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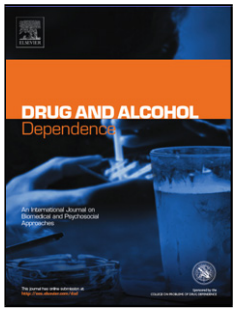

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PII: S0376-8716(14)02008-0
DOI: http://dx.doi.org/doi:10.1016/j.drugalcdep.2014.12.028
Reference: DAD 5410

To appear in: *Drug and Alcohol Dependence*

Received date: 5-7-2014
Revised date: 20-12-2014
Accepted date: 22-12-2014

Please cite this article as: Di Nicola, M., Tedeschi, D., De Risio, L., Pettorruso, M., Martinotti, G., Ruggeri, F., Swierkosz-Lenart, K., Guglielmo, R., Callea, A., Ruggeri, G., Pozzi, G., Di Giannantonio, M., Janiri, L.,Co-occurrence of Alcohol Use Disorder and behavioral addictions: relevance of impulsivity and craving, *Drug and Alcohol Dependence* (2015), http://dx.doi.org/10.1016/j.drugalcdep.2014.12.028

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Co-occurrence of Alcohol Use Disorder and behavioral addictions: relevance of impulsivity and craving

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Running head: Co-occurrence of AUD and behavioral addictions

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ABSTRACT

Purpose. The aims of the study were to evaluate the occurrence of behavioral addictions (BAs) in Alcohol Use Disorder (AUD) subjects and to investigate the role of impulsivity, personality dimensions and craving. **Methods.** 95 AUD outpatients (DSM-5) and 140 homogeneous controls were assessed with diagnostic criteria and specific tests for gambling disorder, compulsive buying, sexual, internet and physical exercise addictions, as well as with the Barratt Impulsiveness Scale (BIS-11) and Temperamental and Character Inventory – Revised (TCI-R). The Obsessive Compulsive Drinking Scale (OCDS) and Visual Analogue Scale for craving (VASc) were also administered to the AUD sample. **Results.** 28.4% (n=27) of AUD subjects had at least one BA, as compared to 15% (n=21) of controls (χ^2=6.27; p=.014). In AUD subjects, direct correlations between BIS-11 and Compulsive Buying Scale (CBS), Internet Addiction Disorder test (IAD), Exercise Addiction Inventory (IAD) scores (p<.01), between OCDS obsessive and CBS and VASc and CBS, IAD scores (p<.003), were found. BIS-11 (t=−2.36; p=.020), OCDS obsessive (Z=-4.13; p<.001), OCDS compulsive (Z=-2.12; p=.034) and VASc (Z=-4.94; p<.001) scores were higher in AUD subjects with co-occurring BAs. The occurrence of BAs was associated with higher impulsivity traits (BIS-11 scores; OR=1.08; p=.012) and higher craving levels (VASc scores; OR=2.48; p<.001). **Conclusions.** Our findings emphasize a significant rate of co-occurrence of BAs in AUD. High levels of impulsivity and craving for alcohol seem to be associated with other addictive behaviors.

KEYWORDS: Alcohol Use Disorder; Gambling Disorder; behavioral addictions; impulsivity; craving; internet addiction.

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1. INTRODUCTION

Gambling disorder is currently conceptualized as a non-substance-related disorder and has been included in the DSM-5 diagnostic category of 'Substance-related and Addictive Disorders' (APA, 2013). Though gambling disorder is the most extensively investigated, several other non-substance behaviors bring about a similar form of behavioral reinforcement, producing short-term reward that may trigger persistent behavioral patterns despite adverse consequences (Grant et al., 2010, 2013). Diagnostic criteria have been proposed for compulsive buying (McElroy et al., 1994; Black, 2001), internet addiction (Young, 1996; Shapira et al., 2000), sexual addiction (Goodman, 1993; Keane, 2004) and physical exercise addiction (Hausenblas and Symons Downs, 2002).

Behavioral addictions (BAs) share important features with substance use disorders (SUDs): persistent and maladaptive engagement in the behavior despite possible harm to oneself and/or others, excessive time spent and diminished control over the behavior, increasing sense of tension or excitement before performing the behavior, a sense of pleasure and gratification or relief when performing the behavior or shortly after (Frascella et al., 2010; Marazziti et al., 2014). Also, like SUDs, BAs present the phenomena of tolerance, withdrawal and craving. In particular, craving has re-emerged as a fundamental construct in the pathophysiology of addictive behaviors with its inclusion in DSM-5 as a key clinical symptom of addictive disorders (APA, 2013).

Similar predispositions (neurobiological, genetic, environmental) underlie the development and maintenance of both substance and behavioral addictions, so that pathophysiological models for drug addiction may be relevant to BAs as well (Potenza, 2008). Natural rewards and abused substances appear to induce similar activity in reward circuitry (i.e., the mesolimbic dopamine pathway, extending from the ventral tegmental area to the nucleus accumbens) and connected regions, including the amygdala, hippocampus and frontal cortex (O'Sullivan et al., 2009). Alterations in brain learning and memory systems have been found in both SUDs and BAs (Everitt et al., 2008), established and maintained by genetic predisposition and pathological neuroadaptation

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in reinforcement systems (Hyman et al., 2006). Dysregulation of multiple neurotransmitter systems (e.g., serotonergic, dopaminergic, noradrenergic, opioidergic, glutamatergic) has also been observed (Pettorruso et al., 2014). In particular, in both BAs and SUDs, noradrenaline has been found to be especially relevant to aspects of arousal and excitement, serotonin to behavioral initiation and cessation, dopamine to reward and reinforcement, and opioids to feelings of pleasure or urges (Grant et al., 2006, 2008; Dagher and Robbins, 2009; Campbell-Meiklejohn et al., 2011; Leeman and Potenza, 2013). Genetic and family history findings, though limited, provide further evidence of commonality between behavioral and substance addictions (Brewer and Potenza, 2008). BAs and SUDs also share similarities in terms of natural history, impulsivity and compulsivity features as well as personality dimensions (Castellani and Bugle, 1995; Lawrence et al., 2009; Ko et al., 2010; Di Nicola et al., 2014).

Some studies have investigated comorbidity between SUDs and gambling disorder (Daghestani et al., 1996; Toneatto and Brennan, 2002; Wareham and Potenza, 2010), compulsive buying (Black et al., 1998; Black, 2001), sexual addiction (Garcia and Thibaut, 2010), internet addiction (Black et al., 1999; Bakken et al., 2009; Ko et al., 2012), obligatory physical exercise (Freimuth et al., 2011). Findings from these studies indicate that BAs and SUDs frequently co-occur, thus supporting the notion that these disorders share a common pathophysiological basis. However, studies investigating the co-occurrence of different BAs in the same sample are limited, and are mostly focused on non-clinical and teenage subjects (Pallanti et al., 2006; MacLaren and Best, 2010; Villella et al., 2011).

Considering the shared vulnerabilities underlying substance and non-substance-related disorders, we hypothesize higher BAs comorbidity rates in subjects with Alcohol Use Disorder (AUD), compared to homogeneous controls. Hence the aims of the present study were: (i) to assess the occurrence of BAs (according to diagnostic criteria for gambling disorder, compulsive buying, Internet addiction disorder, sexual and physical exercise addictions) in a sample of AUD subjects compared to controls, homogeneous with respect to socio-demographic and clinical characteristics;

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(ii) to compare AUD subjects with and without co-occurring BAs for socio-demographic characteristics, clinical variables, impulsivity, personality dimensions and alcohol craving, in order to highlight any significant association.

2. Methods

2.1 Subjects

Data were obtained from 95 AUD outpatients admitted, from January, 2013 to July, 2014, to the Addictive Disorders Unit of the Day-Hospital of Psychiatry of the University General Hospital "A. Gemelli" in Rome.

Inclusion criteria were: age 18 to 65; current DSM-5 diagnosis of AUD (APA, 2013); abstinence from alcohol for at least 8 weeks; a CIWA-Ar (Clinical Institute Withdrawal Assessment for Alcohol - revised) score < 10, indicating mild alcohol withdrawal symptomatology (Sullivan et al., 2000); euthymic mood for at least 12 weeks, as evidenced by clinical and psychometric evaluations [(Hamilton Depression Rating Scale < 8 (Hamilton, 1960) and Young Mania Rating Scale < 6 (Young et al., 1978)]; a MMSE score > 26 (Folstein et al., 1975); fluency of spoken and written Italian.

All subjects were evaluated using the Structured Clinical Interviews for DSM-IV (SCID I; SCID II) (First et al., 1996a, 1996b). AUD subjects were following a naturalistic maintenance treatment with mood stabilizers/anticonvulsant drugs (lithium, valproate, carbamazepine, topiramate), antidepressants (SSRIs, SNRIs, NaSSAs, and unspecific antidepressants), benzodiazepines, naltrexone, acamprosate, nalmefene.

Exclusion criteria included: a history of psychotic disorders, bipolar disorder type I and suicidality, multiple substance abuse with the exception of nicotine, severe cognitive deficits, neurological or medical disorders impairing evaluation, and reduced physical state.

At the same time and in the same geographical area 140 control subjects, homogeneous to AUD subjects for socio-demographic and clinical characteristics, were enrolled among the general

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population. Controls were evaluated using the Structured Clinical Interviews for DSM-IV (SCID I/NP; SCID II) (First et al. 1996b, 1996c).

Exclusion criteria for the control group included lifetime history of alcohol/substance abuse, brain trauma, neurological illnesses. Controls were either occasional alcohol drinkers or non-drinkers.

In AUD and control subjects, BAs were diagnosed according to specific criteria: DSM-5 criteria (APA, 2013) for gambling disorder, McElroy's criteria (McElroy's et al., 1994) for compulsive buying, Goodman's criteria (Goodman, 1993) for sexual addiction, Young's criteria (Young, 1996) for Internet addiction and Hausenblas and Symons Downs's criteria (2002) for obligatory physical exercise.

Anonymity was guaranteed to all participants; the study protocol complied fully with the guidelines of the Ethics Committee and was approved by the Institutional Review Boards in agreement with local requirements. It was conducted in accordance with Good Clinical Practice guidelines and the Declaration of Helsinki (1964) and subsequent revisions. Written informed consent was obtained after a complete description of the study was provided to each subject. All subjects participated without receiving any form of payment.

2.2 Psychometric assessment

AUD and control subjects were administered a battery of self-report questionnaires to assess BAs:

- *South Oaks Gambling Screen* (SOGS; Lesieur and Blume, 1987), a 20-item questionnaire that screens for pathological gambling.

- *Compulsive Buying Scale* (CBS; Christenson et al., 1994), which consists of 13 items; subjects rate how true each item is for them on a scale ranging from 1 (not at all) to 7 (very much). The scale has a negative cut-off, so the more negative the total score the more severe the compulsive buying behavior.

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- *Sexual Addiction Screening Test* (SAST; Carnes, 1991), which assesses sexually compulsive behaviors, and helps discriminate between addictive and non-addictive behavior. It consists of 25 dichotomous yes/no items.

- *Internet Addiction Disorder* test (IAD; 1996), a 20-item questionnaire; items reflect six underlying dimensions of Internet addiction: salience, excessive use, neglect of work, anticipation, lack of control and neglect of social life. Items are rated on a 5-point scale, where 1=very rarely and 5=very frequently.

- *Exercise Addiction Inventory - Short Form* (EAI-SF; Griffiths et al., 2005), which consists of six statements. Each statement is rated on a 5-point scale (1="Strongly disagree", 2="Disagree", 3="Neither agree nor Disagree", 4="Agree", 5="Strongly Agree"), so that high scores indicate addictive exercise.

In the clinical sample, alcohol craving was assessed using:

- The Italian version of the *Obsessive Compulsive Drinking Scale* (OCDS) (Janiri et al., 2004), which consists of 14 questions, each rated on a scale from 0 to 4, and provides a total and two subscale scores (OB-obsessive: 6 items; CP-compulsive: 8 items).

- The *Visual Analogue Scale* for alcohol craving (VASc) (Mottola, 1993), which assesses craving by asking the patient to place a mark on a line approximately 4 inches long and divided into arbitrary units beginning with zero.

In AUD and control subjects impulsivity and personality dimensions were assessed with:

- The *Barratt Impulsiveness Scale* version 11 (BIS-11) (Fossati et al., 2001), a 30 item self-administered questionnaire that investigates impulsivity. It includes three subscales: Attentional (problems related to concentrating/paying attention), Motor (fast reactions and/or restlessness), and Non-planning (orientation toward the present rather than the future).

- The *Temperament and Character Inventory – Revised* (TCI-R) (Martinotti et al., 2008), a true/false self-administered questionnaire measuring temperament (4 dimensions: Novelty

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Seeking/NS, Harm Avoidance/HA, Reward Dependence/RD, Persistence/PE) and character (3 dimensions: Self Directness/SD, Cooperativeness/CO, Self Transcendence/ST).

BAs scales, OCDS and VASc were administered during a morning session lasting one hour, and were always completed in the same order and sequence (day 1). The TCI-R and BIS-11 were filled out on another session lasting about one hour and a half (day 2).

2.3 Statistical analysis

Statistical analysis was conducted using SPSS for Windows, Versions 15.0 (SPSS Inc, Chicago, Illinois). Dichotomous data were compared by chi-square test using the Fisher or the Yates corrections as appropriate. Continuous data were expressed as means ± standard deviation and compared by independent student's t test.

Since all the BA scales' scores were not normally distributed, the principal outcome analysis consisted of non-parametric Mann-Whitney U test for comparison between the two groups.

Spearman's rank correlation coefficient was employed to examine the relationship between continuous variables in the two groups; within each group, the nominal significance level (i.e., $p<.05$) was corrected according to the Bonferroni procedure and set at $p<.003$. In order to determine which factors were associated with the occurrence of BAs, we entered variables that were significant in the logistic regression. Since a multiple regression analysis was performed, the nominal significance level (i.e., $p<.05$) was corrected according to the Bonferroni procedure and set at $p<.01$. We examined all variables for multi-collinearity. The Hosmer-Lemeshow goodness-of-fit statistic was used to check the appropriateness of the model. Findings were reported as Odds Ratios (OR) and p values.

3. RESULTS

3.1 Demographic and clinical data

AUD and control subjects were homogeneous with respect to socio-demographic and clinical characteristics (Table 1). All participants were Caucasians.

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In AUD subjects comorbid disorders were affective disorders (major depressive disorder: n=6, 6.3%; bipolar disorder type II: n=4, 4.2%), anxiety disorders (panic disorder: n=6, 6.3%; agoraphobia: n=3, 3.2%; generalized anxiety disorder: n=4, 4.2%; social anxiety disorder: n=2, 2.1%), eating disorders (anorexia nervosa: n=2, 2.1%; bulimia nervosa, n=3, 3.2%), personality disorders (borderline: n=4, 4.2%; antisocial: n=4, 4.2%; dependent: n=3, 3.2; narcissistic: n=2, 2.1%). In control subjects comorbid disorders were affective disorders (major depressive disorder: n=10, 7.1%; bipolar disorder type II: n=5, 3.6%), anxiety disorders (panic disorder: n=7, 5%; agoraphobia: n=4, 2.9%; generalized anxiety disorder: n=5, 3.6%; social anxiety disorder: n=3, 2.1%), eating disorders (anorexia nervosa: n=3, 2.1%; bulimia nervosa, n=5, 3.6%), personality disorders (borderline: n=3, 2.1%; antisocial: n=5, 3.6%; dependent: n=4, 2.9; narcissistic: n=4, 2.9%).

No difference in impulsivity (BIS-11 total score) and personality dimensions (TCI-R) between AUD and control subjects was observed.

Current pharmacological treatment of AUD and control subjects is presented in Table 2.

3.2 Co-occurrence of BAs in AUD and control subjects

According to diagnostic criteria, 28.4% (n=27) of AUD subjects had at least one BA as compared to 15% (n=21) of controls (χ^2=6.27; p=.014). Table 3 shows associations between specific BAs in both AUD and control subjects.

AUD patients obtained higher scores than the control group on the BAs tests except for physical exercise (Table 4).

3.3 Correlations in AUD and control subjects

Correlations between BA tests, for both AUD and control subjects, are described in Table 5. In AUD subjects, we observed an inverse correlation between CBS and SAST, so that more severe compulsive buying (lower CBS score) correlates with more severe sexual addiction behavior (higher SAST score). We also found an inverse correlation between CBS and IAD, as well as a

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direct correlation between SAST and IAD. In controls, a negative correlation between CBS and SAST, and a positive correlation between SOGS and SAST was noted.

Correlations among BAs, TCI-R, BIS-11, OCDS and VASc scores are shown in Table 6. With regard to impulsivity traits, we found an inverse correlation between CBS and BIS-11 in both AUD and control subjects, so that more severe compulsive buying (lower CBS score) correlates with higher impulsivity levels (higher BIS-11 score). In AUD subjects, we observed a direct correlation between BIS-11 scores and both IAD and EAI scores. With regard to personality dimensions, we found an inverse correlation between CBS and novelty seeking in both AUD and control subjects, so that more severe compulsive buying (lower CBS score) correlates with higher novelty seeking levels (higher TCI-R novelty seeking score). In AUD subjects, SAST scores were inversely correlated with self-directedness. In the control group, we found an inverse correlation between EAI scores and self-transcendence.

With respect to craving, in AUD subjects (Table 6), we observed a significant inverse correlation between CBS scores and both OCDS obsessive and VASc scores, so that more severe compulsive buying (lower CBS score) correlates with higher craving levels (higher OCDS obsessive and VASc scores). A direct correlation between IAD and VASc was also found.

3.4 AUD and control subjects with and without BAs

There were no significant differences between AUD subjects BAs^{+} (n=27) and BAs^{-} (n=68) in terms of gender, age, level of education, employment, age of onset, duration of illness, cigarette smoking, comorbidity, Cloninger typology, DSM-5 severity.

BIS-11, OCDS and VASc scores were significantly higher in AUD BAs^{+} compared to BAs^{-} subjects (Table 7). No difference in TCI-R personality dimensions was found.

Finally, in AUD subjects, multivariate logistic regression analysis indicated that the occurrence of BAs was associated with higher impulsivity traits (as measured by BIS-11 scores; OR=1.08; p=.012) and higher craving levels (as measured by VASc scores; OR=2.48; p<.001).

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There were no significant differences between control subjects BAs^+ (n=21) and BAs^- (n=119) in terms of gender, age, level of education, employment, cigarette smoking, comorbidity. We found a significant difference in impulsivity (63.35 ± 8.22 vs. 52.53 ± 8.31; t=-4.912, p<.001), novelty seeking (113.57 ± 12.61 vs. 102.86 ± 13.69; t=-2.742, p=.007), harm avoidance (85.43 ± 14.33 vs. 94.62 ± 15.42; t=2.086, p=.04).

4. DISCUSSION

The main finding of our study is a significantly higher rate of BAs among AUD subjects (28.4%), compared to the control group (15%). AUD patients reported significantly higher scores on scales for gambling disorder, compulsive buying and sexual addiction, as compared to controls. Furthermore, we observed significant correlations between scores on different BAs scales, thus highlighting the overlap between different addictive behaviors. Though no studies have yet systematically assessed the co-occurrence of these disorders, emerging data suggest an association between AUD and specific BAs (Abdollahnejad et al., 2014). High rates of co-occurrence for SUDs and gambling disorder have been frequently reported, with the highest odds ratios observed with AUD (Cunningham-Williams et al., 1998). A Canadian epidemiological survey estimated that the relative risk for an AUD increased 3.8-fold when in comorbidity with gambling disorder (Bland et al., 1993). Several studies of family history evidenced a high frequency (up to 20%) of alcohol dependence in subjects with BAs, particularly in compulsive buyers (Lejoyeux et al., 2000). Accruing evidence therefore seems to support the high rate of co-occurrence of addictive disorders, and the notion that addiction is a complex construct, involving complementary and overlapping phenomenological, clinical, neurobiological and psychosocial factors (Goodman, 2008; Camardese et al., 2012; Walther et al., 2012). Studies suggest that common biological mechanisms exist for all urge-driven disorders, possibly involving the processing of incoming reward input by the ventral tegmental area/nucleus accumbens/orbital frontal cortex circuit (Dagher et al., 2009). Alterations in dopaminergic pathways have been proposed as underlying the seeking of rewards (i.e., gambling, drugs; Zack et al., 2009). Recent research suggests that dopamine mainly encodes the motivational

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aspects of reward processing ('reward wanting'), but not learning or 'liking' for the same rewards. In this view, dopamine neurotransmission increases the incentive salience of a conditioned cue, causing the cue to increase the motivational state of "wanting" for the reward without necessarily enhancing its hedonic properties (Berridge, 2007). The subjective experience of pleasure (reward liking) seems to be mediated by endogenous opioids (endorphins, enkephalins, dynorphins) and their receptors widely expressed in the ventral striatum (especially the nucleus accumbens) and the ventromedial prefrontal cortex (Di Nicola et al., 2013).

In our sample, AUD patients with co-occurring BAs experienced more severe impulsivity and alcohol craving than those without BAs. In AUD subjects, the occurrence of BAs was associated with higher impulsivity traits (as measured by BIS-11 scores) and higher craving levels (as measured by the VASc). We confirm previous findings of high temperamental impulsivity, defined as lack of behavioral inhibition, in patients with BAs (Kim et al., 2008; Di Nicola et al., 2010b; Pettorruso et al., 2014b). Impulsivity is closely linked to addictive disorders (Leeman and Potenza, 2013). Gambling disorder and AUD share deficits in tasks linked to ventral prefrontal cortical dysfunction. Both gambling disorder and AUD subjects displayed impairments in risky decision-making and cognitive impulsivity (Lawrence et al., 2009). In addition, adolescents with internet addiction showed higher scores on the BIS-11 compared to controls (Cao et al., 2007). Recent studies suggest that addiction, performance on delay discounting/response inhibition tasks, and trait impulsivity constitute a triad associated with difficulty in distinguishing between causes and effects (Torres et al., 2013). In light of our results, we propose that impulsivity traits identify a subgroup of addicted individuals with different clinical presentations and outcomes (Albein-Urios et al., 2014), as well as higher BAs comorbidity rates.

We also found a relevant contribution of craving phenomena in AUD-BAs comorbidity. Craving is commonly thought to play a crucial role both in the transition from controlled drinking to AUD and in the mechanism underlying relapse (Sinha and Li, 2007; Heinz et al., 2009; Martinotti et al., 2013). In addition, craving was found to be a relevant phenomenon in gambling

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disorder (de Castro et al., 2007; Tavares et al., 2005). Interestingly, our results highlight a significant role for craving in the engagement in other BAs as well. Therefore, it is possible to hypothesize that craving, being a core component of AUD, could represent a predisposing factor for the development of BAs. The dopaminergic brain reward system seems to play a fundamental role in the mechanism of craving (Addolorato et al., 2005; Heinz et al., 2009). Although the predominance of dopaminergic transmission is well-established, other neurotransmitter systems also play important roles (Pettorruso et al., 2014a). Craving in AUD patients after detoxification was found to be related to glutamatergic dysfunction in the nucleus accumbens and the anterior cingulate cortex, as measured by proton magnetic resonance spectroscopy (Bauer et al., 2013). Recent findings also suggest that cue-induced activation to internet video game stimuli may be similar to that observed during cue presentation in GD and AUD (Ko et al., 2009; Han et al., 2011). The involvement of the same neurobiological substrates in craving phenomena could contribute to cross-sensitization in different addictive disorders (Pickens et al., 2011), as the behavioral response to a unitary motivational drive (Aston-Jones and Harris, 2004). Further research is certainly needed to define the contribution of substance- (or behavior-) specific as well as non-specific aspects (e.g., dysphoric states, negative affective states) to craving phenomena. Furthermore, the exploration of the impact of different craving typologies (e.g., reward, relief or obsessive craving; Martinotti et al., 2013) could contribute to the understanding of AUD-BAs comorbidity.

Concerning the relevance of personality traits, specific temperamental and character dimensions in AUD subjects were related to different BAs. With regard to temperamental traits, novelty seeking (associated with exploratory activity in response to novel stimulation, impulsive decision making, extravagance in approach to reward cues; Castellani and Rugle, 1995; Cloninger, 1987) was found to be directly related to compulsive buying, confirming previous results from studies on sensation-seeking (Lejoyeux et al., 1997; Frascella et al., 2010). With respect to character dimensions, self-directedness, expressing the individual's competence towards autonomy, reliability, and maturity, showed an inverse relationship with sexual addiction behaviors. Though

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most authors agree that an "addictive personality" is not clearly identifiable, our findings allow us to hypothesize that vulnerable individuals, driven by craving phenomena, show a preference towards specific BAs in accordance with their temperamental and personality traits. It is therefore possible that certain personality profiles are associated with specific BAs, and that some personality traits (i.e., novelty seeking) represent vulnerability factors while others are involved in the persistence of the addictive behavior.

The current study presents several limitations. Some results could not have been detected because of the relatively small number of patients enrolled. The cross-sectional nature of the data precluded the investigators' ability to establish the chronological order between BAs and AUD. In addition, results could have been biased by concurrent pharmacological treatment. However, a strong point of our study was the recruitment of patients abstaining from alcohol use for at least 8 weeks and in a euthymic mood or stabilized by medication for at least 12 weeks, with no relevant confounding factors (e.g., acute withdrawal, alcohol intoxication, any hypomanic/manic or depressed state).

Given the lack of awareness of some of these conditions, our findings may help guide clinicians in the detection of a high risk sub-group of AUD patients, in order to actively screen these subjects for the occurrence of BAs. The assessment of BAs in AUD patients could be useful in predicting the risk of a more severe outcome that usually characterizes comorbid patients (Mandelli et al., 2012). As for other underreported and under-diagnosed conditions, patients' and clinicians' awareness of the co-occurrence of different BAs and AUD may improve diagnosis and treatment, significantly lowering the impact on patients' quality of life. Early recognition of high-risk patients for multiple addictive disorders would also prompt specific monitoring and possibly help define new treatment strategies. Further studies are necessary to assess the role of comorbid BAs in AUD patients in terms of drink relapses and long-term outcomes. Future studies should also contribute to allow consistency in BAs diagnostic category (Clark and Limbrick-Oldfield, 2013), in order to point out common features and improve clinical management. Furthermore, the impact of other

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possible BAs needs to be more thoroughly explored (e.g., mobile phone addiction, punding; (Martinotti et al., 2011; Pettorruso et al., 2014b), particularly among high-risk patients (e.g., addicted patients).

Our findings point to the centrality of craving in the co-occurrence of addictive behaviors, and future research should certainly contribute to shed light on neurobiological underpinnings of craving phenomena, to better understand their role in addictive disorders comorbidity (Pozzi et al, 2006). Our findings need to be replicated in a larger population. Also, future prospective studies might clarify the natural history of these co-occurring disorders and contribute to the development of optimal treatment options. Patients with co-occurring BAs could, in fact, benefit from specific pharmacological treatments and psychological interventions aimed at warding off urges to engage in damaging or risky behavior (Janiri et al., 2007; Di Nicola et al., 2010b, 2014; Marazziti et al., 2014).

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Role of Funding Source: Nothing declared
Contributors: All authors materially participated in the research and/or article preparation
Conflict of interest: No conflict declared

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Highlights

- Alcohol Use Disorder patients reported significantly higher scores on scales for pathological gambling, compulsive buying and sexual addiction, as compared to controls.
- We found a marked overlap between different addictive behaviors.
- Alcohol Use Disorder patients with co-occurring behavioral addictions experienced more severe impulsivity and alcohol craving than those without behavioral addictions.
- Novelty Seeking was found to be directly related to compulsive buying and internet addiction.

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Table 1. Socio-demographic characteristics and clinical data of the samples.

	Alcohol Use Disorder subjects	Controls
N	95	140
Gender (% males)	57 (60)	85 (60.7)
Age (M ± SD)	44.1 ± 9.5	42.4 ± 12.2
Marital status		
single	35 (36.8)	56 (40)
married	35 (36.8)	54 (38.6)
separated/divorced	22 (23.2)	21 (15)
widowed	3 (3.2)	9 (6.4)
Level of education		
elementary school	1 (1.1)	4 (2.9)
lower secondary school	33 (34.7)	38 (27.1)
high school education	47 (49.5)	77 (55)
degree	14 (14.7)	21 (15)
Employment condition		
regular job	47 (49.1)	71 (50.8)
occasionally employed	12 (12.9)	19 (13.7)
unemployed	25 (26.7)	33 (23.8)
student	4 (4.3)	8 (5.3)
retired	7 (7)	9 (6.4)
Smoking	36 (37.9)	49 (35)
Comorbidity	43 (45.3)	58 (41.4)
Pharmacological treatment	43 (45.3)	59 (42.1)
Alcohol-related history		
Age of onset (years: M ± SD)	34.6 ± 9.8	-
Duration of illness (years: M ± SD)	9.5 ± 6.8	-
DSM-5 severity		
Moderate	58 (61.1)	-
Severe	37 (38.9)	-
Cloninger typology		
type 1-like	64 (67.4)	-
type 2-like	31 (32.6)	-
Craving		
OCDS total	5.61 ± 3.74	-
OCDS obsessive	3.38 ± 2.40	-
OCDS compulsive	2.23 ± 1.61	-
VAS craving	2.60 ± 1.68	-

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Table 2. Type of drugs administered to Alcohol Use Disorder (AUD) and control subjects.

Drugs	AUD (n=95)	Controls (n=140)
	N (%)	N (%)
Mood stabilizers/Anticonvulsants	14 (14,7%)	18 (12.9%)
Antidepressants	16 (16.8%)	25 (17.9%)
SSRIs	6 (6.3%)	9 (6.4%)
SNRIs	4 (4.2%)	7 (5)
Unspecific (Trazodone)	4 (4.2%)	6 (4.3%)
NaSSAs	2 (2.1%)	4 (2.8%)
Benzodiazepines	16 (16.8%)	25 (17.9%)
Other		
Nalmefene	9 (9.5%)	-
Naltrexone	5 (5.3%)	-
Acamprosate	8 (8.4%)	-

Legend: SSRIs: selective serotonin reuptake inhibitors; SNRIs: serotonin and noradrenalin reuptake inhibitors; NaSSAs: noradrenergic and specific serotoninergic antidepressants.

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Table 3. Co-occurrence of Behavioral Addictions (BAs) in Alcohol Use Disorder (AUD) and controls subjects.

	AUD (N=95)	**Controls** (N=140)
No BAs	**68 (71.6)**	**119 (85)**
Single BA	**18 (18.9)**	**19 (13.6)**
GD	3 (3.1)	5 (3.6)
CB	11 (11.6)	11 (7.9)
HS	3 (3.1)	2 (1.4)
IA	0 (0)	0 (0)
PEA	1 (1.1)	1 (0.7)
Multiple BAs	**9 (9.5)**	**2 (1.4)**
GD+CB	3 (3.1)	1 (0.7)
GD+CB+HS	1 (1.1)	0 (0)
CB+HS	2 (2.2)	1 (0.7)
CB+PEA	3 (3.1)	0 (0)

Legend: GD: Gambling Disorder; CB: Compulsive Buying; SA: Sexual Addiction; IA: Internet Addiction; PEA: Physical Exercise Addiction.

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Table 4. Mann-Whitney U test for comparison of scores on behavioral addiction scales between Alcohol Use Disorder (AUD) and control subjects.

	AUD	Controls	Mann Whitney U Test	
	M ± SD	*M ± SD*	**Z**	**P value**
South Oaks Gambling Screen	0.72 ± 1.74	0.38 ± 1.67	-3.205	0.001*
Compulsive Buying Scale	0.38 ± 2.67	1.17 ± 2.03	-1.995	0.046*.
Sexual Addiction Screening Test	4.53 ± 4.12	2.32 ± 3.07	-4.854	<0.001*
Internet Addiction Disorder test	27.43 ± 9.44	24.34 ± 4.99	-2.149	0.032*
Exercise Addiction Inventory	10.82 ± 6.12	11.16 ± 4.92	-1.543	NS

* Difference is statistically significant; NS: not significant.

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Table 5. Spearman's correlations between scores on behavioral addiction scales in Alcohol Use Disorder (AUD) and control subjects.

	South Oaks Gambling Screen (SOGS)		Compulsive Buying Scale (CBS)		Sexual Addiction Screening Test (SAST)		Internet Addiction Disorder test (IAD)		Exercise Addiction Inventory (EAI)	
	AUD	***Controls***	***AUD***	***Controls***	***AUD***	***Controls***	***AUD***	***Controls***	***AUD***	***Controls***
SOGS	-	-	-.183	-.081	.180	.295*	.106	.073	.054	.142
CBS	-.183	-.081	-	-	-.366*	-.257*	-.558*	-.169	-.032	.018
SAST	.180	.295*	-.366*	-.257*	-	-	.414*	.214	.067	.149
IAD	.106	.073	-.558*	-.169	.414*	.214	-	-	.197	.206
EAI	.054	.142	-.032	.018	.067	.149	.197	.206	-	-

*: p<.003 according to the Bonferroni procedure; CBS has a negative cut-off.

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Table 6. Spearman's correlations between behavioral addiction scales, TCI-R dimensions, BIS-11 total, OCDS and VASc scores in Alcohol Use Disorder (AUD) and control subjects.

	South Oaks Gambling Screen		Compulsive Buying Scale		Sexual Addiction Screening Test		Internet Addiction Disorder test		Exercise Addiction Inventory	
	AUD	***Controls***	***AUD***	***Controls***	***AUD***	***Controls***	***AUD***	***Controls***	***AUD***	***Controls***
BIS-11 total	.182	.175	-.238*	-.303*	.087	.182	.257*	-.020	.207*	.034
TCI-R										
Novelty Seeking	.210	.176	-.330**	-.383**	.178	.203	.244	.257	.057	.074
Harm Avoidance	.047	-.183	-.108	-.023	.305	-.036	.100	-.116	-.169	-.096
Reward Dependence	-.052	-.212	-.018	.103	.067	-.118	.106	.012	.112	-.167
Persistence	-.134	.180	-.123	-.001	.043	.072	.018	-.182	.218	.099
Self-Directedness	-.225	-.108	.305	.218	-.409**	-.198	-.226	-.125	-.011	-.082
Cooperativeness	-.184	-.117	.269	.191	-.272	-.141	-.220	-.116	-.014	-.227
Self-Transcendence	-.069	.041	-.323	-.071	.262	.206	.232	-.128	.190	-.380**
Craving scales										
OCDS obsessive	.202	-	-.352***	-	.192	-	.266	-	-.064	-
OCDS compulsive	.234	-	-.160	-	.167	-	.149	-	-.057	-
VASc	.116	-	-.345***	-	.095	-	.349***	-	-.074	-

Legend: BIS-11: Barratt Impulsiveness Scale-11; OCDS: Obsessive Compulsive Drinking Scale; VASc: Visual Analogue Scale for Craving.
* = p<.01; ** = p<.001; *** = p<.003. Statistical threshold for correlations was corrected according to the Bonferroni procedure and set at p<.01 between BAs scales and BIS-11 total, at p<.001 between BAs scales and TCI-R dimensions, and at p<.003 between BAs scales and craving measures. CBS has a negative cut-off.

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Table 7. Comparison of BIS-11, OCDS and VASc scores between AUD patients with (BA^+) and without (BA^-) co-occurring behavioral addictions.

	Alcohol Use Disorder Subjects		Mann Whitney U Test/ Independent t Test	
	BA^+ (n=27)	BA^- (n=68)		
	M ± SD	M ± SD	**Z/t**	**P**
BIS-11 total	61.04 ± 9.67	55.49 ± 10.57	t=--2.36	.020*
OCDS total	7.78 ± 2.61	4.75 ± 3.79	Z=-3.35	.001*
OCDS obsessive	4.96 ± 1.93	2.75 ± 2.31	Z=-4.13	<.001*
OCDS compulsive	2.81 ± 1.18	2 ± 1.71	Z=-2.12	.034*
VASc	3.72 ± 1.41	1.79 ± 1.51	Z=-4.94	<.001*

Legend: BIS-11: Barratt Impulsiveness Scale; OCDS: Obsessive Compulsive Drinking Scale; VASc: Visual Analogue Scale for Craving. * Difference is statistically significant.

Accepted Manuscript