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Further evidence of a psychopathology specific to Substance Use Disorder. Relationships between psychopathological dimensions and alcohol craving in recreational drinkers

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Summary

Background. At present, the diagnosis of substance addiction relies on the identification of specific behavioural symptoms. We have proposed an integrated framework of the psychopathology of addiction that comprises possible related psychological symptoms. The first syndrome was the "Worthlessness/Being Trapped" (W/BT) dimension. The second one was related to "Somatic Symptoms" (SS). The third factor identified the "Sensitivity/Psychoticism" (S/P) syndrome. The fourth factor was related to "Panic Anxiety" (PA) symptomatology. The fifth syndrome described a "Violence/Suicide" (V/S) dimension. **Methods**. In this cross-sectional, naturalistic study, involving a single assessment of recreational drinkers, we estimated the magnitude of the correlations between behavioural covariates of alcohol craving and our five psychopathological syndromes. **Results.** The Alcohol Craving Scale and the total score of the Symptomatological Check List (90 items) were positively correlated (n=78; r=0.48; p <0.01). W/BT was positively correlated with the habit of drinking because others are already drinking and personally continuing to drink till late in the day, despite having already drunk profusely. No correlation was found with SS. S/P was positively correlated with the tendency to drink only because others are already drinking. PA was positively correlated with never missing an opportunity to drink the last glass being offered. V/S was positively correlated with almost always feeling like having a drink. Canonical variate set-one (SCL-90 syndromes) was saturated negatively by W/BT and positively by V/S and ACS Set-two (items in ACS) was saturated negatively by never refusing the last glass being offered and positively by always being thirsty enough to drink at any time and often feeling like having a drink. These sets were significantly correlated (p <0.001). **Conclusions**. The current study, because it demonstrated the correlation between psychopathology and craving in recreational alcohol drinkers, has provided further support for the view that our psychopathological structure is specific to SUD.

Key Words: Alcohol craving; Psychopathology specific to Substance Use Disorder; Correlation between craving and psychopathology

1. Introduction

At present, the diagnosis of substance addiction relies on the identification of specific behavioural symptoms **[1]**. These patients, however, often show many other symptoms, such as impulsivity, depression, boredom, novelty seeking, irritability and restlessness, besides attention and concentration difficulties that belong to the domain of psychological issues, such as difficulty in controlling impulses, anxiety and

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mood. Typically, these symptoms are associated with the behavioural symptoms of addiction and contribute to the maintenance of the use of substances, along with the overall psychopathological profile. Regrettably, these symptoms are not included in the diagnostic criteria of substance use disorder (SUD) and have usually been considered as comorbid psychological or personality disorders **[8, 19, 20]**.

In order to overcome this categorical view, we have proposed an integrated framework of the psychopathology of addiction that comprises possible related psychological symptoms **[44, 45]**. We propose that the psychiatric symptoms shown by patients with addiction to substance abuse are closely related to addiction and not to the presence of a Dual Disorder. This assertion is supported by the high frequency of the concurrent manifestation of both symptomatological domains and by the overtly common neurobiological and neurophysiological mechanisms.

The main line of evidence supporting our proposed integrated framework was provided by a study on 1,055 heroin-addicted patients at treatment entry **[37]**. An exploratory principal component factor analysis (PCA) performed on their Self-Report Symptom Inventory (SCL-90) questionnaires **[11]** revealed that, instead of the nine known factors found in psychiatric patients, we obtained a simpler, five-factor solution. The first factor outlined a dimension that was mainly related to depressive feelings like hopelessness, a sense of despair when envisioning the future, sensations of worthlessness and, primarily, being trapped. Accordingly, the first factor was the "Worthlessness/Being Trapped (W/BT)" dimension. The second factor was related to a "Somatic Symptoms (SS)" dimension, with bodily manifestations like dullness felt in the arms, the aching of muscles, hot or cold spells, powerlessness, insomnia, nausea and gastric issues. The third factor pertained to sensations related to other people who are able to know one's own thoughts, experiencing thoughts that are unfamiliar to one's own mind and being talked to or watched by other people. Accordingly, this factor identifies the "Sensitivity/Psychoticism (S/P)" dimension. The fourth factor was related to the "Panic Anxiety (PA)" dimension, concerning being afraid of open spaces and being afraid to travel, feelings of fearfulness culminating in spells of panic or terror. The fifth and last factor takes into account a "Violence/Suicide (V/S)" dimension concerning pervasive thoughts related to death, uncontrollable outbursts, screaming/throwing things, and intense urges to smash things up. These five dimensions were found to be mutually independent **[34, 37, 45]**. All of these findings were replicated in another sample of 1,195 heroin-addicted patients at the beginning of their residential treatment in a therapeutic community **[49]**. The P.C.A. performed on the SCL-90 questionnaires confirmed the five-factor solution observed in our previous study **[37]** related to the dimensions of W/BT, SS, S/P, PA, V/S. In addition, this psychopathological structure proved to be a stable trait across gender, marital status, education, income, living situation, and length of addiction, but not across age. Accordingly, older heroin-addicted patients showed the highest scores in relation to SS and W/BT symptomatology **[35, 37, 41]**.

This psychopathological structure tends to be maintained even across different substance abuse disorders. In one of our studies, 2,314 subjects with alcohol, heroin or cocaine dependence were assigned to one of the five dimensions, and differences between patients dependent on alcohol, heroin or cocaine in the frequency of the five clusters and in their severity were analysed. We confirmed a positive association of the SS dimension with the condition of heroin versus cocaine dependence and of the S/P dimension with the condition of alcohol versus heroin dependence. SS and PA successfully discriminated between patients as being alcohol, heroin or cocaine dependents. Looking at the subsample of heroin dependents, no significant differences were observed. The available evidence coming from our results, taken as a whole, seems to support the extension of the psychopathological structure previously observed in opioid addicts to the population of alcohol and cocaine dependents **[43]**.

Even in the case of alcohol abuse disorder (AUD), its diagnosis is related to the identification of a group of behavioural and physical symptoms, which also comprise craving, withdrawal and tolerance **[1]**. AUD tends to be a common, relapsing condition that generates a threefold increase in early mortality rates **[50, 54]**. AUD affects almost 15 million people in Europe, where its impact is that of a heavy social and economic burden **[24, 56]**. Unfortunately, within the European Union only 10% of AUD patients receive any form of treatment **[23, 53]**. What is more within the first 12 months, more than 75% of the patients that did receive treatment experienced relapse **[38]**.

It has been documented by epidemiological studies that AUD patients show a high prevalence of comorbid psychiatric disorders, while psychiatric patients show a high prevalence of AUD with respect to the general population **[14, 17]**. In addition, comor-

bid symptomatology related to a psychopathological dimension is a common, rather than rare, condition in these patients, as it is for the dimensions of alexithymia **[5]**, impulsiveness **[12]** and anhedonia **[18]**. Though the high frequency of comorbidities, the nature of the psychopathological dimension of patients with AUD and comorbid psychiatric disorders has received little attention. In patients with AUD comorbid psychiatric conditions are able to generate an enhanced risk of suicide, enhanced risk of psychopathology and a global functional decline **[2-4]**.

In the present study we have investigated a sample of recreational drinkers using SCL-90 **[11]** and the Alcohol Craving Scale (ACS.; **[13]**) in order to: A) provide a precise definition of the psychopathological structure of these kinds of subjects, so testing the hypothesis that it will replicate the structure of patients with heroin addiction and comorbid psychiatric conditions; B) analyse the relationships, in terms of non-parametric combinations, between the SCL-90 dimensions and the ACS behavioural covariates through non-parametric canonical correlation analysis.

2. Methods

2.1. Design of the study

In this cross-sectional, naturalistic study, through a single assessment of recreational drinkers, we estimated the magnitude of the correlations between behavioural covariates of alcohol craving and psychopathological syndromes both at univariate and multivariate levels.

2.2. Sample

The sample consisted of 78 subjects, with 32 (41.0%) males and 46 (59.0%) females, mean age 25.53±4.3 (min 19, max 42). Males and females did not differ on the basis of the total score for psychopathology (T=1.43 p=0.156) and for the behavioural covariates of alcohol craving (T=-0.63; p=0.528).

2.3. Assessment

We used the Alcohol Craving Scale (ACS) to evaluate the behavioural covariates of alcohol craving and the Self-Report Symptom Inventory (SCL-90) by Derogatis et al. to record psychopathological symptoms.

2.3.1. SCL-90 Self-Report Symptom Inventory

Originally developed by Derogatis et al. **[11]**, the SCL-90 includes a total of 90 items, each rated on a 5-point scale of severity. It is a self-report clinical rating scale registering the psychopathological symptoms of psychiatric patients. In the case of SUDs, according to the elaboration of Maremmani et al., the 90 items reflect five psychopathological syndromes that are believed to underlie the psychopathology observed in this class of patients. The Maremmani found syndromes are: W/BT, SS, S/P, PA, and V/S **[37]**.

These five dimensions have been empirically established and primarily validated in a sample involving over 2,500 substance use disorder patients **[6, 7, 10, 26-33, 35-37, 46-49, 51]**, On the basis of the highest z scores obtained on the five SCL-90 dimensions, subjects can be clustered in five mutually exclusive groups. A complete description of these syndromes is provided in Maremmani et al. **[37]**.

2.3.2. ACS (Alcohol Craving Scale)

The questionnaire contained 14 items, each of which required a yes or no answer, corresponding to 1 or 0 points, respectively **[13]**. The Italian stereotype investigated is the following: Italian AUD patients often drink outside mealtimes; they almost never think they can eat without taking an alcoholic drink of some kind; they seek medical reassurances that they can continue to drink; they justify taking meals away from home by referring to habit or thirst as their only justification; they often say that they drink because others in their company are already drinking or because they have seen a bottle on the table. They admit their feelings of being 'bottomless', never leave a glass unfinished, drink late in the evening or night, despite having already drunk profusely during the day, never miss an opportunity to drink the last glass offered of wine or an alcoholic digestive at the end of a meal.

2.4. Procedure

In a private recreational club dispensing a variety of alcoholic beverages, we recruited the study participants during the early stages of the evenings when no one had yet stood behind the counter to allow drinking to start. It can, therefore, be assumed that all of them were sober at the time of the testing. Rating scales and questionnaires were administered both during midweek and weekend days to limit the indirect effect of the schedules compared with actual drinking, which, according to studies **[16]** and according to our personal experience, reaches a peak

over the weekend. For further details, please see **[42]**. Participants gave their informed consent to take the test, so responding positively to the request of the examiner after he/she had explained the purposes of the study.

2.5. Data analysis

Using the total score of SCL-90 and ACS, we correlated behavioural covariates of alcohol craving and psychopathological symptomatology according to the non-parametric method. At the multivariate level, we studied the correlations between each psychopathological syndrome and the 14 behavioural covariates of alcohol craving using a Non-parametric Multiple Regression Analysis. M.R.A. is a general statistical technique through which it is possible to analyse the relationship between a dependent or criterion variable and a set of independent or predictor variables. It is a descriptive tool but also an inferential tool. With this analysis, we wished to 'simplify' the prediction equation by deleting independent variables that do not add substantially to prediction accuracy once certain other independent variables are included.

After that, we studied correlations between ACS and SCL-90, at the multivariate level, by means of non-parametric canonical correlation analysis to identify and measure the associations that may connect the two separate sets of variables. Canonical correlation is appropriate in the same situations where multiple regression would be, but where there are multiple intercorrelated outcome variables. Canonical correlation analysis determines a set of canonical variates, orthogonal combinations of the variables within each set that best explain the variability both within and between sets.

3. Results

The ACS and SCL-90 total score were positively correlated (n=78; r=0.48; p<0.01).

Table 1 reports the results of all multiple regression analyses when only significant results were reported.

W/BT was positively correlated with drinking because others are already drinking and drinking late in the day, despite having already drunk profusely. No correlation was found with SS. S/P was positively correlated with drinking because others are already drinking. ACS was positively correlated with never giving up the chance to drink the last glass offered. V/S was positively correlated with almost always feeling like having a drink.

Table 2 shows the results of the canonical correlation analysis. Only one canonical variate was significant. Canonical variate set-one (SCL-90 syndromes) (which explains 41.51% of the total variance) was saturated negatively by W/BT and positively by V/S and ACS Set-two (Items of ACS) (which explains 23.44% of the total variance) was saturated negatively by never refusing the last glass offered, and positively by always feeling thirsty enough to drink at any time and nearly always feeling like having a drink. These sets were significantly correlated (p <0.001).

4. Discussion

If the severity of psychopathological symptoms is higher, then the behavioural covariates of alcohol craving turn out to be more frequent and more severe. Some types of addictive behaviour are more closely linked to specific psychopathological syndromes. Drinking because others are already drinking is related to the sensitivity/psychotic and depressive syndromes. The depressive syndrome is related to drinking late in the day, despite having already drunk profusely. People who never give up a chance to drink the last glass offered, show more severe ACS symptoms, while these people, who almost always feel like having a drink, are distinguished by the impulsivity of the V/S syndrome.

When we studied the relationships between psychopathology and craving, two opposite dimensions were found. At the psychopathological level, recreational drinkers are distinguished by the high severity of W/BT, with V/S and ACS showing low severity, or vice versa. In the first case, craving behaviours are distinguished by drinking because others are already drinking, and continuing to drink late in the day, despite having already drunk profusely. When V/S and ACS are predominant, and W/BT is lower, subjects are always thirsty enough to drink at any time and often feeling like having a drink.

Interestingly, a recent study highlights a neural network where a central role is played by the medial orbitofrontal cortex (mOFC), as well as the dorsal periaqueductal grey (dPAG), the central nucleus of the amygdala (CeA) and the nucleus accumbens, which is consistent with rodent models. This study shows that both inhibitory and excitatory projections by the mOFC to the dPAG are able to lead to alcohol abuse. Thus, two distinct neural pathways are able to generate the same addictive behaviour **[21]**.

Table 1. Regressions between behavioural covariates of alcohol craving and psychopathological syndromess

Behavioural covariates of alcohol craving	Std Error	beta	p
1. Worthlessness/Being Trapped			
6. Drinking because others are already drinking	0.17	0.32	0.013
10. Drinking until late in the day, despite having already drunk profusely	0.35	0.49	0.014
3. Sensitivity/Psychoticism			
6. Drinking because others are already drinking	0.16	0.29	0.032
4. Panic Anxiety			
Never refusing the last glass being offered	0.06	0.28	0.025
5. Violence/Suicide			
12. Almost always feeling like having a drink	0.08	0.40	0.003

Only significant statistically significant results are reported

Notably, the midbrain PAG is a brain region that has been traditionally viewed as an area comprising distinct, longitudinally organised neural substrates which are able to support active or passive emotional coping strategies. The evidence seems to converge, identifying active coping mediated by the activation of either the dorsolateral or lateral PAG columns, while passive coping strategies are mediated by the activation of the ventrolateral PAG column **[22]**. Electrical stimulation of the PAG in humans has been reported to induce extreme fear **[40]**, discomfort, distress, anxiety and weeping **[55]**. Most importantly, the more proximal a "virtual predator" is, the more active the PAG, and the dread of being captured is positively correlated to the PAG signal **[39]**. This finding seems to correlate with the observation that identifies PAG neurons as cells that tend to prioritise threat probability over fear output itself **[57]**. In our sample, PAG activity may be preferentially related to the dimension of W/BT that is typically experienced in life events leading individuals to face threats to their physical or emotional life. Unsurprisingly, PAG activation is critically involved in subjects with post-traumatic stress disorder **[15]**, and the behavioural co-

Table 2. Non-parametric canonical correlations between psychopathological syndromes and behavioural covariates of alcohol craving

	Root N° 1* load
Psychopathological dimensions	
1. Worthlessness/Being Trapped	-0.42
2. Somatic Symptoms	-0.12
3. Sensitivity/Psychoticism	0.10
4. Panic Anxiety	0.38
5. Violence/Suicide	1.08
Behavioural covariates of alcohol craving	
1. Often drinking outside mealtimes	-0.04
2. No eating is possible without taking an alcoholic drink	-0.08
3. Seeking medical reassurance for continuing to drink	0.17
4. Needing absolutely to drink because feeling an urge	-0.08
5. Feeling thirsty because being used to drinking at a specific time of day	0.22
6. Drinking because others are already drinking	0.14
7. Drinking because having seen one's own favourite drink	-0.05
8. Admitting to feelings of being 'bottomless'	-0.13
9. Rarely leaving any drink in the glass after finishing meals	-0.15
10. Drinking until late in the day, despite having already drunk profusely	0.20
11. Always thirsty enough to drink at any time	0.44
12. Almost always feeling like having a drink	0.49
13. Severe difficulties in stopping the drinking habit between meals	0.20
14. Never refusing the last glass offered	-0.37

*Eigenvalue=1.29 F=1.79 p <0.001

variates promoted by dPAG activation that are related to active coping strategies aimed at drinking may be preferred over becoming resigned to the fall into passive and immobilising coping strategies promoted by ventrolateral PAG **[22]**. Thus, in the first dimension distinguished a high severity of W/BT and low severity of V/S and ACS, there may be a prevalent inhibitory activity stemming from mOFC to dPAG and leading to compulsive drinking, such as insensitivity to aversion **[21]**.

Conversely, the correlation between enhanced negative affective and self-referential processing networks has been linked to suicidal ideation. The brain regions involved mainly pertain to the processing of information related to the self and are the ventromedial prefrontal cortex, the rostral anterior cingulate cortex, the insula, and the ventral striatum, besides including the medial OFC **[25, 52]**. In addition, impulsivity has been reported in patients with panic disorder without lifetime comorbidity with major mood episodes, where trait and state impulsivity may be related to the presence of comorbid cyclothymic mood instability **[9]**, while, in a sample of 56 healthy male adults, it has been reported that spontaneous activity in medial OFC correlates with trait anxiety. In particular, the resting-state functional connectivity between the right subregions of the mOFC and the praecuneus was correlated with trait anxiety **[58]**. Overall, these observations suggest in the second dimension, which is marked out by a high severity of V/S and PA and low severity of W/BT, there may be a prevalent excitatory activity stemming from mOFC to dPAG leading to aversive feelings, a lower threshold for escape, and a general sensation of urgency leading to alcohol craving and abuse **[21]**.

The following limitations should, in any case, be borne in mind. 1) Our study is cross-sectional, and the specific temporal order of the variables cannot be defined; alternative orders have not been ruled out, and it is possible that these relationships are bidirectional in nature. Longitudinal studies are essential to allow conclusions to be drawn about changes occurring within the individual over time. 2) All of the data cited here draw on self-report measures; relying exclusively on self-report data tends to reinforce associations between variables.

5. Conclusions

Despite these limitations, the current study identified relationships that would benefit from further evaluation and could have important clinical implications. Specifically, a psychopathological structure specific to SUD has been further confirmed in recreational alcohol users. Canonical correlation analysis revealed that the W/BT dimension was linked to drinking simply because others are already drinking, and extending to drinking late in the day, despite having already drunk profusely. The S/P dimension was related to drinking because others are already drinking; the ACS dimension was correlated with never refusing the last glass offered, and V/P was associated with almost always feeling like having a drink. The presence of this psychopathological structure associated with these behavioural covariates is able to add new insights to psychopharmacological and psychological treatment.

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Contributors

All authors were involved in the study design, had full access to the survey data and analyses, and interpreted the data, critically reviewed the manuscript and had full control, including final responsibility for the decision to submit the paper for publication.

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Conflict of interest

Authors declared no conflict of interest. IM served as Board Member for Angelini, Camurus, CT Sanremo, D&A Pharma, Gilead, Indivior, Lundbeck, Molteni, MSD, Mundipharma.

Ethics

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 has ethics committee approval. All patients gave their informed consent to the anonymous use of their clinical data for this independent study.

Note

It is the policy of this Journal to provide a free revision of English for Authors who are not native English speakers.

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