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Effect of episodic and working memory impairments on semantic and cognitive procedural learning at alcohol treatment entry

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ABSTRACT

Background: Chronic alcoholism is known to impair the functioning of episodic and working memory, which may consequently reduce the ability to learn complex novel information. Nevertheless, semantic and cognitive procedural learning have not been properly explored at alcohol treatment entry, despite its potential clinical relevance. The goal of the present study was therefore to determine whether alcoholic patients, immediately after the weaning phase, are cognitively able to acquire complex new knowledge, given their episodic and working memory deficits.

Methods: Twenty alcoholic inpatients with episodic memory and working memory deficits at alcohol treatment entry and a control group of twenty healthy subjects underwent a protocol of semantic acquisition and cognitive procedural learning. The semantic learning task consisted of the acquisition of 10 novel concepts, while subjects were administered the Tower of Toronto task to measure cognitive procedural learning.

Results: Analyses showed that although alcoholics were able to acquire the category and features of the semantic concepts, albeit slowly, they presented impaired label learning. In the control group, executive functions and episodic memory predicted semantic learning in the first and second halves of the protocol respectively. In addition to the cognitive processes involved in the learning strategies invoked by controls, alcoholics seem to attempt to compensate for their impaired cognitive functions, invoking capacities of short term passive storage. Regarding cognitive procedural learning, although the patients eventually achieved the same results as the controls, they failed to automate the procedure. Contrary to the control group, the alcoholics' learning performance was predicted by controlled cognitive functions throughout the protocol.

Conclusion: At alcohol treatment entry, alcoholic patients with neuropsychological deficits have difficulty acquiring novel semantic and cognitive procedural knowledge. Compared with controls, they seem to use more costly learning strategies which are

nonetheless less efficient. These learning disabilities need to be considered when treatment requiring the acquisition of complex novel information is envisaged.

Keywords: alcoholism, semantic learning, cognitive procedural learning, episodic memory, working memory

INTRODUCTION

There is now evidence that chronic alcoholism results in brain abnormalities (Mann et al., 2001; Moselhy et al., 2001; Rosenbloom et al., 2003; Sullivan and Pfefferbaum, 2005) and long-term cognitive impairments such as episodic memory deficits (Beatty et al., 1995; Fama et al., 2004; Goldstein et al., 2004; Hildebrandt et al., 2004; Nixon and Bowlby, 1996; Nixon et al., 1998; Tivis et al., 1995) and working memory dysfunctions (Ambrose et al., 2001; Joyce and Robbins, 1991; Oscar-Berman et al., 2004). Research into the impact of the cognitive impairments on the ability to learn complex novel information is less frequent. Studies using face-name learning tasks have revealed either an impairment of these abilities (Beatty et al., 1995; Everett et al., 1988) or a reduction in the speed of acquisition stemming from a deficit of acquisition processes rather than an impairment of retrieval abilities (Sherer et al., 1992). A recent study (Fama et al., 2004) investigated perceptual learning in chronic alcoholism and concluded that patients performed at the same level as controls, but implemented different learning strategies requiring higher-order cognitive processes in order to achieve the same performance. Such conclusions are also supported by a series of functional magnetic resonance imaging studies (De Rosa et al., 2004; Desmond et al., 2003; Pfefferbaum et al., 2001; Tapert et al., 2001) showing that alcoholics recruit higher-level cognitive systems than controls for the same tasks.

Semantic and cognitive procedural acquisitions have never been explored in chronic alcoholism contrary to perceptual learning (Fama et al., 2004), and might be impaired given their episodic and working memory dysfunctions. In effect, semantic learning has mainly been investigated in patients with selective and severe episodic memory deficits (Glisky et al., 1986) and results are heterogeneous. While some studies have shown that semantic acquisition is possible in spite of episodic memory impairments (Guillery et al., 2001; Kitchener et al., 1998; O'Kane et al., 2004), others have reported that semantic learning requires efficient episodic memory functioning

(Gabrieli et al., 1988; Verfaellie et al., 2000). No study has investigated the impact of working memory dysfunction on semantic learning, but we can postulate that the dynamic course of learning requires executive functions. We would therefore expect alcoholic patients with episodic memory and working memory impairments to present poor semantic learning abilities.

In the same way, impairments of episodic and working memory in alcoholism may hinder cognitive procedural acquisition. Indeed, according to the Adaptive Control of Thoughts model (Anderson, 1992), cognitive procedural learning occurs in three qualitatively different phases (cognitive, then associative and finally autonomous), involving different types of processing and flagged by specific cognitive determinants (Ackerman and Cianciolo, 2000; Beaunieux et al., 2006). During the cognitive phase, performance levels are mainly associated with nonverbal intelligence, whereas in the autonomous phase, individual differences are largely determined by psychomotor functions. The associative stage is regarded as a transitional phase between the other two learning stages and has no specific cognitive determinant. Given the contribution of episodic memory and working memory to the cognitive stage of cognitive procedural learning (Beaunieux et al., 2006; Butters et al., 1985; Winter et al., 2001; Xu and Corkin, 2001), we would expect these learning capacities to be impaired in alcoholic patients.

An impairment of semantic and cognitive procedural learning abilities at alcohol treatment entry may have a negative impact on the outcome of the treatment. In effect, although nobody has identified precisely which cognitive processes are involved in the treatment of alcohol dependence we can postulate that treatment of alcohol notably based on cognitive behavioral therapy (CBT) requires the learning of novel semantic information and/or novel cognitive procedures. For example, patients have to learn that a glass of wine or a glass of beer or whisky served in a bar contains about 10g of alcohol so that they know that their alcohol intake is the same whether they choose a beer or a whisky. During treatment, patients must acquire other items of semantic information, such as the meaning of alcohol

dependence or the consequences of alcohol consumption on the liver, etc. Treatment also entails learning novel cognitive procedures in procedural memory. Encoding a novel procedure will result in the emergence of a new skill or habit in the subject's behavioral register. In alcoholism treatment, cognitive procedural learning represents the acquisition of novel behavioral responses to the temptation of alcohol. For example, in high-risk situations, alcoholic patients have to search for coping skills learned during treatment to stop or inhibit their customary behavior and adopt a new one. Thus, the treatment of alcohol dependence may rely on the ability to learn semantic and procedural knowledge which, however, may be impaired at alcohol treatment entry.

Even though learning disabilities could prevent alcoholics from benefiting fully from their treatment, there has not been any research into the acquisition of semantic and procedural information in alcoholics at alcohol treatment entry - precisely the time when learning abilities are required in the programs. The objective of the present study was to assess the effects of chronic alcoholism on semantic and cognitive procedural learning abilities at alcohol treatment entry, taking account of episodic memory and working memory dysfunctions. In the light of previous studies of complex novel acquisition abilities (Beatty et al., 1995; Everett et al., 1988; Fama et al., 2004) and the harmful effects of alcoholism on cognition, we tested the following hypotheses: alcoholic patients would, at the least, present a slower rate of acquisition and would use different learning strategies to complete the tasks.

METHODS

Participants

Demographic data

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Twenty alcoholic inpatients and 20 control subjects were examined. All the participants gave their informed consent to the neuropsychological procedure, which was approved by the local ethical committee. Alcohol-dependent participants were recruited by clinicians while they were being treated in the alcoholism department of Caen University Hospital (CHU), on the basis of the DSM IV criteria for alcohol dependence. Patients had no history of other forms of substance abuse (except tobacco) or psychiatric problems. Controls were drawn from a study by Beaunieux et al. (2006) and were recruited by word of mouth, as they were not paid for their participation. They were interviewed to ensure that they did not meet the criteria for alcohol abuse or dependence and were excluded if they reported the consumption of three or more alcoholic drinks a day during the previous year. None of the participants were receiving psychoactive medication or had a history of pathology (head injury, coma, epilepsy, Gayet-Wernicke diagnosis, hepatic cirrhosis, depression, etc.) which might affect their cognitive function. The two groups were matched according to their age and level of education (Table 1).

Drinking history

Although the learning ability assessment was carried out at the start of alcohol treatment, we only selected patients who had already been weaned of alcohol, in order to decrease the likelihood of acute alcohol withdrawal effects. That said, they were at an early stage of abstinence, as we wanted to explore learning abilities at the precise time when treatment is proposed. Patients were interviewed to determine the age at which they had had their first alcoholic drink, the age of onset of alcoholism, the length of time they had abused alcohol and their habitual daily alcohol consumption (Table 1).

Insert Table 1

Neuropsychological data

Immediately after the weaning phase, the patients underwent a neuropsychological assessment comprising an episodic memory test and various working memory tasks.

- Episodic memory

The Spondee test (“Spon” for spontaneous and “dee” for deep) is a verbal learning test comprising two lists of 16 words belonging to 16 different categories. It is derived from the Double memory test (Grober and Kawas, 1997). In the first list, words were encoded spontaneously according to the strategies subjects were able to implement on their own. In this condition, subjects had to point to words as they were read out by the experimenter. In the second list, words were deeply encoded, i.e. in a semantic mode: subjects had to point to words in response to their semantic category. For each list, a free recall test, a semantic cued recall test and a recognition task were then carried out. The main purpose of this task was to assess the depth of encoding processes and the efficacy of retrieval processes. On this task - at alcohol treatment entry -, alcoholic patients presented a slight impairment of episodic memory abilities (Table 2). Cued recall after spontaneous encoding was the score that was most sensitive to the effects of chronic alcoholism, suggesting that patients mainly had difficulty making efficient use of semantic strategies to encode information on their own (Nixon et al., 1998).

Insert Table 2

- Working memory

Working memory is composed of both slave systems and a central executive considered as similar to the executive functions (Baddeley, 1986; Baddeley et al., 1996). The *slave systems* of working memory were assessed by means of three computerized passive storage tasks. The phonological loop and the visuospatial sketchpad (respectively in charge of the short term storage of phonological and visuospatial information) were evaluated by verbal

span and spatial span tasks respectively. The newly-identified slave system of working memory (Baddeley, 2000; Baddeley, 2003), responsible for maintaining multimodal information and known as the episodic buffer, was assessed by means of a multimodal span task (Quinette et al., 2006). Patients were asked to memorize increasingly long strings of letters (verbal span), locations (spatial span) and letters placed in an array (multimodal span) and had to recall them immediately afterwards. The final score corresponded to the number of correctly-reported sequences.

The *central executive* of working memory was assessed using three different types of task involving executive functions. Organization and the ability to self-generate strategies were assessed by two verbal fluency tasks (Cardebat et al., 1990): a letter fluency task and a categorical fluency task. The verbal fluency score corresponded to the number of correct words supplied in both these tasks, minus intrusions and perseverations.

Inhibition ability was assessed by means of the Stroop test (Stroop, 1935). The number of colors named in the interference condition was recorded to gauge inhibition ability. The scores were age-corrected.

Updating abilities were assessed by the n-back (N-2) paradigm (Quinette et al., 2003). The percentage of correct answers was recorded.

Alcoholic patients presented impaired performance on the three span tasks and on the whole executive tests (Table 3). Thus, slave systems and central executive of the working memory were impaired compared with those of the control subjects. Broadly, at alcohol treatment entry, the results of the working memory assessment reflected the executive dysfunctions that are usually reported early in abstinence (Noel et al., 2001; Zinn et al., 2004).

Insert Table 3

Semantic learning paradigm

Learning task and design

This task was inspired by one designed for errorless learning in developmental amnesia (Guillery-Girard et al., 2004; Martins et al., 2006). Subjects had to learn ten novel concepts existing in the real world but quite rare. Each concept consisted of a name or label, its superordinate category and three specific features.

This semantic learning task consisted of 3 stages: a pre-learning assessment, the presentation of the concepts, a learning phase (Figure 1). This pre-learning assessment was conducted before the start of the learning phase in order to check that the semantic concepts were new for all participants and that both groups had the same level of semantic knowledge about these 10 concepts. For each concept, the assessment consisted of 1) a photo-naming task and 2) a 3-choice questionnaire about the superordinate category and the three features. The scores corresponded to the number of correct answers provided. Then, the ten novel concepts were presented to the subjects in the form of photos, labels, categories and features. The learning protocol comprised 8 daily sessions. For each concept, subjects had to provide the label when they were shown the photo and answer 4 open questions (one about the category: and three about the features). The subjects were given the correct response if they failed to answer within 15 seconds or after two incorrect answers. Subjects had to correct their errors themselves from one session to the next, using feedback from the experimenters. The order in which the items were presented was counterbalanced during the learning sessions. The semantic learning scores corresponded to the number of correct answers provided minus errors on the naming task and the category/features questionnaire. Thus, the learning scores took into account both improvements in performance and the correction of errors (scores could be negative if there were more errors than correct answers).

Insert Figure 1

Cognitive procedural paradigm

Learning task and design

The learning of the Tower of Toronto task (TT task) was carried out during 4 daily learning sessions. Subjects were asked to perform 10 trials in each learning session (Figure 2). The TT task consisted of a rectangular base and three pegs. Four different-colored disks were used: one black, one red, one yellow and one white. The disks were initially stacked on the leftmost peg, with the darkest one at the bottom and the lightest one on top. The task consisted in rebuilding this configuration on the rightmost peg, obeying the following two rules: only one disk may be moved at a time, and a darker disk may never be placed on top of a lighter one. The rules were read out to the subjects and they were then required to solve the puzzle. The subjects' performance on the TT task was assessed in terms of completion time and the number of moves needed to complete it (minimum 15). For each variable, learning scores corresponded to the sum of the ten trials in each session.

Insert Figure 2

Specific determinants of the learning phases

In order to delimit the three learning phases, we used highly reliable and specific cognitive determinants, which were assessed using the same tasks as in the study conducted by Beaunieux et al. (2006).

Nonverbal intelligence capacities were assessed by means of two subtests of the Wechsler Adult Intelligence Scale (Wechsler, 2001): Block Design and Matrix Reasoning. The

nonverbal intelligence score consisted of the sum of the standard T scores (average 10 and standard deviation 3) for these two tasks.

To assess psychomotor abilities, a disk transfer task was carried out. Subjects had to transfer the 4 disks of the TT task one by one from the leftmost peg to the middle peg, then to the rightmost peg and finally to the leftmost one. The only instruction they were given was to use only one hand. The total transfer time was recorded (12 moves). This transfer task was performed twice: once before and once after the procedural learning for the TT task. The psychomotor score was an average transfer time based on the two recorded times.

Statistical analysis

Regarding the semantic learning performance, we carried out a statistical analysis in three steps. First of all, repeated-measures analyses of variance with Session repetition as a within-subjects factor were carried out on the results on label naming and category/features learning in order to measure the effect of chronic alcoholism on semantic acquisition. We used post-hoc analyses to compare alcoholic patients and control subjects on each learning session. Secondly, within each subject group, correlations (Bravais-Pearson) were carried out to examine the relationships between semantic learning on the one hand and episodic and working memory on the other hand. Finally, within the context of the correlations observed, multiple regressions were conducted to emphasize the best predictor of each learning session in each group. We compared the β coefficients of the two groups to estimate whether alcoholics invoked the same learning strategies as controls.

As far as the cognitive procedural learning is concerned, the same statistic method was used and an additional analysis was carried out. In accordance with the methodology established

by Beaunieux et al. (2006), the three stages of the procedural learning were pinpointed by assessing correlations (Bravais Pearson) between the learning scores (in terms of time) and the cognitive determinants for each learning phase (nonverbal intelligence and psychomotor abilities). We chose not to consider the number of moves for the correlations and regressions, as it was not sufficiently sensitive. In effect, this variable loses its variability as soon as the subjects find the solution to the problem and thus does not reflect the automation of the cognitive procedure.

RESULTS

Semantic learning

Comparison of learning performance

The comparison of correct answers on the pre-learning assessment did not reveal any significant difference between the two groups for label naming [$t(38)=0.68$, $P=0.50$] or the category and features questionnaire [$t(38)=-0.32$, $P=0.75$].

With regard to the learning sessions, the analysis of variance conducted on label naming scores revealed a significant effect of Group [$F(1,38)=44.8$, $P<0.0001$], Session repetition [$F(7,266)=60.9$, $P<0.0001$] and Interaction [$F(7,266)=13.7$, $P<0.0001$]. Post-hoc analyses showed that the alcoholic patients were significantly impaired compared with control subjects in Sessions 3 to 8 (Figure 3a). The analysis of variance conducted on the category and features learning assessment showed a significant effect of Group [$F(1,38)=18.8$, $P=0.0001$], Session repetition [$F(7,266)=172.1$, $P<0.0001$] and Interaction [$F(7,266)=3.4$, $P=0.001$]. Post-hoc analyses showed that the learning difference was significant in Sessions 2 and 3 (Figure 3b).

Insert Figure 3

Correlations between episodic memory and working memory and label learning

We focused our analysis on label learning because it was the most difficult semantic element for the patients to acquire. Broadly speaking, in the control group, learning performance was linked to the n-back task in Session 1 and to verbal fluency from Sessions 2 to 4. The label naming score was correlated with cued recall after deep encoding in Sessions 3, 4 and from 6 to 8. In the alcoholic group, there was no relationship between learning performance and cognitive scores for the first session. On the whole, semantic learning was correlated with most of the episodic scores after spontaneous encoding, as well as with the verbal span task and the three executive functions tested in the second half of the protocol. Results are summarized in Table 4 and examples of the scatterplots are presented in Figure 4.

Insert Table 4

Insert Figure 4

Predicting semantic acquisition

In the control group, the best predictor of semantic learning performance was the N-Back task in Session 1 (accounting for 27% of the variance), the verbal fluencies in Sessions 2 and 3 (respectively accounting for 25% and 28% of the variance) and the cued recall after a deep encoding in Sessions 4 and from 6 to 8 (accounting for 33%, 22%, 35% and 23%, respectively). In the alcoholic group, 22% of the variance in learning results in Session 2 was accounted for by free recall after spontaneous encoding. Verbal span task was the best predictor from Sessions 3 to 5 and in Session 7 (accounting for 39%, 64%, 46% and 42% of the variance respectively). The best predictor of performance in Sessions 6 and 8 was the verbal fluencies score (accounting for 47% and 41% of the variance respectively).

There was no significant difference between the slopes (β coefficient) of the two groups regarding controls' predictors. On the contrary, the slope differences were significant for the predictors of the alcoholic group from Sessions 2 to 7 (Table 5).

Insert Table 5

Cognitive procedural learning

Comparison of learning performance

Regarding the number of moves (Figure 5a), the repeated-measures analysis of variance showed significant effects of Group [$F(1,38)=7.48, P<0.01$] and Session repetition [$F(3,114)=40.47, P<0.0001$]. There was no significant Interaction effect [$F(3,114)=1.00, P=0.39$]. Regarding the completion time, the repeated-measures analysis of variance showed significant effects of Group [$F(1,38)=22.48, P<0.0001$], Session repetition [$F(3,114)=63.5, P<0.0001$] and Interaction [$F(3,114)=6.82, P=0.0003$]. Post-hoc analyses showed that alcoholic patients significantly differed from control subjects in Sessions 1 and 2 (figure 5b).

Insert Figure 5

Delimitation of the learning phases

Alcoholic patients performed more poorly than the control subjects with regard to nonverbal intelligence [$t(38)=5.00, P<0.0001$] and psychomotor abilities [$t(38)=-3.87; P=0.0004$]. Results are presented in Table 6.

Insert Table 6

Correlations showed that nonverbal intelligence was only linked with procedural performance in Session 1 ($r=-0.47$, $p=0.03$) for the control group, whereas it was linked with it across all the sessions for the alcoholic group ($r=-0.59$, $p=0.006$; $r=-0.58$, $p=0.006$; $r=-0.50$, $p=0.02$; $r=-0.45$, $p=0.04$). Psychomotor abilities were significantly correlated with cognitive procedural learning in Sessions 3 ($r=0.43$, $p=0.05$) and 4 ($r=0.58$, $p=0.007$) for the control group, while there was no significant link for the alcoholic group.

Correlations between episodic memory, working memory and procedural learning

Broadly speaking, the performance of the control group in terms of completion times in Session 1 was correlated with free recall after spontaneous encoding and the span tasks. From Sessions 2 to 4, however, cognitive procedural performance was no longer linked to episodic memory and working memory abilities. For the alcoholic group, verbal span and visuospatial span were correlated with procedural results in Session 1. From Sessions 2 to 4, performance could be predicted by cued recall after deep encoding and the n-back task. Results are summarized in Table 7 and examples of the scatterplots are presented in Figure 6.

Insert Table 7

Insert Figure 6

Predicting cognitive procedural acquisition

In the control group, the sole predictor of the procedural learning performance was the multimodal span task, accounting for 29% of the variance in Session 1. In the alcoholic group, the best predictors of procedural results in Sessions 1, 2, 3 and 4 were respectively the verbal span task, the cued recall after a deep encoding, the N-Back task and the recognition after a deep encoding (accounting for 48%, 48%, 49% and 44% of the variance respectively).

The slopes were significantly different between two groups regarding alcoholics' predictors from Sessions 2 to 4 (Table 8).

Insert Table 8

DISCUSSION

Semantic learning

Statistical analyses showed that regarding label acquisition, the two groups did not differ significantly in the first two learning sessions, as they both performed poorly at the beginning of the learning phase. Nevertheless, over Sessions 3 to 8, the difference in the performance of the two groups became increasingly marked. Controls quickly improved their scores, benefiting from the repetition of sessions and feedback from the experimenters whereas the alcoholic patients acquired few labels. Concerning the learning of the category and features, both groups managed to achieve the same results by the end of the protocol, but learning was slower for the alcoholic group than for the control group (Fama et al., 2004; Sherer et al., 1992).

These data have to be interpreted with a degree of caution, as the category/features learning task may have been less difficult than the label acquisition task and consequently may have made it more difficult to highlight differences between the two groups. It is not possible to determine with the present study whether our results are linked to the construction of the semantic learning task or whether they reflect the special status of names or labels compared with other types of semantic information (Martins et al., 2006; Thoene et al., 1995). Labels are new words which are essentially processed like meaningless words linked together arbitrarily, just as in face-name learning, which has been found to be impaired in alcoholism (Beatty et al., 1995; Everett et al., 1988; Sherer et al.,

1992). Categories and features on the other hand, have a meaning for subjects, as they are already part of an existing semantic network. Learning categories and features is akin to associative learning, which has been shown to be preserved in alcoholism (Oscar-Berman and Pulaski, 1997).

In the control group, regressions analyses showed that learning performance was predicted by executive functions during the first half of the protocol. Updating ability may have been required at the start of acquisition in order to revise working memory according to the corrections provided by the experimenter. In subsequent sessions (2 and 3), organizational strategies may have been used to deploy efficient encoding and retrieval strategies. Thus, from Session 4 onwards, the link between semantic learning and episodic memory may be interpreted as the gradual deep encoding of information so that it could easily be retrieved in response to the photos in the cued recall. These results suggest the existence of relationships between semantic learning and other cognitive functions (Cipolotti et al., 2001; Martins et al., 2006; Verfaellie et al., 1995; Verfaellie et al., 2000).

By contrast, in the alcoholic group, no cognitive functions were predictive of the learning performance during the first learning session. Moreover, unlike the controls, alcoholics' performance was predicted by executive functions only in the second half of the paradigm. Active and strategic learning appeared to lag behind compared with the control group, leading to the shallower encoding of the new information in episodic memory. In effect, semantic learning was correlated with spontaneous encoding processes, which were impaired and did not allow the alcoholics to encode information efficiently. Lastly, and unlike the control subjects, the alcoholics' learning results were predicted by short-term passive storage of verbal information. New labels may have been stored in the slave systems of working memory during each session, thus preventing the patients from remembering the answers from one session to the next.

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The comparison of the β coefficients suggested that new labels acquisition requires different cognitive processes in the two groups. Regarding the predictors of the controls, there was no significant difference between the two groups, suggesting that the cognitive processes invoked by the controls are also invoked by alcoholics. On the contrary, the slopes of the two groups were significantly different with regard to the alcoholics' predictors. Thus, alcoholic patients invoked specific cognitive processes in addition to those invoked by controls. In alcoholic patients, labels acquisition may involve both the same cognitive processes as controls and additional cognitive processes to compensate for the previous impaired ones. These compensatory strategies have already been suggested in a neuroimaging study (Desmond et al., 2003).

To sum up, at alcohol treatment entry, the alcoholic patients presented an impairment of novel semantic learning and more specifically a deficit of label acquisition. Compared with controls, alcoholics invoked different and inefficient cognitive strategies (Fama et al., 2004) to attempt to compensate for their impaired episodic and working memory.

Cognitive procedural learning

Statistical analyses showed that the alcoholic patients acquired the new procedure less efficiently than the controls. On the whole, they solved the problem more slowly than the controls and made more moves. However, in terms of the number of moves, alcoholic patients and controls improved their performance at the same rate, whereas in terms of completion time, the two groups performed differently (interaction effect). Previous studies had already reported that alcoholics are slower than controls (Sherer et al., 1992), sacrificing speed for accuracy during learning (Nixon and Bowlby, 1996). However, although the patients had lower levels of performance in terms of completion time in the first sessions, they did not differ significantly from the controls in the last two sessions (post-hoc analyses). Our cognitive procedural paradigm included a sufficient number

of trials for the alcoholic patients to catch up with the controls and achieve similar performance. Thus, in chronic alcoholism, cognitive procedural acquisition is possible, but it is more difficult and takes longer than in non-alcoholic subjects. Nonetheless, although both groups had equivalent results at the end of the protocol, the alcoholics were not at the same stage of learning.

In effect, the controls' performance was linked to nonverbal intelligence in Session 1, indicating that they had reached the cognitive stage of the ACT model (Ackerman and Cianciolo, 2000; Anderson, 1992; Beaunieux et al., 2006). In Sessions 3 and 4, learning was correlated with psychomotor abilities signposting the autonomous stage (Ackerman and Cianciolo, 2000; Beaunieux et al., 2006). The associative phase is currently regarded as a mixed phase (Sakai et al., 1998) and may have corresponded here to Session 2. Unlike the controls, the performance of the alcoholic patients was linked to nonverbal intelligence across all the sessions and was never correlated with psychomotor abilities, suggesting that, even at the end of the protocol, they were still in the cognitive stage or at the beginning of the associative stage of the ACT model.

Impairment of nonverbal intelligence in alcoholism (Barron and Russell, 1992) may be partly responsible for difficulties in acquiring a novel cognitive procedure. However, the deterioration of procedural learning abilities may also be explained by the visual-related deficits that are frequently reported in the alcoholics (Beatty et al., 1996; Sullivan et al., 2000; Fama et al., 2004). A low level of visuospatial processing may hinder the completion of the task, notably involving the analysis of the disks' place on the tower and the respect of a rule based on the colors of the disks. Lastly, these difficulties may also be due to the adverse effects of chronic alcoholism on episodic memory and executive functions, which are known to play a vital role in the cognitive stage of procedural acquisition (Beaunieux et al., 2006). The specific impact of cognitive and visuospatial impairments on the learning deficits revealed by the Tower of Toronto task should be explored in further studies.

Regression analyses showed that the performance of the control subjects was only predicted by the multimodal span task in the cognitive phase (Session 1), multimodal items of information (verbal strategies, visual images of disk configurations) being stored during the resolution stage. From Sessions 2 to 4 (associative and autonomous stages), learning results were no longer predicted by controlled cognitive functions, reinforcing the theory that cognitive procedural acquisition involves nonprocedural functions (Butters et al., 1985; Winter et al., 2001; Woltz, 1988; Xu and Corkin, 2001), mainly in the cognitive learning phase (Beaunieux et al., 2006).

Contrary to controls, the procedural learning performance of the alcoholics was predicted by short-term storage of verbal information, episodic memory and executive functions throughout the protocol. Moreover, the comparison of the β coefficients showed that the two groups had different learning strategies from Session 2. These results reinforce the hypotheses that the alcoholic patients were still in a problem-solving mode at the end of the learning phase and that they implemented higher-order cognitive processes in order to achieve normal learning levels (Fama et al., 2004). Their episodic and working memory deficits may have prevented them from completing the cognitive and associative stages and thus from automating the cognitive procedure.

Taken as a whole, the data suggest that, at alcohol treatment entry, chronic alcoholism may hinder the acquisition of a new cognitive procedure, as the patients were slower and had to make more moves than controls. Even if they managed to attain the same level of performance, by dint of repeating numerous trials, patients were still at a controlled stage of acquisition, and automation of the cognitive procedure would have required many further trials.

CONCLUSION

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The aim of the present study was to investigate semantic and cognitive procedural learning in alcoholic patients at alcohol treatment entry, taking deficits in episodic memory and working memory into account. Our results show that acquiring complex novel information creates problems for alcoholic patients. With regard to semantic learning, label acquisition is genuinely impaired, whereas the acquisition of the category and features is slow but possible. The present study shows a slowdown in the rate of acquisition and the use of different cognitive strategies to compensate for the cognitive deficits (Figure 7) which confirm previous data reported in perceptual learning (Fama et al., 2004), episodic learning (Nixon et al., 1998) and face-name acquisition (Sherer et al., 1992). The implementation of more cognitively demanding and less efficient cognitive processes during novel acquisition is in accordance with fMRI data showing that in cognitive tasks, alcoholics activate inappropriate brain systems, suggesting a functional reorganization (De Rosa et al., 2004; Pfefferbaum et al., 2001). However, our interpretations are based solely on correlational patterns and need to be confirmed by behavioral and imaging experiments.

Insert Figure 7

These findings could have clinical implications for the treatment of alcohol dependence. In effect, cognitive dysfunctions of alcoholic patients have been showed to be linked with the outcome of the treatment (Tapert et al., 2004). Since the classic treatment of alcoholism, notably based on cognitive behavioral treatment (CBT), may rely on the acquisition of novel semantic information or cognitive procedures, not all alcoholic patients may be cognitively able to acquire such complex novel knowledge. Consequently, the current form of treatment may not be appropriate for alcoholic patients with neuropsychological impairments (Tapert et al., 2004). Thus, the assessment of neuropsychological deficits at alcohol treatment entry may prove useful for clinical decision-making and the choice of the most appropriate treatment (Bates et al., 2002). Lastly, our results are in accordance with the findings of Nixon et al. (1998), who suggested that “repetition of material or procedures to be learned would be a useful strategy with alcoholics who

are in educational treatment programs, wherein they are expected to acquire new information that may relevant in later settings”.

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Figure 1: Semantic learning paradigm

Figure 2: Cognitive procedural learning paradigm

Figure 3: Results of semantic learning in terms of label learning (A) and category/features learning (B)

*: significant difference between alcoholic patients and control subjects ($p < 0.05$)

Figure 4: Scatterplots illustrating the relationship between label learning results and free recall after spontaneous encoding in Session 2 in control (A) and alcoholic group (B)

Significant correlation in the alcoholic group ($r_{BP} = 0.63$)

Figure 5: Results of cognitive procedural learning in terms of the number of moves (A) and completion times in seconds (B)

*: significant difference between alcoholic patients and control subjects ($p < 0.05$)

Figure 6: Scatterplots illustrating the relationship between cognitive procedural results (completion time) and N-back task in Session 3 in control (A) and alcoholic group (B)

Significant correlation in the alcoholic group ($r_{BP} = -0.70$)

Figure 7: Contribution of episodic memory and working memory in the learning strategies used by alcoholics and controls in the dynamic course of semantic acquisition and cognitive procedural learning

A) In the control group, semantic label acquisition was initially predicted by executive functions (EF) which may organize the information before it is gradually laid down in long-term episodic memory (EM).

B) In the alcoholic group, semantic label acquisition was impaired. Compared with controls, alcoholics invoked different learning strategies involving episodic memory and executive functions as well, but also the verbal slave system of working memory. Patients might attempt to compensate for their impaired episodic and working memory.

C) In the control group, cognitive procedural learning performance was predicted by the multimodal slave system of working memory in the first session. Controls subsequently ceased to use controlled processes, indicating that they had automated the cognitive procedure.

D) In the alcoholic group, cognitive procedural learning was impaired, even though the patients' performances were similar to those of the controls by the end of the protocol. Patients had a slower rate of acquisition, which was predicted by controlled processes such as episodic memory and working memory, throughout the protocol, indicating a failure to automate the procedure.

Table 1: Main clinical features of participants

| | Control subjects N=20 mean (SD) | Alcoholic patients N=20 mean (SD) | P value |
|---|--|--|----------------|
| Age | 48.4 (5.9) | 47.2 (5.6) | 0.5 |
| Years of schooling | 11.4 (2.3) | 9.9 (2.9) | 0.08 |
| Age of first alcoholic drink | / | 17.7 (3.9) | / |
| Range | | 10-30 | |
| Age of onset of alcoholism | / | 24.6 (8.0) | / |
| Range | | 18-40 | |
| Years of alcoholism | / | 21.8 (8.8) | / |
| Range | | 10-35 | |
| Days of weaning | / | 9.4 (4.9) | / |
| Range | | 3-21 | |
| Quantity (number of standard drinks) | / | 21.3 (10.9) | / |
| Range | | 8-48 | |

SD = standard deviation

Table 2: Results of the Spondee test used to assess episodic memory in alcoholic patients and control subjects

| Encoding | Retrieval | Control subjects | Alcoholic patients | P value |
|--------------------|---------------|-------------------|--------------------|---------|
| | | N=20 mean (SD) | N=20 mean (SD) | |
| Spontaneous | % free recall | 47.8 (14.52) | 37.8 (21.70) | 0.09 |
| | % cued recall | 59.1 (15.37) | 42.8 (23.06) | 0.01* |
| | % recognition | 85.3 (13.94) | 75.6 (17.19) | 0.05* |
| Deep | % free recall | 52.2 (16.26) | 40.3 (18.75) | 0.04* |
| | % cued recall | 88.1 (15.30) | 80.0 (17.28) | 0.12 |
| | % recognition | 95.9 (6.81) | 92.2 (10.31) | 0.18 |

SD = standard deviation

*: significant difference between alcoholic patients and control subjects

Table 3: Assessment of working memory in alcoholic patients and control subjects

| Cognitive functions | | Tasks | Control subjects N=20 mean (SD) | Alcoholic patients N=20 mean (SD) | P value |
|--------------------------|------------------------|--------------------------|---------------------------------------|---|----------|
| Slave systems | Passive storage | Verbal span | 5.9 (1.41) | 4.35 (1.13) | 0.0005* |
| | | Visuospatial span | 5.2 (0.83) | 3.9 (0.91) | <0.0001* |
| | | Multimodal span | 4.7 (0.86) | 3.7 (0.92) | 0.001* |
| Central executive | Organization | Verbal fluency score | 55.5 (13.67) | 43.05 (13.73) | 0.006* |
| | Inhibition | Stroop test (Word Color) | 42.6 (13.33) | 31.1 (11.22) | 0.005* |
| | Updating | N-back task | 93.8 (0.03) | 80.2 (0.13) | <0.0001* |

SD = standard deviation

*: significant difference between alcoholic patients and control subjects

Table 4: Correlations between episodic memory, working memory and semantic learning (label learning)

| Predictive independent variables | | | Session 1 | Session 2 | Session 3 | Session 4 | Session 5 | Session 6 | Session 7 | Session 8 | |
|----------------------------------|----------------------|------------------------|-------------------|---------------------|----------------------|-----------------------|-----------------------|-----------------------|----------------------|-----------------------|----------------------|
| | | | r_{BP} | r_{BP} | r_{BP} | r_{BP} | r_{BP} | r_{BP} | r_{BP} | r_{BP} | r_{BP} |
| Episodic memory | Spontaneous encoding | Free recall | | <i>0.47*</i> | | <i>0.63**</i> | <i>0.52*</i> | <i>0.63**</i> | <i>0.57**</i> | <i>0.59**</i> | |
| | | Cued recall | | | | <i>0.61**</i> | <i>0.49*</i> | <i>0.63**</i> | <i>0.54**</i> | <i>0.60**</i> | |
| | | Recognition | | | | <i>0.45*</i> | | | | <i>0.51*</i> | |
| | Deep encoding | Free recall | | | | <i>0.44*</i> | | | | | |
| | | Cued recall | | | 0.49* | 0.57** | | 0.47* | 0.59** | 0.48* | |
| | | Recognition | | | | | | | <i>0.46*</i> | <i>0.49*</i> | |
| Working memory | Slave systems | Phonological loop | Verbal span | | <i>0.62**</i> | <i>0.80***</i> | <i>0.67***</i> | <i>0.65**</i> | <i>0.65**</i> | <i>0.60**</i> | |
| | | Visuospatial sketchpad | Visuospatial span | | | | | | | | |
| | | Episodic buffer | Multimodal span | | | | | | | | |
| | Executive functions | Organization | Verbal fluency | | 0.50* | 0.53* | 0.49* | <i>0.59**</i> | <i>0.64**</i> | <i>0.69***</i> | <i>0.64**</i> |
| | | Inhibition | Stroop test | | | | <i>0.49*</i> | <i>0.66***</i> | <i>0.50*</i> | <i>0.50*</i> | |
| | | Updating | N-back task | 0.52* | | | <i>0.49*</i> | <i>0.53*</i> | <i>0.53*</i> | <i>0.45*</i> | 0.46* |

Only significant correlations are reported
 Alcoholic patients' data are in bold and italic
 *: $p < .05$; **: $p < .01$; ***: $p < .001$

Table 5: Best predictors of the semantic learning in alcoholic and control groups

| | Best predictors | β coefficient | | Group differences between β coefficients |
|------------------|----------------------------------|---------------------|--------------------|--|
| | | Control subjects | Alcoholic patients | |
| Session 1 | N-back task | 0.52* | 0.26 | NS |
| Session 2 | Verbal fluencies | 0.50* | 0.43 | NS |
| | Free recall/spontaneous encoding | -0.33 | 0.47* | @ |
| Session 3 | Verbal fluencies | 0.53* | 0.33 | NS |
| | Verbal span | -0.06 | 0.62* | @ |
| Session 4 | Cued recall/deep encoding | 0.57* | 0.28 | NS |
| | Verbal span | 0.15 | 0.80* | @ |
| Session 5 | Verbal span | 0.15 | 0.68* | @ |
| Session 6 | Cued recall/deep encoding | 0.47* | 0.26 | NS |
| | Verbal fluencies | 0.18 | 0.69* | @ |
| Session 7 | Cued recall/deep encoding | 0.59* | 0.39 | NS |
| | Verbal span | -0.08 | 0.64* | @ |
| Session 8 | Cued recall/deep encoding | 0.48* | 0.25 | NS |
| | Verbal fluencies | 0.36 | 0.64* | NS |

NS: not significant

*: significant best predictor of the learning session within the group; $p < .05$

@: significant difference between alcoholic patients and control subjects; $p < .05$

Table 6: Assessment of nonverbal intelligence and psychomotor abilities in alcoholic patients and control subjects

| Cognitive functions | Tasks | Control subjects | Alcoholic patients | P value |
|------------------------|--------------------|---------------------------|---------------------------|----------|
| | | N=20 mean (SD) | N=20 mean (SD) | |
| Nonverbal intelligence | Block Design | 21.70 ^a (4.09) | 14.55 ^a (4.90) | <0.0001* |
| | Matrix Reasoning | | | |
| Psychomotor abilities | Disk transfer task | 14.53 (2.77) | 18.42 (3.52) | 0.0004* |

SD = standard deviation

^a= sum of the standard T scores for the two nonverbal intelligence tasks

*: significant difference between alcoholic patients and control subjects

Table 7: Correlations between episodic memory, working memory and cognitive procedural learning

| Predictive independent variables | | | | Session 1 | | Session 2 | Session 3 | Session 4 |
|----------------------------------|----------------------|------------------------|-----------------------|------------------------|------------------------|------------------------|-----------------------|-----------|
| | | | | r_{BP} | r_{BP} | r_{BP} | r_{BP} | |
| Episodic memory | Spontaneous encoding | Free recall | -0.45* | <i>-0.68**</i> | <i>-0.50*</i> | <i>-0.51*</i> | | |
| | | Cued recall | <i>-0.61**</i> | | | | | |
| | | Recognition | | | | | | |
| | Deep encoding | Free recall | <i>-0.54**</i> | | | | | |
| | | Cued recall | | | <i>-0.69***</i> | <i>-0.67***</i> | <i>-0.57**</i> | |
| | | Recognition | | | <i>-0.46*</i> | <i>-0.62*</i> | <i>-0.66**</i> | |
| Working memory | Slave systems | Phonological loop | -0.45* | <i>-0.69***</i> | <i>-0.50*</i> | <i>-0.51*</i> | | |
| | | Visuospatial sketchpad | -0.46* | <i>-0.47*</i> | <i>-0.53**</i> | <i>-0.46*</i> | | |
| | | Episodic buffer | -0.54** | | <i>-0.51*</i> | <i>-0.44*</i> | | |
| | Executive functions | Organization | <i>-0.51*</i> | | <i>-0.53*</i> | <i>-0.55**</i> | <i>-0.46*</i> | |
| | | Inhibition | | | | | | |
| | | Updating | | | <i>-0.68***</i> | <i>-0.70***</i> | <i>-0.48*</i> | |

Only significant correlations are reported

Alcoholic patients' data are in bold and italic

*: $p < .05$; **: $p < .01$; ***: $p < .001$

Table 8: Best predictors of the procedural learning in the alcoholic and control groups

| | Best predictors | β coefficient | | Group differences between β coefficients |
|------------------|---------------------------|---------------------|--------------------|--|
| | | Control subjects | Alcoholic patients | |
| Session 1 | Multimodal span | -0.54* | -0.40 | NS |
| | Verbal span | -0.45 | -0.69* | NS |
| Session 2 | Cued recall/deep encoding | -0.03 | -0.69* | @ |
| Session 3 | N-Back task | -0.15 | -0.70* | @ |
| Session 4 | Recognition/deep encoding | -0.17 | -0.66* | @ |

NS: not significant

*: significant best predictor of the learning session within the group; $p < .05$

@: significant difference between alcoholic patients and control subjects; $p < .05$