

Alcohol cues increase cognitive impulsivity in individuals with alcoholism

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Abstract

Background Individuals with alcoholism are characterized by both attentional bias for alcohol cues and prepotent response inhibition deficit. We tested the hypothesis that alcoholics exhibit greater cognitive disinhibition when the response to be suppressed is associated with alcohol-related information.

Methods Forty recently detoxified individuals with alcoholism were compared with 40 healthy non-substance abusers on the “Alcohol-Shifting Task”, a variant of the

go/no-go paradigm requiring a motor response to targets and no response to distracters. The aim was to test the ability of alcoholics to discriminate between alcohol-related and neutral words. Sometimes, the alcohol-related words were the targets for the “go” response, with neutral words as distracters, sometimes the reverse. Several shifts in target type occurred during the task.

Results Alcoholics made significantly more commission errors (i.e., press a key when a distracter displayed) and more omission errors (i.e., not press a key when a target displayed) than controls. Moreover, the number of commission errors was greater in alcoholics when alcohol-related stimuli had to be detected.

Conclusions These results demonstrate that alcoholics exhibit a basic prepotent response inhibition deficit, which is enhanced when the response to be suppressed is related to alcohol. We discuss clinical and theoretical implications of these findings.

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Introduction

Like other addictions, alcoholism is characterized by compulsive preoccupation with obtaining the object of addiction (alcohol) in spite of devastating consequences affecting social and occupational functioning (American Psychiatric Association 1994).

In individuals with alcoholism, alcohol-drinking practice can be viewed as encompassing stimulus-driven automatic behaviors (e.g. Tiffany 1990). From an information-processing perspective, three main processes could influence these behaviors: (1) the level of practice leading to a certain

degree of automaticity; (2) the strength of the incentive value for alcohol as defined by Robinson and Berridge (2003); and (3) regulatory processes including the ability to inhibit dominant response, to re-orient attention, and to select an alternative response requiring preserved executive functioning. This view is consistent with neurobiological and functional neuroimaging-based models suggesting that drug-seeking behavior may be due to two related processes: (1) an increase in incentive motivational qualities of the drug and associated stimuli (related to subcortical dysfunction) and (2) impaired inhibitory control (related to frontal cortical dysfunction; for reviews, see Lubman et al. 2004; Goldstein and Volkow 2002; Moselhy et al. 2001). Therefore, abnormal motivational properties of alcohol and/or impaired prepotent response inhibition may lead to loss of control of alcohol use and to alcohol relapse (Noël et al. 2002; Cox et al. 2002).

In this framework where alcohol has acquired strong motivational properties, alcohol-related stimuli may be seen as ‘hijacking’ the attention of heavy drinkers and alcoholics (e.g., Johnsen et al. 1994; Townshend and Duka 2001; Waters and Green 2003; Noël et al. 2005, 2006; Jones et al. 2003). For instance, when performing the alcohol Stroop task, sober alcoholics are slower than non-alcoholic controls in naming the color of alcohol-related words (e.g., Johnsen et al. 1994; Stetter et al. 1995). When performing a selective attentional task (the dot-probe detection task), regular social drinkers show a clear attentional orienting response toward alcohol-related stimuli over neutral stimuli, whereas occasional alcohol drinkers do not (Townshend and Duka 2001; Field et al. 2004).

In addition, recently detoxified alcoholics exhibit executive frontal function deficits (e.g. Noël et al. 2001; Hildebrandt et al. 2004). Among the executive functions, inhibition has been recognized as an essential system (e.g. Collette and Van der Linden 2002). A hypothesis that has attracted increasing attention suggests that alcoholism is a ‘disinhibitory disorder’. This would account for poor performance in a variety of cognitive tasks assessing dominant response inhibition in abstinent alcoholics (e.g. Noël et al. 2001) and in children of alcoholics (e.g. Habeych et al. 2006). It is also supported by abnormalities in brain electrophysiology (e.g. Kamarajan et al. 2006) and brain metabolism (e.g. Scheinsburg et al. 2004) during the performance of response inhibition tasks.

However, little is known about the relationship between enhanced attention for alcohol cues (cognitive bias) and impaired prepotent response inhibition (cognitive deficit). Studies using the alcohol Stroop task did not reveal any significant differences between light and heavy drinkers (Sharma et al. 2001) or between alcoholics and healthy participants (Lusher et al. 2004) in terms of the number of errors made when words are related to alcohol. One reason for the absence of cognitive disinhibition in the alcohol

Stroop task is that both problematic users of alcohol and healthy participants made very few errors, thus reflecting a ceiling effect. Another limitation of the Stroop task is that the inhibitory nature of the involved processes is questionable. Whereas the Stroop task has generally been considered as examining resistance to interference (Nigg 2000), it might also be viewed as taxing mechanisms of inhibitory control involved in suppression of prepotent responses (i.e., read the alcohol-related words rather than the color).

To overcome these limitations, we designed an alcohol version of a go/no-go paradigm (the Alcohol-Shifting task, Noël et al. 2005), which examines distinctly motor response inhibition, shifting of attention, and the influence of alcohol-related stimuli on these functions. We hypothesized that alcoholic subjects exhibit impairments in tasks requiring inhibitory control as well as shifting. Furthermore, we hypothesized that these deficits would be more pronounced when processing and controlling alcohol-related information.

Materials and methods

Participants

All subjects were adults (>18 years old) and provided informed consent that was approved by the appropriate human subject committees at the Brugmann University Hospital. The demographic data on the two groups are presented in Table 1.

Alcoholic participants

Forty alcoholic participants (ALC) were recruited for this study from the Alcohol Detoxification Program of the

Table 1 Demographic and clinical data of subjects who participated in the study

	ALC	CONT
Total <i>N</i>	40	40
Age (years): mean ± SD	44.7±10.8	43.6±10.7
Gender (M/F)	18/18	18/18
Education (years): mean ± SD	10.5±2.3	11.3±1.9
Prior detoxification treatments: mean ± SD	3.9±4.6	–
Years of abuse: mean ± SD	12.8±6.9	–
Duration of abstinence (days): mean ± SD	19.7±2.7	–
BDI ^a	13.7±6.5	3.5±3.9
STAI ^b		
Trait	43.3±17.1	30.4±10.3
State	52.1±6.1	35.6±10.1

^a Beck Depression Inventory (1987, 1993)

^b State Trait Anxiety Inventory (1993)

Institute of Psychiatry, Brugmann Hospital, Brussels, Belgium. They were tested between 18 and 21 days after drinking cessation. They all received complete medical, neurological, and psychiatric examinations at the time of selection. The participants had to meet the Diagnostic and Statistical Manual of Mental Disorders (DSM-IV) criteria for alcohol dependence (ascertained by a board-certified psychiatrist [P.V.]). Reasons for exclusion were other current DSM-IV Axis I diagnoses, a history of significant medical illness, head injury resulting in loss of consciousness for longer than 30 min, use of other psychotropic drugs or substances that influence cognition, and overt cognitive dysfunction. At the time of assessment, ALC were withdrawn from all psychotropic drugs (including diazepam used for alcohol detoxification). To increase the reliability of information, ALC and their families were interviewed separately. Blood levels of folate, vitamin B12, and B-carotene were measured. Current clinical status was rated using the Beck Depression Inventory (BDI; Beck 1987) and the Spielberger State Trait Anxiety Inventory (STAI Trait and State; Spielberger et al. 1993). The Structured Clinical Interview for DSM-IV (SCID-IV) was used to assign Axis I diagnoses (including alcohol and other drug abuse and/or dependence).

Control participants

Forty control participants (CONT), similar for sex, age, and educational level, were recruited by word of mouth from healthy community members; they were not paid for their participation. Exclusion criteria were an Axis I psychiatric diagnosis assessed by the SCID-IV; drug-use disorder during the year before enrollment in the study; or consumption of more than 54 g/day of alcohol for longer than 1 month. On the basis of the results of their medical history and physical examination, they were considered to be medically healthy. CONT were asked to avoid the use of drugs, including narcotic pain medication, for the 5 days before testing and to avoid alcohol consumption for the preceding 24 h.

Procedure

All ALC were inpatients admitted to the Clinic of Addictions for detoxification and treatment. They had serious substance abuse problems requiring professional intervention, which was the reason for their admission.

The duration of their abstinence from substance use was known from the length of their stay at the Clinic of Addictions. The minimum abstinence period was 15 days. Each ALC was tested at the end of treatment, i.e., shortly before discharge. Thus, at the time of testing, the ALC were no longer in acute withdrawal or taking any psychotropic drugs.

ALC were routinely checked for substance abuse during their treatment. They were also breath-analyzed and subject to urine toxicology screening for opiates, stimulants, and marijuana immediately before testing. Therefore, we can be reasonably sure that there was no use of substances during the entire period of abstinence. The duration of abstinence, the number of times in treatment, and the total number of years of abuse were obtained from interviews.

Alpha-span task

Given that ALC exhibited reduced working memory capacities (e.g. Noël et al. 2001), which might decrease performance on the Alcohol-Shifting task, we administered the alpha-span task for assessing working memory (Belleville et al. 1998).

This task investigated the ability to manipulate information stored in working memory by comparing the recall of information in serial order (involving mainly a storage component) and in alphabetical order (involving storage and manipulation of information). After having assessed the verbal span level, the subject was asked to repeat word sequences in two different conditions: direct recall and alphabetical recall. In both conditions, the number of words to be recalled corresponded to the subject's span minus one item. In the direct condition, the subject performed an immediate serial recall of ten sequences of words. In the alphabetical condition, the subject was asked to recall ten sequences of words in their alphabetical order. The comparison of performance in alphabetical recall with that in serial recall assesses the subject's performance.

Alcohol-shifting task

The alcohol-shifting task was adapted from the original task designed by Murphy et al. (1999). In our go/ no-go task, words are briefly displayed, one by one, in the center of the screen. Half of the words are targets and half are distracters. Subjects are instructed to respond to targets by pressing the space bar as quickly as possible but not respond to distracters. Words are presented for 500 ms, with an inter-stimulus interval of 900 ms. A 500-ms/450-Hz tone sounds for each false alarm (i.e., a response to a distracter) but not for omissions (i.e., failures to respond to a target). The task comprises two practice blocks followed by eight test blocks of 18 stimuli each composed of nine 'neutral' (N) and nine 'alcohol related' words (A). In each block, either N or A words are specified as targets, with targets for the ten blocks presented either in the order NNAANNAANN or AANNAANNAA. Due to this arrangement, four test blocks are 'non-shift' blocks, where subjects must continue responding to stimuli in the same way. Four test blocks, however, are 'shift' blocks, where subjects must begin

responding to stimuli, which had been distracters, and cease responding to stimuli, which had been targets.

The 45 neutral and alcohol-related words used were selected, from an original list of 180 words, because they had been consistently rated, by five certified psychologists (from the Department of Psychology of the Free University of Brussels) and 30 alcoholic patients in detoxification treatment (Brugmann University Hospital, Clinic of Addiction) blind to the purpose of this study, as being ‘very related to alcohol’ [on a 7-point Likert scale with endpoints (–3) ‘very unrelated to alcohol’ and (+3) ‘very related to alcohol’]. Words rated –3/–2 were selected as alcohol-related and those rated +2/+3 as neutral. The neutral and alcohol-related words did not differ in terms of word length or word frequency as determined from the norms of Hofland and Johansson (1982). Examples of alcohol related words are ‘drink’, ‘tipsy’, and ‘cocktail’; and neutral words, ‘forest’, ‘cupboard’, and ‘harbor’.

Statistical analyses

Two-tailed repeated-measures ANOVA were used to compare performances on the Alcohol Go/No-Go Task across groups. The within-group repeated measures were type of target (neutral versus alcohol-related words) and shift (shift versus nonshift blocks). Pearson’s product moment correlation coefficients with Bonferroni correction were employed in correlational analyses. All statistical analyses were performed using Statistical Package for the Social Sciences 14.0 (SPSS 14.0; SPSS, Chicago, Ill).

Results

Demographical and clinical variables

ALC and CONT groups were similar in term of age, sex and educational level. However, duration of alcoholism [$F(1,78)=7.6, p<0.001$], daily consumption of alcohol [$F(1,78)=8.6, p<0.001$], the number of prior detoxification treatments from alcohol [$F(1,78)=4.4, p<0.001$], depression [$F(1,78)=5.3, p<0.001$], STAI [$F(1,78)=4.2, p<0.001$] and Spieberger state anxiety inventory (STSI) [$F(1,78)=5.3, p<0.001$] were higher in ALC than in CONT (see Table 1).

Cognitive tasks

Reaction time task

ALC’s mean reaction time (RT) to detect a cross displayed at the center of a computer screen was up to 279.1 ms (SD=52.7), whereas it reached 258.2 ms (SD=

36.9) for CONT. The difference between groups was not significant [$F(1,78)=-0.8, p>0.05$].

Alpha-span task

The scores for serial and alphabetical recall were analyzed using a two-way two (group) × two (serial, alphabetical recall) ANOVA. The analysis revealed a main effect of group [$F(1,78)=6.6, p=0.01$] and of condition [$F(1,78)=87.5, p<0.001$]. A significant interaction between group and type of recall was also found [$F(1,78)=9.1, p<0.01$], with ALC showing a more important decrease in performance from direct to alphabetical recall than CONT ($p<0.01$) despite a similar performance in direct recall.

Alcohol-shifting task

Mean response time, errors, and omissions for each block of 18 trials were initially analyzed by way of repeated ANOVAs, with patient group (ALC and CONT) and target presentation order (alcohol words first, neutral words first) as between-subject factors and type of target (alcohol-related words, neutral words) and type of condition (shift, non-shift) as within-subject factors. As no effects involving target presentation order approached significance, and as no specific prediction involving target presentation order were made on a priori basis, data were reanalyzed for the purpose of clarity; specially, three ANOVAs were performed (on each of the three dependent variables of interest: RT, errors, and omissions), with group, type of target, and shift condition as factors. Response time less than 100 ms (anticipation) were excluded from analysis.

Reaction times

Using RT as the dependent measure, a three-way ANOVA two groups (ALC, CONT) × two types of targets (alcohol, neutral words) × two conditions (shift, non-shift) revealed a main effect of “type of target” [$F(1,78)=91.7, p<0.0001$], with all participants being slower to detect neutral than alcohol-related targets. For the interaction group × type of target [$F(1,78)=9.5, p<0.001$], ALC were slower than CONT to process alcohol cues as target ($p<0.05$; see Fig. 1).

Commission errors (i.e., press the key when a distractor is displayed)

When considering the mean number of no-go errors made by ALC and CONT on shift and non-shift conditions for neutral and alcohol cues, the three-way, two-group (ALC, CONT) × two conditions (shift versus non-shift) × two types of target (neutral, alcohol-related words) ANOVA revealed a signifi-

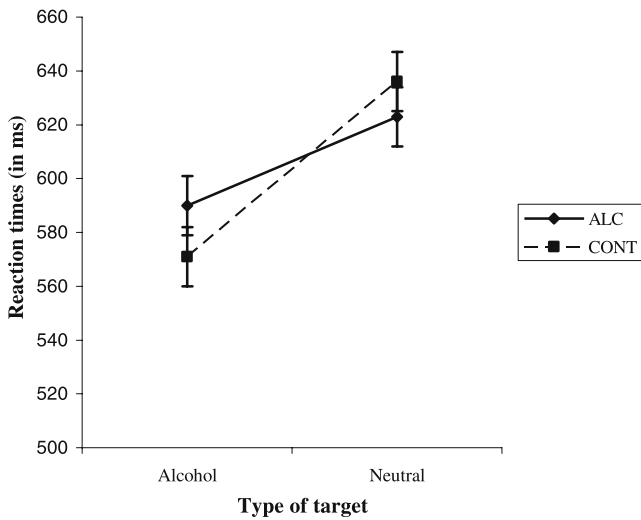


Fig. 1 Reaction times for alcohol and neutral cues in ALC and CONT (+/- standard errors of the mean)

cant main effect of type of target [$F(1,78)=25.6, p<0.001$], with participants making more errors when targets were neutral than related to alcohol. The significant main effect of group [$F(1,78)=8.4, p<0.01$] indicated that ALC made more commission errors. The interaction group \times target was the only significant interaction [$F(1,78)=7.3, p<0.01$], with CONT making more commission errors when the target was related than not related to alcohol (see Fig. 2).

Omission errors (i.e., not press the key when a target is displayed)

When considering the mean number of omissions made by ALC and CONT on shift and non-shift conditions when targets were neutral and related to alcohol, we performed a three-way, two (group) \times two (shift versus non-shift conditions) \times two (alcohol versus neutral stimuli), which revealed a main effect of group [$F(1,78)=9.1, p<0.01$], with ALC omitting more targets than CONT (see Fig. 3). No interaction achieved the significance.

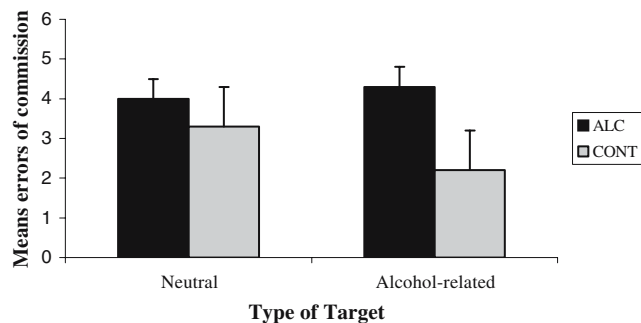


Fig. 2 Mean errors of commission for neutral and alcohol-related words in the alcohol-shifting task for ALC and CONT. Bars represent 1 SEM

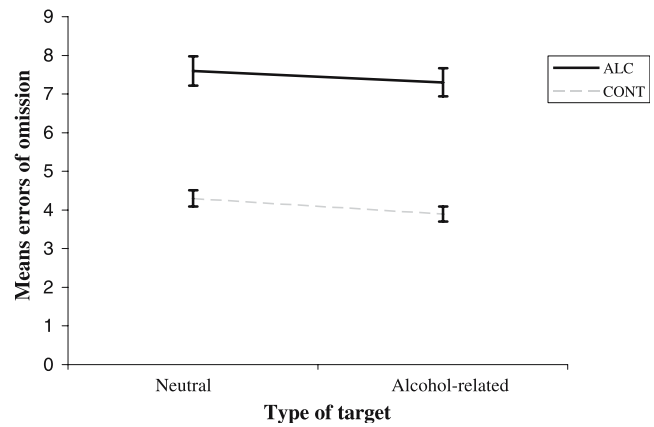


Fig. 3 Mean errors of omission for neutral and alcohol-related words in the alcohol-shifting task for ALC and CONT. Bars represent 1 SEM

Relationship between clinical variables and cognitive measures

When considering the correlation between the number of prior detoxification treatments, the duration of alcoholism, the number of days of abstinence, depression and anxiety scores, and the working memory and Alcohol-Shifting task performances, we found, by using parametric Pearson’s analyses and after correction with Bonferroni method, a significant positive correlation between the severity of alcoholism, as expressed in the total number of prior detoxifications, and the inhibition bias (average of commission errors when target was neutral words–average of commission errors when target was related to alcohol; $r_{40}=0.51, p<0.01$). None of the other correlations was found to be significant.

Discussion

The primary aim of the present study was to examine the presence of cognitive deficits and biases in recently detoxified alcohol-dependent individuals. We studied different mechanisms of executive control (i.e., prepotent response inhibition and shifting) and the cognitive biases for alcohol-related stimuli. For the non-shift (response inhibition) condition of the alcohol-shifting task (Noël et al. 2005), ALC made more commission errors and more omission errors than non-alcoholic participant (CONT). Moreover, analyses indicated that only ALC made still more commission errors when the target was related to alcohol. These results indicate that ALC exhibit both a response inhibition deficit and a bias of inhibition for alcohol-related stimuli.

The ALC’s difficulty in inhibiting a dominant response on the go/no-go task replicates results of a recent study (Goudriaan et al. 2005) and strengthens the hypothesis considering alcoholism as a ‘disinhibitory disorder’. In-

deed, ALC exhibited poor performance in a variety of prepotent response inhibition tasks (e.g. Stop Signal task, Goudriaan et al. 2006; Wisconsin Card Sorting task, Ratti et al. 2002; Stroop task, Dao-Castellana et al. 1998; Hayling task, Noël et al. 2001). For instance, in the Hayling task (Burgess and Shallice 1996), subjects were asked to give a word that made no sense at all in the context of a sentence in which the last, very predictable word was missing. ALC were slower than CONT, and they also gave more words related to the predictable one, thus indicating a response inhibition deficit (Noël et al. 2001).

Another main related finding was that ALC were still more impulsive (made more commission errors) than CONT when targeting alcohol-related cues. This greater impulsivity in ALC when processing alcohol cues suggests that the activation of category-related semantic representations is at an abnormally high level, consistently with the ‘incentive motivational theory’ proposed by Robinson and Berridge (1993, 2003).

The finding that ALC made more omission errors than control, whatever the type of stimuli to be detected, can be explained as the consequence of selective attention deficit (e.g. Lezak 1995).

Interestingly, we found that the meaning of words (related or not to alcohol) impacts RT, ALC being slower than CONT in pressing a key when alcohol-related words rather neutral ones were displayed. This contrasts with findings in a recent study, in which polysubstance abusers with alcoholism took more time than controls to press the key only when neutral targets were displayed (Noël et al. 2005). This could reflect a difference in basic speed processing in alcoholics who use or not other substances. Results on a reaction time task (i.e., task of everyday attention, TEA) indicates that ALC were not slower than CONT, whereas polysubstance abusers were slower than their controls in most of the cognitive tasks used in previous studies conducted in our laboratory (e.g. Bechara et al. 2001). Another explanation could be that, compared to drug users who have been abstinent for a longer period, recently detoxified ALC recruited for this study presented numerous negative consequences associated with their alcohol habits (e.g. withdrawal symptoms, feelings of guilt), thus making alcohol undesirable. This hypothesis is in line with two studies (Stormark et al. 1997; Noël et al. 2006) that showed that on a selective attentional task (the dot-probe detection task), ALC but not CONT exhibited an attentional bias for alcohol cues at the earlier stage of attention (<100 ms) followed by a bias of avoidance (Stormark et al. 1997) or no bias at all (Noël et al. 2006) after a 500-ms-long presentation.

We also found an absence of shifting deficit in ALC as assessed by the alcohol-shifting task. Such a deficit has been observed in ALC by using a version of the Stroop

task, where participants had to name the color of the print of a word printed in an incongruent color and had to read the word’s meaning when it was underlined (Noël et al. 2001). This discrepancy could be due to the fact that different shifting processes are involved in these tasks and are differentially affected by alcoholism. In the alcohol-shifting task, participants were instructed to switch from a target word to another word (perceptual shifting), but the rule governing the task realization remained identical (i.e., pressing a key). In contrast, in the shifting version of the Stroop task, participants were requested to switch from a rule to another (conceptual shifting), that is, to name the color of a word printed and to read the word when it was underlined. Further investigations are needed to validate this distinction in ALC.

Similarly to Noël et al. (2001, 2002; see also Ratti et al. 2002), we observed that ALC exhibited working memory abnormalities. The results of the alpha-span task show that ALC’s ability to store information in working memory (measure the span size and the score of direct recall condition) remained normal, but the ability to manipulate the information stored (measured by the alphabetical recall condition) was impaired. Moreover, the performance in the alpha span task correlated with the number of commission errors made by ALC on the Alcohol-Shifting task, indicating that their response inhibition deficit cannot be explained by this working memory impairment.

Regarding the potential influence of the high levels of depression and anxiety observed in ALC in their cognitive functioning, we did not find a significant correlation between cognitive performance and measures of anxiety and of depression, which suggests that the observed deficits and biases in ALC are not due to these clinical aspects. On the other hand, we found a positive correlation between the number of prior detoxification treatment and the proneness to be disinhibited (more commission errors) when alcohol-related stimuli were targets, thus indicating that this inhibition bias may be involved in the severity of alcoholism. From this study, we cannot determine whether the cognitive deficits and biases found in ALC existed before they became addicted to alcohol. These deficits and biases could have been a cause of their addiction rather than a consequence of alcohol-related neurotoxicity. In support of the hypothesis, a recent functional magnetic resonance imaging study has compared youths with and without a family history of alcoholism, using a go/no-go procedure, and has demonstrated that youths with a family history of alcoholism showed less inhibitory frontal response than other youths, thus suggesting that inhibition deficits could be predisposing factors to alcohol abuse (Schweinsburg et al. 2004). In addition, poor response inhibition has been demonstrated to be a predictor of problem drinking in adolescents at risk for alcoholism (e.g. Nigg et al. 2006).

Increased impulsivity by alcohol cues observed at the end of a detoxification treatment in ALC might have some clinical implications. Indeed, alcohol-drinking practice in individuals suffering from alcoholism can be viewed as encompassing stimulus-driven automatic behaviors (e.g. Tiffany 1990). Besides, the intensity of alcohol-related response may be stronger because of an effect of the behavioral sensitization phenomenon described by Robinson and Berridge (2003). In these circumstances, moderating or stopping alcohol drinking might require the inhibition of prepotent response. The present findings show that the response inhibition deficit seen in ALC is more pronounced when response associated with alcohol-related stimuli is to be suppressed. Thus, psychopharmacological and psychological strategies to improve the prepotent response inhibition capacities and/or to diminish the salience of alcohol-related responses would be fruitful for attenuating the severity of alcoholism and to prevent alcohol relapse.

To summarize, prepotent response inhibition is impaired in ALC, and signs of disinhibition are more pronounced when motor responses to be suppressed have been associated with alcohol cues. These findings underline that alcoholics' cognitive efficacy is dramatically influenced by alcohol cues, which increase cognitive impulsivity.

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