Conditional responding, but not decision-making is impaired in alcohol-dependent participants without amnesia

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Abstract: Bechara (2003) puts forward a model of disturbances in executive functions related to addiction. This model involves deficits in decision-making and in suppressing pre-potent representations or response patterns. In this study we tested this model in 29 individuals with long-term heavy alcohol dependency and compared their performance with that of 20 control subjects. Only individuals without memory impairment, with normal intelligence and normal visual response times were included. We examined word fluency, object alternation, spatial stimulus response incompatibility, extra-dimensional shift learning and decision making using the Gambling task, and subtracted the performance in a control condition from that of the executive condition, in order to focus specifically on the executive component of each task. Only object alternation and incompatibility revealed significant differences between the group of alcoholics and the control group. Moreover, response times in the object alternation task correlated with duration of alcohol dependency. We conclude that long-term alcohol abuse leads to an impairment in conditional responding provided the response depends on former reactions or the inhibition of pre-potent response patterns. Moreover, the results do not argue in favour of a specific deficit in decision-making or in shifting between relevant representations.

Key Words
Addiction
Alcohol
Conditional responding
Risk taking
Response suppression
**Introduction**

In recent years, neuropsychological aspects of addiction have received considerable interest. Bechara (2003) gives a comprehensive review of the kinds of executive function disorders which may contribute to substance dependency. According to his view there are two different kinds of impairment related to addiction. The first concerns the correct representation of gains and losses in ill-defined or partly stochastic environments. Individuals have to weigh the direct and indirect future consequences of choices between action alternatives. Healthy individuals learn to avoid choices which are risky in the long run, although these choices may be superior in terms of short-term reward. Substance dependent individuals may fail to anticipate the future consequences of their behaviour. They may be unable to develop a cognitive and/or affective balance of short-term and long-term consequences. This kind of deficit is related to a lack of emotional threat aroused by an internal representation of future events, maybe due to a loss of specific affective states as such. The Gambling Task (GT), developed to investigate the behavioural consequences of ventromedial prefrontal lesions (Manes et al., 2002; Mavaddat et al., 2000; Bechara et al., 2000; Damasio et al., 1991), has mainly been used to study this kind of deficit, because it allows for an investigation of strategies in relation to actual and future rewards and punishments dependent on the choices an individual makes. Several studies have shown that at least a portion of substance dependent patients behave in the GT like patients with ventromedial prefrontal lesions, i.e. they do not develop a response strategy which avoids risky decisions.

The second cognitive deficit discussed by Bechara (2003) is the inability to suppress responses in specific situations. Obviously, this kind of executive deficit mainly concerns the direct monitoring and controlling of behaviour, because the individual is confronted with a choice affectively and cognitively known to produce negative results, at least in the long run. Bechara (2003) mentions three different explanations for a lack of response suppression. The first is a pre-potent representation of a specific environmental stimulus forcing the individual to look for it and to react to it. The dependence on such a pre-potent stimulus would prevent the individual from changing his behaviour as long as such a stimulus is available. The important paradigms in this context are the Wisconsin Card Sorting Test and the intra- and extradimensional shift learning from the CANTAB. The choice of only one pattern of responding would produce a high number of perseverations and prevent successful shift learning.
The second explanation of a deficit in response suppression concerns a kind of perseveration of a behavioural set. In this case, irrespective of the context, the individual sticks to a specific action pattern. The major impairment is an inability to refrain from a specific behavioural pattern and not from a pre-potent representation of an external stimulus. From a neuropsychological viewpoint, typical paradigms testing for such a deficit are Go/NoGo tasks, in which a specific response is triggered for example by frequency (e.g., the SART) or by features of the stimuli (e.g., the STROOP), but this response has to be inhibited due to the specific task instruction. The third and last explanation concerns the flexibility to shift between different responses solely because of an internal state, i.e., independent of the external situation. On the emotional level, a typical reason to shift behaviour would be saturation, on a cognitive level this could be due to task instructions, like in the object alternation task. In the object alternation task the preferential object is totally determined by an inner rule and not by environmental features. Substance dependency may be related to an inability to follow the rule of avoiding situations risky for abuse, independent of the specific environmental contexts.

Empirical evidence for these different explanations for substance dependence is incomplete. Studies with the GT have revealed statistical differences between normal controls and poly-substance abusers or cocaine-dependent persons (Bechara et al., 2001; 2002a; 2002b, Grant et al. 2000; Goudriaan et al., 2004). But at the same time, a considerable subgroup of poly-substance abusers behave normally in the GT. Moreover, it is not clear if impaired performance can be generalized to all kinds of addictions, for example to pure alcohol dependency. Note that the nature of the substance may be of major importance for the kind of neuropsychological findings. Opiates, amphetamine, and alcohol bind to different neuronal receptors. In the long run, alcohol leads to a shrinking of axons and white matter, especially in the frontal cortex (Adams et al., 1998; Dao-Castellana et al., 1998; Volkow et al., 1994). The neuro-toxic effects of alcohol and its alteration of the synaptic features of specific neuronal receptors may lead to kinds of executive impairments that differ from those induced by other forms of drugs. Deficits in response inhibition have been observed since the beginning of neuropsychological assessment of alcoholics, but with different results. In a considerable number of studies the Trail Making Test has been used and interest has focused on performance in the B trial because of the necessity to shift between sets of stimuli (letters, digits). Most of the investigations came to the conclusion that the Trail Making Task is sensitive for severe long-term alcohol dependence (Chao et al., 2003; Noel et al., 2001; Ihara...
et al., 2000; Lodberg, 1980; Long et al., 1974; Kleinknecht & Goldstein, 1972), but not all of them (Templer et al., 1975). Recovery has been proposed as one reason for these contradictory results: alcoholics show a definite improvement in many cognitive functions during the first two weeks after detoxification (Kleinknecht & Goldstein, 1972), but are quite stable in performance after this first detoxification period (Kish et al., 1980; Mann et al., 1999). Another reason for these contradictory results may be differences present in the group of alcoholics studied. Long-term alcohol abuse may be associated with repeated traumatic brain injuries, states of malnutrition and a sub-clinical development of a Korsakoff’s syndrome (Kleinknecht & Goldstein, 1972). The heterogeneity of cognitive impairments due to such additional factors can lead to divergent results. Therefore, a proper analysis of executive impairments in alcoholics requires the exclusion of other clinical features.

Brokate et al. (2003) and Hildebrandt et al. (2004) made an attempt to exclude from their investigations alcoholics with a high risk of having suffered from falls or malnutrition by focusing on patients of average intelligence and without memory impairment. They investigated performance in a specific variant of the object alternation task, in working memory, word fluency and the modified Wisconsin Card Sorting Test. Alcoholics showed a significant deficit in the Object Alternation (OA) task, but not in working memory and word fluency. They also did not produce more perseverative trials in the modified Wisconsin Card Sorting test, but completed a lower number of categories. This result argues in favour of Bechara's third explanation for a lack of response suppression, without similar impairments in the mechanisms of the first or second explanation. To our knowledge there are no studies that have systematically evaluated the different executive function impairments proposed by Bechara (2003) in a group of pure long-term alcohol dependent individuals. This was the reason for this investigation. To get information about the specific impairments of long-term alcohol dependent patients, we used a set of executive tasks sensitive for the integrity of the frontal lobe (phonological fluency), for following a purely internal sequence of shifting between object preferences (an object alternation task), for a deficit in conditional responding or inhibiting an externally cued response (a spatial stimulus-response incompatibility task, IT), for a deficit in shifting between different stimuli (shift learning task from the CANTAB), and for a deficit in decision-making (GT).
Method

Subjects
The sample consisted of 29 alcoholics and 20 controls, all in-patients of a psychiatric or neurological hospital. Alcohol dependence was diagnosed according to the criteria of the ICD 10, F 10.2. The alcoholics had abstained from alcohol for 19 days on average. Length of alcohol dependency, amount of alcohol consumption and biographical details were established on the basis of a semi-structured interview and the medical record. The control group had been admitted to the hospital for treatment of a peripheral nervous system disease, e.g., inter-vertebral prolapse or peripheral facial paresis. In the control group brain damage was excluded by a clinical MRI scan. A detailed description of the samples is given in Table 1. All subject gave their informed consent before the investigation started. The study was approved by the hospital’s ethic commission.

Neuropsychological Assessment
The groups were first investigated with the subtests 3 and 4 of a test battery ("Leistungsprüfsystem", LPS) developed by Horn (1983), measuring abstract reasoning as a core element of general intelligence, and subsequently with a word/ nonword discrimination test, ("Mehrfachwahl-Wortschatztest" by Lehrl et al., 1991), measuring premorbid intelligence. Verbal memory performance was assessed using the California Verbal Learning Test (CVLT: German version; Ilmberger, 1988). Subjects with low premorbid or general intelligence (LPS or MWT T score of < 39) or a free recall in the CVLT below 6 words were excluded. To match the groups for perceptuo-motor speed we applied the Alertness Test from the Testbattery on Attentional Assessment (TAP: Zimmermann & Fimm, 1992), which measures cued and non-cued simple reaction times.

Within the domain of executive functions we investigated phonological word fluency (with subtest 6 of the LPS; Horn, 1993) and categorical word fluency (naming as many animals as possible in one minute).

The subtest Response Alternation of the TAP was used as an OA task (Zimmermann & Fimm, 1992). In this task, a letter and a digit are presented (each of about 1.2 cm width and 1.8 cm height), each on one side of the screen (6 cm distance between the centres of the stimuli). A left and a right button are available to the subject. In the simple condition, the respondent is asked to press the button on the side on which the digit appears. In the difficult condition, the subject is asked to alternate between letter and digit from trial to trial, pressing
first the button on the side of the letter (first trial), then of the digit (second trial), and so on for 100 trials. The location of the stimuli on the screen (left or right) varies randomly in all trials, but in half of the trials the letter is on the right and in the other half on the left side. Each trial starts directly after the respondent has pressed a response key. Errors are indicated by flashing of the correct stimuli. When the incorrect key is pressed directly after a previous error, i.e. if the flash is ignored, this does not count as an error, but as a missed correct response. Individuals were informed about the response rule and had two training session of 10 trials before each test began.

Deficits in conditional responding or inhibiting an externally cued response were measured by the IT of the TAP (Zimmermann & Fimm, 1992). In this task an arrow (extending 3.5 degrees horizontally) is presented for 100 msec, starting 3.5 degrees lateral of a fixation point. Again, a left and a right button are available to the respondent. The task is to press the button on the side the arrow is pointing to. Each trial is started after the respondent has pressed the button. In half of the sixty trials the direction the arrow points to and the side where it is presented are the same (compatible condition). In the other half the arrow is presented at side opposite to where it is pointing to. These are the incompatible trials, and subjects have to suppress the tendency to respond on the side where the stimulus is presented.

We used the shift-learning task of the CANTAB (Cambridge Neuropsychological Test Automated Battery, Lowe & Rabitt, 1998) to measure intra-dimensional and extra-dimensional shift learning (see Cenes Limited 1999 for a detailed description of the task). In this task, the subject learns a series of discriminations in which the same stimulus dimension is relevant, and which is likely to promote the development of an attentional bias towards that dimension (intra-dimensional shifts). However, the task culminates in the presentation of a second critical discrimination, in which a different stimulus dimension is now relevant (extra-dimensional shift) (Rogers et al., 2000).

The IOWA GT consists of the presentation of four card decks, and the subjects have to choose between the different decks. Two of the decks are “good” decks with relatively low gains, but with lower losses. The other two decks are “bad” decks, with relatively high gains, but with even higher losses. Furthermore, both the good and the bad decks differ in frequency of losses. The probability of losing is high in one of the good and one of the bad decks, but in both these the amount of loss is lower than in the other two decks, in which losses are seldom but comparably higher. In 100 trials subjects have to learn to choose the good decks with relatively low direct outcome, and to avoid the other two decks. For a detailed description of the task see Bechara et al. (2001).
Statistical Analysis
For statistical evaluation we used a subtraction method common in human brain imaging studies in order to focus specifically on the executive component as well as to correct for unspecific differences between the groups. We subtracted

- the score of the semantic fluency task from that of the phonological fluency task to separate the executive aspects of word fluency (Henry & Crawford, 2004);
- the simple condition of the OA task from the difficult condition, to focus on the ability to follow an internal sequence of preferences (Brokate et al., 2003);
- the compatible condition from the incompatible condition in the Incompatibility test to concentrate on suppression of externally cued responses (Merriam et al., 2001);
- the intra-dimensional shift errors from the extra-dimensional shift errors to focus on problems in shifting between two external criteria (Rogers et al., 2000);
- the frequency of choosing the bad decks per 20 trials from the frequency of choosing the good decks in the IOWA GT (Bechara et al., 2001).

All the statistical tests concerning the patients’ data were done with difference scores, i.e. after subtraction of the baseline task from the specific task. A non-parametric Mann-Whitney U-Test was used for all statistical tests between groups.

The association between duration of alcohol dependence, amount of alcohol consumption and neuropsychological task results was analysed using the Spearman rank correlation coefficient. We also calculated the Spearman rank correlation of the executive tasks for both groups separately to investigate if they concern similar cognitive functions.

Results
Due to the exclusion criteria (two alcoholics were excluded because of the low intelligence cut-off score) there were no significant differences between the alcoholics and controls in age, years of education, pre-morbid intelligence, abstract reasoning, cued, and non-cued reaction times.

Executive tasks: The difference score in word fluency was not significant [Z: -1.147, p=0.251]. Response differences for the OA task approached significance [Z: -1.871, p=0.061], as did the number of errors in the incompatibility task [Z: -1.913, p=0.056]. OA errors differed highly significantly between the alcoholics and the control group [Z: -2.347, p=0.019]. Alcoholics produced more errors than controls in the incompatibility test and in OA. Both groups made a similar number of errors in extra-dimensional shift learning [Z: -0.031,
None of the five blocks of the GT yielded a significant difference (first block \[Z: -1.264, p=0.203\]; second block \[Z: -0.031, p=0.975\]; third block \[Z: -0.923, p=0.276\]; fourth block \[Z: -1.090, p=0.276\]; fifth block \[Z: -1.075, p=0.282\].

To analyze whether these negative results are due to our subtraction methods we also calculated post hoc group differences of the single test results. Again there were no significant differences between the groups for the shift learning task (i.e. for the variables total errors, total trials, stages completed, pre-extradimensional shift errors, extradimensional shift errors), and also not for the phonological word fluency, the easy task in the OA paradigm, and the RTs and the errors in the compatible condition of IT. There was a significant difference in the semantic fluency task \[Z:-2.106, p=0.035\] and a highly significant difference for errors in OA \[Z:-2.606, p=0.009\], and for errors in the incompatible conditions of the IT \[Z:-2.624, p=0.009\]).

**Short-term effects of detoxification:** To control for time of sobriety and recovery we replicated all statistical evaluation by comparing those individuals with sobriety for less than 18 days \(n= 17\) and those for more than 17 \((n = 12)\) days. There were no significant differences between these groups in any of the applied tasks.

**Long-term effects of heavy alcohol consumption:** Finally, an analysis of the duration of alcohol dependence, amount of alcohol consumption and the performance in the executive tasks was performed. The only significant correlation for the duration of alcohol abuse concerned the difference score in response time for the OA \[Spearman Rho: 0.384, p=0.04\] and the fifth block of the GT \[Spearman Rho: 0.405, p=0.029\]: patients with long-term heavy alcohol consumption needed significantly more time than patients with a relatively shorter time of dependence in the OA task and they choose more often the safe decks in the GT. The amount of consumed alcohol per day, correlated significantly with the difference score for the RT in the incompatible conditions of the IT \[Spearman Rho: -0.375, p=0.045\]. Although we used a difference score for this calculation, and therefore a kind of age-corrected value for the response time, we used partial correlation partialling out age to see if age may be of influence. This was the case for the IT, partly for the GT but not for the OA: the partial correlation between amount of consumed alcohol and RT in the IT was not significant anymore, the correlation coefficient for duration of abuse and the GT was reduced to 0.3768 \(p=0.048\), but increased for the OA to 0.5283 \(p=0.004\).
Inter-correlations of task performance: Finally, we calculated the correlations between the various difference scores, separately for the groups of alcoholics and of the controls. For the controls, only the difference score of word fluency and the numbers of errors in extradimensional shift learning correlated [Spearman Rho: 0.625 p=0.013]. In the group of alcoholics, the difference score in errors for the OA and the IT correlated [Spearman Rho: 0.428 p=0.020].

Discussion

In this study we used Bechara’s (2003) framework for executive deficits in addicted individuals and we investigated these deficits in long-term alcohol dependent individuals. We used Word Fluency to measure frontal lobe functioning, the Object Alternation (OA) Task from the TAP for deficits in shifting between responses (a pure internal shift between response criteria), the Incompatibility Task (IT) of the TAP for deficits in conditional responding, the Shift Learning Task from the CANTAB for deficits in changing relevant presentations, and responses in the Gambling Task (GT) for decision-making impairments. The main result of our study is that alcoholics are impaired in the OA task and possibly in the IT task, but not on the GT, word fluency, and the Shift Learning task.

Deficits of alcoholics in a specific variant of OA, in which subjects are informed about the underlying rule at the beginning, have been documented twice by our group (Hildebrandt et al., 2004; Brokate et al., 2003), but have not always been found with the original version of this paradigm (Bardenhagen et al., 1998; Oscar-Berman et al., 1982, but see Ambrose et al., 2001). There are several other conditional tasks which have been used in research on alcoholism and which revealed an impaired performance (see Noel et al., 2001; Ihara et al., 2000), the most prominent being the Trail-Making B. Like our OA task, the Trail-Making B Test is an object alternation task in which subjects are fully informed about the relevant rule and get some training before the test starts. The only difference is that in the Trail-Making B Test they can rely on a visual trace of their former response, whereas in our OA task there is no such trace. In agreement with our results, most studies using the Trail-Making B found impairments in alcoholics (Noel et al., 2001; Ihara et al., 2000; Lodberg, 1980; Long et al., 1974; Kleinknecht & Goldstein, 1972, but see Templer et al., 1975). The fact that no visible trace of the last response is available in OA and that it is possible to distinguish between errors and RTs, makes it probably more sensitive than the Trail-Making B.
We also found a weak statistical difference between the alcoholics and the controls in the IT using a subtraction method, and a marked difference using only the incompatible condition of the task for statistical testing. Moreover, there was a correlation between the OA task and the IT for the alcoholics, but not for our control group. Consequently, this study replicates and refines our earlier results (Hildebrandt et al., 2004; Brokate et al., 2003).

What may be the common element(s) of the OA and the IT which are responsible for the impairment of the alcoholics? Within the framework of Bechara (2003), both tasks belong to the group of Go/NoGo tests, which concern the control of responses and not the control of dominant representations as in the WCST and the Shift Learning Task of the CANTAB. We would like to add to this characterization of the OA and the IT the notion that they are conditional response tasks, i.e. tasks which require a response to a given stimulus that differs depending on contextual information (see Passingham, 1993). In the case of the IT task, this conditional aspect is defined in purely environmental terms. The dominant response set, i.e., to react on the same side as the stimulus is shown, has to be suppressed depending on the information signaled by the direction of the arrow. The response is therefore conditional on the direction of the arrow, ignoring its position. In the OA task there is a complete decoupling of stimulus information and response: whether the stimulus requires a response depends completely on the context of an internal sequence which itself is independent from the sequence of external stimulus characteristics.

Why than are in particular these kinds of tasks impaired in alcoholics? One reason could be that deficits in the mechanisms underlying these tasks make individuals prone to become addicted to alcohol. Both tasks measure subjects’ ability to respond to specific stimuli depending on contextual information. Such an ability is of prior importance to control behavior if alcohol is available to the individual, and to avoid situations in which alcohol abuse is probable. In a society in which alcohol is part of many social situations, the ability for such a contextual responding may therefore decide if patients relapse or not. But deficits in OA and IT may also be a result of the neurotoxic effects of alcohol consumption. In order to control for a short-term neurotoxic effect of alcohol abuse, we divided our group in two sub-groups with less or more than 18 days of detoxification and found no significant difference in the performance of these two groups. This argues for a permanent alteration of cognitive performance in the OA and eventually also in the IT. To investigate the question whether long-term heavy alcohol consumption may have a detrimental effect on OA and IT,
we calculated the correlation between performance and the duration of alcohol dependency. There was no significant correlation between the duration of dependence and IT or between the duration of dependence and errors in OA, but we found a significant correlation for the RTs in OA and years of dependence. Two earlier studies (Hildebrandt et al., 2004; Brokate et al., 2003) also revealed inconsistent results in this respect. As argued in these studies, a definite answer to the question to what extent OA deficits predispose individuals to alcohol dependence has to wait for a study with a considerably larger number of patients. Subjective reports about the length of continuous alcohol dependence are generally vague.

Given the increasing number of studies showing impairments of substance dependent individuals in decision-making (Clark et al., 2004) and the central role of risky decision-making in Bechara's (2003) framework, the negative result of the GT is surprising. In our view, there may be two reasons for the lack of a significant impairment of the alcoholics in this task. The first concerns the number of alcoholics investigated, which may have been too small (less than 40 or even 60 individuals as in Bechara et al. 2001, Petry 2001 or Bechara & Damasio 2002a). As can be seen in Figure 1, at least the absolute values of the results point in the direction of a slower learning to avoid risky moves in the group of alcoholics. But on the other hand, the differences between the groups are far from becoming significant (p > 0.20 for each block), and there was a weak positive correlation between the fifth block and duration of alcohol dependence, both arguing for another explanation. This study also differs from others in that our control group consists of patients suffering from peripheral nervous system diseases. Taking the absolute values of Bechara’s (2003) control group, that group performed somewhat better than our control group. But we would argue that including individuals as controls who are in the same psychological situation as the alcoholics could have an advantage over using socially well performing controls, being in a very different general situation from the alcoholics.

Most of the studies with the GT have been done in non-alcoholic substance dependent individuals or in individuals with poly-substance dependency (Bechara & Damasio, 2002a; Bechara et al., 2001). Therefore, another explanation could be that alcohol affects different neurotransmitters than cocaine or amphetamine and that this difference is responsible for positive results in one group and negative results in another group of substance dependent individuals. Comparative neuropsychological studies on long-term effects of other addictive substances are rare. Roberts & Horton (2003) compared 7689 individuals addicted to cocaine, heroin and alcohol with the Trail Making Test. They found remarkably similar results for
heroin and alcohol abusers, but somewhat more impairment in cocaine abusers. Functional brain imaging studies show a specific relation of decision behavior in the GT and subcortical structures, which at the same time are also targets for opiate and dopaminergic modulation (Clark et al., 2004). Therefore, the specific pathways of neurotransmitter binding may also play a role here.

Word fluency and shift learning have been studied extensively with organic brain patients and with functional brain imaging (for reviews see Henry & Crawford, 2004; Clark et al., 2004). For the shift-learning task there are also several studies in animals. Both tasks share some common psychological and physiological mechanisms. In Bechara’s (2003) framework they rely on the intact ability to shift between representations which lose their relevance between trials or sets of trials. Typically, perseverations in word fluency and shift learning are defined as sticking to a formerly correct representation which actually has become irrelevant. This distinguishes them from the OA and IT tasks, in which one has to shift between motor responses. Physiologically, phonological fluency and extra-dimensional shift learning rely on an intact lateral prefrontal cortex (Clark et al., 2004; Rogers et al., 2000), for the shift learning task the upper part of Brodman’s area 10 may also play a role (Rogers et al., 2000). Our study endorses the view that shift learning and phonological word fluency share common psychological resources, because the performance of healthy subjects correlated for these tasks. But at the same time it shows that alcoholics seem to have no problems in either of them. The intra-/ extradimensional shift-learning task has been developed to allow for a more fine-grained analysis of impairments in the WCST (Rogers et al., 2000), but has not yet been used for studying cognitive deficits in alcoholics. Five studies using the WCST (Chao et al., 2003; Brokate et al., 2003; Bechara et al., 2001; Ihara et al., 2000; Joyce & Robbins, 1991) found mild impairments in the number of categories reached, but not in the amount of perseverative errors. Therefore, alcoholics are not impaired in shifting between categories ("representations"), but in keeping their responses in accordance with a relevant response rule, as in the OA or IT tasks.

Few categories in the fluency task and the occurrence of perseverative trials are related to dorsolateral and superior medial prefrontal cortex lesions, but not to lesions of the inferior medial prefrontal cortex (Stuss et al., 2000; Monchi et al., 2001). The lack of significant differences in the shift learning task in our study is therefore in accordance with an only weakly significant difference in the WCST and the assumption of an alteration of the medial areas of the prefrontal cortex in alcoholics, and not so much of the dorsolateral prefrontal
cortex. And it corresponds to investigations showing that alcoholics are not impaired in working memory (Hildebrandt et al., 2004; Brokate et al., 2003; Vogel-Sprott et al., 2001; Finn et al., 1999; Joyce & Robbins, 1992), another function relying heavily on an intact lateral prefrontal cortex.

PET and SPECT studies have also suggested a diminished perfusion in the ventromedial prefrontal cortex in long-term alcohol dependent individuals (Volkow et al., 1994, 1997; Dao-Castellano et al., 1998; Adams et al., 1998; Taber et al., 2000). According to Goldstein et al. (2001), alcoholics and controls show differential neural activity in the orbitofrontal cortex during a response inhibition task. Goldberg (1985) and also Passingham (1993) have argued that there are two major functional areas of the frontal lobes, anterior to the primary motor cortex. One (the lateral parts) is more related to conditional responses to external information, the other (the medial parts) is involved in learning of conditional responses to internal information, i.e. stimuli concerning internal states or goals. In accordance with these assumptions about sub-divisions of the prefrontal cortex, it has been shown by animal (Iversen & Mishkin, 1970; Mishkin & Manning, 1978), human lesion (Freedman et al., 1998) and functional brain imaging (Gold et al., 1996) studies that the ventromedial prefrontal cortex is related to OA tasks. Stimulus-response incompatibility tasks have not been studied as much for their organic basis. But Merriam et al. (2001) showed using fMRI that during the incompatible condition the medial frontal cortex dorsal to the supplementary frontal eye fields become activated. Taken together, the brain imaging and neuropsychological data indicate a specific disturbance of the medial, and not so much of the lateral frontal cortices after long-term heavy alcohol abuse.

As a conclusion of this study we would like to state that one main task for future research is to broaden our knowledge of conditional responding in alcoholics by using experimental paradigms which vary different aspects (conditional on spatial, object or response features) and task loads of conditional responding (complexity of context rules). In this context it seems to be of high interest whether non conditional Go/NoGo tasks like the STROOP and conditional tasks, in which the response is conditional on two object features (i.e. not on former responses), reveal deficits, or if only tasks, which involve an internal contextual response shifts do have such an effect. This question can be easily answered by future investigations.
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Figure 1: A score smaller than zero indicates that risky decks are chosen more often than save decks, a score greater than zero that the save decks are more often chosen. Each block consists of 20 trials. The differences between the control group and the group of alcoholics are not significant in any of the blocks.
Figure 2: Alcoholics produced significantly more errors in the OA task (after subtraction of the errors in the control task) than the control group. They also showed a tendency ($p = 0.056$) to produce more errors in the incompatible trials of the Incompatibility task (after subtraction of the errors in the compatible trials).
Table 1: Group characteristics

<table>
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<tr>
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<th>Alcoholics</th>
<th>Controls</th>
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<tr>
<td>n</td>
<td>29</td>
<td>20</td>
</tr>
<tr>
<td>sex (m/f)</td>
<td>22 / 7</td>
<td>10 / 10</td>
</tr>
<tr>
<td>Days of detoxification mean</td>
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<td>7</td>
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<tr>
<td>Days of detoxification SD</td>
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<td>Age SD</td>
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<tr>
<td>School education in years SD</td>
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<td>Abstract reasoning mean</td>
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<tr>
<td>Abstract reasoning SD</td>
<td>5.9</td>
<td>5.5</td>
</tr>
<tr>
<td>Simple visual RT mean</td>
<td>273.2</td>
<td>290.6</td>
</tr>
<tr>
<td>Simple visual RT SD</td>
<td>67.2</td>
<td>97.4</td>
</tr>
<tr>
<td>Cued visual RT mean</td>
<td>266.7</td>
<td>283.4</td>
</tr>
<tr>
<td>Cued visual RT SD</td>
<td>82.4</td>
<td>81.1</td>
</tr>
</tbody>
</table>

Table 2: Difference scores in the executive tasks

<table>
<thead>
<tr>
<th></th>
<th>Alcoholics</th>
<th>Controls</th>
</tr>
</thead>
<tbody>
<tr>
<td>Word fluency mean</td>
<td>11.4</td>
<td>7.7</td>
</tr>
<tr>
<td>Word fluency SD</td>
<td>6.3</td>
<td>10.2</td>
</tr>
<tr>
<td>Incompatibility, errors * mean</td>
<td>3.3</td>
<td>0.95</td>
</tr>
<tr>
<td>Incompatibility, errors * SD</td>
<td>4.7</td>
<td>1.7</td>
</tr>
<tr>
<td>Incompatibility, RT mean</td>
<td>185.7</td>
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<tr>
<td>Incompatibility, RT SD</td>
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<td>128.4</td>
</tr>
<tr>
<td>OA, errors ** mean</td>
<td>8.9</td>
<td>3.5</td>
</tr>
<tr>
<td>OA, errors ** SD</td>
<td>10.7</td>
<td>4.9</td>
</tr>
<tr>
<td>OA, RT mean</td>
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<td>427.2</td>
</tr>
<tr>
<td>OA, RT SD</td>
<td>679.8</td>
<td>339.6</td>
</tr>
<tr>
<td>Shift learning, errors mean</td>
<td>15.3</td>
<td>12.1</td>
</tr>
<tr>
<td>Shift learning, errors SD</td>
<td>13.1</td>
<td>9.6</td>
</tr>
<tr>
<td>Gambling: 1. Block mean</td>
<td>-1.2</td>
<td>-3.3</td>
</tr>
<tr>
<td>Gambling: 1. Block SD</td>
<td>3.9</td>
<td>6.4</td>
</tr>
<tr>
<td>Gambling: 2. Block mean</td>
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<td>1.4</td>
</tr>
<tr>
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<tr>
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<td>8.5</td>
</tr>
<tr>
<td>Gambling: 4. Block mean</td>
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<td>2.8</td>
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<tr>
<td>Gambling: 4. Block SD</td>
<td>6.9</td>
<td>7.8</td>
</tr>
<tr>
<td>Gambling: 5. Block mean</td>
<td>1.8</td>
<td>4.7</td>
</tr>
<tr>
<td>Gambling: 5. Block SD</td>
<td>5.2</td>
<td>8.6</td>
</tr>
</tbody>
</table>

** p = 0.019, * p = 0.056

Abbreviations: OA = Object alternation; SD = Standard deviation