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# ***Genuine episodic memory deficits and executive dysfunctions in alcoholic subjects early in abstinence***

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## **Abstract**

### **Background**

**Chronic alcoholism is known to impair episodic memory function, but the specific nature of this impairment is still unclear. Moreover, it has never been established whether episodic memory deficit in alcoholism is an intrinsic memory deficit or whether it has an executive origin. Thus, the objectives are to specify which episodic memory processes are impaired early in abstinence from alcohol and to determine whether they should be regarded as genuine memory deficits or rather as the indirect consequences of executive impairments.**

### **Methods**

**Forty recently detoxified alcoholic inpatients at alcohol entry treatment and fifty five group-matched controls underwent a neuropsychological assessment of episodic memory and executive functions. The episodic memory evaluation consisted of three tasks complementing each other designed to measure the different episodic memory components (learning, storage, encoding and retrieval, contextual memory and auto-noetic consciousness) and five executive tasks testing capacities of organization, inhibition, flexibility, up-dating and integration.**

### **Results**

**Compared with control subjects, alcoholic patients presented impaired learning abilities, encoding processes, retrieval processes, contextual memory and auto-noetic consciousness. However, there was no difference between the two groups regarding the storage capacities assessed by the rate of forgetting. Concerning executive functions, alcoholics displayed deficits in each executive task used. Nevertheless, stepwise regression analyses showed that only performances on fluency tasks were significantly predictive of some of the episodic memory disorders (learning abilities for 40%, encoding processes for 20%, temporal memory for 21% and state of consciousness associated with memories for 26%) in the alcoholic group.**

### **Discussion**

**At alcohol treatment entry, alcoholic patients present genuine episodic memory deficits which cannot be regarded solely as the consequences of executive dysfunctions. These results are in accordance with neuroimaging findings showing hippocampal atrophy. Moreover, given the involvement of episodic memory and executive functions in alcohol treatment, these data could have clinical implications.**

**MESH Keywords** Alcoholism ; diagnosis ; physiopathology ; rehabilitation ; Cognition Disorders ; diagnosis ; physiopathology ; Frontal Lobe ; physiopathology ; Hospitalization ; Humans ; Male ; Memory Disorders ; diagnosis ; physiopathology ; Middle Aged ; Neuropsychological Tests ; statistics & numerical data ; Regression Analysis ; Temperance ; psychology

**Author Keywords** alcoholism ; episodic memory ; executive functions ; treatment

## **INTRODUCTION**

Chronic alcoholism is a major public health problem today since approximately 14 million individuals meet criteria for alcohol abuse or dependence in the USA (Grant et al. 1994) and 5 million persons have medical, social or psychological problems due to alcohol abuse in France (Inserm, 2001). Long-term heavy drinking has been shown to cause cognitive deficits (Fox et al. 2000 ; Goldstein et al. 2004 ; Horner et al. 1999 ; Parsons and Nixon 1993 ; Sullivan et al. 2000) including episodic memory impairments. Episodic memory is currently described as the memory system in charge of the encoding, storage and retrieval of personally experienced events, associated with a precise spatial and temporal context of encoding. Episodic memory allows the conscious recollection of personal happenings and events from one's personal past and the mental projection of anticipated events into one's subjective future (Wheeler et al. 1997). Furthermore, recollection of episodic events includes auto-noetic awareness: the impression of re-experiencing or reliving the past and mentally traveling back in subjective time (Tulving 2001).

Most studies investigating episodic memory in chronic alcoholism have used classic psychometric tasks and reported an impairment of episodic memory as measured by the Wechsler Memory Scale (Fama et al. 2004 ; Glenn and Parsons 1992 ; Goldstein et al. 2004 ; Joyce and Robbins 1991 ; Tivis et al. 1995 ) and the learning of face-name associations (Beatty et al. 1995 ; Everett et al. 1988 ; Schaeffer and Parsons 1987 ; Tivis et al. 1995 ) or lists of words (e.g. the Luria memory words test (Sherer et al. 1992 )). However, contradictory conclusions have been reached using the California Verbal Learning Test (Brokate et al. 2003 ; Hildebrandt et al. 2004 ). Even though studies of learning abilities have provided some initial information about the effects of alcoholism on episodic memory, the specific nature of this impairment (for example encoding vs. retrieval processes) has never been clearly determined. Alcoholic patients have sometimes been shown to present retrieval deficits (Weingartner et al. 1996 ; Zinn et al. 2004 ), notably in tasks involving executive control, such as free recall (Weingartner et al. 1996 ), while the preservation of these retrieval processes has also been reported (Nixon et al. 1998 ).

Furthermore, the current and comprehensive definition of episodic memory has not been properly taken into account when evaluating this memory system in alcoholism. When assessed by mean of an order recognition task, contextual memory has been reported to be impaired in alcoholism (Sullivan et al. 1997 ). However, the ability to retrieve the spatiotemporal context of encoding (when and where information was taken in) has never been investigated. As far as auto-noetic consciousness and recollective experience are concerned, only the acute effects of alcohol have been measured, and then only in healthy volunteers (Curran and Hildebrandt 1999 ; Duka et al. 2001 ): it was found that alcohol consumption significantly reduced conscious recollection.

Whereas more studies are required to determine the harmful effects of chronic alcoholism on the various components of episodic memory, particularly at alcohol treatment entry, the sensitivity of the frontal lobes to the toxicity of ethanol has received more attention ( Moselhy et al. 2001 ). Indeed, the central executive of working memory (Baddeley 1986 ), which is regarded as being similar to the executive functions (Baddeley 1996 ; Miyake et al. 2000 ), has been well documented in alcoholic patients. Inhibition, flexibility, categorization, deduction of rules, organization and planning have mostly been found to be impaired in alcoholism (Ambrose et al. 2001 ; Brokate et al. 2003 ; Dao-Castellana et al. 1998 ; Demir et al. 2002 ; Fama et al. 2004 ; Glenn and Parsons 1992 ; Ihara et al. 2000 ; Joyce and Robbins 1991 ; Noel et al. 2001a ; Noel et al. 2001b ; Oscar-Berman et al. 2004 ; Tedstone and Coyle 2004 ; Uekermann et al. 2003 ), although two recent studies concluded that updating abilities may be preserved (Brokate et al. 2003 ; Hildebrandt et al. 2004 ). The binding of multimodal information, carried out by a newly-identified slave system of working memory (Baddeley 2000 ; Baddeley 2003 ) known as the episodic buffer, is also thought to be impaired in alcoholic patients (De Rosa and Sullivan 2003 ), although this has only been tested indirectly.

As highlighted by numerous neuropsychological (Kopelman et al. 1997 ) and functional neuroimaging studies (Habib et al. 2003 ; Kramer et al. 2005 ; Tulving et al. 1994 ), executive functions play a major role in episodic memory functioning (Davidson et al. 2006 ). Consequently, executive dysfunctions in alcoholic patients may have harmful effects on their episodic memory capacities. In effect, executive functions are known to contribute to the strategic organization of information in order to facilitate encoding and retrieval in memory (Kapur et al. 1994 ), maintain items in a fixed sequence and integrate diverse types of information (factual, temporal, spatial) into a meaningful representation (Wheeler et al. 1997 ) in order to form a comprehensive episode (Baddeley 2000 ). Auto-noetic consciousness, which is associated with episodic memory, also seems to be closely related to prefrontal functions (Wheeler et al. 1997 ). Thus, episodic memory is an elaborate memory system which requires a high level of executive processing (Davidson et al. 2006 ). In the light of these arguments, it would appear to be particularly worthwhile investigating whether the episodic memory deficit in alcoholic patients can be even partially explained by their executive dysfunction (Zinn et al. 2004 ).

Until now, studies dealing with episodic memory in alcoholism have failed to take into account the modern and comprehensive definition of this memory system, as most investigations have only assessed the acquisition of factual information. The effects of chronic alcoholism on encoding versus retrieval processes, long-term retention, contextual memory (temporal and spatial context of encoding) and auto-noetic consciousness remain unclear. Thus, because of its potential clinical relevance, the first goal of the present study was to specify the nature of the episodic memory processes early in abstinence from alcohol. In addition, given the close theoretical link between episodic memory and executive functions, the second goal was to determine the origin of the episodic memory impairment: a genuine memory disorder or a consequence of executive deficits. Episodic memory and executive functions were evaluated according to the popular definitions of these cognitive functions (Wheeler et al. 1997 and Tulving 2001 for episodic memory and Baddeley 1996 and Miyake et al. 2000 for executive functions).

## **MATERIALS AND METHODS**

### **Subjects**

Forty alcoholic inpatients and fifty five control subjects, matched for age [ $t_{(93)}=0.53, P=.59$ ] and years of schooling [ $t_{(93)}=1.59, P=.11$ ], were examined in this study (Table 1 ). There were 20 men in the control group and 33 in the alcoholic group. All the participants gave their informed consent to the neuropsychological procedure, which was approved by the local ethical committee. A proportion of the participants were drawn from a previous study (Pitel et al. 2007 ). Alcoholic subjects were recruited by clinicians while they were

receiving alcohol treatment as inpatients at Caen University Hospital, according to the DSM IV criteria of alcohol dependence (American Psychiatric Association 1994 ). Patients had no history of other types of substance dependence (except tobacco) and they had already been weaned off alcohol when they were included. They were interviewed in order to determine the age at which they had their first alcoholic drink, the age of onset of alcoholism, the length of time they had drunk to excess and their usual daily alcohol consumption (Table 1 ). No participants were taking psychotropic medication or presented psychiatric problems or had any history of pathology (head injury, coma, epilepsy, Gayet-Wernicke diagnosis, hepatic cirrhosis, depression, etc.) which might have affected cognitive function. Control participants were interviewed to check that they did not meet the criteria for alcohol abuse or dependence (criteria of the World Health Organization).

### **Episodic memory assessment**

We chose three tests complementing each other in order to assess the various components of the episodic memory system. The various tasks were spread over 9 days since they were proposed at the same time of a learning paradigm (Pitel et al. 2007 ). The Free and Cued Selective Reminding Test (FCSRT), the Ecological Contextual Memory test (ECMT) and the Spondee test were proposed respectively at the beginning, in the middle and at the end of the assessment period in order to reduce the risk of interference among the word lists.

### **Learning abilities**

We selected a French version of the FCSRT (Grober and Buschke 1987 ; Grober et al. 1988 ) to measure learning abilities, i.e. improvements in performance due to the repeated presentation of information. The first phase of this test consisted of encoding 16 words belonging to 16 different semantic categories. Words were displayed 4×4 on a sheet and subjects had to point to words in response to their semantic category. Every four words, an immediate cued recall was performed using semantic category cues, in order to ensure that encoding had taken place. If the subjects failed, the experimenter showed them the sheet again so that all 16 items were retrieved at immediate cued recall. The encoding phase was followed by three recall trials (each comprising free recall and, if necessary, categorical cued recall). Between each trial, subjects were asked to count backwards for 20 seconds. We chose to use the three free recall trials to assess abilities to improve performance in the course of presentation as these are assumed to be variables that are sensitive to deficits in alcoholic patients (Weingartner et al. 1996 ).

### **Storage capacities**

Twenty minutes after the third free recall in the FCSRT, delayed free and cued recall trials were carried out to explore storage capacities. A rate of forgetting, corresponding to the ability to maintain information in memory for 20 min., was calculated:  $((\text{third free recall} - \text{delayed free recall}) / \text{third free recall}) \times 100$ .

### **Encoding and retrieval processes**

In order to preferentially tax either encoding or retrieval processes, we used a specifically designed memory test, inspired by the Double Memory test (Buschke et al. 1995 ), that had already been used in a previous study by our team (Pitel et al. 2007 ). In this task, entitled the “Spondee” (for SPONtaneous-DEEp) test, the subjects had to learn two different lists of 16 words belonging to 16 different categories and encoded in two different ways. The first list was encoded spontaneously according to the strategies that the subjects were able to implement on their own: the words were displayed 4×4 on a sheet and subjects had to point to words read aloud by the experimenter. A recognition phase was then carried out, where patients had to recognize the 16 target words among distractors. Target and distractor words were presented visually one at a time and subjects had to say if they recognized them. Unlike the first word list, the second one was deeply encoded. The words were still displayed 4×4 on a sheet, but subjects had to point to them in response to their semantic category. They were then asked to recall as many words as possible, in any order and without any time limit.

We applied a method used in a previous study by our research team (Chételat et al. 2003 ) to assess encoding and retrieval processes. Thus, following the spontaneous encoding subtest, where the target was presented in order to compensate for any potential retrieval deficits, but where encoding was not supported, recognition was assumed to be mainly dependent on encoding ability. In contrast, after the deep encoding subtest, which represented the opposite situation, given that encoding was reinforced whereas retrieval was self-initiated, free recall was assumed to reflect mainly retrieval ability. They will be designated hereafter by the process they preferentially tax (i.e. “ encoding” and “retrieval” subtests) for the sake of simplicity.

### **Factual, temporal and spatial memory**

The factual, temporal and spatial components of episodic memory were measured by means of an original ECM test. The ECM test consisted of learning six pairs of unrelated words (Danger-Beauty , Student-Tongue , etc) presented at different times (three pairs in the morning and three in the afternoon) and places (different for each subject and each pair of words) in the space of a single day. Each time, subjects had to read the word pair, construct a sentence containing each word and recall both words to ensure that they had been encoded semantically (i.e. deeply and deliberately). Subjects were told that they had to learn all 6 word pairs but not that they had to learn the context. At the end of the day, the subjects performed a recognition task of the factual, temporal and spatial information. The target word

pair was displayed at the same time as three distractors (one word pair that was semantically linked with the target, one that was phonologically linked and one that had no link at all). For each word pair, subjects also had to recognize the temporal and spatial context of encoding, in the presence of a distractor which corresponded to the encoding context of a different word pair. The “total recognition score” corresponded to the recognition of the whole episode: which words were presented and when and where this episode took place.

### ***Autonoetic consciousness***

The subjective reporting of states of consciousness was assessed using the “Remember/Know/Guess” paradigm, which makes it possible to differentiate between auto-noetic and noetic consciousness (Gardiner et al. 2002 ). In the recognition task of the ECM test described above, subjects had to indicate whether they 1) Remembered the specific episode with the impression of reliving some of the details (R answer), 2) just Knew that this episode had happened to them but did not remember any specific event or detail (K answer), 3) Guessed that they might have experienced this episode, but neither remembered nor knew it (G answer). These responses were given independently for each type of content (factual, temporal and spatial). The scores corresponded to the combined percentages of R, K and G answers for each correctly-recognized content.

### **Executive function assessment**

#### ***Organisation***

Organization and the ability to generate strategies were assessed by two verbal fluency tasks (Cardebat et al. 1990 ). In a letter fluency task, subjects were given 120s to utter as many words beginning with the letter p as possible. In a categorical fluency task, subjects were given 120s to utter as many words belonging to the animal category as possible. The fluency score corresponded to the number of correct words supplied in these two tasks.

#### ***Inhibition***

Inhibition ability was assessed by means of the Stroop test (Stroop 1935 ). This test was composed of three conditions, each lasting 45s: 1) a reading task (Word condition); 2) a color-naming task (Color condition); 3) an interference task (Word-Color condition). The Word condition involved reading the names of colors printed in black as quickly as possible. The Color condition involved naming areas of color as quickly possible. In the Word-Color condition, subjects had to name the incongruous color in which a word was printed as quickly as possible. The number of colors named in the interference task (Word-Color condition) was recorded to gauge inhibition ability.

#### ***Flexibility***

Flexibility ability was assessed by the alternate response subtest of the attentional assessment test (Zimmermann and Fimm 1993 ). In this task, a letter and a number were displayed simultaneously. In a random manner, one stimulus appeared on the right side of the computer screen and the other on the left side. A left and a right button were available to the subjects, who had to press the button corresponding to the appropriate stimulus (alternating between letters and numbers). The percentage of correct answers recorded.

#### ***Updating***

Updating abilities were assessed by the n-back (N-2) paradigm (Quinette et al. 2003 ). Single digits were displayed one after the other and a button had to be pressed if the digit on the screen was the same as the penultimate one. The n-back task lasted approximately 15 minutes in all (instructions and carrying out), stimuli presentation was 5000ms and time between stimuli presentation was 500ms. The percentage of correct answers was recorded.

#### ***Integration***

Integration ability was also assessed by a computerised test derived of one used by Quinette et al. (2006) . It required subjects to integrate multimodal information before memorizing it. A target comprised four colored consonants in the center of a grid and four colored crosses placed randomly in the remaining squares. Subjects were shown each target and asked to mentally color-match the consonants with the locations represented by the crosses. They then had to maintain the association for either 1s or 8s. In the test phase, a grid was provided with a single letter printed in black inside one of the squares. Subjects had to decide whether the association between the letter and the location was the same as before or not. The percentage of correct answers was recorded.

### **Statistical analysis**

Since there was no significant difference between performance of men and women in both groups, we pooled the data not taking account of the sex ratio in each group. All the data were then analyzed by means of parametric tests. Our analysis was conducted in 2 steps. In the first step, we investigated the effects of alcoholism on episodic memory and executive functions. A statistical analysis of group differences in learning abilities was carried out with repeated-measures analyses of variance. A significant group effect would mean that alcoholics presented a lower level of performance than controls, whereas a significant interaction effect would reflect the fact that the two groups had different rates of learning. Regarding the forgetting rate, encoding and retrieval processes, contextual memory, auto-noetic

consciousness and executive functions, performances were analyzed by means of Student's t tests. In the second step, the objective was to find out whether executive dysfunction could explain episodic memory impairments in alcoholism. To this end, we firstly carried out correlational analyses between all episodic memory measures and executive scores in the alcoholic group, using Bonferroni's correction for multiple correlations. Then, stepwise regression analyses were carried out in the alcoholic group between executive functions and impaired episodic memory scores. Variables accounting for 10% (or less) of the variance were not interpreted being viewed as inconsiderable. A probability level of 0.05 was adopted for all analyses.

## RESULTS

### Effects of alcoholism on episodic memory

#### *Learning abilities*

The repeated-measures analysis of variance indicated significant effects of list repetitions [ $F_{(2,186)} = 128.40, P < .001$ ] and group [ $F_{(1,93)} = 18.81, p < .001$ ] but no significant interaction effect on the free recall measures in the FCSRT.

A learning score was also chosen in order to be used for the regression analysis (see below). It corresponded to the sum of the three free recall measures, and a t test analysis of the latter revealed a significant difference between the two groups [ $t_{(93)} = 4.33, P < .001$ ].

#### *Storage capacities*

There was no significant difference [ $t_{(93)} = 0.82, P = .41$ ] between the alcoholic group and the control group on the rate of forgetting after 20 minutes (Table 2).

#### *Encoding and retrieval processes*

Analyses showed a significant effect of group on the encoding score (recognition after spontaneous encoding, [ $t_{(93)} = 2.68, P < .01$ ]) and retrieval score (free recall after deep encoding, [ $t_{(93)} = 3.60, P < .001$ ], Table 2).

#### *Factual, temporal and spatial memory*

There was no significant difference on factual recognition, but alcoholic patients achieved significantly lower recognition performances than control subjects for temporal [ $t_{(93)} = 4.40, P < .001$ ] and spatial information [ $t_{(93)} = 2.27, P = .02$ ]. Moreover the analysis revealed a significant effect of group [ $t_{(93)} = 4.38, P < .001$ ] on the total recognition score (Table 2).

#### *Autonoetic consciousness*

On the recognition task of the ECM test, the alcoholic group provided fewer R answers [ $t_{(93)} = 2.22, P = .03$ ] and more G answers [ $t_{(93)} = -2.76, P < .01$ ] than the control group (Table 2). There was no significant difference on the number of K answers.

### Effects of alcoholism on executive functions

There was a significant group effect on the fluency score [ $t_{(93)} = 3.39, P = .001$ ], with alcoholics producing fewer words than controls. Compared with control subjects, alcoholic patients also performed significantly worse in the interference condition of the Stroop test [ $t_{(93)} = 4.26, p < .001$ ] as well as on the Alternate response task [ $t_{(92)} = 3.14, P < .01$ ], the N-back test [ $t_{(93)} = 4.61, P < .001$ ] and the integration task [ $t_{(93)} = 3.82, P < .001$ ]. Results are reported fully in Table 3.

### Relationships between episodic memory and executive functions

After Bonferroni's correction, there was an only one significant correlation between episodic memory scores and executive capacities (Table 4): fluency score was significantly correlated with learning score ( $P < .0009$ ).

In the alcoholic group, the regression analysis showed that the fluency score was the only significant and not inconsiderable predictor of the episodic memory performances. It was predictive of the learning score, the encoding score, the temporal recognition, the total recognition score, the sum of the R answers and the sum of the G answers (Table 5).

## DISCUSSION

The goal of the present study was to investigate episodic memory in alcoholic patients at alcohol treatment entry, in accordance with the current and comprehensive definition of the episodic memory system: encoding, storage and retrieval of factual information located in a precise space-time context and associated with auto-noetic recollection (Tulving, 2001; Wheeler et al., 1997). Furthermore, the present study tested the hypothesis that executive deficits (Baddeley et al. 2000; Miyake et al. 2000) lie behind episodic memory impairment. The present study reports new findings but do not allow us to provide definitive answers on the nature of the episodic memory deficits and their relationships with executive dysfunctions in alcoholics.

Indeed, patients included in the study were early in abstinence from alcohol, the dry-out period being then short. An additional analysis showed firstly that short length of sobriety was not linked with poorer neuropsychological performance, indicating that no cognitive recovery occurred in the course of the first days of abstinence from alcohol. Secondly, we chose a short dry-out period to include patients right at the time when treatment is proposed. Thus, episodic memory deficits described in the present study reflect cognitive impairments potentially compromising the treatment outcome (Zinn et al. 2004 ).

Moreover, the gender distribution was different in the two groups with a majority of women in the control group and a majority of men in the alcoholic group. Even if the gender distribution did not influence our findings (since the neuropsychological performances of men and women were not significantly different in both groups), our results are mainly representative of alcoholic men. Further studies should investigate whether similar results would be found in a group of alcoholic women (Sullivan et al., 2002 ).

### **Effects of alcoholism on episodic memory**

Our data confirmed the findings of most previous studies reporting an impairment of episodic learning abilities (Beatty et al. 1995 ; Goldstein et al. 2004 ; Joyce and Robbins 1991 ). More specifically, they showed that alcoholic patients present lower performance levels than controls on the FCSRT but seem to improve their performance at the same rate as them. Thus, alcoholics would appear to require more learning trials to achieve the same results (Nixon et al. 1998 ), suggesting a slower pace of episodic information acquisition at alcohol treatment entry (Sherer et al. 1992 ). The conflicting conclusions reached in some previous studies (Brokate et al. 2003 ; Hildebrandt et al. 2004 ) may be explained by the way alcoholic patients were matched with control subjects. In these studies (Brokate et al. 2003 ; Hildebrandt et al. 2004 ), patients were not paired with control participants on the basis of their educational level but according to their mental abilities. Thus, patients with an intelligence score lower than one standard deviation of the mean were excluded. However it was reported that chronic alcoholism may induce a deficit in general intelligence (Beatty et al. 2000 ; Joyce and Robbins 1991 ; Tedstone and Coyle 2004 ) which may be related to executive dysfunction. When they are controlled for intelligence, alcoholic patients with the more severe executive deficits are excluded, thereby making it less likely that experimenters will observe episodic memory impairment in a task sensitive to executive dysfunction (California Verbal Learning Test).

Alcoholic patients appeared to present preserved storage capacities (Sherer et al. 1992 ). This finding contradicts a number of previous studies (Beatty et al. 1995 ; Davidson et al. 2006 ; Munro et al. 2000 ) which have found impaired delayed performances by alcoholic patients. However, in these studies, performances at immediate recall were not taken into account and consequently any deficit in immediate recall or learning automatically induced a deficit in delayed recall which did not reflect a genuine deficit in storage capacities. By measuring performances at immediate recall (Sherer et al. 1992 ), the present study was able to demonstrate that alcoholic patients did not forget significantly more information than controls in the 20-minutes interval. Hence, processes of consolidation in memory seem to be effective in alcoholism.

Our data also conflicted with those of another study (Nixon et al. 1998 ) which concluded that memory deficits may be attributed, in part, to a deficit in the retention of information. However, this conclusion was based on a weak effect of cueing on recall performance, which could instead be interpreted as a deficit in encoding processes. In effect, results on the Spondee test suggest that alcoholic patients performed less efficiently than controls on the recognition task after spontaneous encoding and on the free recall after deep encoding. This may mean that, at alcohol treatment entry, patients present an impairment of both encoding and retrieval abilities.

The ECM test provided information about the effects of alcoholism on contextual memory. The spatiotemporal context of encoding appeared to be impaired in alcoholism, with both a deficit in temporal and spatial context. Thus, our study reports contextual memory impairment in alcoholism and similar results have been recorded for patients suffering from frontal lobes lesions or Korsakoff's syndrome ( Kapur et al. 1994 ; Kopelman et al. 1997 ; McAndrews and Milner 1991 ; Postma et al. 2006 ). Alcoholic patients also tend not to recall complete episodes, i.e. correct factual information associated with the correct spatiotemporal context of encoding. This suggests that episodic memories are not complete in alcoholics at alcohol treatment entry.

Lastly, subject's mental states of consciousness assessed by the ECM test were different for each group. Alcoholic patients provided significantly fewer Remember answers and more Guess answers than control subjects. Alcoholism seems to lead to an impairment of auto-noetic consciousness and a lack of confidence in the accuracy of one's decisions (Gardiner et al. 1998 ). This has already been observed in relation to the effects of acute alcoholism (Curran and Hildebrandt 1999 ; Duka et al. 2001 ), but our data provide fresh insight into the effects of chronic alcoholism on the states of conscious state that accompanies retrieval in episodic memory.

To sum up, at alcohol treatment entry, alcoholics present deficits in various episodic memory components: learning abilities, encoding and retrieval processes, the spatiotemporal context of encoding and auto-noetic consciousness. Storage capacities, however, were preserved in our group of alcoholic patients.

### **Effects of alcoholism on executive functions**

Our results corroborate those of previous studies which have highlighted the effects of alcoholism on organizational ability ( Dao-Castellana et al. 1998 ; Joyce and Robbins 1991 ; Noel et al. 2001b ) and inhibition ability ( Dao-Castellana et al. 1998 ; Goldstein et al. 2004 ; Noel et al. 2001a ; Noel et al. 2001b ; Oscar-Berman et al. 2004 ; Tedstone and Coyle 2004 ; Uekermann et al. 2003 ). Our data also confirm that alcoholic patients present reduced mental flexibility ( Brokate et al. 2003 ; Hildebrandt et al. 2004 ; Noel et al. 2001a ; Oscar-Berman et al. 2004 ). The present study suggests that chronic alcoholism leads to a deficit in updating abilities in working memory, even though different results have recently been reported ( Brokate et al. 2003 ; Hildebrandt et al. 2004 ). Once again, the way the two groups were matched may explain the conflicting results. The present study used also a novel task to assess the effects of alcoholism on integration abilities. As suggested earlier, alcoholic patients may present impairments in the associative binding of multimodal information in memory ( De Rosa and Sullivan 2003 ).

In short, the alcoholic patients in our study presented impairments of executive functions at alcohol treatment entry, as all the abilities we assessed were found to be impaired.

### **Link between episodic memory and executive functions**

We then set out to ascertain whether executive performances could explain the episodic memory impairments in alcoholics, i.e. whether executive dysfunction could be responsible for the deterioration of certain episodic memory processes.

The stepwise regression analyses carried out in the alcoholic group showed firstly that fluency score was mainly predictive of learning performance (40%), suggesting that the learning deficits may be closely linked to executive dysfunctions. These findings reinforced the correlational results indicating that the relationship between learning performance and fluency score was the only significant correlation between episodic memory measures and executive scores. In agreement with previous investigations ( Fama et al. 2004 ; Pitel et al. 2007 ), learning new information and improving performances in the course of the presentations seemed, in the alcoholics, to rely on the use of costly cognitive strategies involving executive capacities. However, the fluency score accounted for only a small proportion (about 20%) of the deficit in the encoding processes, the contextual memory (for temporal information exclusively) and the conscious state that accompanies retrieval of episodic memories ( Wheeler et al. 1997 ). We cannot consider that a predictor explaining 20% of the variance is a good predictor since 80% of the variance was not accounted for by any of our executive scores. These 80% of the variance may either be explained by other cognitive functions non tested in the present study (other executive functions, attentional capacities, semantic memory, etc) or reflect the genuineness of the episodic memory deficits. Thus, the impairment of executive functions may contribute to some of the memory disorders, but it does not primarily account for them. Moreover, given fluency scores involve organizational ability, strategies to search information in semantic memory, they involve cognitive processes at the junction of memory and executive capacities. Thus, fluency score prediction may reflect either relationships between episodic memory performance and executive functions or semantic memory. At last, executive dysfunctions were not significantly predictive of deficits in retrieval abilities and spatial recognition performance, suggesting that some of the episodic memory deficits may appear rather independently of executive impairments reported in this study.

Therefore, contrary to previous suggestions ( Zinn et al. 2004 ), the episodic memory impairment observed in alcoholic patients would not appear to be linked solely to executive dysfunction, the one exception being learning abilities, which may draw heavily on strategies to improve performances during repeated presentations of the information. Chronic alcoholism may cause genuine episodic memory deficits, including impairments of encoding and retrieval processes, contextual memory and autoegetic consciousness. Some of these may appear rather independently of executive dysfunctions whereas others may be partially linked with them. Thus, at alcohol treatment entry, episodic memory impairment must not be regarded solely as an indirect consequence of executive function deficits, as this memory system appears to be intrinsically impaired in chronic alcoholism early in abstinence. There may well be a link between this episodic memory disturbance and recent findings of neuroimaging studies highlighting hippocampal atrophy in chronic alcoholism ( Agartz et al. 1999 ; Beresford et al. 2006 ; Bleich et al. 2003 ; Sullivan et al. 1995 ).

### **Potential clinical implications**

These cognitive impairments have to be taken into account in order to make relevant clinical decisions and choose the most appropriate treatment. In effect, during treatment, alcoholic patients have to travel mentally through time in order to consider former and future high-risk situations. They have to picture the contexts in which they were in danger and could be again, i.e. where (at home, in a bar, at a friend's place, etc.) and when (alone, with certain friends, when they are under stress, etc.) they were tempted by alcohol and might be again in the future. They have to remember very precisely, with autoegetic consciousness, what they felt, how they experienced the craving for drink and why they gave into temptation. A recent study ( Blume et al. 2005 ) reported that episodic memory is crucial to changes of behavior where alcohol is concerned and is particularly important during the precontemplation and contemplation stages of the motivational model ( DiClemente et al. 1999 ). Furthermore, alcoholic patients have to search for the information or skills learned during treatment in order to stop or inhibit their customary behavior (drinking alcohol) in order to adopt a new behavior (taking soft drinks). In the face of temptation, they have to resist drinking alcohol, plan efficient avoidance strategies and make the right decision. Executive functions do not seem to be required during the earlier stages of the motivational model ( DiClemente et al. 1999 ), but come into play during the



3-month follow-up period of the alcohol-dependence program (Blume et al. 2005 ). Alcohol treatment and subsequent abstinence require high-level cognitive processes and consequently may not be feasible by alcoholic patients with impaired episodic memory and/or executive functions. The neuropsychological screening of these cognitive impairments may prove extremely useful at alcohol treatment entry, allowing clinicians to ascertain whether alcoholic patients are capable of undergoing standard therapy or whether it needs to be adjusted in order to take account of episodic memory and executive functions impairments.

One of the possibilities could be better to delay the treatment until episodic memory and working memory improve with abstinence since reversibility of neuropsychological deficits with time was previously reported (Bartels et al. 2006 ; Munro et al. 2000 ; Reed et al. 1992 ; Rourke and Grant 1999 ). The first stage of the treatment program could consist of cognitive stimulation which was showed to facilitate the improvement of neuropsychological capacities (Roehrich and Goldman 1993 ). Cognitive stimulation was described as enhancing the alcoholic person's capacities to incorporate and use skills, insight, and knowledge presented as part of most alcoholism treatment protocols, improving then treatment outcomes. Another perspective could be to apply rehabilitation techniques used with brain injured patients to treatment of alcoholics with cognitive deficits. Therapy notably based on cognitive behavioural treatment could be modified to take account of the principle of errorless learning (Baddeley and Wilson 1994 ) or vanishing cues (Glisky and Delaney 1996 ).

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**Table 1**

Main Clinical Features of Participants

	Controls (N=55)	Alcoholics (N=40)	p value
Age	50.46 ± 10.95	49.41 ± 6.82	0.59
Range	30–72	34–74	
Years of education	11.58 ± 3.65	10.50 ± 2.63	0.11
Range	7–23	7–20	
Days of abstinence before inclusion	/	11.57 ± 12.82	/
Range		3–75	
Age of first alcoholic drink	/	16.34 ± 4.30	/
Range		6–25	
Age of onset of alcoholism	/	26.42 ± 11.25	/
Range		17–55	
Years of alcoholism	/	19.67 ± 8.87	/
Range		5–35	
Quantity (number of standard drinks per day)	/	20.26 ± 12.26	/
Range		7–48	

Data are given as means ± SD.

**Table 2**

Assessment of Episodic Memory in Control Subjects and Alcoholic Patients

Tasks	Episodic memory processes	Variable	Control subjects (N=55)	Alcoholic patients (N=40)	p value
FCSR Test	Learning abilities	FR <sub>1+2+3</sub> <sup>a</sup>	33.43 ± 4.88	27.95 ± 7.43	<0.001 <sup>†</sup>
	Retention abilities	Rate of forgetting <sup>b</sup>	0.01 ± 0.20	-0.02 ± 0.23	0.41
Spondee test	Encoding and retrieval processes	Encoding score <sup>c</sup>	84.32%± 13.39	76.25%± 15.77	<0.01 <sup>†</sup>
		Retrieval score <sup>d</sup>	53.64%± 17.50	40.47%± 17.73	<0.001 <sup>†</sup>
ECM test	Contextual memory	Factual recognition	99.09%± 3.82	97.50%± 8.05	0.20
		Temporal recognition	92.12%± 11.93	77.92%± 19.38	<0.001 <sup>†</sup>
		Spatial recognition	88.48%± 16.31	80.00%± 20.04	0.02 <sup>†</sup>
		Total recognition <sup>e</sup>	83.03%± 20.41	62.08%± 26.14	<0.001 <sup>†</sup>
	Autooetic consciousness	R answers	2.25 ± 0.62	1.92 ± 0.82	0.02 <sup>†</sup>
		K answers	0.45 ± 0.40	0.47 ± 0.50	0.87
		G answers	0.29 ± 0.40	0.57 ± 0.61	<0.01 <sup>†</sup>

Data are given as means ± SD.

<sup>†</sup> Significant difference between alcoholic patients and control subjects (p<0.05).

FR, free recall; R, “remember” answers in the R/K/G paradigm; K, “know” answers in the R/K/G paradigm; G, “guess” answers in the R/K/G paradigm; FCSR, Free and Cued Selective Reminding; ECM, Ecological Contextual Memory.

<sup>a</sup> Sum of free recall measures 1, 2, and 3.

**b** [(Third free recall-delayed free recall)/third free recall] × 100.

**c** % of recognition after spontaneous encoding.

**d** % of free recall after deep encoding.

**Table 3**

Assessment of Executive Functions in Control Subjects and Alcoholic Patients

Tasks	Executive functions	Control subjects (N=55)	Alcoholic patients (N=40)	p value
Verbal fluencies	Organization	54.42 ± 14.48	45.29 ± 14.52 <sup>†</sup>	<0.01 <sup>†</sup>
Stroop test	Inhibition	41.75 ± 12.16	31.52 ± 10.85 <sup>†</sup>	<0.001 <sup>†</sup>
Alternate response task <sup>a</sup>	Flexibility	90.80 ± 10.85	85.15 ± 10.39 <sup>†</sup>	<0.01 <sup>†</sup>
n-Back task	Updating	90.20 ± 12.70	79.40 ± 15.70 <sup>†</sup>	<0.001 <sup>†</sup>
Integration task	Integration	70.10 ± 12.70	56.00 ± 18.70 <sup>†</sup>	<0.001 <sup>†</sup>

Data are given as means ± SD.

<sup>†</sup> Significant difference between alcoholic patients and control subjects (p<0.05).

<sup>a</sup> Only 39 alcoholic patients carried out the task (data from one patient are missing).

**Table 4**

Correlational Results Between All Episodic Memory Measures and Executive Scores in Alcoholic Patients

	Verbal fluencies	Stroop test	Alternate response task	n-Back task	Integration task
FR <sub>1+2+3</sub>	0.61 <sup>†</sup>	0.47	0.47	0.41	0.18
Rate of forgetting	-0.17	0.06	0.04	0.004	-0.19
Encoding score	0.44	0.34	0.31	0.27	0.05
Retrieval score	0.34	0.25	-0.02	0.19	0.20
Factual recognition	0.18	0.04	0.21	0.39	-0.03
Temporal recognition	0.46	0.17	0.30	0.10	0.09
Spatial recognition	0.08	0.08	0.24	0.26	-0.08
Total recognition	0.43	0.23	0.36	0.28	0.05
R answers	0.50	0.29	0.25	0.22	0.08
K answers	-0.22	-0.14	0.07	-0.04	-0.07
G answers	-0.46	-0.37	-0.41	-0.28	-0.09

<sup>†</sup> Significant correlations after Bonferroni's correction.

For abbreviations see Table 2.

**Table 5**

Stepwise Regressions Predicting Impaired Episodic Memory Performance in Alcoholic Patients

Dependent measure	Predictor	R <sup>2</sup> change	β coefficient	p Value
FR <sub>1+2+3</sub>	First: Verbal fluency	0.40	0.53	<0.001 <sup>†</sup>
	Second: Flexibility subtest	<0.10	0.29	0.03 <sup>†</sup>
Encoding score	First: Verbal fluency	0.20	0.34	<0.01 <sup>†</sup>
	Second: Flexibility subtest	<0.10	0.18	0.24
Retrieval score	First: Verbal fluency	<0.10	0.29	0.03 <sup>†</sup>
	Second: n-Back task	<0.10	0.29	0.19
	Third: Flexibility subtest	<0.10	-0.23	0.17
Temporal recognition	First: Verbal fluency	0.21	0.39	<0.01 <sup>†</sup>
	Second: Flexibility subtest	<0.10	0.17	0.26
Spatial recognition	First: n-Back task	<.10	0.18	0.13
	Second: Flexibility subtest	<0.10	0.18	0.30
Total recognition	First: Verbal fluency	0.18	0.34	<0.01 <sup>†</sup>
	Second: Flexibility subtest	<0.10	0.24	0.11
R answers	First: Verbal fluency	0.26	0.51	<0.001 <sup>†</sup>
G answers	First: Verbal fluency	0.24	-0.39	0.001 <sup>†</sup>
	Second: Flexibility subtest	<0.10	-0.28	0.06

For abbreviations see Table 2 .

<sup>†</sup> Significant regression (p<0.05).