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Decreased verbal learning but not recognition performance in unmedicated alcohol-dependent patients during early abstinence

Isadora Duncan, PhD,^{1*} Richard Coer de Lion, MD,^{2*} Julia Kropotkin,³ Franziska Nunn,³
Jana Montana, PhD,⁴ Diana Knoll, PhD,¹ Tom Bosch, MD,⁵ Kindli Fresser, PhD,³
Heino, MD,⁴ Thorben Windbald, MD,⁴

¹ *Institute of Medical Psychologology, Topanga, California*

² *Clinic of Psychiatry, Waco, Texas*

³ *Department of Psychology, University of Tobasco*

⁴ *Department of Psychiatry and Psychotherapy, University of Belgravia*

⁵ *Department of Psychiatry and Psychotherapy, Bedlam*

Corresponding author:

Thorben Windbald, MD
Department of Psychiatry and Psychotherapy, Bedlam
Primrose Lane
London, U.K.
Tel. +42-32-4230 2060
Fax +42-32-4230 2903
e-mail: thorben.windbald@bedlam.uk

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Abstract

Objective. Alcoholism ultimately leads to impairment of memory and other cognitive functions. This can interfere in treatment, if cognitively-impaired alcoholics have difficulty recalling and implementing skills acquired during therapy. We predicted that alcoholics without clinically apparent withdrawal symptoms may still be impaired in higher-order cognitive functions. To test this claim, we measured verbal learning and other aspects of cognitive function in unmedicated patients at an early stage of withdrawal.

Methods: 34 severely ill alcohol-dependent patients and 20 matched healthy controls were tested with the Verbal Learning and Memory Test which includes seven measurement points; these include free recall after distraction, and after 30 min delay, and one word recognition task. Testing was performed between day seven and day 10 after the beginning of abstinence, when clinical withdrawal symptoms had ceased.

Results. The patient group performed worse in free recall ($F(1,50)=14.28$, $p<.001$, partial $\eta^2=.22$), but not in word recognition, in comparison to the healthy control group. Furthermore, the patients had reduced total verbal learning efficiency ($F(1,52) = 14.17$, $p < .001$, partial $\eta^2 = .21$). The extent of impaired recall after distraction correlated with the number of years since diagnosis for alcohol dependence ($r=.39$, $p=.01$).

Conclusions. Our results provide evidence that unmedicated alcohol-dependent patients without obvious withdrawal symptoms had impaired verbal recall, but normal recognition performance, at seven to ten days after onset of abstinence. This deficit may impair treatment outcomes due to poorer implementation of skills newly-learned during this time period.

INTRODUCTION

Clinical evidence shows that chronic alcohol consumption, as well as early alcohol withdrawal, leads to long-term cognitive impairment and **decreased memory** function (Brown et al., 2000; Seifert et al., 2003; Seifert et al., 2004). Cognitive deficits related to alcohol consumption have been found in several **domains, including** problem solving, verbal and non-verbal abstraction learning, **and** memory consolidation (Parsons, 1998; Davies et al., 2005). **Results of** a number of studies have **shown impaired** memory capabilities such as verbal recall and verbal recognition performance in alcoholics **as compared** to outcomes in **other (substance abuse?)** clinical groups **or** healthy controls (table 1). Most of **these** studies indicate that alcoholics perform **relatively** worse in recall than in recognition tasks (Tivis et al., 1995; Uekermann et al., 2003; Seifert et al., 2003) ~~compared to different clinical groups as well as healthy controls~~ (**redundant**) (Davies et al., 2005; Pitel et al., 2007).

Studies focussing on the memory dimension of verbal recall revealed impairments in alcoholics on the first day of acute alcohol withdrawal (Seifert et al., 2003). **Furthermore**, impaired cognitive efficiency **and reduced** verbal short-term memory capacity seemed deteriorated compared to healthy controls **for as long as** five weeks after alcohol **cessation of alcohol** consumption (eg. Mann et al., 1999). In **alcoholics**, verbal **free** recall performance was impaired **in comparison** to patients with depression (e.g. Uekermann et al., 2003). The quality of verbal recognition **was poorer in** alcoholics than **in** controls (Sullivan et al., 1997), as **was** order recognition **in comparison to** schizophrenic patients and healthy control subjects (Sullivan et al., 1997). Verbal recall **was impaired in** alcoholics, **and to an even greater extent in patients** suffering from polysubstance abuse and concurrent alcohol abuse (Medina et al., 2006), **although other report that** recognition memory **was impaired to a similar extent** in alcoholic patients **and** polysubstance abusers (Medina et al., 2006). -----

*insert **table 1** (synopsis of articles) -----*

The findings in alcoholics described **above seem reminiscent of the dramatic** loss of verbal memory in patients with dementia, amnesia, Alzheimer's disease (**or dementia?**), or

Korsakoff's syndrome. Thus, recall performance of amnesic patients is poorer than that of control subjects (Giovanello and Verfaellie, 2001), and patients with alcohol-related dementia exhibit more deficits in delayed verbal recall as well as verbal recognition performance than did patients with subcortical vascular dementia (Schmidt et al., 2005). The pattern of greater deficits in recall than in recognition memory in alcohol-dependent patients is itself evocative of the initiation-retrieval difficulties of patients with subcortical dysfunction (Bondi et al., 1998). Alcohol dementia patients seem more impaired in free recall, though, they do not differ from controls in verbal recognition memory, in contrast to patients with Alzheimer's disease, who also had impaired recognition memory (Saxton et al., 2000). Finally, a study on patients with Korsakoff's syndrome provides evidence that recognition memory is facilitated by first learning names of objects, whereas verbal generation as well as performing a specific action facilitate recall performance (Mimura et al., 2005). ~~Therefore, action memory might be of interest regarding consolidation processes in alcoholics. (seems a bit too speculative)~~ These findings suggest that alternate learning strategies may be of general utility in conditions of memory impairment.

It is generally accepted that new acquired memories are normally first retained in a fragile state, and then consolidate over time (McGaugh, 2000). This slow consolidation of memories may serve as an adaptive function, enabling the contribution of physiological processes modulating memory strength (McGaugh, 2000; Nielson and Powless, 2007). It is this consolidation process, rather than retrieval, which may be disturbed in alcoholics (Sherer et al., 1992). The second component of verbal memory, the performance of recognition performance has been modelled as a dual-process (Jacoby, 1991; Mandler, 1980), in which recollection is first obtained by a conscious, effortful process in which a prior aspect of an experience is retrieved, to be followed by the subjective experience of familiarity, which arises when fluent processing of a stimulus is attributed to prior experience with that stimulus (Jacoby and Dallas, 1981; Giovanello and Verfaellie, 2001; Gardiner, 1988). Studies in amnesic patients show disproportionate deficits during recollection of newly acquired

memory contents (Aggleton and Shaw, 1996; Mayes et al., 1995; Verfaellie and Treadwell, 1993; Yonelinas et al., 1998). However, there is also evidence that both axes, i.e., recollection and familiarity, are equally impaired in this group (Reed and Squire, 1997, 1998; Squire and Knowlton, 1995). The status of the dual model of memory retrieval in alcoholics is not yet established.

A number of studies have been investigating the neuropsychological performance of intoxicated alcoholics, or as a function of duration of abstinence (table 1). However, there are no available data on verbal recall and recognition performance of severely ill, but drug-free alcohol-free or non-medicated?, patients in an early condition of withdrawal, just after cessation of acute withdrawal symptoms. This time point is of critical interest, because such patients are often discharged from intense treatment, and have then to implement their newly learned strategies for maintaining abstinence, in spite of possible memory deficits. The only study measuring memory deficits in alcoholics during early abstinence suffers from rather large standard deviation in the cognitive function end point (Pitel et al., 2007).

The objective of this study was to investigate the extent of verbal memory deficits during the first days of abstinence. Because the cognitive deficits found in alcoholics typically manifest in tasks of higher-order cognitive function (Noel, et al., 2001; for a review see Moselhy et al., 2001), we selected (a) task that measures the ability to recall and recognize words without a specific context (VMLT test, Helmstaedter et al., 2001). We tested the prediction performance (of this learning) task would be impaired in a group of alcoholics in comparison with healthy controls, most especially in the more complex task of free recall versus the lower order cognitive task of word recognition.

METHODS

Study population and diagnostic procedures

The local ethics committee approved the study according to the declaration of Helsinki and written informed consent **was provided by** all participants after the procedures had been fully explained. All patients were inpatients, recruited **at** the Psychiatrische Universitätsklinik of the Charité **Hospital**, in the St. Hedwig Hospital, Berlin, as well as in the Jewish Hospital, Berlin. Each patient **had a** physical **examination, and** a psychometric **assessment was based upon** the structured clinical interview for DSM disorders (**SCID-I, First et al., 2001**). **Included patients** fulfilled DSM-IV criteria for alcohol dependency, had no other axis I disorder, and no active medical or neurological disorder **of substantial nature**. The alcoholic group included 34 (28 male) severely ill alcohol-dependent **inpatients of mean age** 44 years (SD = 8). The **mean extent of** school education was **10.0 years (SD = 1.4), and 27 had** completed vocational education, **five had** finished academic degrees, and **one had** started attending university; **one** patient did not respond to the question about **education history**. Patients reported having had their first drink at a **mean** age of **14.9 years (SD = 3.9)**, (**you tend to report too many decimal places; 0.01 years is four days**), and their first intoxication (**do you mean intoxication requiring hospitalization or medical treatment? Intoxication can mean simply to get drunk**) at a mean age of 23.5 years (SD = 9.1). **Nine patients reported no previous hospitalization, whereas the remaining 25 patients** reported a mean of 8.6 (SD = 9.7) prior **detoxifications(??)** in an inpatient setting. Patients had a **mean** of 18.4 years (SD = 10.0) **since** diagnosis with alcohol dependence. The mean pure **ethanol** intake during the past **five** years was 219 kg (SD = 172) alcohol per patient. (**is that per year? 219 Kg in five years works out to a bottle of wine per day, the French national average**) All patients underwent acute alcohol detoxication including complete alcohol abstinence in an inpatient setting starting 7-10 days before **entry** into the study. **Severity of** acute alcohol withdrawal symptoms **was** measured up to a maximum of 12 times a day **with** the alcohol withdrawal scale (**AWS, Wetterling et al., 1997**). **Withdrawal was supported by medication in those with a (daily mean?) AWS score of 10 or higher.** At admission, patients had a mean **AWS score** of 7.5 points (SD = 3.2); 20 patients **exceeded** the AWS cut-off score, **and were consequently** treated with diazepam, clomethiazole, or carbamazepine for a mean of **4.7** days (SD = **3.9**).

In patients reporting history of seizures or delirium during previous withdrawal, medication was administered when AWS scores were 6 to 8. Other than the anti-seizure medications, some patients received haloperidol for the treatment of visual hallucinations, and/or clonidine for the treatment of high blood pressure. Once a treatment was started, the medication was reduced stepwise during the following days. 12 of the 34 patients reported having had delirium, and 12 reported having had seizures during previous withdrawals. Of these, two patients reported having had delirium but no seizures, whereas one patient reported having had seizures but no delirium. During our inpatient program, there were no cases of delirium or seizures. The day before the assessments of cognitive function, no patient showed clinical symptoms of alcohol withdrawal syndrome. Only patients without psychotropic medication (meaning what in this context? I thought psychotropic meant hallucinogenic) or those who at least discontinued four half-lives before study begin were included enter the study.

The comparison group included 20 (13 male) healthy subjects with no lifetime psychiatric diagnosis, no clinically significant medical or neurological history, no acute medication and no history of alcohol abuse or alcohol dependency according to DSM-IV and ICD-10. The mean age was 44.4 years (SD = 13.1), with mean school education of 10.0 years (SD = 1.5). After school, 12 participants had finished vocational education, five had finished their academic studies, two had started attending university; one volunteer did not respond to this question. The comparison group was deliberately matched for age, sex, schooling and vocational education. Where did you find the volunteers? To here