



The contribution of executive functions deficits to impaired episodic memory in individuals with alcoholism

Xavier Noël^{a,*}, Martial Van der Linden^b, Damien Brevers^c, Salvatore Campanella^a, Catherine Hanak^d, Charles Kornreich^d, Paul Verbanck^d

^a Belgium Fund for Scientific Research (F.R.S.-FNRS), Psychological Medicine Laboratory, Université Libre de Bruxelles (U.L.B), Brugmann Campus, 4 place Van Gehuchten, 1020 Brussels, Belgium

^b Department of Cognitive Psychopathology, University of Geneva, Switzerland

^c Belgium Fund for Scientific Research (F.R.S.-FNRS), Psychological Medicine Laboratory, Université Libre de Bruxelles (U.L.B), Belgium

^d Brugmann University Hospital, Department of Psychiatry, Université Libre de Bruxelles (U.L.B), Belgium

ARTICLE INFO

Article history:

Received 26 September 2010

Received in revised form 9 October 2011

Accepted 11 October 2011

Keywords:

Alcoholism

Executive functions

Episodic memory

Relapse prevention

ABSTRACT

Individuals with alcoholism commonly exhibit impaired performance on episodic memory tasks. However, the contribution of their impaired executive functioning to poor episodic memory remains to be clarified. Thirty-six recently detoxified and sober asymptomatic alcoholic men and 36 matched non-alcoholic participants were tested for processing speed, prepotent response inhibition, mental flexibility, coordination of dual-task and a verbal episodic memory task. Compared with non-alcoholic individuals, the alcoholic patients showed impaired executive functions combined with below normal performance on both free and delayed recall. In contrast, processing speed, cued recall and recognition were preserved. Regression analyses revealed that 47% of alcoholics' episodic memory's free recall performance was predicted by mental flexibility and that 49% of their delayed recall performance was predicted by mental flexibility, manipulation of dual-task and prepotent response inhibition. Regarding participants' executive predictors of episodic memory performance, the slopes of β coefficients were significantly different between the two groups, with alcoholics requiring more their executive system than non-alcoholics. Once detoxified, alcoholic patients showed episodic memory deficits mainly characterized by impaired effortful (executive) processes. Compared with controls, patients used effortful learning strategies, which are nonetheless less efficient.

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1. Introduction

Alcohol dependence, characterized by compulsive preoccupation with alcohol consumption despite the devastating consequences, which affects social and occupational functioning (e.g. in the area of employment, family, education and health) (American Psychiatric Association, 1994), is a widespread psychiatric disorder with a reported prevalence of approximately 8–10% in many Western countries (World Health Organization, 2004). In agreement with other addictive disorders, individuals with alcoholism are very vulnerable to relapse after cessation of drinking (Anton et al., 2006). Long-term abuse of alcohol, in association with nutritional deficits (thiamin deficiency), can lead to classical neurological illnesses, i.e. Wernicke-Korsakoff syndrome (for a review, see Kopelman, 1995). However, during the last three decades, evidence for brain abnormalities in 'non-Korsakoff' chronic alcoholics has been presented which includes electrophysiological (for a review, see Campanella et al., 2009), morphological and functional metabolism (for

a review, see Sullivan and Pfefferbaum, 2005) as well as a wide range of neuropsychological deficits (for a review, see Bates et al., 2002).

Typical cognitive deficits which characterize a state of alcohol dependence include impaired episodic memory (e.g., Glenn and Parsons, 1992; Schwartz et al., 2002; D'Argembeau et al., 2006; Pitel et al., 2007a) and executive functions (e.g., Joyce and Robbins, 1991; Tivis et al., 1995; Moselhy et al., 2001; Brokate et al., 2003) which are likely to be predominant. By definition, episodic memory (EM) refers to a neuro-cognitive system that enables conscious recollection of personal happenings and events from one's personal past as well as the mental projection of anticipated events into one's subjective future (Wheeler et al., 1997). Importantly, executive functioning is of the greatest importance in EM functioning (Shallice et al., 1994; Tulving et al., 1994; Fletcher et al., 1995; Davidson et al., 2006), in that it facilitates both encoding and retrieval in this memory system (Kapur et al., 1994), maintaining a fixed sequence, and integrating diverse types of information (factual, temporal, spatial) into a meaningful representation (Baddeley, 2000). In the broadest sense, executive function is an umbrella term for all processes recruited for managing and controlling cognition in situations where the routine selection of actions is unsatisfactory and is involved in the genesis of plans and willed actions (Norman and Shallice, 1986;

* Corresponding author. Tel.: +32 24772705.
E-mail address: xnoel@ulb.ac.be (X. Noël).

Miyake et al., 2000). As explained by Moscovitch and Winocur (1992), executive functions are involved in the conscious and strategic aspects of memory performance which may operate at both encoding and retrieval phases; this can be considered as “working-with-memory processes”, which improve memory functioning through the use of efficient strategies. Our hypothesis therefore relates to the fact that a decline in executive functioning, which is a hallmark of alcoholism, is involved in frequently reported impairments of episodic memory (EM).

In individuals with alcoholism (and abstinent for a period ranging from several days (Pitel et al., 2007), to several months (Munro et al., 2000) and even years (Brandt et al., 1983)), EM disorders have been identified with the help of psychometric tasks such as the Wechsler Memory Scale (e.g., Glenn and Parsons, 1992; Fama et al., 2004), the learning of face-name associations (e.g., Beatty et al., 1995; Tivis and Parsons, 1995), lists of words (e.g., Brokate et al., 2003; Hildebrandt et al., 2004), and even addresses and stories (Fama et al., 2009). However, the underlying processes for this EM impairment and related brain structures remain unclear (see the critical view by Pitel et al., 2007a). Some findings suggest that effortful retrieval and encoding processes are impaired in chronic alcoholism (Weingartner et al., 1996; Schwartz et al., 2002; Pitel et al., 2007a; Chanraud et al., 2009). For example, memory tasks, which measure accuracy in judging the source of what is remembered and require reflective processes (i.e., self-monitoring performance and suppress cognitive responses), showed that a subsample of alcoholics made errors in accurately identifying the source of correctly remembered knowledge (Weingartner et al., 1996). Such findings suggest that cognitive processes underlying alcoholics' episodic memory disorders are worthy of further clarification.

In addition to EM abnormalities in non-amnesic alcoholics who are recently detoxified, disturbances in the executive system are one of the most consistent and predominant impairments in sober alcoholics (e.g., Joyce and Robbins, 1991; Dao-Castellana et al., 1998; Noël et al., 2001b; Brokate et al., 2003; Oscar-Berman et al., 2004). Indeed, such patients are generally less efficient than comparison subjects controls in carrying out two tasks simultaneously; for example, to inhibit prepotent response, to detect rules, to shift between multiple sets of responses and to plan and to generate concepts.

One interesting study showed that alcoholics had reduced mental flexibility, when assessed by verbal fluency tasks, which accounts for approximately 40% of diminished free recall performance (Pitel et al., 2007a). However, some issues remained to be addressed. Firstly, the impact of a general slowing down of processing speed which was not assessed in this study. Secondly, patients were tested only at the start of alcohol detoxification whereas the neuropsychological profile of alcoholic subjects receiving treatment evolves rapidly during the first 3 weeks (e.g., Carlen and Wilkinson, 1983; Bartsch et al., 2007). Thirdly, this study (Pitel et al., 2007a) did not include important aspects of executive functioning that may impact on effortful aspects of both encoding and retrieval of episodic memory. This includes suppression (inhibition) of pre-potent response or the capacity to realize two tasks simultaneously (Repovs and Baddeley, 2006; Clarys et al., 2009). Finally, in the present study, we tested inpatient alcoholic subjects who had been sober for 3 week on average and 1 week after stopping all detoxification medication. This period corresponds to the moment when patients are usually discharged from the alcohol detoxification program, which increases the clinical interest of this article. We hypothesized that poor mental flexibility, prepotent response inhibition and difficulty in the coordination of dual tasks would be responsible for poor verbal recollection in sober alcoholics' episodic memory.

2. Method

2.1. Participants

2.1.1. Alcoholic patients

Thirty-six male alcoholic patients were recruited for this study from the Alcohol Detoxification Program of the Brugmann Psychiatric hospital at Brussels. They all

received a complete medical, neurological, and psychiatric examination at the time of selection. Exclusion criteria were, a) other current DSM-IV (American Psychiatric Association, 1994) diagnoses for axis I than alcohol dependence, b) a history of significant medical illness, c) head injury which resulted in loss of consciousness for more than 30 min that would have affected the central nervous system, and d) prescribed medication that could influence cognition or overt cognitive dysfunction as assessed by the Mini-Mental State Examination (MMSE < 24, Folstein et al., 1975). To increase the reliability of anamnestic information, the patient and their family were interrogated separately. All alcohol abusers had consumed at least 560 g of alcohol (e.g., ± 8 drinks per day) for at least 2 of the 3 years preceding entry into the study. The detoxification regime consisted of B-vitamins and various doses of sedative medication (Diazepam). After a complete description of the study to the subjects, written informed consent in accordance with the declaration of Helsinki was obtained.

Current clinical status was rated on the self-administrated Montgomery and Åsberg depression rating scale (Montgomery and Åsberg, 1979) and the Hamilton Anxiety Rating Scale (Hamilton, 1959). Clinical and demographic measures are presented in Table 1.

2.1.2. Healthy participants (CONT)

The healthy individuals comprised 36 male volunteers, recruited by word of mouth. They were matched for gender, education and age. All the subjects provided written informed consent and were not paid for their participation. All included participants were drug-free (self-report and urine drug screening), had no Axis I diagnoses (American Psychiatric Association, 1994), and, on the basis of their history and physical examination, they were judged to be medically healthy. They were also excluded if there were histories of excessive substance use (e.g., an average of three drinks or more per day over the last year or more than occasional drug use). They were advised to avoid both alcohol and other substance abuse drugs in the 24 h prior to testing as well as narcotic pain medication for the 5 days prior to testing.

All subjects underwent an alcohol breathalyzer test on arrival at the laboratory.

2.2. Cognitive evaluation

2.2.1. Processing speed

In order to measure processing speed, the time to complete the part A of the Trail Making test, the color-naming and the reading parts of the Stroop test were considered.

2.2.1.1. Episodic memory. California Verbal Learning Test (CVLT; Delis, 1987; Delis et al., 1988; French adaptation, unpublished data). The CVLT consists of five learning trials of a 16-word target list comprising four words from four different semantic categories. The list is read aloud by the examiner at the rate of one word per second. After each trial, the examinee was instructed to freely recall as many words as possible, in any order. A similarly constructed interference list was then presented for one learning trial, followed by 'short-term' free and cued recall of the target list. After a 20-min interval filled with non-verbal tasks, 'long-term' free recall, cued recall, and recognition were assessed. The recognition condition used a yes/no paradigm, with 28 distractors mixed in with the 16 targets. The CVLT yields measures of recall, recognition, learning characteristics, and intrusion and perseveration errors. The recall and recognition measures used in this study were (i) free recall on the immediate (as well as the number of intrusions) and long-term conditions, (ii) total number errors (intrusions plus perseveration) and (iii) the number of correct hits on recognition (Table 2).

2.2.2. Working memory, coordination of storage and manipulation of information

Alpha-span task (Belleville et al., 1998). This task investigated the ability to manipulate information stored in working memory by comparing the recall of information in serial order (implicating mainly a storage component) and in alphabetical order (implicating storage and manipulation of information). Firstly, a classical word-span task was administered to assess the span level of each subject. After the span measurement, the subject

Table 1

Mean (SD) scores on demographic and clinical variables of alcoholics and healthy participants.

	Alcoholics (n = 36)	Healthy participants (n = 36)
Age	43.3 (11.1)	40.9 (10.9)
Years of heavy drinking	14.4 (12.0)	-
Education (total years)	12.0 (2.9)	11.8 (3.6)
TLIE (kg/kg) ^a	27.2 (5.2)	2.0 (0.7)***
Number of drinks per day	17.2 (9.3)	1.9 (1.1)***
Number of prior detoxification treatments	2.4 (1.8)	-
Number of abstinence days	21.8 (0.3)	-
MADRS ^b score	11.0(6.3)	3.7 (1.5)***
Anxiety ^c	12.3 (6.2)	3.1 (1.9)***

Significant difference, * $p < 0.05$, ** $p < 0.01$, *** $p < 0.001$.sa.

^a TLIE, total lifetime intake of ethanol.

^b MontgomeryÅsberg Depression Rating Scale.

^c Hamilton Anxiety Rating Scale.

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