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Executive functions in alcohol-dependence: A theoretically grounded and integrative exploration



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ABSTRACT

Background: Alcohol-dependence is related to large-scale cognitive impairments, particularly for executive functions (EF). These deficits persist even after long-term abstinence and have a major impact on patients' everyday life and relapse risk. Earlier studies, based on multi-determined tasks, mostly focused on inhibition and did not offer a theoretically-grounded and exhaustive view of the differential deficit across EF. The present paper proposes a model-based exploration of EF in alcohol-dependent individuals (ALC), to precisely compare the specific deficit related to each executive subcomponent.

Methods: Forty-seven recently detoxified ALC were compared to 47 matched healthy participants on a nine-tasks validated neuropsychological battery, simultaneously exploring and comparing the three main executive subcomponents (shifting, updating, and inhibition). Psychopathological comorbidities were also controlled for.

Results: Reaction time indexes revealed a global slowing down among ALC, whatever the EF explored. Accuracy indexes revealed a moderate deficit for inhibition tasks but a massive impairment for shifting and updating ones. Complementary analyses indicated that the executive deficits observed were centrally related to alcohol-dependence, while comorbid depressive symptoms appeared to intensify the deficits observed.

Conclusions: By offering a direct comparison between the three major EF, these results showed that alcohol-related executive deficits extend beyond the classically described inhibition impairment. This impairment encompasses each EF subcomponent, as ALC actually presented stronger deficits for updating and shifting abilities. This first observation of a multifaceted EF deficit stresses the need for an individualized evaluation and rehabilitation of EF during and/or after the detoxification process.

1. Introduction

Many earlier studies have highlighted the deleterious effects of alcohol-dependence on the brain (Fein et al., 2002; Mason et al., 2005; Meyerhoff et al., 2005), which include notably gray matter atrophy in frontal/parietal lobes, limbic system and cerebellum (Harris et al., 2008; Oscar-Berman et al., 2009; Oscar-Berman and Marinkovic, 2007). Accordingly, alcohol-dependent individuals (ALC) present a wide range of impairments in the cognitive functions underlined by these brain networks (despite some potential cerebral reorganization partly compensating these deficits, Pfefferbaum et al., 2001), encompassing visuo-

perceptive, attentional (Bernardin et al., 2014), memory (Pitel et al., 2014), emotional (D'Hondt et al., 2014; Marinkovic et al., 2009) and interpersonal (Maurage et al., 2016) dysfunctions. The brain modifications among ALC also include white matter shrinkage, notably in the fronto-cerebellar pathways (Sullivan et al., 2010; Sullivan and Pfefferbaum, 2005), leading to working memory, shifting and problem solving impairments (Sullivan et al., 2003).

Beyond these various impairments, the current models of alcohol-dependence (Fleming and Bartholow, 2014; Goldstein and Volkow, 2002; Oscar-Berman et al., 2014) centrally posited that, together with the increased sensitivity to alcohol-related stimuli due to dysregulated

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limbic activity (Field and Cox, 2008; Klein et al., 2013), executive dysfunctions constitute a key focus of interest in alcohol-dependence. Executive functions (EF) can be globally defined as a set of high-level control mechanisms mediating the ability to successfully regulate thoughts and behaviors in order to fulfil a goal (Miyake and Friedman, 2012). They constitute a central topic of investigation in alcohol-dependence (Fama et al., 2004; Field et al., 2010; Maharasingam et al., 2013; Noël et al., 2012; Pitel et al., 2007, 2008) and numerous neuropsychological studies have reported poor executive functioning in ALC (Bernardin et al., 2014; Cohen et al., 1997; Courtney et al., 2013; Field et al., 2010; Jones et al., 2013). Executive dysfunctions lead patients to make risky or thoughtless decisions and to favour immediate reward without considering the delayed deleterious consequences of excessive alcohol consumption (Bechara et al., 2005; Camchong et al., 2014; Noël et al., 2010). In particular, previous results emphasized the crucial role of inhibition deficits among ALC (Le Berre et al., 2014; Noël et al., 2012, 2007; Pitel et al., 2007), which could persist long after drinking cessation and are strongly involved in relapse (Jones et al., 2013). The spontaneous recovery of cognitive functions may require up to one year, the first months of abstinence thus constituting a risky period during which ALC still present reduced executive abilities, thus increasing relapse risk (Stavro et al., 2013).

Previous studies investigating this “cold” EF component (i.e., the purely cognitive processes, mostly associated with dorsolateral prefrontal cortex, as opposed to the “hot” EF component, involving affective and reward processes and mostly associated with orbitofrontal structures, Zelazo and Müller, 2002) among ALC have used classical neuropsychological tools to individually explore each executive sub-component. Most of them focused on inhibition abilities, using for example Go/No-go or Iowa Gambling task (Courtney et al., 2013; Garland et al., 2012; Kamarajan et al., 2005). Other explorations used the Fluency test or Trail making test to evaluate shifting abilities (Oscar-Berman et al., 2009), the N-back test or Digit span to measure updating abilities (e.g., Pitel et al., 2007), or the Wisconsin card sorting test or the Tower of London to explore problem solving (Oscar-Berman et al., 2009). However, these earlier results presented two main limitations: first, each study exclusively focused on a limited number of EF without integrating them into a theoretical model, thus only offering a restricted view of executive functioning and hampering any direct comparison across EF sub-components. Second and conversely, most of the tests previously used were multi-determined and thus simultaneously explored different sub-components of the executive system. For example, ALC are impaired in the Wisconsin Card Sorting Test (Oscar-Berman et al., 2009), which is usually interpreted as reflecting altered set-shifting abilities. However, it has been shown that this task was not a specific measure of shifting as it also requires perceptual and motor abilities, as well as inhibition and updating (Friedman et al., 2008; Miyake et al., 2000). Thus, earlier studies, while showing that EF are impaired in this pathology, did not allow to clarify the specific and differential deficit related to each “cold” executive sub-component.

Yet, over the past few years, theoretical and empirical studies have clearly shown that the executive system can no more be considered as unitary and should rather be viewed as a multi-faceted system consisting of several sub-components that share commonalities but also present specific features (Fournier-Vicente et al., 2008; Hull et al., 2008; Jurado and Rosselli, 2007). In this framework, an influential model based on a factorial analysis in healthy participants (Miyake et al., 2000) proposed to subdivide EF into three basic sub-components: (1) Shifting, the ability to transfer the allocation of cognitive resources from one task to another; (2) Updating, the refreshing of working memory to erase irrelevant information and replace it with pertinent new elements; (3) Inhibition, the control ability preventing a non-pertinent automatic or dominant response to occur. Nine tasks were then proposed on the basis of this model, each being specifically related to one executive sub-component (i.e., three tasks for each subcompo-

nent). While more recent works (Friedman and Miyake, 2017; Miyake and Friedman, 2012) have argued that the inhibition subcomponent could constitute a common underlying factor also partly involved in the shifting and updating subcomponents, this seminal work enabled the isolation of specific executive processes, as well as the reduction of the impurity and multi-determined nature of earlier studies conducted by means of classical neuropsychological tests (Fournier-Vicente et al., 2008). Applying this theoretically and empirically grounded approach to alcohol-dependence could thus offer new insights by clearly determining the different deficits related to these three main executive sub-components.

The present study capitalized on this model to offer the first integrated exploration of the three main executive sub-components (shifting, updating, inhibition) in alcohol-dependence, with a strict control of frequent psychopathological comorbidities, namely depression (de Timary et al., 2013; Schuckit, 1994) and anxiety (Kushner et al., 2000). By offering a direct comparison between the three EF, this study aimed to capture the specific nature of executive deficits in ALC, notably to test the hypothesis that alcohol-dependence is centrally characterized by an inhibition deficit, as suggested by earlier work (Stavro et al., 2013).

2. Materials and methods

2.1. Participants

Two groups of 47 participants [ALC and healthy control participants (CP)] took part in the study. As shown in Table 1, participants were matched for gender [$\chi^2(1, n = 94) = 1.59, p = 0.147$], age [$F(1, 93) = 0.002, p = 0.961$] and education level [i.e., the number of years of education completed since starting primary school; $F(1, 93) = 1.70, p = 0.193$]. ALC were diagnosed for alcohol-dependence according to DSM-IV criteria and recruited during their third week of detoxification treatment at the Neuropsychiatric Hospitals of Saint-Martin and Beau-Vallon (Belgium). They had all been abstinent for 14–20 days, in order to avoid any influence of acute alcohol withdrawal and to ensure the exploration of chronic alcohol effect on executive functioning, before the potential recovery following mid to long-term abstinence (Pitel et al., 2009; Segobin et al., 2014). CP had low alcohol consumption (i.e., lower than two alcohol doses per day for women and three for men) and did not consume alcohol during the three days preceding testing session. All participants were free of any major medical, psychiatric or neurological disorder (including head trauma and epilepsy), and did not present any history of polysubstance abuse (except tobacco), as assessed by a clinical interview. The study was approved by the Ethics Committee of the Medical School (Université

Table 1
Demographic and psychopathological measures for control (CP) and alcohol-dependent (ALC) participants: mean (S.D.).

	CP (N = 47)	ALC (N = 47)
Demographic Measures		
Age ^{ns}	48.8 (9.3)	48.9 (7.4)
Gender ratio (F/M) ^{ns}	22/25	16/31
Education Level (in years) ^{ns}	14.7 (2.5)	14.1 (2.5)
Alcohol consumption (units/day) ^{**}	0.8 (0.8)	17.2 (13.7)
Number of previous detoxification treatments	/	1.9 (2.2)
Alcohol-dependence duration (in years)	/	12.9 (9.9)
Psychopathological Measures		
Beck Depression Inventory ^{**}	2.3 (2.7)	11.2 (7.8)
State Anxiety Inventory [*]	31.3 (8.3)	38.9 (21.6)
Trait Anxiety Inventory ^{ns}	38.6 (7.8)	44.1 (20.9)

ns = non significant.

* $p < .05$.

** $p < .001$.

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