Response Inhibition and Decision–Making of Alcohol - Dependent Patients without Amnesic Syndrome

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Introduction

Most of the research on alcohol toxic effects on the brain revealed neuronal degeneration, hypoperfusion and functional changes of the prefrontal cortex in detoxified alcoholics without amnesic syndrome, but with a long history of alcohol dependence. Recently, the results of two studies of our group suggested a non impaired dorsolateral prefrontal cortex, indicated by the unaffected working memory performance, irrespective of increasing interference (Brokate et al., 2003, in press, Hildebrandt et al., submitted). We concluded that the ventromedial prefrontal cortex was sensitive for the alcohol toxic effects, resulting in deficits regarding response inhibition, object alternation and set shifting. Moreover, the alcoholics could not reliably maintain internal cues, maybe because of the problem with reward learning. Bechara et al. (1998, 2001) pointed out that alcoholics and patients with ventromedial lesions had a lot of similarities in proceeding on the gambling task. They showed no advantageous strategy but were insensitive to positive or negative future consequences. Their behavior was guided by immediate prospects. Disinhibition and sensibility for reward were an important issue for alcoholics, both on a behavioral and on an experimental level. Our aim was to replicate the results of Bechara et al. (2001, 2002) that alcoholics were impaired in decision-making in the gambling task, and to compare the results with several flexibility and shifting tasks, which are sensitive to the ventromedial frontal cortex. We further included the incompatibility task, in order to determine whether spatial effects had an influence on the performance of the executive tasks.

Methods

Patients

The sample consisted of 30 alcoholics and 15 controls. Alcohol dependence was diagnosed according to the criteria of ICD 10, F 10.2. The alcoholics were inpatients of a psychiatric hospital in a detoxification program. They abstained from alcohol for, on average, 18.6 days before participation. At that time, they had no withdrawal symptoms and no medication treatment except for Vitamin B. Length of alcohol dependence, somatic illness and biographical details were established on the basis of a semi-structured interview and of the medical record. Subjects with a history of head injury, an important liver disease, other somatic illnesses or polydrug use were excluded. None of the patients had a history of Wernicke encephalopathy or could be regarded as suffering from an amnesic syndrome. For a more detailed description of the alcoholic sample, we used the Beck Depression Inventory (German version: Hautzinger et al., 1994) and the Michigan Alcoholism Screening Test (Selzer, 1971). Subjects were matched on intelligence scores, age and education, so that we had to exclude 2 alcoholics and 2 members of the control group from further investigation. The control group had been admitted to the hospital for treatment of a disease of the peripheral nervous system, e.g., intervertebral prolapses or peripheral facial paresis, the participants were treated for about 3 to 10 days. A detailed description of the participants is given in Table 1.

Table 1: Description of the samples in means and standard deviations

Sample	Alcoholics N = 28	Controls N = 13
Age (years)	45.79 +/- 9.71	48.69 +/-11.06
Years of Education at School	9.64 +/- 1.47	10.31 +/- 1.67
Years of Alcohol Dependence	14.21 +/- 9.14	
Days after Detoxification	18.68 +/- 8.94	
Beck Depression Inventory	16.29 +/- 11.19	
Michigan Alcoholism Screening Test	33.36 +/- 9.89	
MWT Intelligence (T–score)	53.96 +/- 11.02	52.77 +/- 10.47
LPS Intelligence (T-score)	51.59 +/- 5.22	54.83 +/- 5.01
TAP Alertness without warning tone (reaction time in ms)	273.43 +/- 68.45	311.77 +/- 113.57
TAP Alertness with warning tone (reaction time in ms)	266.95 +/- 83.88	298.31 +/- 92.67

Procedure

First, we used the subtests 3,4 of the ”Leistungs-prüfsystem” (LPS; Horn, 1983) as a measure of general intelligence. These subtasks require the subject to find an abstract rule underlying a particular sequence of symbols (numbers, letters, geometrical figures), in order to reject a false item within a series. Premorbid intelligence was subsequently assessed with a word/non-word discrimination test, (”MWT” by Lehrl et al., 1991). The Alertness Test of the ”Testbattery of Attention Assessment” (TAP; Zimmermann & Fimm, 1992) was used to measure simple reaction time in two different conditions: with and without a warning tone. Then the verbal memory performance was assessed using the California Verbal Learning Test (CVLT: German version, following Ilmberger, 1988) to make sure that only alcoholics without amnesic syndrome were included.

Additionally, we used the subtest ”alternate response" (Stage II & Stage III) of the TAP. In this task, a letter and a number were presented simultaneously on a computer screen for 100 trials. One stimulus appeared on the right, the other on the left side; sides varied randomly. A left and a right response button were available to the participant. In the spatial response condition, the subject had to press the button on the side the number appeared. In the response shift condition, the subject had to press on the side of the letter and of the number, alternately.

The reaction times, number of errors and hits were used for analysis. In the “incompatibility” of the TAP, a point in the middle of the computer screen had to be observed, while an arrow on the left or on the right side appeared. The arrows pointed to the right or to the left in a random sequence. The participant had to press the right button if the arrow pointed to the right side, and the left button if the arrow pointed to the left side. The reaction times and errors were compared under two conditions : the compatible condition, in which the position and the direction of the arrow corresponded, and the incompatible condition, in which they did not. Furthermore, we used two different word fluency tasks, category word fluency (animals, jobs and furniture) and phonologic fluency (words on L, P, R).

Gambling task: “The task involves four decks of cards called A, B, C, and D. In two decks (A and B), choosing a card is followed by a high gain of money, but at unpredictable points, the selection of a card is followed by a high penalty, so that in the long run, these decks are disadvantageous. In the other two decks (C and D), the immediate gain is smaller, but the future loss is also smaller, so that in the long run, these decks are advantageous. More specifically, the schedules of reward and punishment are structured in such a way that the discrepancy between reward and punishment in the disadvantageous decks (A and B) is rendered larger in the negative direction. That is, the net difference between reward and punishment in each block of 10 cards was set up in such a way that this difference in decks A and B increased in the negative direction across each block (i.e. towards larger loss). By contrast, this discrepancy between reward and punishment in the advantageous decks (C and D) is rendered larger in the positive direction, i.e. this difference in decks C and D increased in the positive direction across each block (i.e. towards larger gain). The total number of trials was set at 100 card selections. To score the performance of the subject on the GT, the number of cards picked from decks A and B are added in each block of 20 cards, and the number of cards picked from decks C and D are added separately in each block of 20 cards. A net score is then obtained by subtracting the total number of cards selected from advantageous minus disadvantageous decks ((C+D)-(A+B)) for each block of 20 cards.” (Bechara et al., 2002).

Intra- Extradimensional Shift of CANTAB: Subjects were tested in their ability to attend to specific attributes of compound stimuli and to shift that attention when required. Color filled shapes and white lines were used as test dimensions, and the subject had to learn which of the stimuli and the compound stimuli is correct, and had to react flexibly when the category changed.

We compared all the data of the alcoholics with those of the controls by means of non parametric Mann Whitney U- Tests, and we computed Spearman correlation coefficients for the executive data and the data of the alcoholic history.

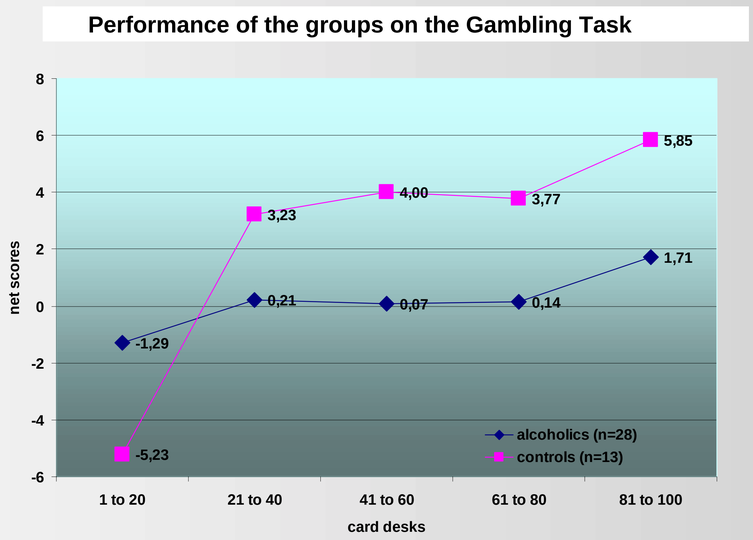

Figure 1: The figure shows net scores ((C+D)-(A+B))of cards selected by each group across different blocks expressed as mean. Positive net scores reflect advantageous performance while negative net scores reflect disadvantageous performance.

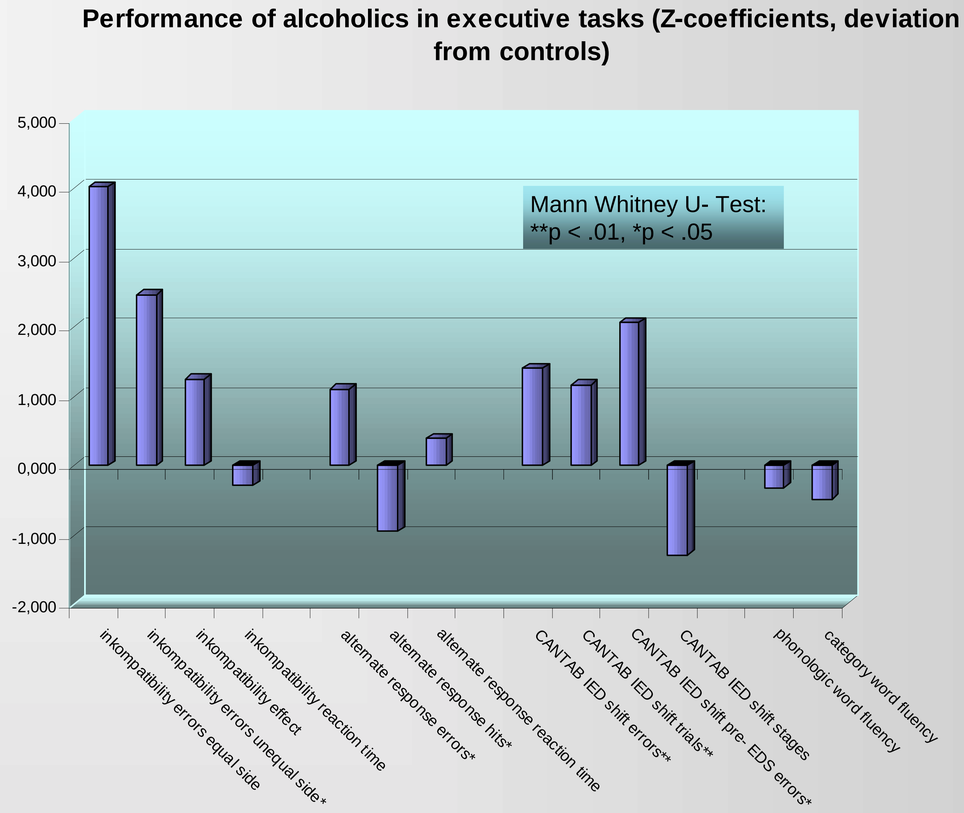

Table 2: Significant Spearman Rho correlation coefficients between the executive tasks for alcoholics (irrespective of logical thinking ability scores (LPS))

	Alternate response hits	Alternate response errors	Gambling 61 to 80	Gambling 81 to 100
IED total errors	-.550**	.494**		-.388*
IED completed stage trails	.392*	-.379*		
IED stages	.567**	-.519**		
IED pre EDS errors			-.491**	-.427*

*p < .05; **p < .01

Results

The alcoholics and the control group did not differ in age, education and aspects of pre-morbid and logical intelligence. Alcoholics showed no memory dysfunction in the CVLT. The results indicated a significant difference between alcoholics and controls in alternate response, in the errors of the incompatibility task, in the gambling task and the shift task of the CANTAB, but no differences in the word fluency tasks. (see figure 2). Though the non parametric Mann Whitney U-Test showed a significant difference in the gambling task at one stage only, a variance analysis with repeated measures yielded a significant interaction effect of group* net scores [F (1,39) = 3,564; p=.008]. At the beginning of the gambling task the controls showed a decision behavior which was highly risky, but they adapted after 20 trials. They reacted differentially after punishment and reward. The decision making of the alcoholics remained at the same level throughout the 100 trails, meaning the alcoholics chose in approximately equal frequency from the four decks. Because of the unchanging reaction behavior in all five levels, we interpreted the behavior of the alcoholics as ineffective, inadequate and lacking a learning effect. In the shift task of the CANTAB alcoholics produced significantly more errors and a lower number of correct trials, while the completion of stages was not different for the groups. The error control was generally diminished for alcoholics in the incompatibility task, but there were no group differences in the subtraction score of compatible and incompatible errors, which indicated no disturbed inhibition effect for spatial attention shifting. In the alternate response task alcoholics produced significantly more errors, which could be interpreted as a deficit in response inhibition. The executive tasks were correlated for alcoholics and controls, but there were some group differences. For alcoholics, the performance in the gambling task and the alternate response task was related to the CANTAB IED, if influences of intelligence were deleted, while for controls the performance in the gambling task correlated with the CANTAB parameters and word fluency (see table 2).

Discussion

Our aim was to investigate the performance of alcoholics and controls in the gambling task, which has been recently shown to be sensitive for the ventromedial cortex, but not for areas of the dorsolateral prefrontal cortex. Several studies by Bechara et al. (1998, 2002), using this task, revealed clear evidence for this assumption and showed deficits of alcoholics and substance abusers in this task. We were able to replicate this finding: alcoholics and controls differed significantly in advantageous strategies and revealed net scores of performance nearly equal to those of the subjects of the Bechara et al. (2002) study. Furthermore, we could replicate the results of our earlier studies concerning the deficiencies in the alternate response task of the TAP (Brokate et al., 2003; Hildebrandt et al., submitted). The alcoholics showed deficits in response inhibition in the alternate response task and in the incompatibility task in general, but not concerning the inhibition of a false spatial reaction. In the shift task of the CANTAB alcoholics produced significantly more errors and a lower number of correct trials, whereas the amount of completed stages was not different for both groups. We interpreted these results in line with the TAP results as indicating a diminished response inhibition and error control. The important parameters of the alternate response task, the gambling task and the shift task of the CANTAB were significantly correlated for alcoholics, so that we concluded that the diminished maintenance of internal rules by the alcoholics leads to dysfunctions in action control. On a behavioral level alcoholics tend to repeat actions, for example drinking related actions, while they believe to be engaged in abstinent behavior. Another inter-pretation, which we were not able to prove with neuropsychological tests only, is that alcoholics use different frontal areas to perform tasks of response inhibition compared to controls, as Pfefferbaum et al., (2001) could show concerning spatial working memory. Furthermore, two variables of the IED Shift task were correlated with the amount of daily alcohol consumption, which indicated a relation between diminished error control and alcohol toxic effects. Our results support the assumption that alcohol affects cortical areas which have been associated with reward circuits. Chronic alcohol consumption destroys the brain reward system, followed by alcohol craving and ignorance of relevant internal cues (Braus et al., 2001; Robinson et al., 2003).

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