to the development of SUDs. Specifically, the period between drug experimentation and the onset of a disorder is more restricted for girls than for boys (Palmer et al. 2009, Quiñones-Jenab 2006).

With regard to boys, the higher involvement in criminal activity may be associated with the higher rate of antisocial features detected in males' personality profiles (Brennan et al. 2017). This result can also be interpreted in light of a developmental pathway that associates early externalizing problems in childhood, namely oppositional defiant and conduct disorders, with later antisocial behavior and drug use in adolescence and adulthood (Elkins et al. 2007, Fergusson et al. 2007, Pingault et al. 2013). Correlational results strengthen the role played by these adverse past experiences in females' and males' individual functioning. As regards girls, research demonstrated that their having experienced early traumatic events (often of an interpersonal nature) is capable of compromising optimal cognitive development (Bennett et al. 2008, El-Sheikh and Buckhalt 2003, Mayes 2002, Singer et al. 2008) and personality disorders (Afifi et al. 2011, Gibb et al. 2001). The inverse association between criminal activity and cognitive abilities in male inpatients is in line with a review study indicating that clinically significant frontal lobe dysfunction is associated with aggressive dyscontrol (Brower and Price 2001).

Overall, our study contributes to the literature indicating that sex differences in drug-addicted individuals can be detected as early as adolescence and emerging adulthood and not only in older age. According to the present results, gender differences encompass cognitive profiles, symptomatological distress and adverse past experiences. Consequently, some implications for treatment can be hypothesized. In fact, gender differences do not merely compromise SUD development and the clinical condition (Palmer et al. 2009, Quiñones-Jenab 2006), but they tend to persist during treatment, affecting its process and outcomes (Becker and Curry 2008, Fox and Sinha 2009, Greenfield et al. 2010).

The present results point out that a gender-oriented approach might represent a valuable option, due to the earlier stages of SUD development and the earlier phases of intervention, including early assessment. Second, intervention programs should be ideated and implemented taking into account the specific constellation of risk factors that characterize young women and young men. Tailored interventions for women should directly address early adverse experiences and their potential traumatic effect in order to buffer adverse implications; 45% of adults with SUDs meet the criteria for complex trauma diagnosis (Ford and Smith 2008), that is, the experience of multiple, chronic and prolonged developmentally adverse traumatic events, most often of an interpersonal nature and occurring in early development (Kearney et al. 2010, Van der Kolk et al. 2005). Complex trauma mediates the association between early adverse experiences and drug problems in young people (aged 16–24) (Rosenkranz et al. 2014). Moreover, women with traumatic experiences and related sequelae comprise 30–59% of patients with SUDs, and they face a more severe course (Najavits et al. 1998). However, despite the acknowledged need for trauma-focused work (Brown et al. 2008, Taplin et al. 2014), only a few protocols address trauma experiences that pre-exist/co-exist with SUDs in young adulthood (Rosenkranz et al. 2014), and even fewer for women (Marich 2009, Marich 2010, Najavits 1993).

By contrast, males could benefit from a cognitive

rehabilitation approach, aimed to restore those impairments in neuropsychological functioning that might negatively influence the treatment process and outcome (Aharonovich et al. 2006, Grant et al. 2013).

Our study may contribute to the topic of gender differences in drug addiction, constituting an original work with respect to the previous literature on this theme. A primary aspect relates to the specificity of the clinical group, indicating that sex differences in drug-addicted individuals can be detected as early as emerging adulthood and may also affect the domain of neuropsychological functioning. The assessment instruments included in the study are also largely validated and widely used. Finally, some useful considerations can be drawn from the present results in terms of clinical implications, offering indicators for the ideation and implementation of tailored treatment protocols.

Besides some strengths, this study has some limitations, the first being the small size of its samples. However, as reported by Streiner (2006), the sample size does not always represent an obstacle in psychiatric research. Second, the study addresses a very specific group of individuals with SUDs, in terms of age and the severity of the disorder (i.e., characterized by high frequency of use and disturbance in social functioning); thus, the results cannot be generalized to other drug-dependent individuals, such as outpatients. The preliminary and cross-sectional nature of the study constitutes other limits of the research; thus, we cautiously proposed an interpretation of our results, recognizing the limitedness of the study. Replication of the present data is necessary in order to increase confidence in the results and to better guide the clinical implications that the study has preliminarily indicated.

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