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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 subcomponent. 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 subcomponents. 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 subcomponent.

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 subcomponents: (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 subcomponent (i.e., three tasks for each subcomponent). 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 subcomponents.

The present study capitalized on this model to offer the first integrated exploration of the three main executive subcomponents (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.
* $p < .05$.
** $p < .001$.

catholique de Louvain, Belgium) and participants provided written informed consent. The complete evaluation required five one-hour sessions, participants being given breaks between tasks. Subclinical psychopathological comorbidities were assessed with self-reported questionnaires measuring depression [Beck Depression Inventory, BDI, (Beck et al., 1996)] and anxiety [State and Trait Anxiety Inventory, forms A and B (Spielberger et al., 1983)].

2.2. Task and procedure

All participants completed nine computerised tasks adapted from Miyake et al. (2000), namely the "Plus-Minus", "Local-Global" and "Number-Letter" tasks for Shifting; the "Tone Monitoring", "Keep Track" and "Letter Memory" tasks for Updating; the "Antisaccade", "Stop-Signal" and "Stroop" tasks for Inhibition. Each task comprised both control (parts A and B) and executive (part C) subparts, which were identical in their structure and requirements except that parts A and B did not involve executive functions while part C did. This design thus enabled to compute accuracy and RT indexes serving as dependent variables, which were based on the extraction of the specific executive subcomponent while controlling for visual and motor involvement. Namely, the average percentage of correct answers (for accuracy) or the average reaction times for correct answers (RT) for the non-executive parts A and B were subtracted from those observed in the executive part C (C-[(A + B)/2]). This method was used to remove task impurity by comparing each experimental task with control conditions only differing regarding EF involvement. This was done for each task except the Stop-Signal task, which did not include a subpart C and in which the dependent variables were the percentage of efficient inhibition in part B (as adapted from Miyake et al., 2000) and a "subpart B- subpart A" RT index. Tasks were administered in a pseudo-random order with the following constraints: (1) the control subparts of a given task were always administered before the executive subpart; (2) the successive presentation of two tasks related to the same executive sub-component was avoided. Each task started with 10 practice trials, repeated if needed, to ensure a correct task understanding. The number of trials per condition slightly varied depending on the task duration (10–20 min). Participants were required to perform the task as quickly and accurately as possible while accuracy (percentage of correct answers) and reaction times (RT) were recorded using either a voice or motor response key. Methodological details regarding tasks design are presented in the Supplementary Materials section. A graphical illustration of the nine tasks is proposed in Fig. 1.

2.3. Statistical analyses

Statistical analyses were performed using SPSS 21.0 (SPSS Inc., Chicago, IL., USA). The raw analyses related to each subpart [i.e., control (A-B) and executive (C)] are described in the Supplementary Materials section as the focus of the present analysis was to extract the executive component using indexes computation. This preliminary step used repeated measure ANOVAs to compare the results (accuracy and RT) in the subparts of each task separately, with groups (ALC, CP) as between-subjects factor and experimental measure (subparts of each task) as within-subjects factors. Statistical analyses were then based on a three-step procedure. The first step explored EF deficits among ALC for each task. Following the procedure described by Miyake et al. (2000), and in order to decrease the non-executive variance (e.g., visuomotor impairment) from the performance, accuracy and RT indexes were computed by extracting the executive component (directly representative of an executive process) from the manifest performance (including non-executive process). This index approach offers a genuine exploration of EF and reduces the task impurity problem. The executive cost for each task was thus the difference between performance (accuracy or RT) for the trials requiring executive processing and performance (accuracy or RT) for the trials in which no EF was involved. We used the following formula: EF Index = Executive part − Mean of non-executive parts [e.g., Stroop RT index = interference RT − (mean of reading RT and denomination RT)]. Analyses of variance (ANOVAs) were then carried out for executive accuracy and RT indexes (violations of sphericity were corrected by the Greenhouse–Geisser correction when appropriate). The second step compared each executive subcomponent (i.e., Shifting, Updating and Inhibition) by grouping the three corresponding tasks between and within groups. To allow comparing tasks, standardized z-scores were computed for each executive index. Then, in order to combine performances from the three tasks assessing a same EF, a composite executive index was computed. While the task index analysis listed all dependent variables (accuracy and RT), the composite executive index analysis only combined the most sensitive variables related to each task (see Miyake et al., 2000). A mean z-index ($M = 0$ and $SD = 1$) was computed for each executive subcomponent [z-shifting index (comprising Plus-Minus, Local-Global, Number-Letter RT indexes); z-updating (comprising Tone Monitoring, Keep Track, Letter memory accuracy indexes); z-inhibition (comprising Antisaccade accuracy index, Stop-Signal percentage of efficient inhibition and Stroop RT index)]. It should be noted that for each composite executive index, RT and accuracy tasks indexes were adapted such as a higher index reflected worse performance for all measures. Repeated measures ANOVAs were then carried out for accuracy and RT with groups (ALC, CP) as between-subjects factor and experimental measure (the three executive z indexes) as within-subjects factors. (violations of sphericity were corrected by the Greenhouse–Geisser correction when appropriate). This second step is reported in the second results section, that gathers the comparison across functions. The alpha level was set at 0.05 for analyses. Effect sizes (Cohen's d) were calculated for group comparison in the index tasks and in the EF subcomponent analysis of variance (ANOVAs). The third step examined the role played by ALC characteristics (e.g., education level, age, alcohol consumption characteristics) and comorbidities (depression and anxiety) on EF deficits among ALC using Pearson's correlations. Given the high comorbidity of alcohol use disorders, depression and anxiety, complementary analyses of covariance (ANCOVAs) were then performed to explore group differences on the tasks indexes and executive subcomponents for which an association with comorbidities was found.

3. Results

3.1. Executive indexes analyses

These results are presented in Table 2 and group comparisons are illustrated in Fig. 2.

3.1.1. Shifting tasks

For the ***Plus-Minus task***, a significant group effect was found for the *accuracy index* [$F(1,92) = 6.60$, $p = 0.012$], showing that ALC had lower accuracy than CP, but not for the *RT index* [$F(1,91) = 3.51$, $p = 0.064$]. For the ***Local-Global task***, a significant group effect was found for the *accuracy index* [$F(1,91) = 11.75$, $p = 0.001$], showing that ALC had lower accuracy than CP, but not for the *RT index* [$F(1,91) = 3.85$, $p = 0.053$]. For the ***Number-Letter task***, a significant group effect was found for the *accuracy index* [$F(1,92) = 11.09$, $p = 0.001$], showing that ALC had lower accuracy than CP, but not for the *RT index* [$F(1,92) = 3.41$, $p = 0.068$].

3.1.2. Updating tasks

For the ***Tone monitoring task***, a significant group effect was found for the *accuracy index* [$F(1,90) = 8.10$, $p = 0.005$], showing that ALC had lower accuracy than CP, but not for the *RT index* [$F(1,89) = 1.76$, $p = 0.188$]. For the ***Keep track task***, no significant group effect was found, for the *accuracy index* [$F(1,92) = 0.14$, $p = 0.701$]. For the ***Letter Memory task***, a significant group effect was found for the

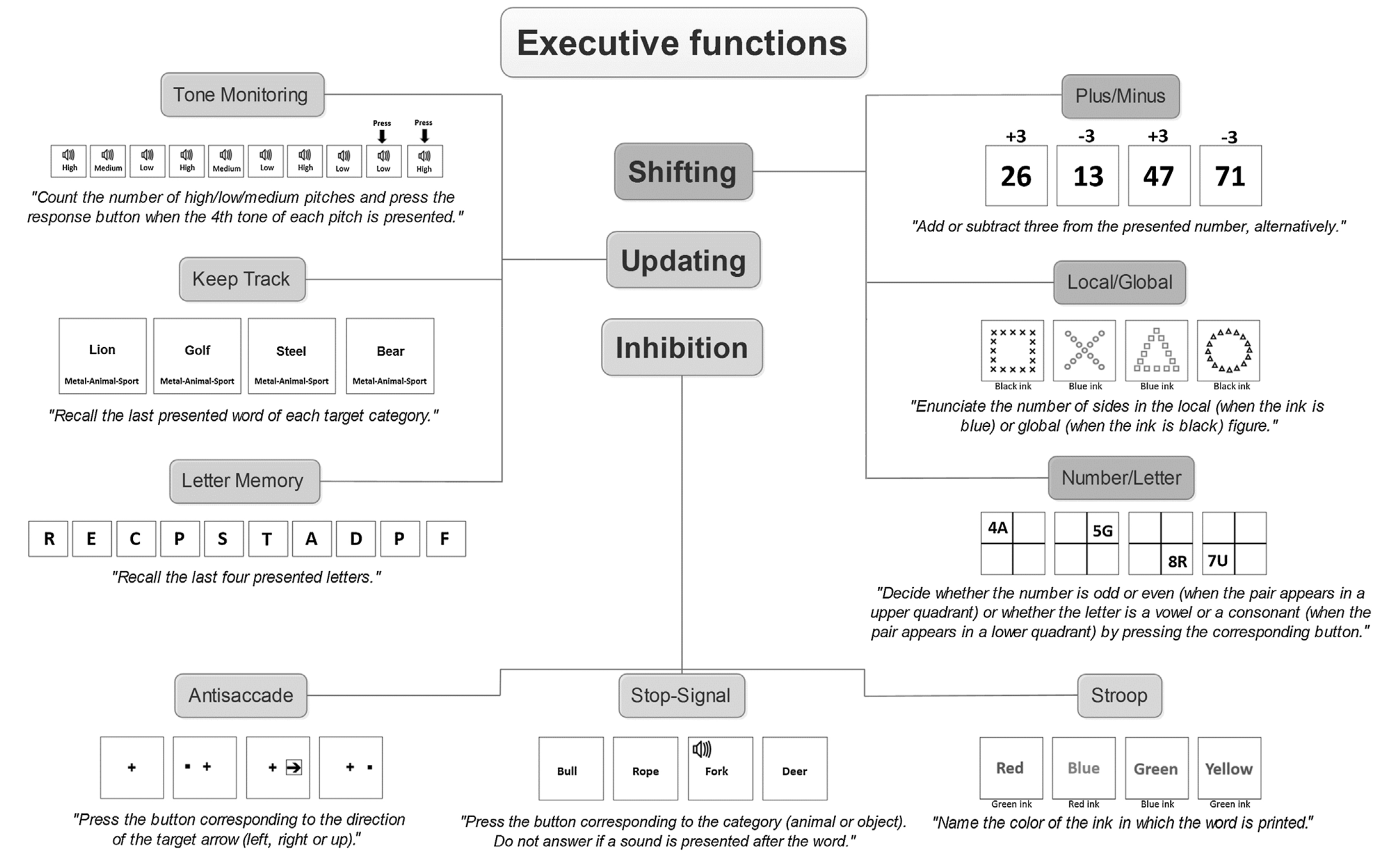

Fig. 1. Illustration of the nine executive functions tasks adapted from Miyake et al. (2000).

Table 2
Executive indexes (Accuracy and RT) for control (CP) and alcohol-dependent (ALC) participants for each experimental task: mean (S.D.).

	CP	ALC	N[b]	p-value for group effect	p-value for group effect with depression as covariate
Shifting 1: Plus-Minus					
Accuracy[a]	−5.9 (14.1)	−14.8 (19.1)	47	0.012	0.595
RT[a]	54.7 (162.5)	126.4 (204.3)	47/46	0.064	0.740
Shifting 2: Local-Global					
Accuracy	−5.5 (6.6)	−14.3 (16.4)	47	0.001	0.010
RT	367.3 (226.3)	462.9 (242.9)	47/46	0.053	0.216
Shifting 3: Number-Letter					
Accuracy[a]	−7.5 (15.4)	−19 (17.9)	47	0.001	0.113
RT	437.4 (217.3)	520.1 (216.4)	47	0.068	0.075
Updating 1: Tone Monitoring					
Accuracy	−38.2 (19.5)	−50.9 (23.3)	47/45	0.005	0.093
RT	476.8 (216.8)	406.2 (286.7)	46/45	0.188	0.133
Updating 2: Keep Track					
Accuracy	−21.9 (9.6)	−22.4 (14.8)	47	0.701	0.556
Updating 3: Letter Memory					
Accuracy[a]	−14.4 (11.8)	−31.5 (18.5)	47	< 0.001	0.018
Inhibition 1: Antisaccade					
Accuracy	−13.8 (15.9)	−19.8 (17.5)	46/43	0.090	0.836
RT	43.7 (76.8)	37.8 (139.2)	46/43	0.803	0.272
Inhibition 2: Stop-Signal					
Accuracy	−8.7 (26.6)	−36.5 (38.9)	47	< 0.001	< 0.001
RT	105.7 (78)	113.0 (101.7)	47	0.695	0.740
Percentage of efficient inhibition	92.3 (7.4)	86.7 (8.5)	47	0.001	0.028
Inhibition 3: Stroop					
Accuracy	−1.1 (2.5)	−4.2 (10.6)	47	0.070	0.527
RT[a]	178.6 (94.4)	285.4 (180.0)	47	0.001	0.108

[a] Significant correlation between the executive index and the Beck depression scale using Bonferroni adjusted alpha level of .0026 (0.05/19).
[b] Due to missing data for some participants in some tasks, the sample size finally included in the analyses slightly varied across subtasks.

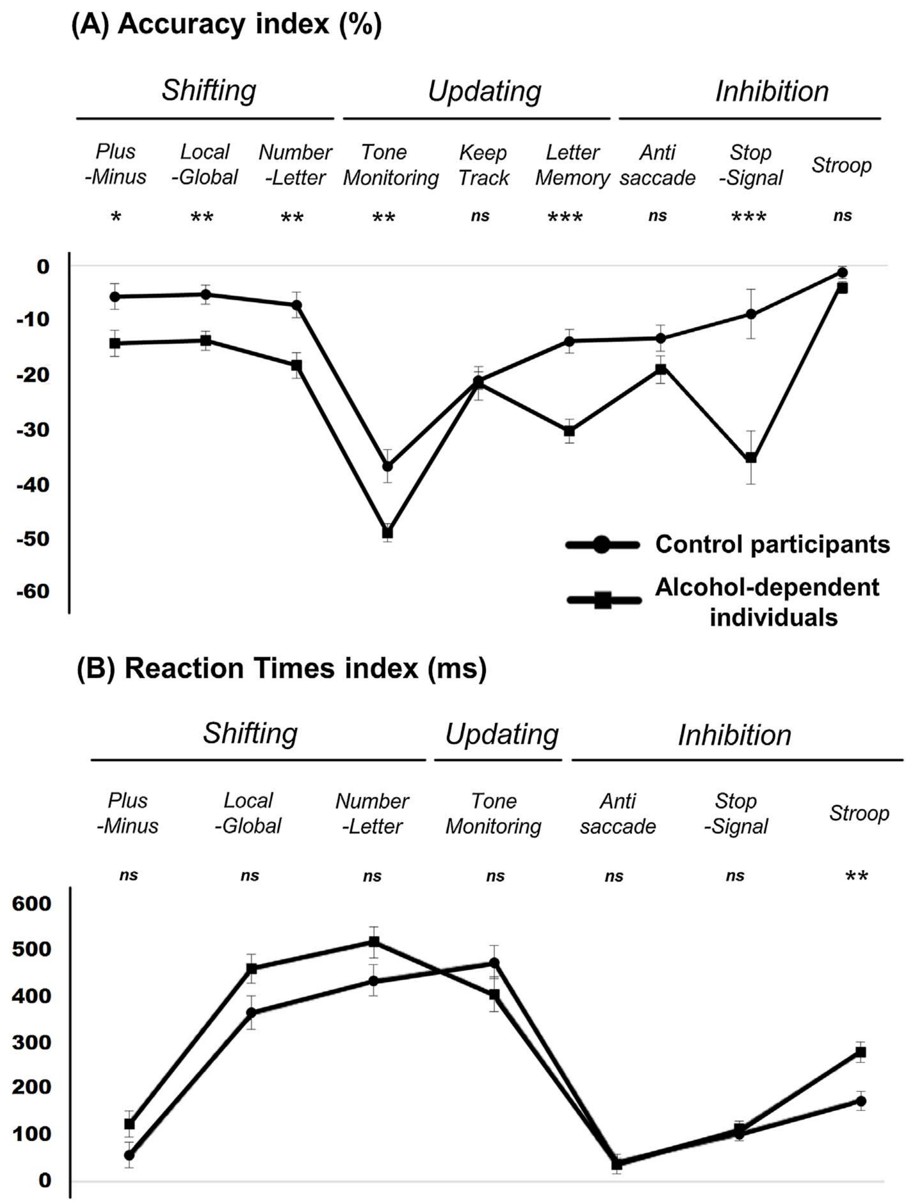

Fig. 2. Comparison between control participants and alcohol-dependent individuals on the experimental measures (accuracy and reaction times indexes) for the nine executive tasks. ns = non-significant; * = $p < 0.05$; ** = $p < 0.01$; *** = $p < 0.001$.

accuracy index [F(1,92) = 28.5, $p < 0.001$], showing that ALC had lower accuracy than CP. It should be underlined that no RTs were recorded for Keep track and Letter memory tasks.

3.1.3. Inhibition tasks

For the ***Antisaccade task,*** no significant group effect was found, neither for the *accuracy index* [F(1,87) = 2.93, p = 0.090] not for the *RT index* [F(1,87) = 0.06, p = 0.803]. For the ***Stop-Signal task***, a significant group effect was found, for the *accuracy index* [F(1,92) = 16.37, $p < 0.001$] showing that ALC presented more categorisation errors than CP, but not for the *RT index* [F(1,92) = 0.15, p = 0.695]. The percentage of efficient inhibition revealed a significant group effect [t(92) = 3.41, p = 0.001], ALC presenting a lower percentage of efficient inhibition than CP. It has to be underlined that, for the Antisaccade and Stop-Signal tasks, the measures specifically indexing inhibition were the accuracy index and the percentage of efficient inhibition, respectively, as the other results (i.e., RT index for the Antisaccade task, accuracy and RT indexes for the Stop-Signal task) reflect more general cognitive and visuo-motor abilities. For the ***Stroop task***, no significant group effect was found for the *accuracy index* [F (1,92) = 3.36, p = 0.070], but a significant group effect was observed for the *RT index* [F(1,92) = 12.98, p = 0.001], showing that ALC were slower than CP.

3.2. Comparison between executive subcomponents

A significant group effect was found [F(1,92) = 32.35, $p < 0.001$] showing that ALC had higher indexes, reflecting worse executive performance. No condition effect was found [F(2,184) = 1.84, p = 0.162]. No interaction between group and executive subcomponent was found [F(2,184) = 1.85, p = 0.160]. These results are presented in Table 3.

3.3. Influence of alcohol-consumption characteristics

Correlations within the ALC group between alcohol-related variables (alcohol consumption intensity, number of previous detoxification processes, alcohol-dependence duration) and tasks indexes were not significant (all $r < 0.268$, $p > 0.02$) after using Bonferroni adjusted alpha levels of 0.002 per test (0.05/19). Therefore these variables were

Table 3
Z-scores for each executive subcomponent (Shifting, Updating, Inhibition) for control (CP) and alcohol-dependent (ALC) participants: mean (S.D.), p-values [without covariate (with depression as covariate)] and effect-size (Cohen's d).

	CP	ALC	N	p-value for group effect	p-value for interaction	p-value for post-hoc *t*-tests on group comparison	Effect size
z-Shifting[a]	−0.15 (0.46)	0.21 (0.55)	47	< 0.001 (0.007)	0.160 (0.787)	< 0.001 (.122)	0.71
z-Updating[a]	−0.27 (0.40)	0.06 (0.52)	47			0.001 (0.075)	0.70
z-Inhibition	−0.34 (0.53)	0.23 (0.65)	47			0.001 (0.037)	0.96
Subcomponents comparison	No difference	No difference	47				

[a] Significant correlation between executive index and the Beck depression scale.

not considered as covariates in the subsequent analyses.

3.4. Influence of comorbidities

Groups did not significantly differ for trait anxiety [F(1,92) = 2.846, p = 0.095], but ALC presented higher state anxiety [F(1,92) = 5.123, p = 0.026] and depression [F(1,92) = 50.95, p < 0.001] scores than CP. Bonferroni-adjusted alpha level was set at 0.002 per test (0.05/19) for correlational explorations of task indexes. Anxiety was not significantly correlated with accuracy and RT indexes (r < 0.230, p > 0.026) after using Bonferroni adjusted alpha levels. Significant correlations were however found between depression scores and several tasks indexes, namely: Plus-minus RT (r = 0.36, p < 0.001) and accuracy (r = −0.36, p < 0.001), Number-Letter accuracy (r = 0.34, p = 0.001), Letter Memory accuracy (r = −0.49, p < 0.001), and Stroop RT (r = 0.38, p = 0.001). While all other correlations were non-significant (r < 0.10, p > 0.002), depression was considered as a meaningful factor for further analyses.

Complementary analyses of covariance (ANCOVAs) were thus used to explore group differences on task indexes and on subcomponent indexes with depression as covariate. Regarding task indexes, when depression was included as a covariate, the accuracy index remained significant for three tasks, namely Local-Global [F(1,91) = 6.88, p = 0.010], Letter Memory [F(1,91) = 5.80, p = 0.018] and Stop-Signal [F(1,91) = 23.25, p = 0.001], as well as for the percentage of efficient inhibition on the Stop-Signal [F(1,91) = 4.9, p = 0.028]. These results are presented in Table 2. Regarding the subcomponent indexes, a main group effect was found [F(1,91) = 7.62, p = 0.007] showing reduced executive functioning in ALC. No condition effect was found [F(2,182) = 1.88, p = 0.151]. No interaction between group and executive subcomponent was found [F(2,182) = 0,24 p = 0.787]. These results are presented in Table 3.

4. Discussion

Earlier studies using classical neuropsychological tests have repeatedly suggested that deficits in EF constitute an important factor in alcohol-dependence (Field et al., 2010; Noël et al., 2007). To overcome limitations of previously used multi-determined executive tasks, the present study capitalized on Miyake's model (Miyake et al., 2000) to compare the performance of ALC and matched controls on a neuropsychological battery assessing three main executive subcomponents: shifting, updating and inhibition. An index was computed to remove the non-executive variance from the performance (e.g., visuomotor impairment), and to offer more specific measures of executive processes.

The task index analysis provided a more precise approach of executive functioning, which is particularly interesting to identify between- and within-group differences on each subcomponent. Regarding RT, while raw analyses (see Supplementary Materials) totally confirmed the classical slowing down in alcohol-dependence (Fama et al., 2004; Knight and Longmore, 1996), specific comparisons performed on EF indexes did not reveal any strong difference between ALC and CP, as ALC were only impaired in the Stroop task, this difference even disappearing when depression was included as a covariate. In other terms, the RT impairment among ALC during executive tasks, repeatedly reported in earlier studies, might actually be explained by the fact that previous explorations did not take into account the non-executive and general slowing down related to alcohol-dependence, thus confounding non-executive and executive impairments. However, when the RT specifically related to EF are isolated as it is conducted here, it appears that RT do no constitute a key deficit in alcohol-dependence. Conversely, strong group differences were found for accuracy indexes, as ALC were impaired in the three shifting tasks as well as in two updating tasks, and in one inhibition task. It thus appears that when EF subcomponents are isolated, alcohol-dependence is associated with a global impairment for executive accuracy, encompassing inhibition but also shifting and updating abilities. Regarding these task indexes, it has to be acknowledged that, while they offered a reliable measure of executive functioning for most tasks, some indexes (i.e., RT index for the Antisaccade task and RT-accuracy indexes for the Stop-Signal task) were not specifically measuring the targeted executive subcomponent (which was respectively measured by accuracy index and percentage of correct inhibition for those tasks) but rather more general cognitive functioning, as underlined above.

In line with the recent call for a more in-depth exploration of EF processes among clinical populations (Friedman and Miyake, 2017), the present study also provided an integrated approach of EF subcomponents by merging individual tasks in a subcomponent z-score index allowing the direct comparison between the three subcomponents: ALC were impaired for shifting, updating and, inhibition. While this global approach of performance per subcomponent integration may miss more subtle differences that are tasks-specific, it offers an efficient overview of impaired subcomponents. This observation of a generalized deficit for the three EF subcomponents leads to an in-depth reinterpretation of earlier works exploring EF in ALC, which used multi-determined tasks not allowing to extract more refined measures of the executive processes at stake: when the specific performance related to EF is isolated from more global deficits, alcohol-dependence is not merely associated with inhibition alterations, but it rather appears that ALC present a global dysexecutive pattern, also characterized by shifting and updating deficits. The present study confirms earlier results on these subcomponents (Noël et al., 2012; Oscar-Berman et al., 2009; Pitel et al., 2007; Stavro et al., 2013) but nevertheless provides the advantage of using theoretically-grounded tasks design and analysis. The inability to make efficient choices in everyday life and to avoid alcohol consumption in ALC could thus be underpinned, rather than by a mere inhibition deficit, by a constellation of executive dysfunctions reducing their ability to inhibit erroneous decisions but also to take into account new pertinent information (updating deficit) and to adapt their behaviour following environmental changes in a flexible way (shifting deficit). Moreover, the present study underlines the need to use neuropsychological batteries proposing several tasks for each subcomponent and leading to the computation of executive indexes. Indeed, despite the fact that each task specifically focused on one EF subcomponent, some variability still remains across tasks (e.g., regarding the response mode or the involvement of visuo-motor processes). It is thus important to remain cautious in the interpretation of a single task and to explore the global pattern of results observed across different tasks to have a reliable measure of each EF subcomponent.

Another important insight of the present study is its control of psychopathological biasing variables, allowing to disentangle the respective influences of chronic alcohol consumption and psychopathological comorbidities. While anxiety levels were not related to executive impairments, five indexes were correlated with depression levels. The complementary analyses of covariance revealed that most of the significant group differences did not survive when depression was included as a covariate. This suggests that, alcohol consumption *per se* is not solely involved in EF deficits, comorbid depressive symptoms might further hamper executive functioning, leading to a cumulative deficit. In most cases, alcohol use disorders and depression are deeply intertwined (Schuckit, 2006), which is confirmed here as only fifteen ALC presented none-to-low depressive symptoms. Therefore, special caution should be taken with regard to depressive symptoms among ALC, especially during alcohol withdrawal (Luty and O'Gara, 2006; Schuckit, 1994). Conversely, no significant correlations were found between alcohol consumption characteristics and executive performance, which might be at least partly due to the difficulty to efficiently measure such parameters by self-report measures (Fein et al., 2006; Stavro et al., 2013). The causal link between EF deficits and alcohol consumption should thus be further explored, as pre-existing EF deficits may expose these individuals to heavy drinking behaviours (Volkow and Baler, 2012). Future studies should also further explore each executive component, as the three EF explored here might be further subdivided in subcomponents presenting differential deficits in alcohol-dependence. For example, it has been proposed that inhibition might encompass prepotent response inhibition (explored with the present inhibition tasks), but also resistance to distractor interference and resistance to proactive interference (Friedman and Miyake, 2004). While the present study focused on the initial tasks proposed by Miyake et al. (2000), future studies should also take into account the modifications proposed more recently for some of these tasks, for example by using an adjusted Stop-Signal reaction time as the dependent measure for the Stop-Signal task (Verbruggen and Logan, 2009)]. In the same vein, regarding shifting tasks, it should be noted that mechanisms measured by shifting indexes in the present study reflected mixing costs (i.e., poorer performance in mixed-task blocks compared to single task blocks) although switch cost (i.e., longer responses during switch trial compared to task-repetition trial within a block) is now considered as a more sensitive shifting measure (e.g., Kiesel et al., 2010; Monsell, 2003). Future studies should thus refer to more recent papers (Friedman et al., 2008) assessing EF by means of revised tasks, offering more precise measures than those used in Miyake et al. (2000). Specifically for shifting, these revised tasks present randomized switch and repetitive-trials, the switch cost being computed by comparing these two types of trials (Friedman et al., 2008). Moreover, while the present design focused on the initial theoretical assumptions of the model (Miyake et al., 2000), recent work (Friedman and Miyake, 2017; Miyake and Friedman, 2012) has argued that the inhibition subcomponent could constitute a common factor and share similar mechanisms with shifting and updating subcomponents. Future studies should thus explore whether the dissociation between EF subcomponents proposed here is strict or whether the deficits observed for shifting and updating abilities could be partly explained by impairments in a common inhibitory factor. Furthermore, future studies should investigate other key EF, beyond the model presented here, like planning or problem solving. As cognitive and cerebral changes occur after mid to long-term abstinence (Rosenbloom et al., 2004; Sullivan et al., 2010 for reviews), upcoming works could use the present subcomponent approach to explore the evolution of executive functioning with abstinence. It should also be acknowledged that a ceiling effect in the control group for some tasks (e.g., Stroop task) might have influenced our group comparisons, and that the quite limited sample led us to focus our analyses on individual accuracy and RT indexes scores rather than on the confirmatory factor analyses using latent-variables approach used in the original study (Miyake et al., 2000). Finally, not considering smoking information as a control factor might constitute a limitation of the present study: while contradictory results have been reported, nicotine dependence is known to influence EF (e.g., Flaudias et al., 2016; McClernon et al., 2016; Meyerhoff et al., 2006), the executive impairments found in ALC thus being potentially influenced by concurrent nicotine dependence.

Beyond these limitations, the present study claims for a more stringent approach when assessing EF in alcohol-dependence, by computing the executive subcomponent underlying observed performance. It also underlines the usefulness of capitalizing on model-based approaches, allowing a theoretically-grounded exploration of each executive subcomponent to go beyond the mere description of isolated cognitive deficits in psychiatric disorders. Finally, our results also bare critical implications for both prevention and treatment of alcohol-dependence, claiming for extending the role played by neuropsychological evaluation and rehabilitation in psychiatry care. Indeed, most current rehabilitation programs lead to an improvement in tasks' performance but fail to have a real impact on clinical symptoms and daily life (Snyder, 2015). Therefore, the present study, together with other recent ones using more specific EF tasks, should encourage the development of an integrative and individualized neuropsychological evaluation of EF among ALC during detoxification. This approach would allow to precisely determine impaired subcomponents and to propose individual rehabilitation strategy involving the creation of personalized material (e.g., inhibition task with alcohol-related items) that would favor the transfer of acquired competence in daily-life. Since executive training effectively reduces alcohol use in alcohol-related disorders (Houben et al., 2011), specifically targeting and training impaired EF subcomponent in ALC would help to promote sustainable abstinence, and would therefore contribute to reduce the high risk of relapse after detoxification (Finney et al., 1996).

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Contributors

M.B. and P.M. designed the study; M.B., F.D. and P.M. performed the literature review; M.B., B.L., M.F., P.d.T. and P.M. managed data collection; M.B., F.D., A.-L.P. analysed the data; all authors participated to the writing of the manuscript and approved the final version.

Conflict of interest

No conflict declared.

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Appendix A. Supplementary data

Supplementary data associated with this article can be found, in the online version, at http://dx.doi.org/10.1016/j.drugalcdep.2017.03.018.

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