Alcohol-Attentional Bias in Alcohol-Dependent and Cocaine-Dependent Patients

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ABBREVIATIONS


INTRODUCTION

Addictive behaviors are frequently associated with reactivity to substance-related cues, also known as substance-related attentional bias [1]. In the study of addiction, attentional bias refers to the observation that substance-related cues capture the attention of experienced substance users [2], and this is based on the theory that the substance and its associated cues increase motivational incentive and salience with each new administration [3,4]. As is commonly understood [3], substances of abuse can operate as Unconditioned Stimuli (US) that elicits Unconditioned Responses (UR). Through conditioning a substance can become associated with environmental stimuli that are contiguous with and contingent on the effects of that substance. That is, after repeated pairings of US with a Conditioned Stimulus (CS), the CS will elicit a Conditioned Response (CR) in the presence of the US. Additionally, substances of abuse can operate as conditioning stimuli, where the US is the substance and the CS is any environmental stimulus that is contiguous with and contingent on the effects of that substance. That is, after repeated pairings of US with a CS, the CS will elicit a CR in the presence of the US.

Background: Substance-related attentional bias refers to the reactivity to substance-related cues. This attentional bias to drugs has been examined in different addictive disorders such as cocaine, alcohol or tobacco dependence. There is extensive evidence regarding the attentional bias to alcohol-related cues in Alcohol Dependent (AD) patients. Furthermore, there is evidence regarding the higher attention bias to cocaine-related cues in Cocaine Dependent (CD) subjects after the exposure to alcohol consumption. However, there are still no data on the potential attentional bias to alcohol-related cues in patients diagnosed with CD.

Objectives: we aimed to assess attentional bias in a sample of alcohol and cocaine users with a visual probe task.

Material and methods: We used a sample of 35 AD patients, 30 CD patients and a control group formed by 35 healthy volunteers. Moreover, and to further study alcohol attentional bias in CD subjects, we divided this group in terms of their history of alcohol consumption. All subjects were examined using the visual probe task, in order to study the attentional bias to alcohol-related cues.

Results: The patients that showed the greater attentional bias to alcohol-related cues were the AD subjects, followed by the CD patients and finally by controls. AD and CD exhibited lower reaction times to alcohol-congruent condition compared to the alcohol-incongruent, whereas in controls the opposite effect was found.

Discussion: Our results indicated that although attentional bias to alcohol-related cues was clearly found in AD and CD patients, these data are in accordance with the hypothesis about the fact that cocaine dependence increases the attentional bias to other drugs, such as alcohol.
dependent subjects would show greater attentional bias for alcohol-related cues in subjects without any alcohol use disorder. In clinical samples and in the general population [18,17]. Now, if cocaine consumption is associated with alcohol consumption, the observation extends to those findings with cocaine-related stimuli compared to the neutral stimuli, and this increased activation under low load in presence of the alcohol-related visual stimuli in a dot probe detection task. In patients who use cocaine, the underlying cognitive processes are unknown.

Alcohol and cocaine are used in higher quantities with concomitant use than when either of the substances are used individually [14], and it is proven by a wide variety of studies that cocaine and alcohol combination produces additive psychological and physiological effects [15]. Therefore, and given that dopamine activity in the mesolimbic pathway is hypothesised to be responsible for incentive salience attribution and attentional bias [3,16], acute administration of drugs that increase dopaminergic activity should lead to increases in attentional bias for any drug-related cues. In addition, Montgomery et al. found increased attentional bias for cocaine cues following preload with alcohol in regular cocaine users, by means of a visual probe task [17]. In cocaine attentional bias, researches using the cocaine emotional Stroop task showed that subjects who use cocaine had slower reaction time compared to controls [8]. Other authors also observed that regions implicated in the general orientation of attention also showed significantly increased activation under low load in presence of the alcohol-associated stimuli compared to the neutral stimuli, and this observation extends to those findings with cocaine-related stimuli [17]. Now then, if cocaine consumption is associated with alcohol consumption in clinical samples and in general population [18], it can be hypothesised that cocaine may increase attentional bias for alcohol-related cues in subjects without any alcohol use disorder (e.g., abuse or dependence).

The present study sought to assess attentional bias in a sample of alcohol and cocaine users with a visual probe task. We hypothesised that Alcohol Dependent (AD) patients and cocaine-dependent subjects would show greater attentional bias for alcohol stimuli compared to controls.

METHODS

Subjects

A sample of 100 individuals was recruited for the study. Groups were divided into 35 AD patients, 35 CD patients and a control group formed by 35 healthy volunteers. In the AD group (26males/9females), the average age was 47.20 years (SD=1.26); the average age for the CD group (30males/5females) was 42.63 years (SD=7.162) and within the control group (23males/12females) the average age was 43.26 years (SD=1.34).

All AD and CD patients underwent detoxification before assessment for this study, and were referred for treatment from Primary Care and Mental Health centres. Patients included fulfilled DSM-IV criteria for diagnosis of alcohol or cocaine dependence (DSM-IV-TR) [19], determined using the validated Spanish version of the Psychiatric Research Interview for Substance and Mental Disorders (PRISM) [20]. Exclusion criteria for patients were current drug abuse other than alcohol, cocaine or nicotine, and any medication that could influence psychophysiological parameters. In the CD group, patients who also fulfilled alcohol dependence criteria were also excluded. Five subjects from the initial 35 CD patients were finally rejected, in order to control possible confounding variables in these patients. Therefore, the final sample of CD patients was composed of 30 subjects. All the patients were abstinent from alcohol and/or cocaine for more than one month (a mean of 35 days). This abstinence was confirmed by toxicological analyses every three days. Patients and controls performed a urine drug test before the task-dot session.

Regarding controls, they were recruited from the local community and from the mental health service staff. Before inclusion, a semi-structured interview was used to screen control subjects for exclusion criteria: thyroid dysfunction, heart disease, hypotension or hypertension, regular drug prescriptions, a history of mental illness (psychotic disorders, bipolar disorders, panic and generalized anxiety disorders), rapid mood changes, drug use (determined by urine toxicology screening) and alcohol abuse, and alcohol dependence in first-degree relatives. Subjects taking psychotropic medications were excluded from the study.

The local ethics committee approved the study. All patients gave written, informed consent.

METHODS

Clinical assessment

For the clinical assessment, the following scales were used:

- The Hamilton Depression Rating Scale (HDRS) [21]
- The Severity of Alcohol Dependence Scale (IADS) [22]

This scale is a multiple item questionnaire used to provide an indication of depression. This questionnaire is designed for adults and is used to rate the severity of their depression by probing mood, feelings of guilt, suicide ideation, insomnia, agitation or retardation, anxiety, weight loss, and somatic symptoms.
is composed of 30 items subdivided into 6 subscales: symptoms of physical and psychological abstinence; behaviors for the relief of abstinence; regular alcohol consumption; difficulties for alcohol control; and symptomatology restoration after relapse.

- The Barrat Impulsiveness Scale (BIS) [23]

The BIS is a questionnaire designed to assess the personality/behavioral construct of impulsiveness. This scale consists on 30 items and it is scored to yield a total score, three second-order factors (attentional, motor and non-planning), and six first-order factors (attention, motor, self-control, cognitive complexity, perseveration and cognitive instability).

**Psychophysiological assessment**

For the psychophysiological assessment, we used the Visual Probe Task (VPT), which was based on the Lubman [24] task. In this task, twenty-seven alcohol-related pictures ("cue pictures") were matched to 27 non-alcohol-related pictures ("neutral pictures"). Cue pictures included different types of alcohol stimuli, such as a can of beer, a bottle of alcohol, a glass of wine, a brewery...To select the cue pictures, we initially preselected 40 alcohol-related images available in "Google Images". From those initial 40 pictures, we selected those with the most motivational relevance [25]. To do this, we administered the Self-Assessment Manikin Visual Analogue Scale (SAM-VAS) to a sample of 20 subjects with AD diagnosis and in 20 subjects without any psychiatry diagnosis as assessed by the PRISM [19]. From the 40 preselected images, 27 pictures had a score on the SAM-VAS scale larger than the mean and were selected as the cues for this study. To find a matching neutral image, another search was performed in Google Images for each cue picture. Pictures were matched on shape, size, and color to the cue pictures [2]. They were selected from the International Affective Picture System [26] on the basis of low arousal and neutral affect. All pictures were resized to the same dimensions, 6.35 cm x 6.35 cm, using Microsoft Paint and were presented on a gray background.

**Procedure**

Both psychological and psychophysiological assessments were performed on two different days. The first day, participants were informed about the procedures. Using a semi-structured interview, a psychiatrist assessed the presence of psychiatric comorbidity and family history of alcoholism. Finally, the clinical evaluation using the three scales described above was carried out by an expert. On the second day, participants were assessed with the VPT. Participants were seated in a comfortable chair in front of a high-resolution monitor. Subjects were informed that they would watch a series of slides and they were asked to read the instructions on the screen. After reading the instructions, they were told that their reaction time (RT) was going to be measured and were instructed to look at a fixation cross when it appeared on the screen. A pair of pictures ("cue" and "neutral" images) appeared after the cross: one to the right and one to the left of the screen. This was followed by a dot to the left or right of the screen in the position of one of the pictures. Participants were instructed to press the space bar as quickly as possible to indicate the position (left or right) where the dot had appeared. They were given 6 practice trials [27]. Regarding the measures that

we used from the VPT in order to study the attentional bias was: the alcohol-congruent and the alcohol-incongruent measures, and the attentional bias measure. Alcohol-congruent meant that both the image and the dot appeared on the same position (left-left or right-right), whereas alcohol-incongruent was used when the image and the dot appeared on the opposite position (left-right or right-left). Finally, attentional bias was obtained from the substraction of alcohol-congruent minus alcohol-incongruent. Higher negative values involve greater attentional bias to alcohol-related cues.

**Statistical analysis**

The SPSS statistical package version 15 was used for the statistical analysis. Continuous sociodemographic variables were evaluated using one-way analysis of variance (ANOVA) and categorical variables using Chi-square test.

For the psychophysiological analysis, we used a 2-way ANOVA repeated measures design, incorporating groupXcondition, with condition as within-subject factor (alcohol-congruent, alcohol-incongruent), and group (AD, CD and controls) as between-subject factor. Significant main and interaction effects were further analyzed by post-hoc comparisons with Bonferroni adjusted alpha level. Regarding the differences within the CD subgroup, another 2-way ANOVA repeated measures design was performed, with condition as within-subject factor (alcohol-congruent, alcohol-incongruent), and group (CD-AC and CD-NAC) as between-subject factor. Finally, and in order to study attentional bias differences between the three groups we used a one-way ANOVA, with attentional bias measure as the within-subject factor and group (AD, CD and controls) as the between-subject factor. For specifically examine alcohol attentional bias in CD, we divided this subgroup in terms of history of alcohol abuse

**RESULTS**

As shown in Table 1, we did not find statistically significant differences between groups in the sociodemographic variables, as the three groups were paired by age and gender, whereas in clinical variables, we did found statistical differences for the Barrat and the Hamilton scales.

Regarding the psychophysiological measures, we found some statistical differences. Firstly, there was a significant conditionXgroup interaction, F (2,97)=5.367, p=0.05. We obtained that in the AD significant statistical differences appeared between the mean reaction times in the alcohol-congruent condition compared to the alcohol-incongruent (p=0.040), with lower reaction times for the congruent condition. However, within the control group, the reaction times for the incongruent condition were statistically lower than the congruent (p=0.013) (see figure 1 for the mean reaction times in the two conditions within the three different groups).

Within the CD group, we obtained a significant condition X group interaction, F (1,58)=7.303, p=0.03. CD with alcohol use patients had greater attentional bias to the congruent stimuli than the CD without alcohol use subgroup (p=0.045).

Finally, and regarding the attentional bias differences between groups, we also obtained statistical significant
Table 1: Sociodemographic and clinical variables [mean (standard deviation)].

<table>
<thead>
<tr>
<th></th>
<th>AD (n=30)</th>
<th>CD (n=30)</th>
<th>Controls</th>
<th>P</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age</td>
<td>47.20 ± 7.40</td>
<td>41.80 ± 6.91</td>
<td>43.26 ± 10.11</td>
<td>Ns</td>
</tr>
<tr>
<td>Gender</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Male / Female</td>
<td>26 / 9</td>
<td>26 / 4</td>
<td>23 / 12</td>
<td>Ns</td>
</tr>
<tr>
<td>Age of onset of alcohol use (years)</td>
<td>15.20 (3.71)</td>
<td>15.93 (2.90)</td>
<td>16.02 (4.32)</td>
<td>NS</td>
</tr>
<tr>
<td>Age of onset of alcohol dependence (years)</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Drinking days (previous month)</td>
<td>27.30 (2.13)</td>
<td>19.21 (2.15)</td>
<td>16.23 (6.90)</td>
<td>&lt;0.05</td>
</tr>
<tr>
<td>Standard drinks per drinking day</td>
<td>20.01 (9.20)</td>
<td>3.18 (2.11)</td>
<td>2.11 (1.34)</td>
<td>&lt;0.01</td>
</tr>
<tr>
<td>BARRAT</td>
<td>77.17 (11.97)</td>
<td>63.07 (13.89)</td>
<td>38.00 (13.38)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Hamilton</td>
<td>10.80 (6.61)</td>
<td>8.07 (5.96)</td>
<td>6 (1.98)</td>
<td>&lt;0.001</td>
</tr>
</tbody>
</table>

Abbreviations: AD: Patients Diagnosed with Alcohol Dependence; CD: Patients Diagnosed with Cocaine Dependence

Figure 1 Mean reaction times for alcohol-congruent and alcohol-incongruent conditions in AD patients, CD patients and controls.

differences, F (2.97)=5.399, p=0.05. Bonferroni post-hoc test showed that AD had higher attentional bias for alcohol stimuli than controls (MD=25.404, p=0.005). Despite we did not find in this study significant differences within CD patients for the attentional bias measure, this group did also obtained negative values, which indicated attentional bias to alcohol, whereas in controls the vaules were positive (AD<CD<Controls) (see table 2 for the means of attetional bias in the three groups).

DISCUSSION

To the best of our knowledge this is the first study regarding attentional bias to alcohol-related cues in patients with cocaine dependence. The most relevant result of our study was the fact that CD subjects showed greater attentional bias to alcohol stimuli than controls. Our data are in accordance with other authors that also reported greater attentional bias in alcohol dependent patients.

Our results supported our hypothesis concerning the potential greater attentional bias to alcohol-related stimuli in CD patients. Some theoretical models emphasize that once subjects are addicted to any drug, the attentional bias to drugs is already established, and it may theoretically contribute to increased motivation to consume any drug in the future [1]. Furthermore, alcohol priming doses can also increase attentional biases for cues associated with other drugs in drug abusers. For example, in regular smokers alcohol administration (0.4 g/kg) increased attentional bias for tobacco cues and craving for cigarettes [28]. Therefore, alcohol may increase the incentive-motivational properties of a variety of abused substances. This phenomenon
Table 2: Comparisons between AD, CD and controls on attentional bias congruent.

<table>
<thead>
<tr>
<th></th>
<th>AD (SE)</th>
<th>CD (SE)</th>
<th>Control group Mean (SE)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Attentional bias</td>
<td>11.48 (6.54)</td>
<td>-2.05 (5.24)</td>
<td>13.92 (4.91)* (minus incongruent)</td>
</tr>
</tbody>
</table>

*Bonferroni adjustment p <0.05
AD<CD<Controls. Higher values mean greater attentional bias to alcohol-related cues.

Figure 2 Mean reaction times for attentional bias measure (congruent minus incongruent) in AD patients, CD patients and controls.

CONCLUSION

This is the first study focused on examining the attentional bias to alcohol-related stimuli in AD patients and in CD patients. Our results indicated that although in AD group there was greater attentional bias to alcohol stimuli, a similar effect occurred in CD subjects. Consequently, we concluded that although attentional bias to alcohol-related cues was clearly found in AD patients, this might also appear in subjects diagnosed with cocaine dependence, as we observed in our sample of research.

Nevertheless, this study is at least subject to some limitations.

of cross-sensitization suggests that dopaminergic sensitization produced by repeated use of one drug (e.g., cocaine) could render the mesolimbic dopamine system hypersensitive to other drugs and then cues associated with any drug [29]. Thus, regular use of cocaine may produce dopaminergic sensitization that renders the individual hypersensitive to alcohol’s dopaminergic effects. Nevertheless, most of the studies have focused on the attentional bias to cocaine-related stimuli in cocaine abuse patients in terms of the influence that alcohol abuse may exert on it [17], but to the best of our knowledge there are no studies focused on the effects that alcohol abuse has on the attentional bias to alcohol-cues in cocaine abusers. Therefore, these current findings may suggest that CD patients might show an attentional bias to other drugs (alcohol in this case) that have been used with cocaine through the addictive course. When we considered alcohol consumption within this CD group, we did find differences in attentional bias to alcohol-stimuli. These data may explain why alcohol use is highly widespread in cocaine abusers [14], and thus this should be an issue of great relevance when studying attentional bias in these patients.

As expected, our results found that attentional bias is impaired in AD patients, with greater attentional bias to alcohol-stimuli. Schema-based theories of addiction suggest that drug using behaviours tend to be automatic, difficult to impede in the presence of triggering stimuli and may occur in the absence of awareness [30], and incentive theories of addiction propose that stimuli associated with drug taking become particularly salient [3]. Both of these theories highlight the ability of drug-related stimuli to capture attention, and support the idea that attentional biases play an important part in drug dependence [9]. Townsend et al found that stimuli associated with alcohol tend to acquire incentive salience as related theories suggest [31] and capture the attention of the individual who uses the drug [9]. Furthermore, these authors also showed that this attentional bias to alcohol-related cues is still found in non-dependent social drinkers, which suggests that cue-reactivity is sensitive to non-dependent individuals and that cue-reactivity may develop through a history of alcohol use, from first experimentation to abuse and possible dependence [30].

Firstly, there was higher incidence of male subjects within the three groups, and the gender variable may be influencing the results. However, this difference between genders is representative of the prevalence in substance abuse that is commonly found in the clinical population. Secondly, patients with AD showed higher score in the Hamilton scale and the Barrat scale than CD patients and controls. Therefore, this should be a variable to consider for future studies. Finally, within the CD patients, there was a high prevalence of alcohol abuse. However, this is the representative incidence that occurs in the general population of cocaine abusers, and thus this should be considered when studying attentional bias in these patients.

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REFERENCES


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