

ORIGINAL ARTICLE

Distinct Effects of Protracted Withdrawal on Affect, Craving, Selective Attention and Executive Functions among Alcohol-Dependent Patients

Mariana Cordovil De Sousa Uva^{1,4,*,**}, Olivier Luminet^{1,2,**}, Marie Cortesi¹, Eric Constant⁴, Marc Derely⁵ and Philippe De Timary^{2,3,4}¹Department of Psychology, Université Catholique de Louvain, Louvain-la-Neuve, Belgium, ²The Belgian National Fund for Scientific Research (FRS-FNRS), Belgium, ³The Unité d'Hépatologie Intégrée, Cliniques Universitaires St Luc, Université de Louvain, Brussels, Belgium, ⁴Department of Adult Psychiatry, Cliniques Universitaires St Luc, Université de Louvain, Brussels, Belgium and ⁵Clinique La Ramée, Brussels, Belgium

*Corresponding author: Université Catholique de Louvain, Place du Cardinal Mercier 10, B-1348 Louvain-la-Neuve, Belgium. Tel.: +32-27649047. E-mail: Mariana.Cordovil@uclouvain.be. **These authors contributed equally in the conception of the study and the writing of this paper.

(Received 21 August 2009; in revised form 3 December 2010; accepted 19 January 2010)

Abstract — **Aims:** The present study examined the effects of protracted alcohol withdrawal on affectivity, craving, selective attention and executive functions (EFs) in alcohol-dependent patients. **Methods:** Selective attention (The D2 Cancellation Test), flexibility (Trail Making Test), inhibition (Stroop Task), decision making (Iowa Gambling Task), craving (Obsessive–Compulsive Drinking Scale) and state affectivity (Positive and Negative Affectivity Schedule) were assessed in alcohol-dependent patients (DSM-IV, $n = 35$) matched to non-alcohol-dependent participants ($n = 22$) at the onset (T1: day 1 or 2) and at the end (T2: days 14–18) of protracted withdrawal during rehab. **Results:** Alcohol-dependent patients' abilities to focus their attention on relevant information, to switch from one pattern to another, to inhibit irrelevant information and to make advantageous choices were lower than those of control participants during both times of a withdrawal cure. No effect of time emerged from analyses for selective attention and EF deficits. Conversely, significant differences between T1 and T2 were observed for craving and affect scores indicating a weakening of alcohol craving and negative affect as well as an improvement of positive affect among patients from onset to the end of cure. **Conclusion:** Control functions of the Supervisory Attentional System (Norman and Shallice, 1986) were impaired and did not improve during a 3-week withdrawal cure, whereas alcohol craving and negative state affectivity significantly improved in parallel during this period. Implications for understanding the clinical processes of withdrawal are discussed.

INTRODUCTION

Protracted alcohol withdrawal constitutes an important initial step of the treatment and the rehabilitation of alcoholic patients. When performed in hospital, the appearance of withdrawal symptoms (i.e. shakes, sweats, rapid heartbeat and depressive symptoms) are minimized by the implementation of a withdrawal substitution treatment usually consisting of appropriate doses of benzodiazepines. Withdrawal provides alcoholics with a subjective feeling of attaining better control over their drinking. Indeed, the DSM-IV (American Psychological Association, APA, 1994) supports the view that the failure of efforts to cut down alcohol drinking due to the inability to control alcohol use is an important factor of alcohol dependence. Moreover, according to the DSM-IV, the persistence of the drive to drink and the disturbance of affectivity are two important diagnostic criteria of alcohol dependence.

The drive to drink, affectivity and control abilities are therefore three important facets of alcohol dependence, but to date there has been no attempt to evaluate in parallel the ways in which these three factors are affected by alcohol withdrawal. Recent studies using questionnaires have shown significant improvements in craving and affective states (i.e. depression, anxiety) (Andersohn and Kiefer, 2004; de Timary *et al.*, 2008) during a 3-week alcohol withdrawal.

Regarding control abilities, Norman and Shallice (1986) introduced the notion of Supervisory Attentional System (SAS), a system required at the highest level of action control that helps individuals to cope with novelty. Therefore, the SAS provides high level control functions which notably include executive functions (EFs), which are cognitive operations that guide complex behaviour over time such as planning, abstraction, cognitive flexibility, inhibition, concept generation and

decision making. Several previous neurocognitive studies investigated a number of EFs among recently abstinent alcoholic individuals (i.e. sober for 3 weeks) and reported deficits of inhibition of prepotent response (Noël *et al.*, 2001) and cognitive flexibility decision making (Goudriaan *et al.*, 2006), planning (Joyce and Robbins, 1991) and abstraction (Parker *et al.*, 1991). To date, only one study tested the evolution of EFs during withdrawal, but it only focused on flexibility (Mann *et al.*, 1999). It is therefore critical to better understand the influence of withdrawal on a wider selection of EFs. Importantly, the SAS is also involved in attentional control. The issue of attention has not been much explored in research on alcohol addiction (Becker *et al.*, 1983; Tedstone and Coyle, 2004) and never in test–retest settings during withdrawal.

The goals of the present study were therefore to examine whether a 3-week detoxification programme exerts similar or distinct effects on drive for drinking, affectivity, selective attention and a number of EFs, in order to compare these changes to those observed in a control group in a test–retest design.

MATERIALS AND METHODS

Participants

A group of 35 alcoholic patients and a control group of 22 alcohol non-abusers, matched for age, gender and educational level (see Table 1) were tested. All the participants in the alcoholic patient group were recruited among alcohol-dependent patients during a detoxification and rehabilitation programme at the Department of Adult Psychiatry at the Cliniques Universitaires St Luc and Clinique La Ramée, Brussels. They received a diagnosis of alcohol dependence as first axis I diagnosis according to DSM-IV criteria (American Psycho-

Table 1. Sociodemographic data for the clinical and the control groups

Variable	Alcoholic group AT1/AT2 <i>n</i> = 35	Control group C <i>n</i> = 22	Significance
Mean age, ± SD	48.40 ± 8.2	44.36 ± 9.64	ns ^a
Gender, <i>n</i> (%)			
Male	17 (48.5%)	14 (63.63%)	ns ^b
Female	18 (51.5%)	8 (45.47%)	ns ^b
Gender age, ± SD			
Male	46.76 ± 8.22	43.28 ± 8.73	ns ^a
Female	49.94 ± 8.09	46.25 ± 11.45	ns ^a
Educational level, <i>n</i> (%)			
Secondary education	15 (42.85%)	7 (31.81%)	ns ^b
Higher Education	20 (57.14%)	15 (68.18%)	ns ^b

ns, not significant. ns = $P > 0.05$.

^aIndependent *t*-tests for independent samples.

^bPearson chi-square test.

logical Association, APA, 1994), clinically evaluated by psychiatrists (P.dT., M.D.). At onset of withdrawal, systematically patients received a withdrawal substitution treatment consisting of appropriate doses of benzodiazepines (diazepam: usually 30–40 mg per day) to minimize withdrawal symptoms. This medication was progressively tapered during detox. Vitamin B1 was also given to all patients. Only the patients that had drunk alcohol on the date of application or the day before were included in the study. Patients who relapsed during their stay, or who consumed addictive substances other than alcohol (and cigarettes) or presented symptoms of dementia were also excluded. The alcohol non-abusers were recruited by word of mouth and were paid for their participation. They did not report any history of alcoholism or other addiction. The current study was accepted by the ethical committee of the hospitals, and all patients signed an informed consent form.

Measures

Two questionnaires evaluated craving and state affectivity, whereas four tests evaluated selective attention and some EFs such as flexibility, inhibition and decision making, respectively.

A questionnaire on cognitive aspects of alcohol craving, the Obsessive–Compulsive Drinking Scale (OCDS)¹ (Anton *et al.*, 1995, 1996), was administered in a French version (Ansseau *et al.*, 2000). The OCDS is a self-report questionnaire, which can be divided into two subscales, an ‘obsessive’ subscale and a ‘compulsive’ subscale. We used a modified version that excluded items related to drinking, as alcohol consumption was prohibited during the stay. Positive (PA) and negative (NA) mood states were assessed by a validated French version (Gaudreau, 2000) of the Positive and Negative Affectivity Schedule (PANAS) (Watson *et al.*, 1988). The first cognitive task was the D2 Cancellation Test (Brickenkamp, 1981) which assesses selective attention, visual scanning ability and mental concentration. The test is composed of several lines with letters, in which participants have to mark as many targets per line as possible. The dependent variables are total number of items identified in the total lines (GZ) and the total number of errors (F). A second task, the Trail Making Test

(Lezak, 1983), measures visual-motor scanning abilities and the flexibility of cognitive sets and consists of two parts (A and B). The dependent variables are the time spent (milliseconds) and the number of errors for the first (TMT A) and second part (TMT B) of the test. The switching index (i.e. the difference score (B–A)) is also calculated in order to remove the speed component from the test evaluation. The third task, the classical Stroop Task (Stroop, 1935) assessed cognitive selective attention processes and higher control processes related to inhibition of prepotent responses. Three types of items were presented to participants: congruent items (i.e. when two stimulus dimensions are congruent: colour words presented in their ink colour), incongruent (i.e. when two stimulus dimensions are incongruent: colour words presented in another colour) and neutral (i.e. percentage marks). Median reaction times (median RTs) were determined for each type of stimulus (congruent vs incongruent vs neutral). From these median RTs, an interference index is calculated as follows: median RTs incongruent items – median RTs neutral items. The interference index has the advantage of removing the psychomotor component, taking into account only the executive component. It is therefore a good index of inhibition deficit. To administer this task, we used a computerized version of the Stroop Task (Constant *et al.*, 2006) using the E-Prime software system version 1.0. Finally, decision-making processes were tested by the Iowa Gambling Task (IGT; Bechara *et al.*, 1994) with financial rewards and penalties written on cards and converted into Euros. Two measurements, the total number of cards from advantageous decks A' and B' (A' + B') and the total numbers from disadvantageous decks C' and D' (C' + D'), are assessed. A net score (A' + B') – (C' + D') was also calculated.

Statistical analyses

All variables were tested at the onset (T1 = day 1) and end (T2 = days 14–18) of withdrawal in the same subjects with the exception of the GT task which could not be repeated due to potential learning test–retest effects (Tranel *et al.*, 2000). Therefore, the GT was not conducted twice on the same cohort but on two different cohorts by splitting the alcohol group in two, which performed GT either at T1 or at T2. A 2 (Group) × 2 (Time) MANOVA was conducted with Time (T1 vs T2) as a within-subjects factor and with Group (alcoholics vs controls) as a between-subjects factor to test for differences in all scales and tests except for the IGT. The observed interactions were supplemented by calculating *t*-tests for dependent samples. The magnitude of observed effects was directly calculated: η^2 for *F*-test and Cohen's *d* for *t*-test (Cohen, 1988). Student's *t*-tests for independent samples were used to specifically compare the evolution of IGT scores between T1 and T2.

Scores exceeding three standard deviations (SD) from the mean (for the alcoholic and the control groups, respectively) were excluded from analysis. Consequently, the number of participants differs slightly for each variable as shown in Table 2.

RESULTS

Craving questionnaire

Analyses revealed a main effect of Time, $F_s(1,51) > 11.51$, $P_s < 0.001$, $\eta_s^2 > 0.18$, a main effect of Group, $F_s(1,51) >$

¹ Regarding the OCDS, it was necessary to use a modified scale during the second period of assessment in which patients were totally abstinent. Thus, participants were given a version in which several items related to consumption (including some compulsion items) had been removed because the patients had not consumed alcohol for 3 weeks at that point.

Table 2. Cognitive measures^a in alcoholic patients (AT1 and AT2) vs control participants (CT1 and CT2)^b

Tests and parameters	Alcoholic patients		Control participants		Main effects ^d	
	Time 1 AT1 (<i>n</i>)	Time 2 AT2 (<i>n</i>)	Time 1 CT1 (<i>n</i>)	Time 2 CT2 (<i>n</i>)	Effect of time Time 1 vs Time 2	Effect of group A vs C
DII, mean ± SD						
GZ	386.07 ± 107.14 (30)	448.03 ± 106.38 (30)	505.23 ± 80.05 (22)	534.77 ± 73.39 (22)	***	***
F	16.93 ± 12.08 (30)	14.97 ± 9.37 (30)	15.09 ± 15.66 (22)	9.95 ± 7.70 (22)	*	ns
TMT, mean ± SD						
TMT A	36.34 ± 11.35 (31)	31.22 ± 9.69 (31)	29.99 ± 10.16 (21)	24.55 ± 4.77 (21)	***	**
TMT B	88.30 ± 31.39 (31)	73.29 ± 24.50 (31)	67.08 ± 16.21 (21)	63.17 ± 18.92 (21)	**	**
TMT B–A	51.95 ± 25.90 (31)	42.02 ± 18.72 (31)	37.09 ± 15.04 (21)	38.61 ± 16.48 (21)	ns	*
Stroop Test, mean ± SD						
Congruent	1125.19 ± 462.49 (34)	882.06 ± 310.42 (34)	663.43 ± 167.28 (21)	673.28 ± 168.79 (21)	**	***
Neutral	1049.85 ± 350.32 (34)	862.73 ± 288.11 (34)	645.59 ± 141.79 (21)	627.19 ± 123.93 (21)	**	***
Incongruent	1307.18 ± 485.29 (34)	1097.47 ± 399.03 (34)	807.95 ± 244.74 (21)	813.43 ± 293.95 (21)	**	***
Interference index ^c	285.21 ± 210.54 (31)	253.35 ± 186.17 (31)	162.36 ± 143.49 (21)	186.24 ± 189.91 (21)	ns	*

* $P < 0.05$, ** $P < 0.01$, *** $P \leq 0.001$, ns = $P > 0.05$. A, alcoholics; C, controls; DII, D2 Cancellation Test; GZ, total number of items read in 20 s; F, total number of errors (omission and confusion errors); TMT, Trail Making Test; TMT A, part 1 of the test: psychomotor speed component (milliseconds); TMT B, part 2 of the test: flexibility component (milliseconds); TMT B–A, difference between two parts: pure reactive flexibility index; median RTs, median reaction times (milliseconds); ns, non-significant.

^aAll data (except F for DII Test) concern RTs in milliseconds.

^bOnly cases excluding outliers and missing participants are included.

^cInterference index (I) is calculated as median RTs on incongruent items – median RTs on neutral items.

^dMain effects were calculated by a 2 (Group) × 2 (Time) MANOVA.

15.85, $P_s < 0.001$, $\eta^2 > 0.23$, and an interaction between Time and Group, $F_s(1,51) > 12.18$, $P_s < 0.001$, $\eta^2 > 0.19$, for the total score of craving and also for obsessive and compulsive components of craving. The interaction is explained by a significant decrease of craving from onset to end of withdrawal among alcohol-dependent patients by using t -tests, $t_s(31) > 4.26$, $P_s < 0.001$, Cohen's $d_s > 0.62$, as compared to the control group, $t_s(20) < 0.1$, ns. However, the alcoholics 'craving scores' remained higher than controls at the end of the withdrawal cure, $t_s(51) > 2.1$, $P_s < 0.04$, Cohen's $d_s > 0.59$ (see Fig. 1).

Affective state questionnaire

Concerning the score of PA, a main effect of Time, $F(1,52) = 7.14$, $P = 0.01$, $\eta^2 = 0.12$, and an interaction between Time and Group, $F(1,52) = 5.39$, $P = 0.027$, $\eta^2 = 0.09$, were shown while no Group effect was observed, $F(1,52) = 0.21$, ns. The interaction is explained by a significant increase of PA scores from onset ($M = 26.9$, $SD = 7.37$) to end ($M = 33.47$, $SD = 6.86$) of withdrawal among alcohol-dependent patients, $t(29) = -5.02$, $P < 0.001$, Cohen's $d = -0.92$, as compared to the control group, $t(20) = 1.92$, ns (T1: $M = 29.48$, $SD = 7.4$) to end ($M = 29.19$, $SD = 7.91$). The PA scores were not different from those of controls at both times of withdrawal cure, $t_s(49) < 2$, ns.

Analyses revealed a main effect of Time, $F(1,52) = 13.13$, $P = 0.001$, $\eta^2 = 0.2$, a main effect of Group, $F(1,52) = 16.25$, $P < 0.001$, $\eta^2 = 0.24$, and an interaction between Time and Group, $F(1,52) = 5.52$, $P = 0.02$, $\eta^2 = 0.1$, for the NA score. The interaction is explained by a significant decrease of NA scores from onset ($M = 22.5$, $SD = 7.42$) to end ($M = 18.3$, $SD = 8.4$) of withdrawal among alcohol-dependent patients, $t(29) = 3.62$, $P < 0.001$, Cohen's $d = 0.53$, as compared to the control group, $t(20) = 1.92$, ns (T1: $M = 12.9$, $SD = 2.68$) to end ($M = 12.33$, $SD = 2.94$). However, NA scores remained higher than controls at the end of the withdrawal cure, $t(49) = 3.12$, $P = 0.003$, Cohen's $d = -0.88$.

Neuropsychological testing

Selective attention. Regarding the speed of attentional processing (i.e. the selective attention index (GZ) measuring the total items identified), a main effect of group, $F(1,50) = 16.45$, $P < 0.001$, $\eta^2 = 0.25$, emerged from the analyses; the performance of patients was lower than that of controls in general during withdrawal (see Table 2). A main effect of time was also observed, $F(1,50) = 29.27$, $P < 0.001$, $\eta^2 = 0.37$, indicating that participants in general had lower scores at T1 than at T2. Conversely no Time × Group interaction, ($F_s(1,50) < 3$, ns), was revealed. Concerning the number of errors, only a main effect of time appeared, $F(1,50) = 5.72$, $P =$

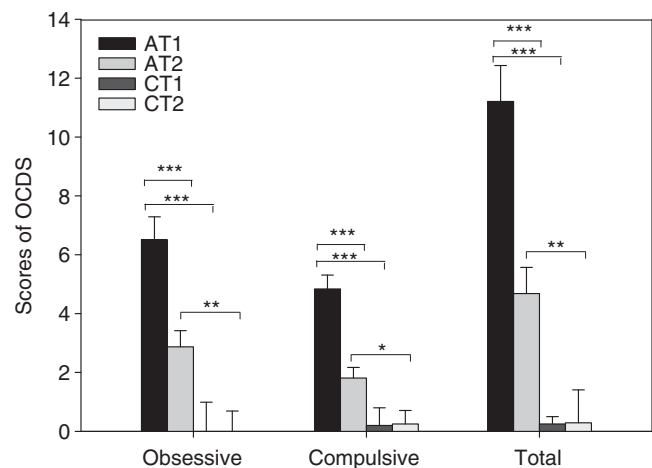


Fig. 1. Evolution of craving (OCDS) during both times of alcoholics' withdrawal (AT1 and AT2) and among control participants (CT1 and CT2) ^a(Results are means ± SEM. Compulsive factor scores and total scores were recalculated from original OCDS scores by excluding items that directly reflect alcohol consumption, which was influenced by the withdrawal procedure.). * $P < 0.05$, ** $P < 0.01$, *** $P \leq 0.001$. OCDS, Obsessive–Compulsive Drinking Scale.

0.02, $\eta^2 = 0.10$, indicating that participants in general committed more errors at T1 than at T2. To determine whether a speed accuracy trade-off (i.e. a relation between quantity (total number of items identified) and quality (total number of errors)) was present or not, a Pearson correlation was computed between speed (GZ) and errors (F). The non-significant correlations GZ and F ($r_s < 0.24$, ns) allowed us to eliminate the possibility of a speed accuracy trade-off at both times for each group.

Cognitive flexibility. Given that the error rate in the TMT was low (<4%) for both parts A and B of the test and that no differences between groups were observed, analysis was focused only on RTs. Concerning the psychomotor speed component (TMT A), a main effect of group ($F(1,50) = 6.96$, $P = 0.01$, $\eta^2 = 0.12$) and a main effect of time ($F(1,50) = 22.011$, $P < 0.001$, $\eta^2 = 0.31$) were evidenced, while no Time \times Group interaction, ($F(1,50) = < 1$, ns), was observed, indicating that patients spent in general more time compared to controls and that all participants spent more time at T1 than at T2 (see Table 2). Regarding TMT B, a cognitive flexibility index, patients were also impaired compared to controls as shown by a main effect of group, $F(1,50) = 6.62$, $P = 0.013$, $\eta^2 = 0.12$ (see Table 2). A main effect of time was also observed, ($F(1,50) = 8.19$, $P = 0.006$, $\eta^2 = 0.14$), showing that all participants at T1 had lower performance than participants at T2. However, no Group \times Time interaction was present, $F(1,50) = < 3$, ns. Finally, for TMT B–A, a more accurate index of cognitive flexibility without any speed component, the MANOVA revealed only a main effect of group, $F(1,50) = 3.77$, $P = 0.05$, $\eta^2 = 0.10$, indicating that the switching performance of patients was lower than that of controls in general during withdrawal.

Prepotent response inhibition. Given a floor effect of error rates (<6%) for all categories of stimuli, the analyses only focused on the median RTs for congruent, neutral and incongruent stimuli rather than on the number of errors. A main effect of group, $F_s(1,53) > 14.80$, $P_s < 0.001$, $\eta_s^2 > 0.23$, revealed that alcoholic patients were slower than controls in general and for all stimuli. A main effect of time was also observed for all stimuli, $F_s(1,53) > 8.10$, $P_s < 0.01$, $\eta_s^2 > 0.13$, indicating that all participants had lower performance at T1 than at T2. Moreover, the Group \times Time interaction for all stimuli was also significant, $F_s(1,53) > 8.98$, $P_s < 0.01$, $\eta_s^2 > 0.14$. As shown by paired *t*-tests, for all types of stimuli an improvement was found only for alcoholic patients, $t_s(33) > 3.94$, $P_s < 0.001$, Cohen's $d_s > 0.47$. However, this improvement was partial as the performance of patients was lower than that of controls at the end of the withdrawal as shown by *t*-tests for independent samples comparing groups, $t_s(53) > 2.82$, $P_s < 0.01$, Cohen's $d_s > 0.78$.

The interference index, the most reliable index to assess inhibition or interference of the prepotent response, was computed as follows: median RTs incongruent items – median RTs neutral items. On this measure, there was only a significant main effect of group, $F(1,50) = 3.90$, $P = 0.05$, $\eta^2 = 0.07$, showing more interference for patients than controls during withdrawal. Overall, this result supported the hypothesis that alcohol-dependent patients have similar difficulty inhibiting interference responses at both times of a 3-week withdrawal cure.

Decision making. The alcoholic group was randomly split into two independent groups. Indeed, the IGT was only ad-

ministered once because of the potential for test–retest effects. Results showed that alcohol-dependent patients at both times took more cards from disadvantageous decks ($A' + B'$) (i.e. two high reward decks but which also give higher levels of punishment compared to advantageous decks ($C' + D'$) with low levels of reward but low levels of punishment) (T1: ($M = 47.04$, $SD = 8.99$), T2: ($M = 48.80$, $SD = 6.99$) than controls did ($M = 41$, $SD = 8.01$) as shown by *t*-tests for independent samples, T1: $t(41) = 2.33$, $P = 0.025$, Cohen's $d = 0.71$, and T2: $t(30) = 2.65$, $P = 0.013$, Cohen's $d = 1.01$). In addition, patients had lower net scores ($(A' + B') - (C' + D')$) (i.e. the difference between advantageous and disadvantageous decks was smaller) (T1: ($M = 6$, $SD = 17.72$), T2: ($M = 4.11$, $SD = 10.22$) than controls ($M = 17.54$, $SD = 15.50$), T1: $t(41) = -2.855$, $P = 0.025$, Cohen's $d = -0.69$, and T2: $t(29) = -2.391$, $P = 0.024$, Cohen's $d = -0.96$). In the alcohol-dependent groups, no significant differences were observed for both indexes between the group tested at T1 and the one at T2. Fig. 2 shows a sample line graph displaying the net scores $(C' + D') - (A' + B')$ of cards selected (20 by 20) for each group. The learning of the task appears graphically quicker for controls than alcoholics at T1 and T2. Nevertheless, the difference was statistically significant only for the 4th block (61–80 selected cards) ($t_s(40) > -1.99$, $P_s < 0.05$, Cohen's $d_s > 0.66$).

DISCUSSION

In the current study, we addressed the question of whether a withdrawal cure among alcohol-dependent patients has an effect on craving, affectivity and control abilities such as selective attention and EFs. We observed a partial decrease in the obsessive, compulsive and total self-reported craving scores as well as in negative affect scores during withdrawal. At the end of withdrawal, however, values remained higher than those of the controls. Moreover, the effect sizes concerning the improvement in craving and negative affect were similar according to Cohen's indexes (Cohen, 1988). In fact, the scores of both variables decreased with a large magnitude between both times. In addition, concerning positive affective state, we also observed a significant increase during withdrawal although at both times scores were not different from those of controls.

Concerning control abilities, we first measured selective attention. A deficit in procession speed was observed at the D2 task among alcoholic patients during withdrawal. These findings regarding selective attention are not in parallel with those of a previous study (Tedstone and Coyle, 2004), which found no differences between sober alcoholics and controls in the Eriksen task. However, this difference may be explained by the fact that in the latter work, patients were tested after 6 weeks of residential rehabilitation, which in comparison with our shorter 2–3-week period of abstinence may permit a recovery of attention. Regarding cognitive flexibility, measured by the TMT B–A, alcoholic patients exhibited impaired performance during the 3-week withdrawal and no improvement between the two time periods. This is consistent with previous studies performed with early abstinent alcoholics using the TMT (Noël *et al.*, 2001) in addition to other tasks (Hildebrandt *et al.*, 2004). However, another study (Mann *et al.*, 1999) found some recovery of TMT performance after 6 weeks of cure.

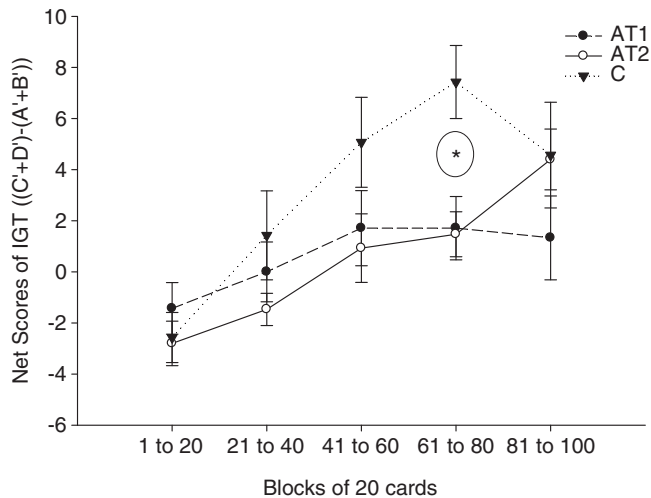


Fig. 2. Net scores $(C' + D') - (A' + B')$ of cards selected (20 by 20) by alcoholic (AT1 and AT2) ^a(The two groups AT1 and AT2 of IGT corresponded to two independent groups of alcoholics coming from the alcoholic group randomly split into two independent groups tested either at T1 ($n = 21$) or at T2 ($n = 11$.) and control participants (C) ^b(Results are means \pm SEM. Positive net scores reflect advantageous performance while negative net scores reflect disadvantageous performance.) across the IGT. * $P_s < 0.05$ between C and AT1 or AT2. IGT, Iowa Gambling Task.

Concerning the performance of prepotent response inhibition, previous studies using a paper version of the Stroop Task (Stroop, 1935) observed deficits in early abstinent alcoholics (Goudriaan *et al.*, 2006). Our study which used a computerized version of the task (which gives better accuracy in measuring reactions times) confirmed that the performance of alcoholics was impaired both at onset and end of withdrawal and that no improvement of the interference index was observed.

A decision-making deficit among alcoholics was also observed both at onset and end of withdrawal. Indeed, controls learned to make the right decision quicker than the alcoholics, but the difference was only significant after the 4th block. As in ventromedial prefrontal lesion patients, alcoholic subjects have tendencies to favour large immediate rewards while disregarding long-term negative consequences (Bechara and Damasio, 2002). This deficit in learning in the face of negative events may be relevant for alcoholic patients in that it may prolong their drinking habit despite the negative consequences of intoxication (Clark and Robbins, 2002).

Overall, the findings presented in this study are consistent with the idea that some SAS high level control functions involved in the genesis of plans and in willed actions (Norman and Shallice, 1986) were impaired among alcohol-dependent patients in the beginning of withdrawal and in an early abstinent state (effect sizes for these comparisons ranged from 0.07 to 0.25). This sharply contrasts with the improvement in alcohol craving and affective states observed during the withdrawal cure. Consequently, these findings suggest that either sobriety has no positive effect on cognitive function in alcoholics or that 3 weeks of sobriety is too short to observe cognitive recovery. The latter proposal is supported by the observation of some cognitive functions after 6 weeks of sobriety in a previous study (Mann *et al.*, 1999; Tedstone and Coyle, 2004).

Importantly, results concerning selective attention scores and other scores involving basic processes such as perceptual and motor (i.e. GZ, TMT A, TMT B, congruent, neutral and incongruent stimuli) show differences between T1 and T2 for both alcoholics and controls, indicating a test–retest effect between T1 and T2. However, because these indexes (i.e. TMT B–A and interference index of the Stroop (Stroop, 1935)) remained stable at both times for both alcoholics and controls, the learning effect did not affect performance of pure EFs that are not affected by these basic processes (Lezak, 1995).

From a clinical standpoint, we frequently observe that alcoholic individuals at the end of withdrawal are excessively optimistic about their ability to remain abstinent, a factor that we intuitively do not consider as a good predictor of future sobriety. The remaining deficits in selective attention and in EFs may contribute to their inability to anticipate the difficulties they might meet after going back home, and thus increase the possibility of relapse. Indeed, the EF deficits and the persistence of significant levels of negative affect and craving suggest that alcohol-dependent patients have only weak abilities to resist drinking after a classical 3-week withdrawal period. Therefore, it would be of interest to examine empirically if these executive deficit factors may serve as predictors of relapse (Noël *et al.*, 2002; Moriyama *et al.*, 2002). Future research should also be dedicated to investigating the evolution of these cognitive functions over a longer time period after withdrawal to better understand if spontaneous improvement may be expected during long-term abstinence (Pitel *et al.*, 2009) or if EFs and selective attention deficits remain altered as in short-term abstinence (Zinn *et al.*, 2004). This knowledge could be used to form the basis of specific rehabilitation programmes to prevent relapse.

This study is not without limitations. First of all, some uncertainty remains as to the exact conditions that were obtained by our specific design (T1 vs T2) to understand observed effects. At T1, the subjects had stopped drinking for <24 h and were starting or about to start a medication of benzodiazepines. At T2, most subjects had stopped benzodiazepines. We therefore compared a status induced by a period of alcohol drinking or perhaps of early withdrawal (T1) with early sobriety (T2). We do not believe, however, that the observed negative affect at T1 might be attributed solely to effect of withdrawal. Indeed, in an earlier publication of our group (de Timary *et al.*, 2008), there were no significant changes in negative affect as assessed by depression and anxiety measures between onset of withdrawal (equivalent to T1 in the present study) and 3 days after the onset, which is commonly considered as the time for peak withdrawal effects (Kosten and O'Connor, 2003). Therefore, we believe that negative affect observed at T1 is mainly due to the effects of a prolonged period of alcohol drinking that induces negative mood (Schuckit, 1994). The recovery at T2 is due to early sobriety. Secondly, a larger sample size could have increased the significance of the effects, considering the number of variables. In addition, the lack of information about any other secondary axis I diagnosis (such as mood or anxiety disorders) does not preclude the fact that some of the observed scores on the PANAS or on the neuropsychological tests might not be due to alcohol dependence. However, it is difficult if not impossible to give a diagnosis of anxious disorder or major depression when patients are in a state of alcoholization (de Timary *et al.*, 2008; Schuckit, 1994).

CONCLUSION

In conclusion, these results suggest that a 3-week alcohol detoxification period affects only the drive for drinking alcohol and state affectivity does not affect selective attention or EFs, which remained impaired at both time periods of the cure. These observations may be relevant for clinicians to better understand the abilities and deficits of their patients during and after a 3-week detoxification period and to implement new neurocognitive treatments to decrease the risk of relapse.

Funding—This work was supported by FSR 2004 (P.T.), FSR 2007 (M.C.S.U.) and 1.5.175.06 and 3.4585.07 from FNRS-FRS (O.L.).

REFERENCES

- Andersohn F, Kiefer F. (2004) Depressive mood and craving during alcohol withdrawal: association and interaction. *German J Psychiatry* **7**:6–11.
- Ansseau M, Besson J, Lejoyeux M *et al.* (2000) A French translation of the Obsessive-Compulsive Drinking Scale for craving in alcohol-dependent patients: a validation study in Belgium, France, and Switzerland. *Eur Addiction Res* **5**:51–6.
- Anton RF, Moak DH, Latham PK. (1995) The Obsessive Compulsive Drinking Scale: a self-rated instrument for the quantification of thoughts about alcohol and drinking behaviour. *Alcohol Clin Exp Res* **19**:92–9.
- Anton RF, Moak DH, Latham PK. (1996) The Obsessive Compulsive Drinking Scale: a new method of assessing outcome in alcoholism treatment studies. *Arch Gen Psychiatry* **53**:225–31.
- American Psychological Association (APA). (1994). *Diagnostic and Statistical Manual of Mental Disorders (DSM-IV)*. Washington DC.
- Bechara A, Damasio AR, Damasio H *et al.* (1994) Insensitivity to future consequences following damage to human prefrontal cortex. *Cognition* **50**:7–15.
- Bechara A, Damasio H. (2002) Decision-making and addiction (part I): impaired activation of somatic states in substance dependent individuals when pondering decisions with negative future consequences. *Neuropsychologia* **40**:1675–89.
- Becker JT, Butters N, Hermann A *et al.* (1983) A comparison of the effects of long-term alcohol abuse and aging on the performance of verbal and nonverbal divided attention tasks. *Alcohol Clin Exp Res* **7**:213–9.
- Brickenkamp R. (1981) *Test D2: Aufmerksamkeits-Belastungs-Test: Handanweisung*. Gottingen: Verlag fur Psychologie Dr C.J. Hogrefe.
- Clark L, Robbins T. (2002) Decision-making deficits in drug addiction. *Trends Cogn Sci* **6**:361–3.
- Cohen JS. (1988) *Stastical Power Analysis for the Behavioural Sciences*. N.J. Hillsdale: Erlbaum.
- Constant E, Adam S, Seron X *et al.* (2006) Hypothyroidism and major depression: a common executive dysfunction? *J Clin Exp Neuropsychol* **28**:790–807.
- de Timary P, Luts A, Hers D *et al.* (2008) Absolute and relative stability of alexithymia in alcoholic inpatients undergoing alcohol withdrawal: relationship to depression and anxiety. *Psychiatry Res* **157**:105–13.
- Gaudreau P. (2000) *Vers une version française du PANAS: Analyses en composantes principales avant, pendant et après une compétition sportive*. Paris: Communication présentée au Congrès International de la Société Française de Psychologie du Sport.
- Goudriaan AE, Oosterlaan J, De Beurs E *et al.* (2006) Neurocognitive functions in pathological gambling: a comparison with alcohol dependence, Tourette syndrome and normal controls. *Addiction* **101**:534–47.
- Hilbrandt H, Brokate B, Eling P *et al.* (2004) Response shifting and inhibition, but not working memory, are impaired after long-term alcohol consumption. *Neuropsychology* **18**:203–11.
- Joyce EM, Robbins TW. (1991) Frontal lobe function in Korsakoff and non-Korsakoff alcoholics: planning and spatial working memory. *Neuropsychologia* **29**:709–23.
- Kosten TR, O'Connor PG. (2003) Management of drug and alcohol withdrawal. *N Engl J Med* **348**:1786–95.
- Lezak MD. (1983) *Neuropsychological Assessment*. New York: Oxford University Press.
- Lezak MD. (1995) Executive functions and motor performance. In Lezak MD (ed). *Neuropsychological Assessment*. New York: ResultsOxford University Press. 650–85.
- Mann K, Günther A, Stetter F *et al.* (1999) Rapid recovery from cognitive deficits in abstinent alcoholics: a controlled test-retest study. *Alcohol Alcohol* **34**:567–74.
- Moriyama Y, Mimura M, Kato M *et al.* (2002) Executive dysfunction and clinical outcome in chronic alcoholics. *Alcohol Clin Exp Res* **26**:1239–44.
- Noël X, Sferrazza R, van der Linden M. (2002) Median frontal hypometabolism measured by ^{99m}Tc-Bicistate SPECT procedure in the prediction of short term alcohol abstinence in alcohol-dependent patients. *Alcohol Alcohol* **37**:347–54.
- Noël X, van der Linden M, Schmidt N *et al.* (2001) Supervisory attentional system in nonamnesic alcoholic men. *Arch Gen Psychiatry* **58**:1152–8.
- Norman DA, Shallice T. (1986) Attention to action: willed and automatic control of behavior: center for human information processing. In David RJ, Schwarte GE, Shapiro D (eds). *Consciousness and Self Regulation: Advances in Research*. New York: Plenum Press. 1–18.
- Parker ES, Parker DA, Harford LC. (1991) Specifying the relationship between alcohol use and cognitive loss: the effects of frequency of consumption and psychological distress. *J Stud Alcohol* **52**:366–73.
- Pitel AL, Rivier J, Beaunieux H *et al.* (2009) Changes in the episodic memory and executive functions of abstinent and relapsed alcoholics over a 6-month period. *Alcohol Clin Exp Res* **33**:490–8.
- Schuckit MA. (1994) Alcohol and depression: a clinical perspective. *Acta Psychiatr Scand* **89**:28–32.
- Stroop JR. (1935) Studies of interference in serial verbal reactions. *J Exp Psychol* **18**:643–62.
- Tedstone D, Coyle K. (2004) Cognitive impairments in sober alcoholics: performance on selective and divided attention tasks. *Drug Alcohol Depend* **75**:277–86.
- Tranel D, Bechara A, Damasio AR. (2000) Decision making and the somatic marker hypothesis. In Gazzaniga MS (ed). *The New Cognitive Neurosciences*. Cambridge: MIT Press. 1115–31.
- Watson D, Clark LA, Tellegen A. (1988) Development and validation of brief measures of positive and negative affect - the PANAS scales. *J Pers Soc Psychol* **54**:1063–70.
- Zinn S, Stein R, Swartzwelder HS. (2004) Executive functioning early in abstinence from alcohol. *Alcohol Clin Exp Res* **28**:1338–46.