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**Mind reading abilities in opiate-dependent patients: An exploratory study**

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## **Abstract**

### **Objectives**

Impairments in social cognition have been described as playing a major role in the maintenance of addictive behavior in substance abusers. This study aimed to investigate the Theory of Mind (ToM) ability of opiate-dependent (OD) patients and to explore whether TOM ability was correlated with length of substance abuse, age at onset of substance abuse and length of abstinence.

### **Methods**

OD patients (N = 29) and non-dependent individuals (NDI) (N = 29) were submitted to the Theory of Mind Assessment Scale (Th.o.m.a.s.), a semi-structured interview, and to the *Versailles-Lecture Intentionnelle en Situation* (V-LIS), a movie paradigm in which participants have to infer the characters' intentions.

### **Results**

The results confirmed a deficit in ToM ability in OD patients, with OD patients demonstrating poorer performance than NDI on both the V-LIS and the Th.o.m.a.s. The combination of perspective taking and reflecting on others' mental states was particularly difficult for OD patients. Furthermore, impairments in ToM abilities were not correlated with the age at onset of substance abuse or to the duration of substance abuse or abstinence.

### **Conclusions**

The results suggest OD patients may have impaired social cognition, demonstrating deficits in even basic social interaction skills, which may constitute a risk factor for addiction. These findings underline the importance of developing interventions to improve social cognition ability during the rehabilitation of OD patients.

**Keywords:** Theory of mind, social cognition, emotion recognition, opiate-dependence, substance abuse.

## 1. Introduction

Deficits in emotional information processing in patients with substance use disorders (SUD) and especially in opiate-dependent (OD) patients have been first studied in terms of difficulties in identifying and expressing one's own emotions through the concept of alexithymia [1] [2]. Since, these deficits have been observed at different levels of the emotional processes (identification, categorization, expression) demonstrating both a prominent difficulty in identifying their own emotions but also those of other people [3] [4] [5] [6]. Thus, these emotional deficits would affect the way individuals with SUD assess the intentions or the mental states of others [7] [8] and could constitute a major risk factor for maintaining substance use behaviors as it may trigger stressful interpersonal situations that patients with SUD may try to cope by consuming psychoactive substances [9] [10] [11]. However, regarding the methodology employed to investigate emotional processes in these patients, previous studies have revealed mixed findings that in fact, could be related to different processes of social cognition.

The first studies conducted on the socio-affective abilities of OD patients assessed their ability to recognize emotional facial expressions (EFE) alone or in combination with other emotional indicators such as prosody and body postures [4] [10] [7]. These studies provided convergent evidence, suggesting that OD patients displayed impairment in their ability to decode other people's emotions and seemed to be unaware of their own emotional difficulties [12]. In line with these studies, further researches have investigated social cognition mainly through "Theory of Mind" (ToM) (also called 'mentalizing' or 'mind reading'). ToM is defined as the ability to explain and predict one's own and other individuals' behaviors by inferring mental states [13]. It is acquired during childhood and could be considered as an elementary and basic process in social activities. There is today growing evidence that impaired ToM may also lie at the core of inadequate behaviours observed in different psychiatric disorders [14]. ToM ability is characterized by two dimensions: a cognitive one, which requires a cognitive understanding of

other's mental states, and an affective one which refers to the ability to infer the emotions of others. These two components are underpinned by two different neuronal networks [15] and are differently impaired in various mental disorders. Thus, this distinction between cognitive and affective ToM may constitute a starting point for understanding mentalization in patients suffering from addiction. Nevertheless, beyond these dimensions, ToM also refers to different types of mental states: volitional states that refer to desires and intentions; epistemic states that refer to knowledge and beliefs; and positive and negative emotional states [16]. The distinction between the ability to infer others' beliefs about the state of the world (defined as first-order ToM) and the ability to understand nested mental states, that is, to infer others' beliefs about the mental state of someone else (defined as second-order ToM) can also be noted [17]. ToM also refers to the ability to understand one's own mental states (first-person ToM) and the ability to understand others' mental states (third-person ToM) [18]. Finally, one can distinguish between an egocentric perspective, in which others are represented in relation to the self, and an allocentric perspective, in which the mental states of others are represented independently of the self. [19] Importantly, these different ToM dimensions are underpinned by different brain networks [20] [21], suggesting that ToM is complex constructs that should be more in-depth examined.

Rare studies have focused on ToM abilities in alcohol-dependent patients [22] [23] [24] [25] [26] and abusers of other substances such as cocaine, methamphetamine and cannabis [27] [28] [29] [30] [31] [32]. Furthermore, some of the studies focusing on mentalistic capacities in patients with SUD have been conducted in patients with comorbid personality disorder [33] [34] [35] which must be distinguished from patients with SUD [36].

Among patients with SUD, the literature highlights that alcohol-dependent patients showed deficits in humor processing related to their abilities to interpret scenes [37] and detect "Faux Pas" [38] [23]. However, distinguishing the cognitive and affective dimensions of the ToM, stronger evidence supports the presence of an impairment in the ability to infer emotional states (affective

ToM) in alcohol-dependent patients based on the results of self-report questionnaires [26] [39] [23] and performance tasks such as the “Reading the Mind in the Eyes Test” (RMET) [40] [25] or the “Movie for Assessment of Social Cognition” (MASC), multiple-choice tasks requiring the identification of mental states [24].

In patients with OD, the study by McDonald et al. has especially investigated their social inference ability. In that study, opioid maintenance patients demonstrated difficulties in inferring meaning from conversations, with their ability to decode sarcastic situations identified as especially deficient, whereas abstinent OD patients did not present significant deficits [7]. In addition, based on the results of a self-report questionnaire (Empathy Questionnaire), Ferrari et al. found that recently abstinent poly-substance-dependent patients (including OD patients) scored lower than controls on the total score of empathy, and especially on the emotional dimension [41]. These different findings in OD patients at different stages of their withdrawal question the effect of duration of abstinence on social cognition. Overall, studies of SUD patients show considerable heterogeneity in the duration of abstinence, ranging from few weeks [39] [40] to several months of abstinence [22], with rare studies conducted among active consumers [31] when some do not even specify this information [32]. Nevertheless, the effect of abstinence on ToM has never been studied, as has the impact of the history of addiction.

As strong conclusions cannot be drawn from the limited number of studies available, it is now essential to better identify whether specific ToM deficits exist in OD patients and to clarify the effects of the duration of abstinence, the duration of substance abuse, and the age of onset of substance abuse on social cognition. In that line, first we aimed to overcome the limitations of previous studies, particularly regarding their lack of ecological validity and the lack of precision of the different dimensions of the ToM investigated, by examining whether the ability to interpret and identify intention in simple situations of social life are impaired in OD individuals without personality disorder. Thus, as proposed by Bazin et al. [42], we investigated ToM skills using

more ecological tasks, which offer a good trade-off between enriched social contexts (video scenes with sound) and precisely defined cognitive measures targeting aspects of social cognition. We proposed to use the *Versailles-Situational Intention Reading* (V-SIR) to assess the subject's ability to infer mental states through the presentation of short video clips showing complex interactions between one or more individuals [42].

Considering its complex nature, it is also important to better identify different inherent ToM abilities in the study of ToM processes (ability to infer emotions, volitional and epistemic states, first versus second-order ToM, first versus third-person ToM, egocentric versus allocentric perspective taking). To this end, Bosco et al. developed a semi-structured interview assessing different aspects of ToM: the Theory of Mind Assessment Scale (Th.o.m.a.s.) [16], which was subsequently used to evaluate alcohol-dependent individuals [22]. They observed impairments in all ToM dimensions, identifying more difficulties related to third-person ToM than first-person ToM and the allocentric perspective than the egocentric perspective.

Thus, using the V-SIR task, we seek to verify first if simple ecological tasks are impaired in OD patients. Then, using the Th.o.m.a.s., we expected that the ToM abilities should be impaired according to the level of complexity of the intention reading tasks. We hypothesized that the items for third-person ToM would be more highly affected than those for first-person ToM and that the items for allocentric performance would be more highly affected than those for than egocentric performance, as similar results have previously been observed in other substance-dependent patients [22]. We also expected that first-order ToM would be less impaired than second-order ToM, as commonly observed, because of the higher degree of mindreading ability required for second-order tasks [43].

Finally, we proposed to explore whether these ToM performances differed in OD patients with a longer period of substance abuse, an earlier onset of substance abuse and a recent period of abstinence.



## 2. Material and methods

### 2.1. Participants

Demographic data are presented in Table 1. Twenty-nine patients who met the DSM-IV TR criteria for opiate dependence (OD) participated in the study. These patients were recruited from addiction treatment centers in Switzerland (the reinsertion and residential centers of “Association Argos”) and France (the reinsertion center of “CHRS Renovation”, and the addiction departments of the Hénin-Beaumont and Felleries-Liessies hospitals). The diagnosis of opioid dependence was made by a physician specializing in addictology. Included patients did not have recent antecedent indications of addictive behaviors other than substance dependence. Patients who had been abstinent for less than 48 hours and more than one year were excluded.

Twenty-nine age- and gender-matched participants were selected to constitute the group of non-dependent individuals (NDI). They were recruited from the general population or at the University of Lille. They were excluded if they presented a history of any form of addictive behavior (except nicotine).

All participants were native French speakers. For both groups, the exclusion criteria included a history of psychotic disorders and personality disorder, bipolar disorder, neurological disorders or head injury, intellectual deficiency or neuroleptic or mood stabilizer treatment. All participants were volunteers and provided informed consent prior to participation.

(Insert Table 1 about here.)

### 2.2. Procedure

Data for substance dependence and consumption were obtained from the medical records of the patients; substance consumption was regularly evaluated by urinalysis in the addiction treatment centers.

Clinical assessments were individually conducted by two psychologists specifically trained for this study.

Levels of depression and anxiety were assessed using the Hospital Anxiety and Depression Scale (HADS) [44], a self-report questionnaire containing 14 items (7 for anxiety and 7 for depression). This scale provides an overall score, a score for depression and a score for anxiety. Higher scores depicted higher levels of anxiety or depression.

Two tasks were used to measure cognitive and affective ToM and their different their aspects: the Theory of Mind Assessment Scale (Th.o.m.a.s.) [16] and the *Versailles-Situational Intention Reading* (V-SIR) [42].

The Th.o.m.a.s. is a semi-structured interview composed of 39 open-ended questions through which the participant is directly asked to express how he/she understands his/her own mental states and those of others. For each question, the participant is invited to illustrate their answer with examples from everyday life.

The questions are organized in 4 main subscales:

- Subscale A (I-me) refers to the perception the participant has of his/her own mental states. When answering subscale A questions, participants were asked to provide their own point of view (egocentric perspective) regarding their own mental states (first-person ToM) (e.g., “Do you ever experience emotions that make you feel good?”).
- Subscale B (other-self) refers to the ability of the participant to perceive the mental states of others. When answering subscale B questions, participants were asked to describe the manner in

which other individuals (allocentric perspective) view their own mental states (third-person ToM) (e.g., “Do other people ever experience emotions that make them feel good?”).

- Subscale C (I-other) refers to the perception the participant has of the mental states of others.

When answering subscale C questions, participants were asked to provide their own point of view (egocentric perspective) about the mental states of others (third-person ToM) (e.g., “Do you notice when others feel good?”).

- Subscale D (other-me) refers to the perception of the participant regarding the view others have of his/her mental states. When answering subscale D questions, participants were asked to perceive the point of view of others (allocentric perspective) regarding their mental states (first-person ToM). This scale can be considered a second-order ToM task (e.g., “Do others notice when you feel good?”).

Each of the 4 subscales included an evaluation of the participant's perspectives on volitional states (which refer to desires and intentions), epistemic states (which refer to knowledge and beliefs) and emotional states (positive and negative).

Each answer was analyzed and scored from 0 to 4, according to the rating criteria described by Bosco et al. [16]. A rich and contextualized answer with a congruent real-life example was considered to reflect a greater ability to understand mental states. The absence of an answer, an inconsistent answer, and a "yes" or "no" answer without providing an argument were rated 0. For complete responses, the levels of consistency, richness, contextualization and diversity of the statements were used to scores ranging from 1 to 4. A detailed and consistent answer describing various contextualized mental states that were supported by relevant examples was rated 4.

Answers were analyzed by two independent judges. To evaluate inter-judge agreement, an intraclass coefficient correlation (ICC) was calculated based on 10 Th.o.m.a.s. ratings (5 from each group of participant). The resulting ICC was high at 0.93.

The V-SIR aims to explore cognitive ToM through the presentation of six short video clips. Each video depicts two or more protagonists in a complex social interaction such as lies, allusions or indirect speech. For each video, the participant is asked to infer the mental state of one of the protagonists. Five possible answers are given, and the participant must rate each proposal according to its probability. Among participants, the ability to rate the probabilities correctly is considered to reflect their ability to understand the mental states of others. Each V-SIR score corresponds to the Manhattan distance between the score of the participant and the mean score of a reference control sample. The overall score for each participant was computed as the sum of the absolute values of the differences between the participant's score and the mean rating of the reference control group for each item. Higher scores indicated greater ToM impairment.

#### 2.4. Statistical analysis

Chi-square tests were performed to compare the gender distributions in the OD patient and NDI groups. The t-test for independent samples was used to compare education level, age, and depression and anxiety severity (HADS scores) between the two groups. Cohen's *d* was used to measure the effect size for these comparisons. The effect size was categorized based on the following Cohen's *d* values: .20 = small, .50 = medium, .80 = large.

Analysis of covariance (ANCOVA) tests were carried out to control for a possible effects of depression and anxiety severity (using the HADS overall score) and education level on ToM performance. Before performing these analyses, the following assumptions for ANCOVA were verified: significant correlations between the covariables (HADS overall score and educational level) and ToM scores (Th.o.m.a.s. and V-SIR) and parallel regression lines [38]. For significant results, effect sizes were evaluated by estimating the partial eta-squared (partial  $\eta^2$ ), and the effect

sizes were considered to be small when partial  $\eta^2 = .01$ , medium when partial  $\eta^2 = .06$  and large when partial  $\eta^2 = .14$  [46].

Analysis of variance (ANOVA) tests were performed to evaluate the main effect of the Th.o.m.a.s. subscales on ToM performance in OD patients. Each effect size was evaluated by estimating a partial  $\eta^2$ . Post hoc pairwise comparisons were then conducted using the Bonferroni correction. Pearson's correlation coefficients were also calculated to explore possible bivariate relationships between ToM (Th.o.m.a.s. and V-SIR) scores and variables related to substance abuse (length of substance abuse, age at onset of substance abuse and length of abstinence) in OD patients. Analyses were conducted using SPSS for Windows version 18.

### 3. Results

#### 3.1. Group characteristics

There were no differences between the OD patient and NDI groups with regards to gender ( $\chi^2(1) = .34, p > .10$ ). The mean education level was higher in the NDI group ( $M_{education} = 11.62, SD = 1.92$ ) than the OD patient group ( $M_{education} = 14.55, SD = 2.28; t(56) = 5.30, p < .001, d = 1.39$ ). Age did not differ significantly between the two groups ( $t(56) = 1.52, p = .88$ ).

OD patients were more depressive and anxious ( $M_{HADS\ total} = 17.41, SD = 7.10; M_{HADS\ anxiety} = 10.55, SD = 3.90; M_{HADS\ depression} = 6.86, SD = 4.22$ ) than were NDI ( $M_{HADS\ total} = 9, SD = 3.86; M_{HADS\ anxiety} = 5.86, SD = 2.25; M_{HADS\ depression} = 3.14, SD = 2.37$ ). These differences were significant, with large effect sizes identified for the differences in HADS total score ( $t(56) = 5.61, p < .001, d = 1.47$ ); HADS anxiety score ( $t(56) = 5.62, p < .001, d = 1.47$ ) and HADS depression score ( $t(56) = 4.14, p = .001, d = 1.09$ ).

### 3.2. ToM performance

The ANCOVA tests revealed lower Th.o.m.a.s. scores overall, on the different Th.o.m.a.s., subscales (A, B, C, D) and on the different domains of concern (epistemic, volitional, and emotions) among OD patients when compared with NDI (see Table 2, Figures 1 and 2). Similar results were identified for the V-SIR score.

Insert Figures 1 and 2 about here.

Concerning the Th.o.m.a.s. subscale results, the different subscales were identified to have a significant main effect on ToM performance in OD patients ( $F(3, 96) = 3.25, p = .02, \eta^2 = .08$ ).

Bonferroni *post hoc* tests revealed that subscale A performance was significantly better than subscale B performance among OD patients ( $p = .01$ ). No other differences in performance were found between the different subscales.

### 3.3. Correlations between ToM scores and variables related to substance abuse.

Based on the calculated Pearson's correlation coefficients, there were no significant correlations between ToM (V-SIR and Th.o.m.a.s.) scores and clinical variables related to substance abuse (length of substance abuse, age at onset of substance abuse and length of abstinence) in OD patients.

## 4. Discussion

The main objective of this study was to determine if OD patients would display ToM impairments in simple social situations of social life. The poorer performance of OD patients when compared with NDI on the V-SIR suggests that in standard, everyday life situations, these patients have difficulties inferring the intentions and mental states of others. Given that the participants were presented with five possible answers, we can conjecture that this task was easier than the mental state inferences that would be involved in real life situations. This may suggest a greater impairment in inferring the mental states of others in OD patients than in alcohol-dependent patients, who previously were observed to not differ from control individuals when performing this type of task [25] but were found to fail more complex mental inference tasks [37] [38]. The results are in concordance with the scarce available data that describe deficits in social cognition skills in OD patients or opioid maintenance patients based on impaired EFE decoding [10] [4] [7] and ToM disturbances [7].

Moreover, the results obtained with the Th.o.m.a.s highlighted the presence of difficulties in the understanding of their own and others' mental states among OD patients, including positive and negative emotions, volitional states and epistemic states. The OD patients also performed worse than did NDI on the following different subscales: scale A (first-person ToM, egocentric perspective), scale B (third-person ToM, allocentric perspective), scale C (third-person ToM, egocentric perspective) and scale D (second-order ToM). These observations suggest that both first-order and second-order ToM, first-person and third-person ToM, and the egocentric and allocentric perspectives are impaired in OD patients. Until now, the Th.o.m.a.s. has only been used to assess alcohol-dependent patients, who also displayed impairment in these different dimensions [22]. Our findings are also in line with previous findings suggesting heterogeneous performance on different ToM subscales in OD patients. OD patients performed better on scale A (first-person ToM, egocentric perspective) than on scale B (third-person ToM, allocentric perspective). A task that combined both the ability to take the perspective and to reflect on the

mental states of others (scale B) seems to be more difficult than expressing their own mental state from their own point of view (scale A) in OD patients. This finding suggests that interpersonal skills seem to be more impaired than intrapersonal skills in OD patients. Indeed, taking another's perspective is a more complex operation, first requiring the ability to infer one's own mental states, which may be impaired in dependent patients, and then requiring the ability to differentiate clearly between oneself and another person.

This observation seems to confirm previous studies arguing that impaired social skills are a core issue in the addictive process, as they may generate additional stress with which patients cannot cope, leading to substance consumption [47] [11]. The supposed role played by these deficits in maintaining substance use disorders does not seem to be specific to alcohol-dependent patients and, thus, needs to be considered a priority in the rehabilitation of OD patients.

In addition, there were no differences between scale D (measuring second-order ToM) and the other scales (measuring first-order ToM), whereas the general population has been found to demonstrate worse performance on this type of task because of the advanced degree of mindreading ability required for second-order ToM [43]. It seems that the mindreading impairment in OD patients is already consistently observable on tasks that require lower mindreading ability.

Concerning the relationships between ToM scores and variables related to substance abuse, no significant correlation between Th.o.m.a.s. and V-SIR scores and the length of abstinence, age at onset of substance abuse and length of substance abuse were identified. In OD patients, there was no change in ToM performance after the cessation of substance use. Our results are in line with those of Foisy et al. who described similar findings regarding differences in emotional recognition ability in substance dependent patients who had experienced short-term (less than two months) and a mid-term abstinence (between two and ten months) [4]. Nevertheless, to conclude that ToM deficits remain stable over time, future research assessing patients following a longer period of



abstinence is needed. Furthermore, in our study, the age at onset of opiate use was not correlated with more pronounced ToM deficits. These results are in line with those of Preller et al., who reported that individuals who initiated cocaine use before the age of 18 were less emotionally responsive but did not have poorer mind reading ability [32]. In addition, our results suggest that the duration of substance abuse was not correlated with deficient ToM ability. This result for OD participants is different from those of Bosco et al. observed in alcohol dependent patients, which showed a general progressive impairment in ToM abilities, possibly due to the neurotoxic effects of alcohol abuse [22]. This difference between alcohol-dependent and OD patients is consistent with reports indicating that alcohol was associated with more toxic neurological effects than were opiates [10] [4]. Overall, the lack of correlation between ToM skills and variables related to substance use may suggest that some ToM deficits could be present before the initiation of addictive behavior and could, thus, be considered as a risk factor for the development of addiction. However, it is important to note that our results must be considered in the light of some limitations. First, we must pay attention to the generalization of the results given the relatively small size of our sample. Furthermore, the effect of the history of substance abuse across our sample may imply the risk of cognitive impairments for some participants, that have not been controlled by an effective measure of cognitive capacities. Indeed, as ToM abilities requires executive functioning which is generally impaired in some clinical populations [49] [50] and especially in OD patients, cognitive function efficiency could be considered as a significant predictor of difficulties in social cognition [5]. In the same vein, the substance maintenance treatment was not controlled in our OD sample although methadone treatment may be associated with additional cognitive impairment [48]. In their study, McDonald et al. found that opioid maintenance patients had poorer social emotional skills than did OD abstinent individuals; however, it was unclear whether they showed more deficits at baseline (prior to treatment entry) [7]. Therefore, the involvement of substitution treatment in emotional abilities remains an

unresolved issue in OD patients, and the lack of an overall cognitive measurement constitutes a limitation of the present study. Consequently, it would be relevant to take into account the cognitive performance of participants, which may be related to the severity and duration of substance consumption or substitution treatment. This question of impaired cognitive abilities should be addressed in future research among OD patients since ToM ability implies different but interconnected neural mechanisms and requires varying cognitive efforts according to the form of ToM considered (such as Self/Other or Cognitive/Affective) [21].

Finally, some other variables could also underlie social emotional skills in substance-dependent patients, such as a family history of substance abuse [11] or overdose history [7], but also variables related to the social and occupational functioning of the participants. Indeed, pre-existing social deficits or the amount of social contacts of the participants, that may be influenced by their marital status or their professional situation, as well as their socioeconomic status should be considered in future research.

To conclude, this study in OD individuals was the first to investigate ToM abilities in an ecological task and in taking into consideration their different levels of complexity (first-person and third-person ToM, egocentric and allocentric perspective, first- and second-order ToM).

Although this study presents certain limitations and remains exploratory, it constitutes a supplementary step in the understanding of social functioning in these patients. Our results highlighted the fact that ToM deficits related to basic social inference skills were observable in OD patients, which suggests the presence of difficulties in adaptation to a wide range of social interactions, and not only those greater complexity. This finding is even more relevant with the knowledge that the combination of perceiving third person effects and taking the perspective of others seemed to be particularly difficult for OD patients. From a clinical perspective, these findings underline the importance of developing emotional and social cognition interventions for application during the rehabilitation of OD patients. Beyond the importance to improve social

functioning at an individual level, interventions can also be considered in a larger perspective for developing prevention programs among children of substance abusers who may be themselves affected by socially non-adapted parental interactions. In this perspective, some rehabilitation programs have already given promising results [51] [52] which must be pursued and developed.

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Figure 1: OD group versus NDI group scores on Th.o.m.a.s. different subscales (A, B, C and D).

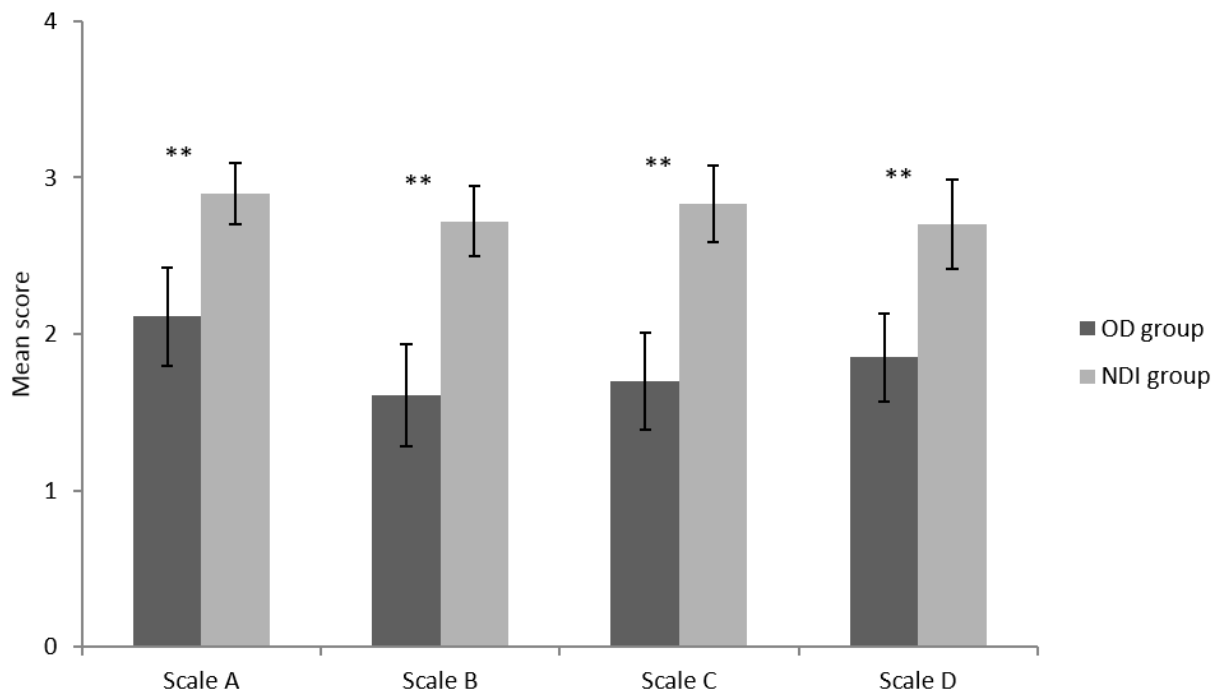


Figure 2: OD group versus NDI group scores on reading mental states (epistemic states, volitional states and emotions) measured with the Th.o.m.a.s.

