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Original article

Impaired decision-making and brain shrinkage in alcoholism

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ABSTRACT

Alcohol-dependent individuals usually favor instant gratification of alcohol use and ignore its long-term negative consequences, reflecting impaired decision-making. According to the somatic marker hypothesis, decision-making abilities are subtended by an extended brain network. As chronic alcohol consumption is known to be associated with brain shrinkage in this network, the present study investigated relationships between brain shrinkage and decision-making impairments in alcohol-dependent individuals early in abstinence using voxel-based morphometry. Thirty patients performed the Iowa Gambling Task and underwent a magnetic resonance imaging investigation (1.5T). Decision-making performances and brain data were compared with those of age-matched healthy controls. In the alcoholic group, a multiple regression analysis was conducted with two predictors (gray matter [GM] volume and decision-making measure) and two covariates (number of withdrawals and duration of alcoholism). Compared with controls, alcoholics had impaired decision-making and widespread reduced gray matter volume, especially in regions involved in decision-making. The regression analysis revealed links between high GM volume in the ventromedial prefrontal cortex, dorsal anterior cingulate cortex and right hippocampal formation, and high decision-making scores ($P < 0.001$, uncorrected). Decision-making deficits in alcoholism may result from impairment of both emotional and cognitive networks.

1. Introduction

In everyday life, alcohol-dependent patients are facing high-risk situations threatening their continuous abstinence from alcohol. They generally opt for instant gratification of alcohol use, despite its long-term negative consequences, possibly reflecting impaired decision-making in alcoholism. Decision-making abilities and the tendency to adopt risky behavior under ambiguous conditions are usually assessed with the Iowa Gambling Task (IGT) [4]. Simulating a real-life situation, this task yields a decision-making measure that has been particularly used in clinical and neurological populations with risky behaviors such as pathological gambling [30,39], eating disorders [18], HIV [31] and also substance dependence/abuse involving cocaine, opioids, marijuana, or alcohol [7,8,11,45,48]. Impaired decision-making has been found in both long-term abstinent [25] and recently detoxified [30,43] alcohol-dependent patients.

The IGT was initially created to assess decision-making problems in patients with ventromedial prefrontal cortex (vmPFC) damage [4]. These patients performed poorly on the IGT by making choices that bring immediate reward but lead to severe delayed punishment. They also displayed emotional deterioration, but preserved intellectual abilities. This clinical observation has given rise to the somatic marker hypothesis [3,22], which says that emotion plays a critical role in guiding decision-making. This theory is based on the notion of somatic (i.e. bodily) state activation mediated by two types of neural circuitry. The impulsive system, where the amygdala is the main substrate, triggers somatic states from unconditioned or conditioned stimuli present in the immediate environment [6], while the reflective system, where the vmPFC is the main substrate, activates somatic states through the recall of previous emotional events that are not directly available in the environment [6]. The role of vmPFC is to couple "memory" processes (dorsolateral prefrontal cortex and hippocampus) with structures holding previous feeling states (insula, surrounding

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somatosensory cortices, posterior cingulate cortex and precuneate cortex). A general somatic signal emerging from these different somatic states acts on the insula and the surrounding somatosensory cortices, causes them to generate a feeling about the overall emotional state. This signal also influences the striatum, the anterior cingulate cortex and the adjacent supplementary motor area (SMA), which allow us to select and implement appropriate behaviors. Decision-making is therefore a very complex activity, subtended by an extensive brain network. Depending on the location of the brain damage, the same maladjusted risky behavior may be the result of a range of damaged cognitive mechanisms, such as impaired somatic state activation for positive or negative events, failure to anticipate the long-term outcome of actions (i.e., difficulty associating events with the emotional features of their consequences), working memory dysfunction and deficits in the implementation and monitoring of the different behaviors available.

Several regions belonging to the somatic marker hypothesis network are known to be damaged in chronic alcoholism [20,51], especially the frontal cortex [23,42], amygdala [41], hippocampus [35], striatum [41,50], insula [41] and cerebellum [49]. To our knowledge, the relationship between brain shrinkage and impaired performance on a simulated gambling task (SGT) [26] in long-term abstainers has been investigated only once. Using a region of interest, the analysis focused on the vmPFC and the amygdala, the authors reported a bilateral gray matter (GM) volume reduction in the amygdala, but not in the vmPFC. They also failed to find any link between GM shrinkage and decision-making deficits. This absence of association may have been partly due to the long-term abstinence of these alcoholics.

The goal of the present study was therefore to conduct a correlational analysis of the relationship between brain shrinkage and decision-making deficits in alcohol-dependent patients early in abstinence and at alcohol treatment entry. Considering the extent of the decision-making network, we believed that this neuroimaging approach would provide a better understanding of the neuropathological processes underlying the decision-making impairment observed in recently detoxified alcohol-dependent patients. In the framework of the somatic marker theory of addiction [55], we hypothesized that decision-making impairment will be related to brain shrinkage in regions implicated in the somatic marker brain network, including the amygdala, the dorsolateral prefrontal cortex and hippocampus, the insula, the posterior cingulate cortex and the precuneate cortex, the ventromedial prefrontal cortex and finally the striatum, the anterior cingulated cortex and the supplementary motor area (SMA).

2. Materials and methods

2.1. Participants

Thirty alcohol-dependent patients (26 men) early in abstinence were included in this study. They were recruited by clinicians on the basis of the DSM-IV criteria for alcohol dependence [2] and were receiving inpatient treatment for alcohol dependence at Caen University Hospital. Even though all patients were in early abstinence from alcohol, we only selected those who did not present physiological symptoms of alcohol withdrawal any more, as established by the Cushman score [21]. Patients had no history of other types of substance dependence (except tobacco). They were interviewed to determine the age at which they had their first alcoholic drink, the age of onset of alcoholism, the duration of time they were drunk to excess, their regular daily alcohol intake and the number of withdrawals (Table 1). Age, education level, Mini-Mental State Examination (MMSE) [29] results, depression level (Beck Depression Inventory) [10] and anxiety level scores (State-Trait Anxiety Inventory (STAI) for adults with two forms: Y-A for "state anxiety" and Y-B for "trait anxiety") [47] are summarized in Table 1.

Two control groups were included in this study. First, for the gambling task, patients were compared with forty-five control participants matched for age, $t(73) = -0.62$, $P = 0.54$, level of education, $t(74) = -0.29$, $P = 0.77$ and gender χ^2 $(1, n = 75) = 0.07$, $P = 0.79$ (Table 1). Those control participants were interviewed to ensure that they did not drink more than 21 (men) or 14 (women) weekly standard drinks and no more than four at a time (World Health Organization criteria). Second, for the neuroimaging examination, patients were compared with another independent sample of 27 control participants drawn from our database and matched for age, $t(55) = 0.42$, $P = 0.68$ (Table 1). The neuroimaging data were collected in the same magnet and using the same

Table 1
Patients' main demographic, clinical and alcoholic features.

	Decision-making controls	Neuroimaging controls	Alcohol-dependent patients
Number	45	27	30
Women/men	7/38	12/15	4/26
Age	44.76 (7.78)	44.80 (11.35)	43.67 (7.04)
Range	32–58	29–60	31–56
Years of education	10.69 (2.25)	–	10.53 (2.32)
Range	5–17	–	5–15
Mini-Mental State Examination	29.20 (0.97)	–	27.27 (1.68)
Beck Depression Inventory	–	–	8 (3.36)
State-Trait Anxiety Inventory "State anxiety" (STAI Y-A)	–	–	33.13 (10.06)
State-Trait Anxiety Inventory "Trait anxiety" (STAI Y-B)	–	–	50.27 (14.22)
Days of abstinence before inclusion	N/A	N/A	12.63 (7.08)
Range	–	–	7–40
Years of alcohol use	N/A	N/A	27.97 (8.23)
Range	–	–	14–51
Years of alcohol misuse	N/A	N/A	15.60 (9.69)
Range	–	–	2–36
Years of alcoholism	N/A	N/A	9.03 (9.37)
Range	–	–	0.5–33
Quantity per day (in units of alcohol)	N/A	N/A	24.16 (15.44)
Range	–	–	3.5–77.50
Number of withdrawals	N/A	N/A	2.20 (1.16)
Range	–	–	1–6

Data are shown as means (standard deviation).