

Attentional Alterations in Alcohol Dependence Are Underpinned by Specific Executive Control Deficits

Pierre Maurage, Philippe de Timary, Joël Billieux, Marie Collignon, and Alexandre Heeren

Background: Attentional biases and deficits play a central role in the development and maintenance of alcohol dependence, but the underlying attentional processes accounting for these deficits have been very little explored. Importantly, the differential alterations across the 3 attentional networks (alerting, orienting, and executive control) remain unclear in this pathology.

Methods: Thirty recently detoxified alcohol-dependent individuals and 30 paired controls completed the Attention Network Test, which allow exploring the attentional alterations specifically related to the 3 attentional networks.

Results: Alcohol-dependent individuals presented globally delayed reaction times compared to controls. More centrally, they showed a differential deficit across attention networks, with a preserved performance for alerting and orienting networks but impaired executive control ($p < 0.001$). This deficit was not related to psychopathological comorbidities but was positively correlated with the duration of alcohol-dependence habits, the number of previous detoxification treatments and the mean alcohol consumption before detoxification.

Conclusions: These results suggest that attentional alterations in alcohol dependence are centrally due to a specific alteration of executive control. Intervention programs focusing on executive components of attention should be promoted, and these results support the frontal lobe hypothesis.

Key Words: Alcohol Dependence, Attentional Networks, Attention Network Test, Executive Control.

ALCOHOL-related problems constitute one of the major public health issues worldwide, leading to 2.5 million deaths per year (World Health Organization, 2011). It is clearly established that alcohol dependence is associated with large-scale impairments at the cerebral level (Harper, 2007), centrally affecting white matter, subcortical areas, and frontal lobes (Harper and Matsumoto, 2005). Many studies have explored the behavioral correlates of these frontal alterations, repeatedly showing a large range of memory and executive functions impairments among alcohol-dependent subjects (ADS; Pitel et al., 2007). These numerous results have reinforced the “frontal lobe hypothesis” (Tarter, 1975), postulating that ADS centrally present frontal lobe abnormalities. Nevertheless, this focus on memory-executive dysfunctions has led to neglect the exploration of several other high-level cognitive functions and has thus hampered to obtain an exhaustive view of the neuropsychological alterations among ADS.

Centrally, attentional abilities have been little studied among ADS, as confirmed by a recent meta-analysis (Stavrou et al., 2013) showing that <10 studies have focused on attention deficits in alcohol dependence, and that only 3 explored attentional abilities after short-term abstinence. This lack of data appears surprising in view of the central role played by attentional alterations in the development and maintenance of this psychopathological state. Particularly, the presence of a strong attentional bias (i.e., a preferential allocation of attentional resources toward alcohol-related stimuli) has been documented among ADS during the last decade (Noël et al., 2005). As the extent of this attentional bias has been shown to be highly correlated with the intensity of craving and with the relapse risk after detoxification (Field et al., 2009), it might constitute a central variable underlying the persistence of alcohol dependence. Recent clinical trials reinforced this proposal by showing that attention retraining programs lowering this attentional bias efficiently reduced alcohol consumption in alcohol-related problems (Schoenmakers et al., 2010). However, while the central role of attentional bias among ADS is now widely recognized, the underlying attentional processes accounting for this bias remain poorly understood. Centrally, it is unclear whether these attentional alterations are only present for alcohol-related stimuli or whether the attentional bias partly relies on a more general impairment of the attentional system.

Indeed, only few studies investigated the behavioral, neurophysiological, and neuroimaging correlates of attentional deficits with nonalcohol-related stimuli among ADS. Several

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explorations, based on neuropsychological batteries exploring a wide range of cognitive functions (e.g., Nixon et al., 2007; Parsons and Nixon, 1998), first suggested the presence of attentional impairments in alcohol dependence. Neuroscience studies also showed that the electrophysiological components related to the attentional processing of auditory stimuli are delayed and reduced in alcohol dependence (Cohen et al., 1995; Ramachandran et al., 1996), and that white matter alterations and reduced activation of frontal areas contribute to this altered attentional performance (Oscar-Berman and Marinkovic, 2003; Pfefferbaum et al., 2001; Schulte et al., 2012; Sullivan, 2000). However, the studies focusing on specific subcomponents of the attentional system led to mixed results, some showing altered performance for selective and divided attention in ADS (Cordovil de Sousa Uva et al., 2010; Evert and Oscar-Berman, 2001; Fein and Andrew, 2011; Kopera et al., 2012; Maurage et al., 2008) while others described preserved attentional abilities (Bijl et al., 2005; Ceballos et al., 2005; Fein et al., 2006; Smith and Fein, 2010; Tedstone and Coyle, 2004; Zinn et al., 2003). A possible explanation for these discrepancies among earlier results is the use of very diverse tasks, simultaneously exploring several attentional abilities. These earlier studies were in fact not based on a recognized theoretical framework of attention and were thus not able to precisely compare the impairments across different subcomponents of the attentional system.

As a whole, the very limited number of studies currently available do not allow to draw reliable conclusions concerning attentional alterations in ADS (Stavro et al., 2013) and, as suggested in earlier studies (Tedstone and Coyle, 2004), a more systematic and reliable exploration of the attentional system is thus needed to better understand these attentional impairments. This exploration should be conducted by means of a unified task relying on a cognitive model and offering a specific evaluation of each attentional subcomponent. The Attention Network Test (ANT; Fan et al., 2002), based on a strongly validated model of attention (Petersen and Posner, 2012; Posner and Petersen, 1990), constitutes an adapted tool for this purpose. This task, based on a combination of Posner's cueing task (Posner, 1980) and Flanker task (Eriksen and Eriksen, 1974), provides a reliable assessment of the 3 independent attentional networks identified in the model, namely (i) The alerting network, allowing to achieve and maintain a state of high sensitivity or readiness in preparation for incoming stimulation; (ii) The orienting network, allowing to select information from sensory input by engaging, disengaging, and shifting the attentional resources from one stimulation to another; and (iii) The executive attention network, allowing to resolve conflicts among responses and involving the top-down control of attention. Neuroimaging studies reinforced the validity of this task by showing distinct cerebral activations related to each network, that is, superior temporal and thalamic activations for alerting, superior parietal lobule and fusiform gyrus activations for orienting, and thalamic and

superior-inferior frontal gyri activations for executive control (Fan et al., 2005).

Recent studies used the ANT to evidence differential attentional deficits across a wide range of clinical states. For example, multiple sclerosis leads to alerting impairment (Urbanek et al., 2010), while mild cognitive impairment leads to a specific orienting alteration (Fernández et al., 2011), and abnormalities in the executive control network were found in schizophrenia and anxiety disorders (Oggen-Rhein et al., 2008; Pacheco-Unguetti et al., 2011). Autism spectrum disorders are associated with a global impairment of the 3 attentional networks (Keehn et al., 2013). Moreover, recent studies described altered performance related to the executive attention network among cocaine (Woicik et al., 2009) and cannabis (Abdullaev et al., 2010) abusers. These studies clearly showed the high interest of the ANT to better understand the differential attentional deficits in psychopathological states, and notably in addictions. However, this task has surprisingly not yet been used in ADS, despite it could bring insights on the attentional deficit having a crucial role in this pathology. The main aim of the present study was thus to offer the first insights concerning the integrity of the 3 attentional networks in ADS, to better understand the attentional impairments in this pathology, and to explore the hypothesis of a differential deficit between these networks. Following the frontal lobe hypothesis, it could be hypothesized that ADS will present a specific deficit for the executive network of the attentional system, as this network mostly relies on frontal areas.

MATERIALS AND METHODS

Participants

Thirty inpatients (8 women) were recruited during the third week of their treatment in a detoxification center (StLuc Hospital, Brussels, Belgium). Alcohol-dependence diagnosis was established according to DSM-IV criteria (American Psychiatric Association, 2000) during an exhaustive interview performed by a trained psychiatrist. This semi-structured interview was also used to precisely determine medical history, alcohol-consumption characteristics, and psychopathological comorbidities. The demographic characteristics of alcohol-dependent participants appear in Table 1. They had all abstained from alcohol for at least 2 weeks (mean: 17.21 days; SD = 2.89) and were free of any other psychiatric diagnosis. Their mean alcohol consumption just before detoxification was 23.3 alcohol units per day (SD = 17.9) and the mean number of previous detoxification treatments was 1.43 (SD = 2.59). Patients were matched for age, gender, and education with 30 control subjects (CS) who were free of any history of psychiatric disorder or drug/substance abuse (excluding nicotine dependence). CS were recruited among the experimenters' acquaintances and the hospital employees. Each CS consumed <10 alcohol units per week and abstained from any alcohol consumption for at least 3 days before testing. Exclusion criteria for both groups included major medical problems, neurological disease (including epilepsy), visual impairment, and polysubstance abuse. Each participant had a normal-to-corrected vision. Education level was assessed according to the number of years of education completed since starting primary school. Nine ADS and 6 CS presented nicotine dependence. The mean number of cigarettes per day was 13.7 among CS (SD = 6.7)

Table 1. Demographic and Psychopathological Measures for Alcohol-Dependent Subjects (ADS) and Control Subjects (CS): Mean (SD)

	ADS (N = 30)	CS (N = 30)
Demographic measures		
Age ^{NS}	51.1 (11.62)	49.63 (12.61)
Gender ratio (female/male) ^{NS}	8/22	8/22
Educational level (in years) ^{NS}	14.93 (3.55)	16 (2.39)
Psychopathological measures		
Beck Depression Inventory (BDI)**	17.2 (10.35)	4.43 (4.38)
State and Trait Anxiety Inventory A (STAI-A)**	39.8 (10.77)	28.92 (8.27)
State and Trait Anxiety Inventory B (STAI-B)**	47.25 (9.66)	32.78 (9.45)
Toronto Alexithymia Scale (TAS)*	51.23 (10.12)	44.27 (11.11)

NS, nonsignificant.

* $p < 0.05$, ** $p < 0.001$.

and 11.3 among ADS (SD = 7.1). Participants were requested to abstain from smoking during the hour preceding the testing phase. Although all CS were free of any medication, 14 ADS still received moderate doses of benzodiazepines (mean: 15.23 mg/d; SD = 23.39). Participants were provided with full details regarding the aims of the study and the procedure to be followed. After receiving this information, all participants gave their informed consent. The study was approved by the Ethical Committee of the Medical School and carried out according to the Declaration of Helsinki. Participants were not paid for their participation.

Procedure and Analyses

Control Measures. ADS and CS were assessed using several psychological measures. Validated self-completion questionnaires were used to assess depression (Beck Depression Inventory; Beck and Steer, 1987), state and trait anxiety (State and Trait Anxiety Inventory; Spielberger et al., 1983), and alexithymia (20-item Toronto Alexithymia Scale; Bagby et al., 1994).

Experimental Measure. The ANT was administered to determine the efficiency of 3 independent attention functions: alerting, orienting, and executive control (Fan et al., 2002). Participants had to determine as fast and accurately as possible the direction of a central arrow (the target) by pressing the corresponding button (left or right) on a mouse. These targets were preceded by a cue, with 4 possible cue types (Fig. 1, upper part): no cue, center cue (an asterisk replacing the fixation cross), double cue (2 asterisks respectively appearing above and below the fixation cross), or spatial cue (an asterisk appearing above or below the fixation cross and indicating the location of the upcoming target). Moreover, flankers were located on each side of the target, with 3 possible flanker types (Fig. 1, middle part): 2 arrows in the same direction than the target (congruent condition), in the opposite direction (incongruent condition), or 2 lines (neutral condition). As shown in Fig. 1 (lower part), each trial had the following structure: (i) a central fixation cross (random duration between 400 and 600 ms); (ii) a cue (100 ms); (iii) a central fixation cross (400 ms); (iv) a target and its flankers, appearing above or below the fixation cross (lasting until the participant responded or for 1,700 ms if no answer was given); and (v) a central fixation cross (lasting for 3,500 ms minus the sum of the first fixation period's duration and the reaction time [RT]). RT (in milliseconds) and accuracy (percentage of correct responses) were recorded for each trial.

The experiment comprised 288 trials, divided in 3 blocks of 96 trials each (with a short break between blocks). There were 48 possible trials, based on the combination between 4 cues (no cue, center cue, double cue, spatial cue), 3 flankers (congruent, incongruent, neutral),

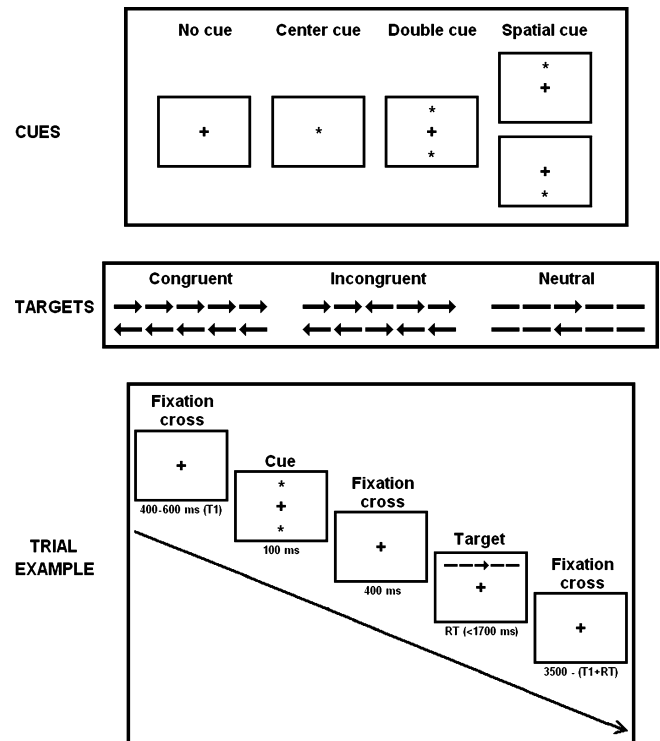


Fig. 1. Description of the Attention Network Test, illustrating the 4 possible cues (upper part), the 6 possible targets (middle part), and an example of the trials used in the task (lower part, i.e., neutral trial preceded by a double cue, the correct response being "right"). Adapted from Fan and colleagues (2002).

2 directions of the target arrow (left, right), and 2 localizations (upper or lower part of the screen). Trials were presented in a random order and each possible trial was presented twice within a block. The task was programmed and presented using E-Prime 2 Professional (Psychological Software Tools Inc., Sharpsburg, PA). The distance between participant's eyes and the screen was around 50 cm, and the target stimuli subtended a visual angle of about 4° in the horizontal field. The task was administered individually in a dark and quiet room, and was performed in 1 session of 70 minutes. The participant first signed the informed consent and read the instructions on the computer screen. Then, these instructions were emphasized by the experimenter and a training session started, consisting in 24 randomly selected trials. Finally, the experimenter recalled the instructions and answered the remaining questions before starting the experimental task. After the experimental task, the participant filled in the questionnaires.

Statistical Analyses. Data reduction was first performed: (i) trials with incorrect responses were excluded from the RT analyses (2.97% of trials); (ii) RT lower than 200 or >2,000 ms were removed from analyses (0.002% of trials with correct responses); and (iii) RT more than 2 standard deviations below or above each participant's mean for each experimental condition were discarded as outliers (0.013% of the remaining trials). A preliminary analysis showed no difference in RT or accuracy according to the direction (left or right) and localization (upper or lower) of the arrow, and these trials were thus merged, leading to 24 trials for each of the 12 experimental conditions (4 cues × 3 flankers).

A first general 2 × 4 × 3 analysis of variance (ANOVA) was then performed separately for RT and accuracy with Group (ADS, CS) as between-subjects factor, Cue (no cue, center cue, double cue, spatial cue) and Flanker (congruent, incongruent,

neutral) as within-subjects factors. Then a subtraction method (Fan et al., 2002) was used to isolate the evaluation of the 3 attentional networks: (i) The alerting effect was calculated by subtracting the mean result (i.e., RT or accuracy score) for double cue trials from the mean result for no cue trials (No cue – Double cue); (ii) The orienting effect was calculated by subtracting the mean result for spatial cue trials from the mean result for center cue trials (Center cue – Spatial cue); and (iii) The executive conflict effect was calculated by subtracting the mean result for congruent trials (summed across cue types) from the mean result for incongruent trials (Incongruent – Congruent). For both alerting and orienting effects, higher subtraction scores for RT (and lower for accuracy) indicated greater efficiency. On the contrary, higher subtraction scores for RT (and lower for accuracy) on executive conflict effect indicated increased deficit in the executive control of attention, as conflicts in the incongruent conditions increased the RT as compared to congruent ones (Fan et al., 2005). On the basis of these subtraction effects, a second general 2×3 ANOVA was performed separately for RT and accuracy with Group (ADS, CS) as between-subjects factor and Attention Network (Alerting, Orienting, Executive Conflict) as within-subjects factor. For each ANOVA, significant main effects and interactions were followed by univariate contrasts (post hoc independent samples *t*-tests). Independent samples *t*-tests were also computed to explore group differences on control measures. Two-tailed Pearson's correlations were performed to (i) test the influence of potential biasing variables on the results, particularly concerning psychopathological measures; and (ii) explore the links between the different experimental data. As our main focus concern the exploration of a potential deficit in ADS as compared to CS, the results section will focus on group comparison. Overall effects for each ANOVA (i.e., significant results nonrelated to group differences) are reported in Data S1.

RESULTS

Control Measures

As shown in Table 1, ADS and CS did not significantly differ in terms of age, $t(58) = 0.47$, $p = 0.64$, gender, and education, $t(58) = 1.36$, $p = 0.18$, thus confirming the correct matching between groups. Nevertheless, ADS showed higher scores than CS for depression, $t(58) = 6.24$, $p < 0.001$, trait

anxiety, $t(58) = 4.39$, $p < 0.001$, state anxiety, $t(58) = 5.86$, $p < 0.001$, and alexithymia, $t(58) = 2.54$, $p < 0.05$.

Experimental Measures

General Analysis. A 2 (groups) \times 4 (cues) \times 3 (flankers) ANOVA was performed separately for RT and accuracy. The results for each group in each experimental condition are presented in Table 2.

Accuracy: No main effect of group was found, $F(1, 58) = 0.95$, $p = 0.33$, nor any interaction with Cue, $F(3, 174) = 0.73$, $p = 0.54$, or Flanker, $F(2, 116) = 0.85$, $p = 0.43$.

RT: A main group effect was found, $F(1, 58) = 22.56$, $p < 0.001$: ADS presented higher RT than CS. An interaction between Group and Flanker was also found, $F(2, 116) = 15.59$, $p < 0.001$: ADS presented higher RT than CS for Congruent, $t(58) = 4.09$, $p < 0.001$, Incongruent, $t(58) = 4.53$, $p < 0.001$, and Neutral, $t(58) = 3.95$, $p < 0.001$, flankers, but this group difference was significantly higher for Incongruent than for Congruent, $t(29) = 4.22$, $p < 0.001$, and Neutral, $t(29) = 4.46$, $p < 0.001$, flankers.

Attentional Networks Analysis. A 2 (groups) \times 3 (attentional networks) ANOVA was performed separately for RT and accuracy. The results related to the RT indexes of these 3 attentional networks are illustrated in Fig. 2.

Accuracy: No main effect of Group, $F(1, 58) = 0.18$, $p = 0.67$, nor interaction between Group and Attentional Network, $F(2, 116) = 1.41$, $p = 0.25$, were found.

RT: A main effect of Group, $F(1, 58) = 10.26$, $p < 0.01$, was found, the Attentional Network indexes being higher among ADS than CS. Centrally, an interaction between Group and Attentional Network was found, $F(2, 116) = 10.78$, $p < 0.001$: As compared to CS, ADS were impaired for the Executive Conflict index, $t(58) =$

Table 2. Reaction Time (RT) (in Milliseconds) and Accuracy (Percentage of Correct Answers) Measures for Alcohol-Dependent Subjects (ADS) and Control Subjects (CS) in Each Experimental Condition of the Attention Network Test: Mean (SD)

	Group	No cue	Center cue	Double cue	Spatial cue
Congruent RT (ms)	ADS	714 (135)	689 (135)	667 (125)	641 (138)
	CS	580 (94)	559 (101)	547 (91)	502 (93)
Accuracy (% correct)	ADS	97.08 (12.19)	97.22 (12.15)	97.08 (12.29)	96.81 (12.26)
	CS	99.44 (1.44)	99.72 (1.05)	99.86 (0.76)	99.72 (1.06)
Incongruent RT (ms)	ADS	877 (168)	876 (180)	857 (171)	778 (178)
	CS	688 (105)	685 (113)	670 (97)	596 (119)
Accuracy (% correct)	ADS	93.33 (13.47)	92.22 (14.38)	95 (12.64)	95.28 (12.27)
	CS	95.41 (6.51)	94.03 (8.86)	95 (7.84)	96.81 (4.73)
Neutral RT (ms)	ADS	700 (134)	679 (132)	675 (129)	630 (138)
	CS	585 (95)	560 (97)	541 (87)	496 (87)
Accuracy (% correct)	ADS	95.83 (12.47)	97.08 (12.14)	97.22 (12.2)	96.94 (12.13)
	CS	98.89 (2.43)	99.17 (2.01)	99.58 (1.27)	99.86 (0.76)

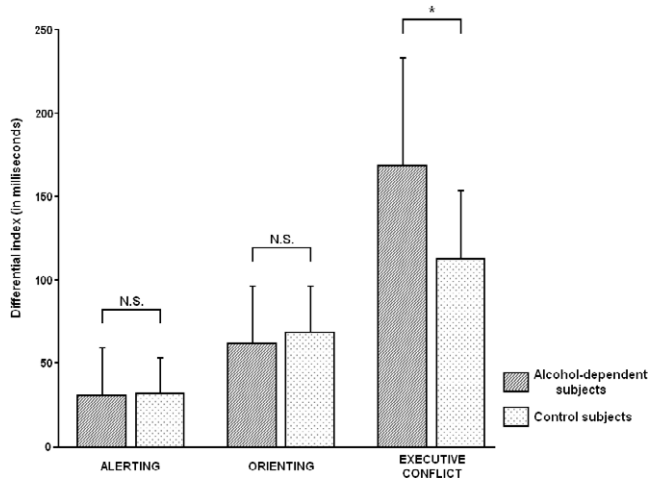


Fig. 2. Differential reaction time (RT) indexes (in milliseconds) among alcohol-dependent and control subjects for the 3 attentional networks, namely Alerting ($RT_{\text{No Cue}} - RT_{\text{Double Cue}}$), Orienting ($RT_{\text{Central Cue}} - RT_{\text{Spatial Cue}}$), and Executive Conflict ($RT_{\text{Incongruent}} - RT_{\text{Congruent}}$). Alcohol dependence is associated with a specific alteration for executive control ($*p < 0.001$), but preserved alerting and orienting abilities.

4.22, $p < 0.001$, but not for Alerting, $t(58) = 0.23$, $p = 0.82$, and Orienting, $t(58) = 0.83$, $p = 0.41$, ones.

Complementary Analyses. Complementary analyses were performed to:

Test for potential biasing effect of demographic and psychopathological variables: Pearson's correlations were performed in both groups between demographic-psychopathological variables (i.e., gender, age, cigarette consumption, benzodiazepine consumption, depression, anxiety, and alexithymia measures) and experimental results. No significant correlation was observed ($p > 0.05$ for every correlation).

Test for the links between alcohol-consumption characteristics and experimental results: Pearson's correlations were performed in ADS to explore the links between alcohol-consumption variables and experimental results. While no significant correlations were found for alerting ($r < 0.18$, $p > 0.33$) and orienting ($r < 0.24$, $p > 0.19$), the extent of the executive control impairment was significantly correlated with the duration of alcohol dependence ($r = 0.42$, $p < 0.05$), the number of previous detoxification treatments ($r = 0.51$, $p < 0.01$), and the alcohol consumption just before detoxification ($r = 0.46$, $p < 0.01$).

DISCUSSION

This study was the first to directly investigate the integrity of attentional networks in ADS by means of the ANT, a reliable and theoretically grounded task. While most other cognitive functions have been extensively explored, attentional

abilities have only been scarcely studied in ADS, some studies showing large-range attentional deficits (Evert and Oscar-Berman, 2001; Fein and Andrew, 2011; Kopera et al., 2012) while others described undamaged performance (Ceballos et al., 2005; Tedstone and Coyle, 2004; Zinn et al., 2003). These inconclusive data confound direct conclusions regarding the specific attentional networks impaired by alcohol dependence. The central result of the present study is the observation that ADS do not present a general attentional deficit but rather a specific deficit for the attentional network related to executive control.

Indeed, ADS first presented globally slower RT than CS, which is in line with earlier results (Maurage et al., 2013) showing visuo-motor slowing down in ADS. More interestingly, executive control network was strongly impaired among ADS as indexed by increased RT for incongruent trials (as shown in the General Analysis), and centrally by the higher executive conflict index (reflecting the RT delay provoked by incongruent flankers) than CS. This delay is present in CS (mean: 122 ms), which confirms several earlier results (Fan et al., 2009), but it is significantly stronger in ADS (mean: 168 ms; see Fig. 2). This reflects impaired executive control ability which are necessary to focus the attentional resources on pertinent information (i.e., central arrow) and inhibit the processing of confusing and irrelevant stimuli (i.e., incongruent flankers). In other words, this impairment suggests that the attentional deficits in ADS are mostly due to an inability to detect and resolve the conflict between task-relevant stimulus and the interference provoked by task-irrelevant stimuli. It is worth noting that executive attention as assessed by the ANT could partly depend on the ability to suppress an ongoing motor response (i.e., prepotent response inhibition), which is impaired in ADS (Goudriaan et al., 2006). This executive control impairment in ADS appears specifically associated with excessive alcohol consumption, as no influence of comorbid depressive or anxious states was found in correlational analyses.

Conversely, alerting and orienting attentional networks appear preserved among ADS, showing that they are able to take the cues into account to improve their performance. More specifically, ADS have a preserved ability to (i) increase one's phasic alertness and establish a vigilance state to prepare the processing of an upcoming stimulus (as indexed by alerting index); and (ii) orient attentional resources toward specific information by successively disengaging attention from earlier focus, moving it toward the new target and engaging attention at it. This differential deficit cannot be explained by a higher complexity of executive control as compared to alerting and orienting, as earlier studies have clearly shown a reverse deficit (preserved executive control network with impaired alerting or orienting ones) in other clinical populations (Fernández et al., 2011). The absence of correlation found here between the performances for each network further shows this independence between the subcomponents of the attentional system. Finally, no group difference was observed for the accuracy levels in any

attention network, which clearly proves that ADS correctly understood the requirements of the task, and which is in line with earlier studies among clinical populations (Fernández et al., 2011; Pacheco-Unguetti et al., 2011) showing a ceiling effect for accuracy in the task, hampering to identify group differences.

While no causal link can be inferred from our design, highly significant correlations were observed between the intensity of the executive deficit and alcohol-consumption characteristics (duration of alcohol dependence, number of previous detoxification, and daily consumption). These results support the proposal that the executive control deficit could be a direct consequence of alcohol neurotoxicity: the more and the longer the excessive alcohol consumption, the stronger the attentional executive deficit. This hypothesis makes sense in view of the current knowledge on the cerebral correlates of attentional networks and the brain impairments in ADS. Indeed, on the one hand, executive control of attention is related to frontal activations (centrally in the superior frontal gyrus) while alerting and orienting mostly rely on temporal-thalamic and parietal-fusiform activations, respectively (Fan et al., 2003, 2005). On the other hand, the frontal lobes are particularly altered in ADS (Harper and Matsumoto, 2005). Our results, by showing a specific alteration of the attentional network relying on frontal areas, thus support the frontal lobe hypothesis postulating that most neuropsychological deficits observed in ADS are underpinned by alterations of frontal areas (Tarter, 1975). Nevertheless, this proposal should be directly tested by neuroimaging studies. Moreover, as a family history of alcohol dependence is known to be related to executive control impairments independently of personal alcohol consumption (e.g., Acheson et al., 2011; Silveri et al., 2011), it cannot be excluded that some of the attentional impairments observed here might be related to the presence of positive family history of alcohol dependence in several ADS, and thus be present before the appearance of alcohol dependence.

At the fundamental level, the present result further confirm the validity of the attention model underlying the ANT by showing that differential deficit between networks, thus reinforcing earlier results suggesting a clear independence of the 3 networks (Fan et al., 2002; Urbanek et al., 2010). At the therapeutic level, our results underline the need to develop rehabilitation programs focused on executive control. Several efficient cognitive rehabilitation programs have recently been proposed in addiction (Rupp et al., 2012; Sofuoglu et al., 2013). Nevertheless, these programs only propose a global rehabilitation of attention using multidetermined tasks. In view of the present results, they should be adapted to focus the attentional remediation on executive control, as rehabilitating the preserved alerting and orienting networks appears of little usefulness. Several proposals have already been developed to specifically rehabilitate each attentional network (Thimm et al., 2006), and those focusing on executive control rehabilitation (Serino et al., 2007) should be adapted to ADS. Stimulating frontal areas in ADS by

means of neuromodulation, such as transcranial magnetic stimulation or transcranial direct-current stimulation, also constitutes a promising therapeutic tool, as these techniques have been successfully used in various psychiatric states to durably increase brain activation (Herremans and Baeken, 2012).

While our results are highly significant and based on a sound experimental design, they will have to be replicated in larger groups of ADS. Moreover, while some studies already explored the brain correlates of attentional deficits in ADS (Cohen et al., 1995; Oscar-Berman and Marinkovic, 2003; Ramachandran et al., 1996; Schulte et al., 2012), further neuroimaging studies should be conducted to confirm the implication of frontal areas in executive control impairments. Another limitation is the absence of control for family history of alcohol dependence, hampering to draw any strong conclusion concerning the causal link between alcohol dependence and attentional deficits. Despite these limitations, we believe that the present study, by offering the first exploration of attentional networks using the ANT and by showing a clear differential deficit between impaired executive control and preserved alerting and orienting, is a valuable first step toward a better understanding of the cognitive processes involved in attentional deficits in ADS.

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SUPPORTING INFORMATION

Additional Supporting Information may be found in the online version of this article:

Data S1. Overall effects for each ANOVA, describing the significant results nonrelated to group differences.