Theory of Mind Difficulties in Patients with Alcohol Dependence: Beyond the Prefrontal Cortex Dysfunction Hypothesis

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Background: Previous studies have shown that alcohol-dependent (AD) individuals have difficulties inferring other people's emotion, understanding humor, and detecting a faux pas. This study aimed at further understanding the nature of such "Theory of Mind" (ToM) difficulties.

Methods: A total of 34 recently detoxified AD and 34 paired controls were compared based on 2 nonverbal and video-based false belief tasks. These tasks were designed to identify 3 different types of deficits: (i) a deficit in dealing with the general task demands, (ii) a selective deficit in self-perspective inhibition, and (iii) a deficit in tracking the other person's mental state. (i) and (ii) are compatible with the hypothesis of a prefrontal cortex dysfunction being at the origin of AD individuals' social difficulties, while (iii) would suggest the possible contribution of a dysfunction of the temporo-parietal junction in explaining the social difficulties.

Results: Group analyses highlighted that AD individuals performed worse on the 2 false belief tasks than controls. Individual analyses showed, however, that just under half of the AD individuals were impaired compared to controls. Moreover, most of the AD individuals who were impaired showed a deficit in tracking the other person's belief. This deficit was linked to disease-related factors such as illness duration, average alcohol consumption, and craving but not to general reasoning abilities, depression, anxiety, or demographic variables.

Conclusions: Just under half of the AD individuals tested showed a ToM deficit, and in most cases, the deficit concerned the tracking of other people's mental states. Such a type of deficit has previously been associated with lesions to the temporo-parietal brain areas, indicating that a prefrontal cortex dysfunction may not be the sole origin of the social cognition deficits observed in alcohol dependence.

Key Words: Theory of Mind, False Belief, Mentalizing, Prefrontal Cortex, Temporo-Parietal Junction.

ALCOHOL DEPENDENCE WHICH is a very frequent psychiatric disorder with very important consequences for mortality and morbidity is associated with deficits in social interactions (Kornreich et al., 2011; Levola et al., 2014), poor ties to social groups (Chou et al., 2011), and tendencies to social estrangement (Thompson et al., 2010). Furthermore, difficulties in social interactions appear as a major factor of relapse in detoxified alcohol-dependent (AD) individuals (Zywiak et al., 2003) and improvement in the social network and social self-efficacy as a main predictor of recovery in abstinent alcoholics (Kelly et al., 2012).

However, the reasons for these social difficulties have still been scarcely explored. Most studies aiming at identifying the sources of social difficulties in AD individuals have focused on difficulties in emotional processing. For example, it has been shown that AD individuals have difficulties recognizing emotion expressions (especially anger) from faces (Kornreich et al., 2003; Maurage et al., 2011), postures (Maurage et al., 2009), or voice prosody (Monnot et al., 2001).

A few studies have also shown that AD individuals have difficulties in detecting humor (Uekermann et al., 2007), detecting that someone said unintentionally something hurtful, that is, a faux pas (Thoma et al., 2013) or reflecting on their own or other people's mental states (Bosco et al., 2014). This suggests that they may have a "Theory of Mind" (ToM) impairment, that is, difficulties inferring not only emotions but also other mental states such as desires, intentions, and beliefs. This study focuses on this particular aspect and aims at narrowing down the type of difficulties that AD

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individuals may have when confronted with mentalizing tasks.

The emerging view is that ToM is not a unitary function and that difficulties in ToM tasks may take various forms (Hartwright et al., 2012; Le Bouc et al., 2012; Samson, 2009). First of all, many ToM tasks are story based and place high demands on general cognitive control abilities (keeping track of the story, remembering who is who and who did what). Such general cognitive control abilities mostly depend on the integrity of the prefrontal cortex (Kane and Engle, 2002). Given that AD individuals have been shown to have memory and executive function impairments (Cordovil De Sousa Uva et al., 2010; Noël et al., 2001; Pitel et al., 2009), it may well be that this interferes with the patients' abilities to deal with the incidental demands of ToM tasks, while their ToM abilities per se may still be preserved. For instance, deficits in complex ToM tasks such as faux pas or humor processing have been related to deficits in working memory (Thoma et al., 2013) and executive functions (Uekermann et al., 2007), respectively.

It may also be that the processes that are core to ToM reasoning are impaired in AD individuals. Neuropsychological evidence obtained out of the field of alcohol dependence, from patients with acquired brain damage, suggests that these core processes are of 2 types. On the one hand, there are processes that allow us to track other peoples' mental states (their desires, beliefs, and intentions) and that recruit the temporo-parietal junction (Samson, 2009; Samson et al., 2004). Patients with such deficits have difficulties realizing that someone else's mental state is relevant to a particular situation and do not spontaneously infer the other person's mental state unless explicitly asked to do so. In daily life, such deficits manifest themselves through misunderstandings during social interactions because the patients have not inferred all the relevant information about the other person's mental state. On the other hand, there are processes that allow us to resist interference from our own perspective (Samson et al., 2005), in situations where an agent's desires, intentions, or beliefs are incongruent with our own mental states. The latter processes have been shown to recruit the lateral prefrontal cortex (Hartwright et al., 2012; Samson, 2009). Patients suffering from such a deficit become extremely egocentered and find it very hard to realize that other people may have a different view.

With the aim of identifying the types of ToM difficulties associated with AD, we used 2 nonverbal mentalizing tasks: one which placed high demands on self-perspective inhibition but which had direct mentalizing instructions and placed therefore low demands on the spontaneous tracking of the other person's mental state (we will refer to this task as the "Inhibit-Task") and one which has no direct mentalizing instructions and places therefore high demands on the spontaneous tracking of the other person's mental state but where the demands in terms of self-perspective inhibition were reduced (we will refer to this task as the "Track-Task"). In both tasks, there were nonmentalizing control items allowing us to see whether the participant could deal with the general and incidental task demands. The 2 tasks have been used previously to understand the origin of ToM impairments in healthy elderly subjects (Bailey and Henry, 2008), schizophrenic individuals (Bailey and Henry, 2010), and individuals with acquired brain damage (Apperly et al., 2004, 2005) and showed distinct types of mentalizing impairments, but these tasks have never been used with AD individuals before. If AD individuals have mentalizing problems due to a general reduction in cognitive resources, then we should expect that their impairment on the mentalizing items in any of the 2 tasks will be accompanied by an impairment on the nonmentalizing control items. On the other hand, if AD individuals have mentalizing problems because of a dysfunction of the core ToM processes, then we should observe selective impairments on the mentalizing items with spared performance on the nonmentalizing control items. Furthermore, depending on the task which is affected, we could further narrow down the ToM processes affected to either the processes involved in the inhibition of one's own perspective (which could be linked to the known prefrontal cortex dysfunction associated with AD) or the processes involved in tracking the other person's mental state (which may suggest that dysfunction in other areas than the prefrontal cortex also contribute to the social cognition deficits in AD).

Because different types of ToM deficits may be associated with alcohol dependence, we decided, in addition to group comparisons, to also compare the performance of each AD subject to the performance of the subset of controls that were best matched for demographic variables. This allowed us for each AD subject to identify whether the subject was impaired in the tasks and, if so, which type of deficit explained the performance.

MATERIALS AND METHODS

Participants

Thirty-four inpatients (8 women), presenting with a DSM-IV diagnosis of alcohol dependence (American Psychiatric Association, 1994), were recruited during the fourth week of their treatment in a detoxification center ("Chêne aux Haies Hospital," Mons, Belgium). They had all abstained from alcohol for at least 3 weeks (M = 25.12 days, SD = 3.08). The exclusion criterion was the existence of a history of any other Axis I DSM-IV disorder and specifically the existence of dependence to any other drug except nicotine.

The mean alcohol consumption among AD participants before detoxification was 20.12 alcohol units (=10 g of pure ethanol) per day (SD = 9.45). The mean duration of alcohol dependence was 12.26 years (SD = 8.53). The mean number of previous detoxification treatments was 2.06 (SD = 1.91).

AD individuals were matched for age, gender, and education levels (measured as the number of years of education completed since starting primary school) with a control group composed of 34 volunteers (8 women) recruited by means of advertisement and who participated in a larger study in exchange of a compensation of 30 euros. Controls were free of any history of Axis I DSM-IV psychiatric disorder or substance abuse/dependence except for nicotine. The mean alcohol consumption among controls was 0.79 units per

Table 1. Comparison Between Demographic, Psychological, Cognitive, and Illness-Related Measures of Healthy and Alcohol-Dependent (AD) Individuals

	Healthy controls (N = 34) (n or mean ± SD)	AD individuals (N = 34) (n or mean ± SD)
Demographic variables		
Male/female ratio	26/8	26/8
Age (years)	47.15 ± 10.42	48.85 ± 8.75
Education (years)	11.50 ± 2.79	11.56 ± 3.07
Cigarettes per day	3.44 ± 7.06	10.85 ± 10.28**
Smokers	11	22
Control measures		
Raven Matrix	48.00 ± 6.44	39.53 ± 9.89***
STAI-state[a]	30.38 ± 10.01	41.68 ± 14.26***
STAI-trait[a]	36.26 ± 9.51	49.47 ± 12.56***
BDI[b]	3.06 ± 2.42	10.24 ± 7.29***
Interpersonal Reactivity Index		
Empathic concern	27.15 ± 5.03	25.03 ± 5.62
Personal distress	18.32 ± 3.91	19.82 ± 6.11
Fantasy scale	20.44 ± 5.07	18.41 ± 5.61
Perspective taking	24.65 ± 4.40	20.74 ± 4.99**
Disease-related factors		
Obsessive-Compulsive Drinking Scale (OCDS) obsessive thinking	1 ± 2.50	5.79 ± 4.25***
OCDS compulsive behavior	0.62 ± 1.44	3.68 ± 3.39***
OCDS global score	1.65 ± 3.83	9.15 ± 7.05***
Number of drinks per day	0.79 ± 1.12	20.12 ± 9.45***
Number of inpatient days	–	25.12 ± 3.08
Alcoholism duration (in years)	–	12.26 ± 8.53
Previous hospitalization	–	2.06 ± 1.91

[a]State Trait Anxiety Inventory for adults.
[b]Beck Depression Inventory Scale.
**$p < 0.01$, ***$p < 0.001$.

day (SD = 1.12), and they abstained from any alcohol consumption for at least 3 days before testing.

Twenty-two AD participants and 11 controls were smokers: the mean number of cigarettes per day was 3.44 among controls (SD = 7.06) and 10.85 among AD individuals (SD = 10.28). Controls were free of medication. Eight AD individuals still received low benzodiazepines doses (i.e., diazepam or lorazepam). The mean benzodiazepine doses received (expressed in diazepam equivalents) was 7.44 mg/d (SD = 12.56). Table 1 summarizes the characteristics of the AD and healthy control groups.

Procedure

After providing written informed consent, participants were tested individually on a large battery of control measures and social cognition tasks. Testing was divided into 2 sessions of 2 hours. The results of only 2 of these tasks are presented here.

Experimental Tasks

The 2 experimental tasks were based on the false belief paradigm, which explores the ability to infer that someone else's representation of the state of the world does not match the real state of the world. The false belief task is a key task widely used in the literature to assess someone's ability to infer other people's mental states in order to understand and predict their behavior (i.e., "ToM"; Premack and Woodruff, 1978). The 2 tasks were nonverbal and video based. The tasks varied along 2 characteristics: (i) the demands in self-perspective inhibition and (ii) the explicitness with which participants were invited to take the protagonist's perspective (to test whether participants spontaneously engage in belief reasoning).

Track-Task. Participants were presented with 48 short videos: 12 false belief, 12 memory control, and 24 filler trials (these filler trials were used to ensure that subjects did not base their responses on superficial strategies; for details about the task, see Apperly et al., 2004; Samson et al., 2004). Participants were instructed to find in which of 2 identically looking boxes a green cube was located. They were told that the woman in the video will help them find the green object. In the false belief trials (see Fig. 1), participants saw the woman watching in which box the green object was located—the angle of the camera was such that participants could not see where the green object was located (Fig. 1*A*). The woman then left the room, and while she was out, the man swapped the 2 boxes (Fig. 1*B*). Once back, the woman pointed to one of the boxes (Fig. 1*C*). To find the green object, participants had to infer that the woman had a false belief (given that she did not see the swap of boxes) and that, therefore, the green object was located in the opposite box to the one the woman pointed at. Importantly, at the time participants could infer that the woman had a false belief (i.e., when the man swapped the boxes), participants had no idea where the green object was located. There was thus no need to resist interference from one's own knowledge of the true location of the green object when reasoning about the woman's belief (low self-perspective inhibition demands). However, because the main task instruction consisted in finding the green object, participants had to realize that paying attention to the woman, and more particularly her belief, was useful for their task (high spontaneous tracking demands). The memory control and filler trials could be solved without false belief reasoning (see Method S1). For each participant, we recorded the number of correct responses for the false belief trials (maximum score: 12/12), the memory control trials (maximum score: 12/12), and the filler trials (maximum score: 24/24).

Inhibit-Task. Participants were presented with 36 short nonverbal videos: 12 false belief, 12 memory control, and 12 filler trials (for details about the task, see Samson et al., 2005). The videos were similar to the ones used in the Track-Task except that the participants were asked to indicate which of the 2 boxes the woman would open first to find the green object and that, this time, the camera angle allowed the participant to see in which box the man was hiding the green object (see Fig. 1*D*,*E*). Thus, in this task, inferring the woman's false belief required from participant that they inhibit their own knowledge about the true location of the object (high self-perspective inhibition demands; Fig. 1*F*). However, the task instructions invited directly the participants to pay attention to the woman for their task (low spontaneous tracking demands). Here again, the memory control and filler trials could be solved without false belief reasoning (see Method S1). For each participant, we recorded the number of correct responses for the belief trials (maximum score: 12/12), the memory control trials (maximum score: 12/12), and the filler trials (maximum score: 12/12).

Each of the 2 experimental tasks was presented at the beginning of 1 session. The Track-Task was always presented before the Inhibit-Task so that the extent to which a participant spontaneously tracks the woman's belief could be reliably tested without contamination from the explicit instructions of the Inhibit-Task.

Besides the global comparison of the scores of the AD and control subjects on the false belief and memory control trials of both tasks, each AD individual was categorized as having either spared belief reasoning or 1 of 3 types of deficits. To achieve this, results of each AD individual on the false belief and memory control trials of the Track-Task and Inhibit-Task were compared with the score of 5 controls[1] matched by age, sex, and education level. In line with Crawford and colleagues (2003) operationalized definition of a deficit in single-case studies, we considered that a patient's performance in a task was impaired when the performance was significantly dif-

[1]This meant that 2 additional female controls were recruited.

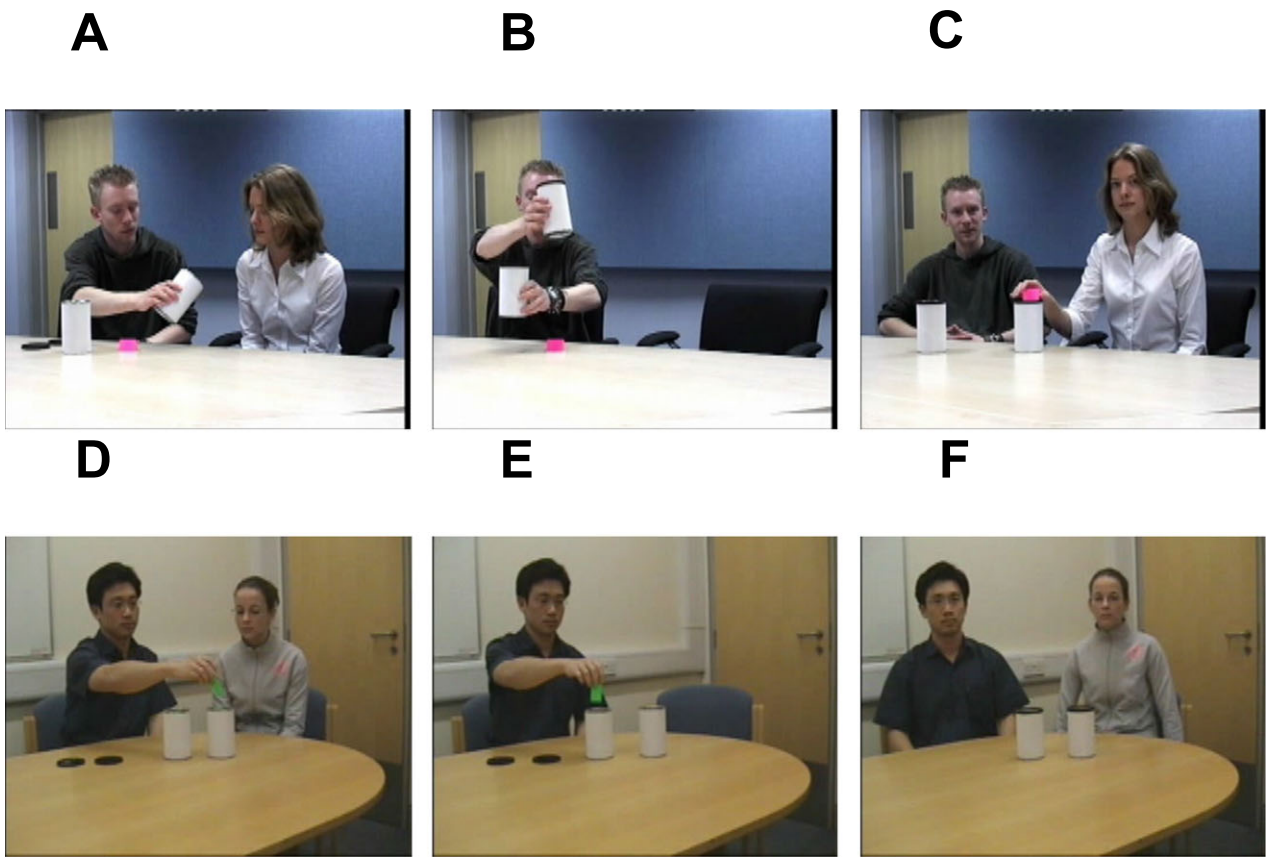

Fig. 1. Schematic representation of the sequence of events in the false belief trials of the task that places high demands on the spontaneous tracking of the other person's perspective (Track-Task; top panel) and the false belief trials of the task that places high demands in self-perspective inhibition (Inhibit-Task; bottom panel). In the Track-Task (**A, B, C**), participants are instructed to find in which of 2 identically looking boxes a green cube is located (implicit belief reasoning instruction). (**A**) The woman watches in which box the green object is located (while the participant cannot see the object location). (**B**) The woman leaves the room, and while she is away, the man swaps the 2 boxes. (**C**) The woman returns and points to one of the boxes to help finding the green object. At this point, participants are asked to point to the box containing the green object. In the Inhibit-Task (**D, E, F**), participants are asked to indicate which of the 2 boxes the woman will open first to find the green object (more explicit belief reasoning instruction). (**D**) The woman watches in which box the green object is located (and this time the participant can also see the object location). (**E**) The woman leaves the room, and while she is away, the man changes the object location. (**F**) The woman returns and participants are asked to point to the box the woman will open first. Note that a feedback about the correct response is provided after each trial of both tasks.

ferent from controls ($p < 0.05$, 1-tailed) in a modified *t*-test adapted to single-case studies (Crawford and Howell, 1998).

Based on these analyses, participants were considered as having no belief reasoning deficit when they showed a comparable performance to that of the controls on all the different trials of the Track-Task and Inhibit-Task (see Table 2). In addition, it was important to ensure that the good performance on the false belief trials was not just resulting from the use of a superficial response strategy (such as always choosing the box opposite to the one the woman pointed at in the Track-Task, for example). The good performance on the false belief trials needed thus to be accompanied by a good performance on the filler trials.

The other participants were classified in 1 of 3 deficits depending on their pattern of performance across the different trial types of the Inhibit-Task and the Track-Task (see Table 2 for a summary):

Type 1 Deficit. A selective self-perspective inhibition deficit whereby the participant wrongly attributes his own knowledge of the state of the world to other people. We expect here that the participant will only have difficulties when he has privileged access to some information that the other person does not have (such as in the Inhibit-Task). The participant's performance would thus be expected to be significantly below the controls' performance on the false belief but not the memory control trials of the Inhibit-Task, while the performance on the false belief trials of the Track-Task should be spared.

Type 2 Deficit. A deficit in tracking the other person's belief whereby the participant does not spontaneously track the other person's belief and/or does not know which cues from the environment to consider to ascribe a belief content to the other person. We expect here that the participant will have difficulties especially when the task instructions do not draw attention to the other person (such as in the Track-Task), but such difficulties could also be observed in the Inhibit-Task (where belief tracking is also required). The participant's performance would thus be expected to be significantly below the controls' performance on the false belief but not the memory control trials of the Track-Task, and this could happen with or without impairment on the false belief trials of the Inhibit-Task.

Type 3 Deficit. A general cognitive deficit whereby the participant loses track of the events and applies his or her belief reasoning on wrong or incomplete information. The participant's performances on the false belief and the control trials of the Track-Task or Inhibit-Task would thus expected to be significantly below the controls' performance.

Table 2. Criteria for Participants's Classification as a Function of Their Performance on the Various Trials of the Inhibit-Task and the Track-Task

	Inhibit-Task High self-perspective inhibition demands Low spontaneous tracking demands			Track-Task Low self-perspective inhibition demands High spontaneous tracking demands		
	False belief	Memory control	Filler	False belief	Memory control	Filler
No belief reasoning deficit	Spared	NA[a]	Spared	Spared	NA[a]	Spared
Type 1 deficit: Selective deficit in self-perspective inhibition	**Impaired**	Spared	NA[b]	Spared	Spared	Spared
Type 2 deficit: Deficit in spontaneous belief tracking	Spared or Impaired[c]	Spared	Spared	**Impaired**	Spared	NA[b]
Type 3 deficit: General cognitive deficit	**Impaired**	**Impaired**	NA[b]	**Impaired**	**Impaired**	NA[b]

NA, not applicable. Impairment in responses to specific tests allow to classify the alcohol-dependent individuals according to deficit types and are depicted in bold.

[a]Control trials do not require belief reasoning, and thus, impairment on these trials but spared performance on belief reasoning trials is not informative about belief reasoning.

[b]Filler trials are only taken into account for the classification when the performance is preserved on false belief trials as this ensures that successful belief reasoning was not achieved via the reliance on a superficial strategy.

[c]A deficit in spontaneous belief tracking must result in an impairment on the false belief trials of the Track-Task. It may, however, also result in difficulties in the Inhibit-Task if, even in that task, participants cannot track the relevant elements in the scene to infer that the woman in the video has a false belief.

Interpersonal Reactivity Index

The Interpersonal Reactivity Index (IRI) is a 28-item self-administered questionnaire (Davis, 1983; French validation by Gilet et al., 2013). The IRI assesses different aspects of social cognition on the basis of 4 subscales: (i) "Empathic Concern," that is, the ability to be emotionally concerned by others' feelings, (ii) "Personal Distress," that is, the tendency to have self-oriented negative feelings in response to others' distress, (iii) "Perspective Taking," that is, the ability to adopt other's point of view at a cognitive level, and (iv) "Fantasy," that is, the ability to project oneself into fictional characters. Each subscale had 7 items to be rated on a 5-point Likert scale (from 1 "it does not describe me at all" to 5 "it describes me very well").

Other Control Measures

Because of the frequent comorbidity between alcoholism and symptoms of depression and anxiety, patients and control participants were presented with the Beck Depression Inventory Scale (BDI short version in 13 items; Beck et al., 1961) and State Trait Anxiety Inventory for adults (STAI A-B; Spielberger et al., 1983).

Global intelligence was assessed by the Raven's Progressive Matrix (Raven et al., 1998).

Alcohol craving was measured with the Obsessive-Compulsive Drinking Scale (OCDS; Anton and Drobes, 1998; Roberts et al., 1999) in a validated French version (Ansseau et al., 2000). The OCDS questionnaire can be divided into an obsessive and a compulsive subscale. Because alcohol drinking was prohibited during detox, we used a modified version of the OCDS where the 4 compulsive items that are directly related to current alcohol drinking were removed.

The study was approved by the ethical committee of the Centre Hospitalier Universitaire, Chêne aux Haies, Ambroise Paré.

RESULTS

Group Level Analysis

AD individuals scored significantly higher than controls for trait anxiety, state anxiety, depression, and alcohol craving and significantly lower for global intelligence (see Table 1).

Regarding the IRI, AD individuals only differed from controls for the "Perspective taking" subscale, $t(66) = -3.43$, $p = 0.001$ (see Table 1).

AD individuals (mean = 8.79; SD = 3.41) also had significantly lower scores than controls (mean = 11.50; SD = 0.9) on the false belief trials of the Track-Task, $t(37.54)^2 = -4.48$, $p < 0.001$ (see Fig. 2). They also had significantly lower scores (mean = 9.5; SD = 3.53) than controls (mean = 11.76; SD = 0.55) on the false belief trials of the Inhibit-Task, $t(34.63)^2 = -3.7$, $p < 0.01$. However, the 2 groups did not differ on the memory control trials of the Track-Task (AD: mean = 11.59; SD = 0.96; CT mean = 11.74; SD = 0.45; $t(66)<1$, $p = 0.42$) or the Inhibit-Task (AD: mean = 11.18; SD = 1.19; CT mean = 11.56; SD = 0.75; $t(55.41)^2 = -1.59$, $p = 0.119$.

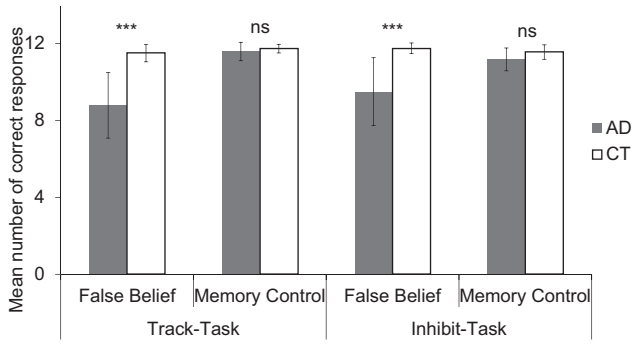

Fig. 2. Group analysis: Alcohol-dependent (AD) and control (CT) participants' number of correct responses on the false belief and memory control trials of false belief task that places high demands in the spontaneous tracking of the other person's perspective (Track-Task) and false belief task that places high demands on self-perspective inhibition (Inhibit-Task). Error bars represent standard errors. ns = nonsignificant; ***$p < 0.001$.

[2]Test corrected for unequal variances.

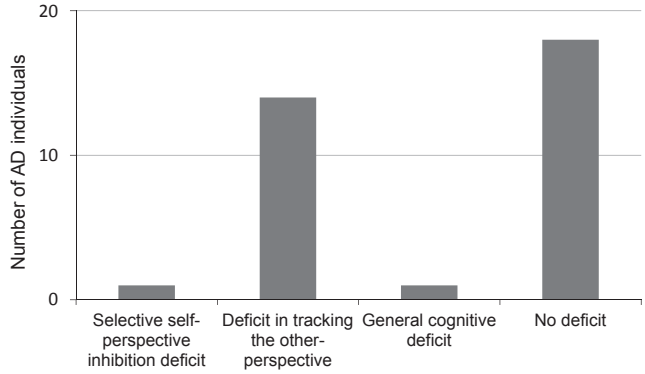

Fig. 3. Single-case analyses: Distribution of the alcohol-dependent (AD) individuals as a function of whether their pattern of performance showed a self-perspective inhibition deficit, a deficit in tracking the other perspective, a general cognitive deficit, or no deficit.

Individual Case Analyses

The majority of AD individuals presented with no deficit (52.94%; see Fig. 3). The second most frequent pattern of performance was that conforming to a deficit in tracking the other person's perspective (41.18%). Among the patients conforming to this type of deficit, 71.43% had also a significantly lower score on the Inhibit-Task. The 2 other types of deficit, that is, a selective self-perspective inhibition deficit and a general deficit, only occurred once (3%).

To explore the characteristics of the AD individuals with versus without a deficit in tracking the other perspective, we performed a series of independent sample *t*-tests on demographic, disease-related measures, control measures, and the IRI subscales (see Table 3). The measures that significantly differed across the 2 groups were disease-related variables. AD individuals showing a deficit in tracking the other perspective also displayed longer years of alcohol abuse, a higher level of alcohol consumption, and higher levels on the obsessive, compulsive, and global ODCS scores. There was also a significant difference on Raven's Progressive Matrix, $t(30) = 2.25$, $p < 0.05$, with those individuals showing a deficit in tracking the other perspective scoring lower as a group. The relation between the false belief reasoning profile and the general reasoning profile was, however, not straightforward. Several AD individuals having no deficits in belief reasoning had a general reasoning score that placed them lower than the 25th percentile, while several individuals with a deficit in false belief reasoning had a general reasoning score placing them above the 25th percentile (sometimes even between the 75th and the 90th percentile). Hence, impaired false belief reasoning performance was not necessarily associated with impaired general reasoning performance as assessed by Raven's Progressive Matrix.

Table 3. Comparison of Demographic, Psychological, Cognitive, and Illness-Related Variables Between Alcohol-Dependent (AD) Individuals With Versus Without Theory of Mind Deficits

	AD with a deficit in tracking the other perspective ($N = 14$) mean ± SD	AD with no deficit ($N = 18$) mean ± SD
Demographic variables		
Male/female ratio	10/4	14/4
Age (years)	48.50 ± 9.46	48.72 ± 8.82
Education level (years)	11 ± 2.48	11.83 ± 3.33
Cigarettes per day	12.14 ± 10.75	8.39 ± 9.41
Smokers	9	11
Psychological and cognitive measures		
Raven Matrix	35.71 ± 11.18	43.17 ± 7.56*
STAI-state[a]	44.07 ± 16.36	39.33 ± 13.31
STAI-trait[a]	50.93 ± 12.44	48.94 ± 13.14
BDI[b]	10.86 ± 7.58	9.56 ± 7.60
Interpersonal reactivity Index		
Empathic concern	26.50 ± 5.69	23.50 ± 5.56
Fantasy scale	19.86 ± 6.01	17.39 ± 5.50
Personal distress	19.71 ± 6.33	19.39 ± 6.25
Perspective taking	22.07 ± 3.69	19.39 ± 5.79
Disease-related factors		
Obsessive-Compulsive Drinking Scale (OCDS) obsessive thinking	7.29 ± 4.46	4.06 ± 3.40*
OCDS compulsive behavior	4.86 ± 3.42	2.44 ± 3.11*
OCDS global score	12.14 ± 7.64	5.89 ± 4.99**
Number of drinks per day	24.29 ± 9.66	17.06 ± 8.71*
Number of inpatient days	25.29 ± 3.17	24.56 ± 2.94
Alcoholism duration (in years)	15.64 ± 9.90	9.00 ± 5.99*
Previous hospitalization	2.14 ± 1.92	1.83 ± 1.98

[a]State Trait Anxiety Inventory for adults.
[b]Beck Depression Inventory Scale.
*$p < 0.05$, **$p < 0.01$.

DISCUSSION

In this study, we presented AD individuals with 2 false belief tasks which allow to specify the types of ToM impairments that these individuals may have. When considering the whole group, we observed that AD individuals had significantly lower scores on both ToM (false belief) tasks when compared to controls. These findings are in line with previous observations of a general ToM deficit in AD individuals (Thoma et al., 2013; Uekermann et al., 2007).

However, when each AD individual was compared to a group of matched controls using single-case statistical analyses (Crawford and Howell, 1998), we showed that the AD group was far from homogeneous: Some subjects presented with severe deficits on the ToM tasks that can be compared to what is observed in brain-damaged individuals (Apperly et al., 2004) or schizophrenic patients (Bailey and Henry, 2010); other AD subjects did not differ from controls. Furthermore, the difference in ToM abilities among the AD subjects was not related to differences in demographic variables, intelligence scores, depression, or anxiety. However, there was a significant difference between the impaired and spared AD individuals on disease-related variables. AD individuals who presented with deficits in the ToM tasks had a longer history of alcoholism, used to consume a higher number of alcohol units per day, and presented with higher craving scores.

It is now increasingly acknowledged that ToM, and particularly belief reasoning, is a multifaceted ability which is underpinned by distinct cognitive and neural processes (Hartwright et al., 2012; Samson, 2009) any of which can be selectively impaired and lead to ToM impairments. The 2 false belief tasks that we used allowed for the first time to explore the types of mentalizing process that may be impaired in AD. More specifically, the tasks allowed us to disentangle 3 types of deficits that can lead to impaired performance in ToM tasks: (i) a deficit in dealing with the general task demands (the subject loses track of the events and applies his or her belief reasoning on wrong or incomplete information), (ii) a selective deficit in self-perspective inhibition (the subject wrongly attributes his or her own mental state to other people, Samson et al., 2005), and (iii) a deficit in tracking the other person's mental state (the subject does not spontaneously track the other person's belief and/or does not know which cues from the environment to use in order to ascribe a belief content to the other person, Samson et al., 2004). Quite strikingly, 14 of the 16 AD individuals who showed an impairment in the ToM tasks showed a deficit in tracking the other person's belief.

Two additional observations are worth highlighting. First, the good performance of these 14 AD individuals on the memory control trials of both tasks suggests that the patients' difficulties were not merely the result of general cognitive deficits that interfered with the tracking of any event. Moreover, some of these 14 AD individuals scored better than the unimpaired AD individuals in a reasoning task outside the social domain (as assessed by the Raven's Progressive Matrix; Raven et al., 1998). This thus indicates that the difficulties were relatively specific to belief reasoning. Second, a majority of the 14 AD individuals who showed a deficit in tracking other people's belief had difficulties not only in the false belief task that placed the highest demands in belief tracking (i.e., the Track-Task) but also in the false belief task that placed high demands on self-perspective inhibition (i.e., the Inhibit-Task). This could be explained in 2 ways: either the deficit in tracking other's belief is so important that it affects performance irrespective of the false belief task (this would mean that a single deficit affected both tasks) or the AD patients showed, in addition to their belief tracking difficulties, difficulties in self-perspective inhibition (this would mean that there were 2 deficits, each affecting one of the tasks). The current data cannot disentangle these 2 possibilities, but the data clearly exclude the interpretation that AD patients suffer *solely* from a deficit in self-perspective inhibition as has been reported in some brain-damaged patients (Samson et al., 2005) or in the healthy elderly (Bailey and Henry, 2008).

While self-perspective inhibition processes have been found to be sustained by the right lateral prefrontal cortex (Hartwright et al., 2012; Samson et al., 2005), the processes involved in belief tracking have been associated with the temporo-parietal junction (Samson, 2009; Samson et al., 2004). This highlights that ToM deficits in AD individuals cannot be only explained by a frontal lobe dysfunction and that a dysfunction of the temporo-parietal areas could also contribute to explain the deficits. Dysfunctioning of the temporo-parietal junction is in line with evidence of decreased parietal lobe volume in AD adolescents (Fein et al., 2013) and adults (Jernigan et al., 1991; Sullivan, 2003; Sullivan et al., 1996). Furthermore, it has been shown that the parietal lobe volume decrease is positively correlated with alcohol dose (Fein et al., 2009) and predictive of relapse within 90 days (Rando et al., 2011). In 1 study, decrease in parietal lobe volume has also been associated with the AD individuals' performance with social stimuli (i.e., in a face name association learning; Pitel et al., 2012). We thus concur with the suggestion by Uekermann (Uekermann and Daum, 2008; see also Bosco et al., 2014) to explore the role of other brain areas than the frontal areas in the social cognition deficits observed in AD individuals.

From a clinical standpoint, further explorations are still needed to evaluate the relation between ToM and interpersonal difficulties such as frequent family or couple difficulties, professional impairments, aggression, and legal problems. ToM deficits might also influence the probability of relapse or other difficulties encountered by AD patients, especially difficulties of care access (Uekermann and Daum, 2008) which result in an important treatment gap (Kohn et al., 2004). Moreover, our study also highlighted that about half of the AD individuals had spared ToM capacities. This implies that, before considering a treatment to improve the capacity of mentalizing among AD individuals, it seems essential to determine which patient needs such remediation. To meet this goal, more research must be carried out to develop specific diagnostic tools for the clinicians. Finally, the possibility of spontaneous recovery of ToM abilities after prolonged abstinence, as it has been shown for other cognitive abilities (Pitel et al., 2009), should also be tested.

CONCLUSION

In line with previous studies, we show in this study that, as a group, AD individuals have difficulties in ToM. Single-case analyses showed, however, that this is only the case for less than 50% of the sample. The AD individuals who were impaired consistently showed difficulties in tracking other people's mental state. Such difficulties have previously been found following focal brain lesions to the temporo-parietal junction, highlighting that frontal dysfunctions may not be the sole origin of the social cognition deficits observed in alcohol dependence.

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SUPPORTING INFORMATION

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

Method S1. Memory control and filler trials in the Track-Task and Inhibit-Task.