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The association between depression and craving in alcohol dependency is moderated by gender and by alexithymia factors



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ABSTRACT

Alexithymia is a multifaceted personality trait that involves difficulties in identifying and describing feelings to others, a poor fantasy life and an externally oriented cognitive style. Alexithymia has been described as a vulnerability factor for mental and physical diseases.

We investigated in a group of 158 alcohol-dependent patients (103 men, 55 women) the association between depression and craving for alcohol when these patients were starting a detoxification program, and the moderating impact of gender and alexithymia on this relation.

We first found an interaction between depression and gender in the prediction of craving in the sense that only for women an increase in depressive mood was related to an increase in total craving. When examining gender separately, we found that alexithymia factors acted as moderators. For women, the link between depression and craving was strengthened for the ones scoring higher on "difficulties describing feelings". But for men, the link between depression and craving was reduced for the ones scoring higher on "externally-oriented thinking". These findings suggest that in some cases that need to be identified more systematically in the future, the "externally-oriented thinking" alexithymia factor can exert – at least in the short term – some protective effects.

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1. Introduction

Craving is a core symptom of addictions that has attracted much attention in recent years. The central role ascribed to craving in addiction by the scientific community is reflected by the introduction of craving as a new diagnostic factor for the definition of substance-use disorders in the DSM 5 (American Psychiatric Association, 2013). In the case of alcohol-dependence (AD), which is with smoke-addiction the most frequent dependence worldwide, a major cause of mortality and burden for society (Whiteford et al., 2013; Dawson et al., 2014), high craving at the end of a detoxification period is frequently associated with strong tendencies for relapse (O'Malley et al., 1992; Volpicelli et al., 1992; Paille et al., 1995). Numerous models of the mechanisms

underlying craving have been suggested (i.e., based on conditioning vs. cognitive mechanisms). All assume that craving is a multifaceted phenomenon that is influenced by a variety of factors (Melchior and Tabakoff, 1984; Tiffany and Carter, 1998; Anton, 1999; Kavanagh et al., 2005). One central factor for explaining relapses after midterm abstinence is the experience of negative affect (Hartka et al., 1991), possibly related to social pressure (Zywiak et al., 2003) or to self related stresses (Hull et al., 1986). Baker et al. (2004) considered that the stimulation of craving by the negative emotion processing system allowed the elicitation of drinking as a mean to escape negative affect. Consistent with this view, several authors have found positive correlations between depressive state and craving during alcohol-withdrawal (Andersohn and Kiefer, 2004; Lukasiewicz et al., 2005b; Oslin et al., 2009).

In this paper, we want to examine two potential key moderators in the relation between affective factors (negative affect and depression) and craving for alcohol in a population of alcohol dependent patients (AD).

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The first moderator is gender. We make the hypothesis that affective factors may be a stronger risk factor for one gender as compared to the other one in AD patients. Despite its theoretical and practical importance, the issue of gender moderation in the relation between affective factors and craving for alcohol has been largely neglected. For instance, Thorberg et al. (2009) reviewed 25 studies on alexithymia and alcohol dependence. Fifteen of them only considered men. Within the 10 remaining studies, which potentially allow for testing gender moderation, only two explicitly considered it (Junghanns et al., 2005; de Timary et al., 2008). Also the analyses were limited to mean comparisons across gender and never examined how gender can moderate the relations between the variables considered. When looking at more recent studies, gender moderation remains a neglected issue (e.g., Cordovil de Sousa Uva et al., 2010b; de Timary et al., 2013).

The second moderator is personality. We already found that the link between negative affect and craving for alcohol is moderated by emotional intelligence (EI). Negative mood at the onset of the cure was linked to craving at the end of the withdrawal period but only among patients with low trait EI scores (Cordovil De Sousa Uva et al., 2010a). We also found that trait self-consciousness (SC) moderated the impact of depression on craving for alcohol. Depressive symptoms were related to alcohol craving but only among patients with high trait SC scores (de Timary et al., 2013). In the present study, we will examine another personality dimension, alexithymia.

Alexithymia is a construct targeting basic socio-emotional competencies. Individuals who score high on this dimension take little interest in their inner emotional and fantasy life, have a cognitive style that is literal, utilitarian, and externally oriented, and experience difficulties in identifying emotions and describing what they feel to others (e.g., Taylor and Bagby, 2004). Importantly, the prevalence of alexithymia ranges from 40 to 67% in AD subjects (Haviland et al., 1988; Taylor et al., 1990; Cecero and Holmstrom, 1997; Taieb et al., 2002; Thorberg et al., 2009).

Alexithymia has been described as a vulnerability factor for various mental diseases such as depression (e.g., Luminet et al., 2001; Mikolajczak and Luminet, 2006; Viinamaki et al., 2006), panic disorder (e.g., Marchesi et al., 2005; Galderisi et al., 2008); alcohol-dependence (e.g., de Timary et al., 2008), other substance dependencies (Taylor et al., 1990; Haviland et al., 1994; Lumley et al., 1994), or eating disorders (e.g., Bydlowski et al., 2005; Speranza et al., 2005; Carano et al., 2006). Alexithymia also increases the vulnerability for physical health. For instance, Kauhanen et al. (1996) showed in a prospective study that individuals high in alexithymia exhibited an increased risk for mortality. A reasonable prediction will thus be that the association between affective factors (negative affect and depression) and craving will be stronger when AD patients score higher on alexithymia.

One key improvement of the present study in comparison with all the previous ones is that we will investigate these *two moderation factors (gender and alexithymia) concurrently*, while previous studies only examined one moderator at a time. This is critical as previous studies showed that alexithymia can have opposite effects when considering men or women. To illustrate, one study showed that higher alexithymia was associated with the frequent use of health care among men, but not among women (Jyvasjarvi et al., 1999). Jula et al. (1999) showed that alexithymia was associated with elevated blood pressure and therefore acted as a risk factor for hypertension but only for men. These studies suggest that, in specific diseases, alexithymia can act as a risk factor only for one gender.

In this paper, we consider the role of each alexithymia factor as the moderating impact of alexithymia might be stronger for some of its factors. The importance of examining the specific effects of alexithymia factors instead of alexithymia total scores has been

already suggested in previous studies. For instance, Larsen et al. (2006) showed in a group of obese patients that two alexithymia factors (“difficulties identifying feelings” and “difficulties describing feelings”) were more strongly associated with emotional eating in men than in women but that was not the case for the factor “externally-oriented thinking”. Emotional eating is a health risk factor characteristic of people who respond to emotional arousal by enlarging their food intake instead of decreasing it. In our previous studies looking at the moderating impact of alexithymia on different aspects of emotion information processing, we also made specific predictions regarding the impact of each alexithymia factor with the rationale that the factors involved different types of deficits in the processing of cognitive and emotional information. Our results support the view of differential effects (e.g., Luminet et al., 2004; Konrath et al., 2011; Dressaire et al., 2015).

In the field of alcohol dependency, however, the vast majority of studies considered only total alexithymia scores (e.g., Bruce et al., 2012; Coriale et al., 2012; Shishido et al., 2013; Stasiewicz et al., 2012; Lyvers et al., 2014), which is pointed out as a shortcoming in the literature review on alexithymia and alcohol-dependence by Thorberg et al. (2009). The authors emphasized that “*there is a need to examine the multifaceted nature of alexithymia in relation to alcohol consumption*” (Thorberg et al., 2009, p. 243).

If we look at the few available data in the population of alcohol dependency that consider alexithymia factors separately, we found support for such an approach.

Thorberg et al. (2011a, 2014) showed that anxiety and/or depression are highly correlated with Difficulties identifying feelings (DIF) and Difficulties describing feelings (DDF), but the correlation with Externally oriented thinking (EOT) is much lower, and usually not significant. Regarding the association with craving, Thorberg et al. (2011a, 2014) using the OCDS-total score found significant correlations with DIF and DDF but not with EOT.

In summary, this paper will first examine if gender moderates the association between affective factors and craving. If gender is a significant moderator, the second step will be to examine whether alexithymia factors would be additional moderators. These two steps will allow to answer the critical question of how gender (men vs. women) and alexithymia factors (DIF vs. DDF vs. EOT) interact in modifying the association between affective factors and craving.

2. Methods

2.1. Participants

This sample included 158 CE participants (103 men, 55 women) with a mean age of 48.76 years (SD=10.39, range from 28 to 79 years). They had on average 9.52 (SD=8.04) years of alcohol addiction. Regarding education, they spent on average 13.98 (SD=3.31) years at school. All patients were recruited during a detoxification and rehabilitation program at the Unité Intégrée d'Hépatologie, Department of Adult Psychiatry at the Academic Hospital Saint-Luc, Belgium. Patients who were addicted to substances other than alcohol (and cigarettes) such as illicit drugs or benzodiazepines were also excluded from the study. Indeed, these substances may influence their affective and craving states and the withdrawal duration of these substances is different from that of alcohol (Kosten and O'Connor, 2003). Participants were tested on the 16th to 18th day of abstinence, just before the end of detoxification. The current study was approved by the ethical committee of the hospital. All patients signed an informed consent form given before starting the data collection. No financial or material incentive was provided.

2.2. Measures

Three state-related dimensions (craving, depression and positive and negative affect state) and the personality trait alexithymia were evaluated by questionnaires.

2.2.1. Obsessive–compulsive drinking scale (OCDS)

The Obsessive–compulsive drinking scale (OCDS) measures the cognitive and behavioral aspects of alcohol-craving during the preceding 7 days (Anton et al., 1996). The OCDS is a self-report questionnaire that is comprised of a total (Tot) of 14 items, which can be divided into two subscales, a 6 item 'obsessive' subscale (Ob) (e.g., How much of your time where you're not drinking is occupied by ideas, thoughts, impulses, or images related to drinking?) and an 8-item 'compulsive' subscale (Co) (e.g., How much of an effort do you make to resist consumption of alcoholic beverages?). All items are rated along 5-point Likert scale (0=least, 4=most) referring to 5 statements which express the degree of the severity of craving. Four compulsive items, which corresponded to items number 7, 8, 9 and 10 of Anton's questionnaire (Anton et al., 1995; Anton et al., 1996), are related to alcohol consumption (e.g., How many drinks do you drink each day?) and therefore are not adapted to the evaluation of craving during detoxification of inpatients. Indeed alcohol consumption is prohibited during withdrawal and therefore these items represent an inaccurate index of compulsion to drink at T2. Thus, they were eliminated and a modified 4-item compulsive subscore (Com) and a modified 10 item total score (Totm) was computed. The scale has been validated into French (Ansseau et al., 2000) and already used in its shortened version in our previous studies (Cordovil De Sousa Uva et al., 2010a; Leclercq et al., 2012; de Timary et al., 2013; Leclercq et al., 2014a). Cronbach α for this shortened version was very high, Totm=0.92, Ob=0.92, Com=0.84.

2.2.2. Positive affectivity negative affectivity schedule (PANAS)

The PANAS is a 20-item scale, which assesses positive and negative mood states (Watson et al., 1988). It consists of 10 positive (e.g., inspired) and 10 negative (e.g., guilty) adjectives rated along five-point scales ranging from 1 (not at all) to 5 (extremely). The PANAS is the most widely used scale for the assessment of current mood states. The French validation was used for this study (Gaudreau et al., 2006). For each subscale, scores range from 10 to 50. Cronbach's coefficients for PA and NA were high, both in the original English version (Watson et al., 1988), Cronbach's α : PA=0.90; NA=0.87) and in the French validation (Cronbach's α : PA=0.90; NA=0.84) (Gaudreau et al., 2006).

2.2.3. Beck depression inventory (BDI)

The BDI is a self-report inventory designed to measure severity of depressive symptoms. The BDI is reliable and valid and thought to be a good measure of depressive state severity in alcohol-dependent patients (Clark et al., 1985; Clark et al., 1993b). The French validation of the second version of the BDI (BDI-II) (Beck et al., 1961) used in this study was published by Bourque and Beaudette (1982). The BDI-II consists of 21 items measuring characteristic attitudes and symptoms of depression (Beck et al., 1961). The items are rated along 4-point Likert scales ranging from 0 "least" to 3 "most" referring to 4 statements, which express the degree of severity of depression. The total score is the sum of all items. The scale asks about feelings in 'the past week including today'. Therefore depression is considered in the present study as a state variable. The BDI is a reliable and valid instrument to assess depression severity in alcohol-dependent patients both in English- and French-speaking populations (Lemperiere et al., 1984; Clark et al., 1993a;). Cronbach α for the French version is very high, usually above 0.90.

2.2.4. Toronto Alexithymia Scale (TAS-20)

The Toronto Alexithymia Scale (TAS-20) is the most widely used measure of alexithymia (Bagby et al., 1994a, 1994b). It is comprised of 20 items that are rated on 5-point Likert scales ranging from 1 (strongly disagree) to 5 (strongly agree). The items load on three factors: a) difficulty identifying feelings (e.g., "when I am upset, I don't know if I am sad, frightened, or angry"); b) difficulty describing feelings (e.g., "I find it hard to describe how I feel about people"); and c) externally oriented thinking (e.g., "I prefer talking to people about their daily activities rather than their feelings"). The present study used a validated French translation of the scale (Loas et al., 1997). Total scores range from 20 to 100.

Cronbach's α coefficients were always found to be high for total alexithymia and the factors DIF and DDF. For instance, in a large study comparing the original English version with the French translation, Cronbach α were above 0.80 for the English version and above 0.70 for the French one. For EOT, values were lower but at least reaching 0.64, which is still acceptable (Zech et al., 1999).

2.3. Analytic plan

We will start by examining how alexithymia (total score and factors), negative affect, depression and craving (total and factors) are interrelated by using Pearson-moment correlations. These analyses will point out some gender differences that will deserve a thorough examination. A first step will be to look at mean group differences across gender for all the variables considered through Student's *t* tests for independent samples. Then, a more crucial issue will be to examine whether the association between depression and craving is moderated by gender. We will conduct hierarchical regression analyses with the total and factor scores of craving as the dependent variables, negative affect, depression and alexithymia factors as the direct predictors and the interaction between depression and gender. If we find a significant interaction between gender and craving, it will indicate that men and women AD do not behave in the same way when being in a depressive mood. In a last step, we will examine for men and women separately how the association between depression and craving is moderated by alexithymia factors. This will be done through hierarchical regression analyses considering the total and factor scores of craving as the dependent variables, negative affect, depression and alexithymia factors as the direct predictors, and the interactions between alexithymia factors and depression.

3. Results

3.1. Relations between alexithymia and negative affectivity, depression and craving dimensions at the end of the treatment

We investigated the extent to which alexithymia (total scores and factor scores) is related to negative affect, depression and craving, both for the total sample and when considering gender separately. Table 1 shows that, for the total sample, depression was highly related to alexithymia total scores and to the three alexithymia factors. Negative affectivity was only related to DIF. Finally, among the dimensions of craving, the only significant relation was between total alexithymia and the obsessive dimension and this was mainly driven by the DIF factor. When comparing results for total alexithymia and for alexithymia factors it is clear that results do not present the same pattern. We will therefore focus on the results for the alexithymia factors in the next sections of the results.

A descriptive examination of the correlations across gender also revealed some interesting differences. The correlation between depression and total alexithymia were almost identical for men and women. But looking only at total alexithymia scores obscured the pattern of results. Indeed, the magnitude of the

Table 1

Pearson-moment correlation matrix between alexithymia (total scores and factor scores) and negative affectivity, depression and craving at the end of treatment.

	DIF			DDF			EOT			Total Alex		
	M	W	Total	M	W	Total	M	W	Total	M	W	Total
NA	0.15	0.25 [†]	0.19*	−0.00	0.06	.02	0.13	0.13	0.11	0.14	0.23 [†]	0.17*
BDI	0.27**	0.47**	0.33***	0.26*	0.25	.24**	0.40***	0.11	0.26**	0.44***	0.43**	0.41***
Ob-OCDS	0.09	0.21	0.14 [†]	0.06	0.16	.10	0.12	0.09	0.09	0.12	0.24 [†]	0.16*
Co-OCDS	0.00	0.28*	0.11	−0.03	0.28*	.09	0.09	0.15	0.11	0.04	0.35**	0.15 [†]
Tot OCDS	0.06	0.25 [†]	0.14 [†]	0.02	0.22	.10	0.12	0.12	0.11	0.09	0.30*	0.17*

Note. DIF=difficulties identifying feelings factor from the Toronto Alexithymia Scale (TAS-20). DDF=difficulties describing feelings factor from the TAS-20. EOT=externally-oriented thinking factor from the TAS-20. Total Alex=total alexithymia score on the TAS-20.

NA=negative affectivity from the PANAS. BDI=Beck Depression inventory. Ob-OCDS=obsessive factor of the obsessive-compulsive drinking scale (OCDS). Co-OCDS=compulsive factor of the OCDS. Tot OCDS=total score of the OCDS.

N=103 for men (M) and N=55 for women (W), except for the line including BDI for which N=82 for men and N=35 for women.

[†] : $p < 0.10$,

* : $p < 0.05$,

** : $p < 0.01$,

*** $p < 0.001$.

correlation between depression and DIF was larger for women than for men. But for EOT, the correlation with depression was present only in men. Regarding the association between craving and alexithymia, a significant correlation was found for women between the compulsive dimension and two alexithymia factors (DIF and DDF), while the correlation was around 0 for men.

3.2. Gender differences

A first step in examining the specific role of gender will be to look at mean differences between men and women for all the key variables. Table 2 reports gender differences for craving for alcohol (obsessive, compulsive and total score), negative affect, depression and alexithymia (factor scores and total score). Only two differences were observed. Men scored higher on the externally-oriented thinking factor of alexithymia and women scored higher on depression. We computed g Hedges effect sizes, which are effect size corrected for unequal sample. They were respectively .35 and $-.36$, which corresponds to small effect sizes.

3.3. Predicting craving by negative affect, depression and alexithymia factors

In this section, we examined the possible direct association between craving on the one hand (obsessive factor, compulsive

Table 2

Mean groups differences across genders for alexithymia (total scores and factor scores), negative affect, depression and craving.

	Men	Women	t
DIF	17.68 (6.05)	17.89 (6.18)	−0.21
DDF	14.36 (3.87)	13.64 (4.27)	1.08
EOT	18.50 (4.44)	16.82 (4.42)	2.27*
Total alexithymia	50.53 (10.33)	48.35 (10.21)	1.27
NA	16.90 (5.99)	18.20 (8.27)	−1.13
BDI	13.05 (6.75)	16.20 (10.29)	−1.96*
Ob-OCDS	5.56 (3.15)	5.95 (4.04)	−0.66
Co-OCDS	3.84 (2.55)	3.76 (2.76)	0.16
Tot OCDS	9.40 (5.22)	9.71 (6.50)	−0.33

Note. DIF=difficulties identifying feelings factor of the Toronto Alexithymia Scale (TAS-20). DDF=difficulties describing feelings factor of the TAS-20. EOT=externally-oriented thinking factor from the TAS-20. Total Alex=total alexithymia score on the TAS-20.

NA=negative affectivity from the PANAS. BDI=Beck Depression inventory. Ob-OCDS=obsessive factor of the obsessive-compulsive drinking scale (OCDS). Co-OCDS=compulsive factor of the OCDS. Tot OCDS=total score of the OCDS.

N=103 for men and N=55 for women, except for the line including BDI for which N=82 for men and N=35 for women.

factor and total score) and negative affect, depression and alexithymia factors on the other hand, through hierarchical regression analyses. As shown in Table 3, the three hierarchical regression analyses were significant (respectively $F(5, 116)=6.04$, $p < 0.001$ for the obsessive factor, $F(5, 116)=2.97$, $p < 0.05$ for the compulsive one and $F(5, 116)=5.40$, $p < 0.001$ for the total score). NA was a significant predictor for the obsessive factor of craving and for the total score. Depression was always found to be significant, over and above NA. Finally, the three alexithymia factors were never significant.

3.4. Gender acts as a moderating variable in the relation between depression and craving

Based on results presented in Table 3, one could conclude that none of the alexithymia factors are related to craving in alcohol-dependent patients. Beyond direct relations between alexithymia and craving, it is important to test the hypothesis that alexithymia factors could act as moderating variables in the relation between depression and craving. In the next section, we will thus examine interaction effects between alexithymia factors and depression. But before doing that, we explained in the introduction that the association between depression and craving is likely to be moderated by gender. We thus first conducted hierarchical regression analyses in which we considered the interaction between

Table 3

Hierarchical regression analyses predicting craving by negative affect, depression and alexithymia factors.

	Ob-OCDS		Co-OCDS		Tot OCDS	
R ² Adj.	β	η^2_p	β	η^2_p	β	η^2_p
NA	0.25**	0.25	0.17 [†]	0.17	0.23**	0.24
BDI	0.35***	0.32	0.26*	0.23	0.33***	0.31
DIF	−0.02	−0.02	−0.04	−0.03	−0.03	−0.03
DDF	−0.01	−0.01	0.00	0.00	−0.01	−0.01
EOT	−0.04	−0.04	0.03	0.03	−0.01	−0.01

Note. DIF=difficulties identifying feelings factor from the Toronto Alexithymia Scale (TAS-20). DDF=difficulties describing feelings factor from the TAS-20. EOT=externally-oriented thinking factor from the TAS-20. Total Alex=total alexithymia score on the TAS-20.

NA=negative affectivity from the PANAS. BDI=Beck Depression inventory. Ob-OCDS=obsessive factor of the obsessive-compulsive drinking scale (OCDS). Co-OCDS=compulsive factor of the OCDS. Tot OCDS=total score of the OCDS.

[†] : $p < 0.10$,

* : $p < 0.05$,

** : $p < 0.01$,

*** $p < 0.001$.

depression scores and gender. In these regressions, we entered NA, depression and gender and then the interaction between depression and gender. Importantly, we found that the interaction was significant for the three measures of craving. We will now detail the results for each craving component.

In the regression predicting the total dimension of craving, $F(4, 112)=9.44$, $p \leq 0.001$, $R^2=0.25$, depression was significant ($\beta=0.33$, $p \leq 0.001$), as well as NA ($\beta=0.21$, $p=0.03$). But gender was not significant ($\beta=-0.04$, $p=0.83$). A significant interaction was found between BDI and gender ($\beta=0.49$, $p=0.004$, $\Delta R^2=0.06$). The simple slopes showed that the regression of total craving on depression was significant for women ($\beta=0.58$, $p \leq 0.001$) but not for men ($\beta=0.09$, $p=0.46$). In other words, for women, an increase in depressive mood was related to an increase in total craving. In men, however, an increase in depressive mood did not affect craving.

The same pattern of results holds for the two sub-dimensions of craving. For the obsessive dimension, $F(4, 112)=9.40$, $p \leq 0.001$, $R^2=0.25$, gender was not a significant predictor ($\beta=0.03$, $p=0.86$) but BDI was significant ($\beta=0.33$, $p=0.002$), as well as NA ($\beta=0.23$, $p=0.01$). The interaction between BDI and gender ($\beta=0.40$, $p=0.01$, $\Delta R^2=0.04$) was also significant. The simple slopes showed that the regression of obsessive craving on BDI was significant only for women ($\beta=0.53$, $p \leq 0.001$) but not for men ($\beta=0.13$, $p=0.26$). For the compulsive dimension, $F(4, 112)=6.23$, $p \leq 0.001$, $R^2=0.25$, gender was not a significant predictor ($\beta=-0.12$, $p=0.53$), as well as NA ($\beta=0.13$, $p=0.19$), while BDI was significant ($\beta=0.27$, $p=0.003$). A significant interaction was also found between BDI and gender ($\beta=0.53$, $p=0.003$, $\Delta R^2=0.07$). The simple slopes showed that the regression of compulsive craving on BDI was significant for women ($\beta=0.54$, $p \leq 0.001$) but not for men ($\beta=0.00$, $p=0.94$).

These results strongly suggest that men and women alcohol dependent patients do not behave in the same way when they are depressed. Therefore, in the next analyses we computed hierarchical regression analyses predicting craving dimensions by negative affect, depression, alexithymia factors and the interaction between alexithymia factors and depression first for men and then for women.

3.5. Alexithymia factors act as moderating variables in the relation between depression and craving as a function of gender

For *men*, the overall craving score as well as the compulsive craving dimension were not predicted by NA, BDI or alexithymia factors, nor by their interactions (see Table 4 for details). In the regression predicting the obsessive dimension of craving, $F(4, 77)=2.55$, $p \leq 0.05$, $R^2=0.12$, EOT was not a significant predictor ($\beta=0.08$, $p=0.50$) but BDI was significant ($\beta=0.29$, $p=0.05$). A significant interaction was found between BDI and EOT ($\beta=-0.23$, $p=0.01$, $\Delta R^2=0.08$). The simple slopes showed that the regression of obsessive craving on EOT was significant only at low levels of EOT ($\beta=0.46$, $p=0.01$) but not at high levels ($\beta=0.05$, $p=0.70$) (see Fig. 1). In other words, for low EOT scorers, an increase in depressive mood was related to an increase in obsessive craving. But for high EOT scorers, changes in depressive mood did not modify craving, suggesting that EOT can act in men alcohol dependent patients as a protective factor against obsessive craving.

For *women*, the overall craving scores and obsessive craving scores were only predicted by depression and by negative affect, which together explained between 68% and 72% of the variance scores (see Table 5 for details). It means that alexithymia factors never predicted the cognitive dimension of craving. Interestingly, the compulsive factor, which represents the behavioral dimension of craving was not only predicted by depression ($\beta=0.45$, $p \leq 0.001$), but also by the interaction between DDF and BDI

Table 4

Hierarchical regression analyses predicting craving dimensions by negative affect, depression, alexithymia factors and the interaction between alexithymia factors and depression in men.

Dependent variables	Predictors				R ²	F(4, 44)	p
	β	β	β	β			
OCDS total	NA	BDI	DIF	BDI X DIF	0.04	0.70	0.59
	0.16	0.15	-0.01	-0.12			
	NA	BDI	DDF	BDI X DDF			
	0.16	0.03	-0.03	0.13			
OCDS obsession	NA	BDI	EOT	BDI X EOT	0.04	0.70	0.59
	0.09	0.19	0.10	-0.18			
	NA	BDI	DIF	BDI X DIF			
	0.11	0.20	0.01	-0.12			
OCDS compulsion	NA	BDI	DDF	BDI X DDF	0.12	2.54	0.05
	0.08	0.29*	0.08	-0.23**			
	NA	BDI	DIF	BDI X DIF			
	0.11	0.07	-0.04	-0.10			
	NA	BDI	DDF	BDI X DDF			
	0.16	-0.10	-0.03	0.21			
	NA	BDI	EOT	BDI X EOT			
	0.16	0.03	0.11	-0.08			

* : $p < 0.05$,

** : $p < 0.01$.

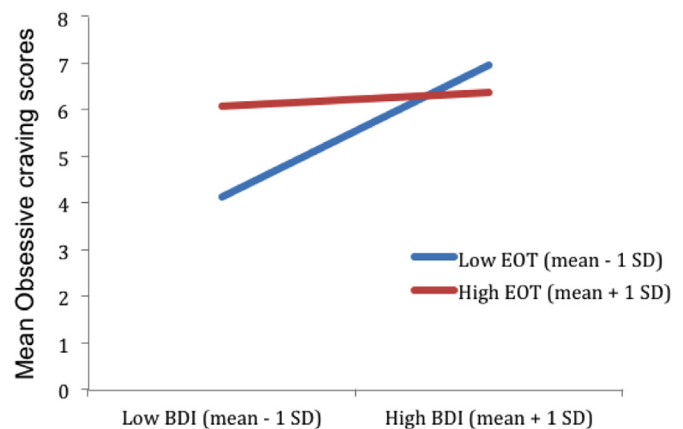


Fig. 1. Moderating effect of Externally-oriented thinking (low EOT vs. high EOT) on the relation between depression (low BDI vs. high BDI) and obsessive craving in men.

($\beta=0.26$, $p=0.02$, $\Delta R^2=0.06$). The simple slopes showed that the regression of compulsive craving on DDF was significant only at high levels of DDF ($\beta=0.71$, $p \leq 0.001$) but not at lower ones ($\beta=0.16$, $p=0.37$) (see Fig. 2). This means that, when women have low DDF scores, an increase in depressive mood is related to a small increase in compulsive craving. However, when they have high DDF scores, any increase in depression is related to a strong increase in compulsive craving. This suggests that a deficit in the ability to verbalize feelings to others in women alcohol dependent patients is related to a high vulnerability for the behavioural component of craving.

4. Discussion

4.1. Summary of the results

The results first showed that gender differences were only found for two variables. Men were higher than women on the

Table 5
Hierarchical regression analyses predicting craving dimensions by negative affect, depression, alexithymia factors and the interaction between alexithymia factors and depression in women.

Dependent variables	Predictors				R ²	F(4, 30)	p
	β	β	β	β			
OCDS total	NA	BDI	DIF	BDI X DIF	0.71	18.26	0.001
	0.34*	0.48***	-0.05	0.09			
	NA	BDI	DDF	BDI X DDF	0.71	18.57	0.001
	0.39**	0.43***	0.06	0.15			
	NA	BDI	EOT	BDI X EOT	0.72	19.40	0.001
	0.49***	0.43***	-0.02	0.18			
OCDS obsession	NA	BDI	DIF	BDI X DIF	0.69	16.61	0.001
	0.51**	0.38***	-0.03	0.07			
	NA	BDI	DDF	BDI X DDF	0.68	16.14	0.001
	0.57***	0.37**	0.01	0.05			
	NA	BDI	EOT	BDI X EOT	0.70	17.91	0.001
	0.65***	0.34**	-0.08	0.17			
OCDS compulsion	NA	BDI	DIF	BDI X DIF	0.62	12.33	0.001
	0.05	0.52***	-0.05	0.11			
	NA	BDI	DDF	BDI X DDF	0.66	14.87	0.001
	0.09	0.45***	0.11	0.26*			
	NA	BDI	EOT	BDI X EOT	0.64	13.09	0.001
	0.20	0.48***	0.07	0.17			

* : $p < 0.05$,

** : $p < 0.01$,

*** $p < 0.001$.

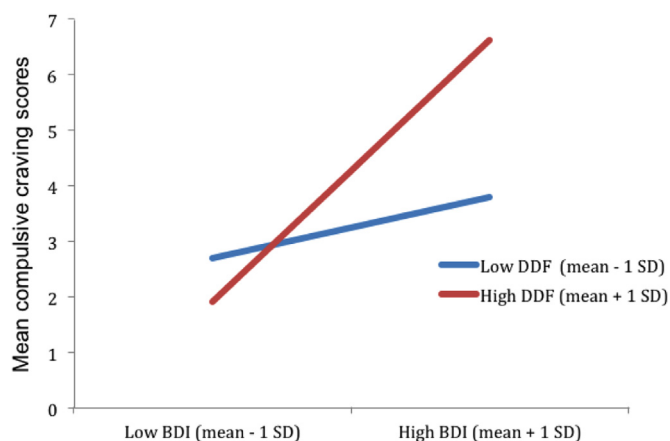


Fig. 2. Moderating effect of Difficulties describing feelings (low DDF vs. high DDF) on the relation between depression (low BDI vs. high BDI) and compulsive craving in women.

alexithymia factor externally-oriented thinking and women were higher than men on depression. Moreover, these differences were only of small effect size. Another important result is that alexithymia factors are related in a very different way to depression across gender. While in men, there is mainly an association with the externally-oriented thinking factor, in women the highest association is with difficulties identifying feelings.

When examining how negative affect, depression and alexithymia factors predicted craving, we found no direct association between alexithymia factors and craving dimensions. This suggests that alexithymia factors do not represent a direct risk factor for craving. However, the results highlighted two important

moderation effects. Firstly, we systematically found an interaction between depression and gender. Analyses of simple slopes revealed that only for women an increase in depressive mood was related to an increase in total craving. In men, however, changes in depressive mood were unrelated to changes in craving. Secondly, these interactions allowed us to test the hypothesis that alexithymia factors moderate the association between depression and craving, but in different ways for both genders. In men, scoring higher on externally-oriented thinking was related to a decrease in the magnitude of the association between depression and craving, but only in the case of the cognitive dimension of craving (obsessions). In women, scoring higher on difficulties describing feelings was related to an increase in the magnitude of the association between depression and craving, but only in the case of the behavioral dimension of craving (compulsions). A first conclusion is that one gender (female) when combined with high difficulties describing feelings scores is associated to more vulnerability for alcohol, while the combination of male gender with high externally-oriented thinking is associated to less vulnerability. It is also noticeable that the alexithymia factors involved in the moderation differ as a function of gender. Another issue is that the interaction between depression and alexithymia factors is not related to the same dimensions of craving: cognitive for men and behavioral for women. We will now discuss these issues.

4.2. Relations between depression, negative affectivity and alexithymia

One important conclusion of the results is that while the association between alexithymia (total scores and factor scores) and depression was strong, the one with NA was of small magnitude, almost always non-significant. Previous studies also showed that alexithymia and depression were associated in alcohol-dependency (De Rick and Vanheule, 2007a, 2007b; de Timary et al., 2008; Evren et al., 2008). In their study examining the associations between alexithymia total scores and the Five-Factor Model, Luminet et al. (1999) found that when the six facets of Neuroticism involved in the NEO PI-R were entered in regression analyses, the “Depression” facet was the only predictor of total alexithymia. This suggests that the depression aspect is central among the different facets composing neuroticism in their relation with alexithymia.

Regarding the association between alexithymia and negative affect, previous studies usually found a positive association, but of moderate magnitude, with total alexithymia scores. The explanation for low magnitude correlations in the present study is that the strength of association varied across alexithymia factors. Whilst the externally oriented thinking subscale has consistently been found not to be significantly associated with NA (e.g., Modestin et al., 2004; Waller and Scheidt, 2004), studies usually found that difficulty identifying and describing feelings are related to NA (e.g., Deary et al., 1997; Sayar et al., 2003). The association with difficulties identifying feelings is usually stronger than the one with difficulties describing feelings (e.g., Bailey and Henry, 2007). In our study, the correlation is just significant for difficulty identifying feelings, but an unexpected result is the absence of correlation with difficulties describing feelings.

4.3. Relations between alexithymia factors and craving in alcohol dependence

The presence of high alexithymia scores among alcohol dependent individuals was always considered as a vulnerability factor. Previous studies showed that alexithymic alcoholics consumed significantly more alcohol and were less abstinent than non-alexithymic alcoholics (Coriale et al., 2012), that total alexithymia predicts alcohol consumption (Bruce et al., 2012), that

higher total alexithymia scores were associated with poorer emotion regulation skills, fewer percent days abstinent, greater alcohol dependence severity, and several high-risk drinking situations (Stasiewicz et al., 2012), or that individuals with higher total alexithymia scores are more likely to act impulsively when experiencing heightened negative or positive affect, and thus engage in more drinking or experience more negative consequences after drinking (Shishido et al., 2013).

Regarding alexithymia and craving, our results suggest almost no direct association, except for women where significant relations were found between compulsive craving on the one hand and difficulties identifying feelings and difficulties describing feelings on the other hand. Our results contrast with those found in a cross-sectional study by Thorberg et al. (2011a) in which a positive association between alexithymia and craving was observed. The correlations were the highest for difficulties identifying feelings. They were lower for difficulties describing feelings, but still significant. For externally-oriented thinking, however, the correlations were not significant. More recently, Thorberg et al. (2014) assessed alcohol dependent patients undertaking cognitive-behavioral therapy in a longitudinal study. They were examined before the start (baseline) and at the end (12 weeks-follow-up) of a treatment program. Multiple regression analyses controlling for baseline age, gender, anxiety and depression found that alexithymia was associated with higher total and obsessive craving at 12 weeks follow-up. A major difference between those studies and the present one is that Thorberg et al. (2014, 2011a) considered outpatients that could still drink alcohol, while our data concern abstinent patients, and the difference in the strength of craving is important between drinking and abstinent alcohol-dependent subjects (Andersohn and Kiefer, 2004; Cordovil De Sousa Uva et al., 2010a; Leclercq et al., 2014b). In addition, these authors did not consider gender differences, while our results suggest that it can be a critical moderator.

4.4. Predictors of craving

Regarding the prediction of the two types of craving by both depression and negative affect, the present results are similar to previous studies (Andersohn and Kiefer, 2004; Lukasiewicz et al., 2005a; Oslin et al., 2009). In our research group, Cordovil De Sousa Uva et al. (2010a) found strong correlations between negative affect and craving in alcohol-dependent patients. At the start of treatment, correlations ranged from .33 for the compulsive component to .41 for the obsessive one. At the end of treatment, correlations ranged from .48 for the compulsive component to .57 for the obsessive one. Very similar relations were found between depression and craving, with correlations ranging from .47 for the compulsive component to .60 for the obsessive one, both at the beginning and at the end of treatment (de Timary et al., 2013). Interestingly, these results show that the associations with the obsessive dimension of craving tend to be of higher magnitude than the ones with the compulsive dimension.

One important result of the present study is that the predictive value of depression on craving was systematically moderated by gender. We found that only for women an increase in depressive mood was related to an increase in craving. Among women, those scoring higher on difficulties describing feelings are even more at risk for compulsive craving, which is in keeping with previous data (Boykoff et al., 2010). In men, however, changes in depressive mood were unrelated to changes in craving. This observation is consistent with the observation that relapse is more frequently related to negative affect in women than men (Zywiak et al., 2003) but also more generally with the observation in male AD patients of a large subgroup namely the type 2 Cloninger for whom the dependence is tightly related to impulsive behaviors and not to

affect related processes (Sigvardsson et al., 1982). Furthermore, brain imaging studies have shown that striatal activation was preferentially elicited by drug cues in men versus stress cues in women cocaine addicts, and that these activations correlated with the level of cocaine-craving (Potenza et al., 2012). Our assumption is that similar gender differences could occur in AD subjects between cues elicited (in the present case alcohol cues) and stress elicited craving.

4.5. Gender differences in alexithymia

Our study revealed only significant differences across gender for depression and the Externally-oriented thinking factor of alexithymia, and the effect size was only of small magnitude. This very small gender difference and for only one alexithymia factor somewhat contrasts with the existing literature. When considering the total alexithymia score, the majority of studies found higher scores for men. At the factor score level, men were usually higher on Difficulties describing feelings and/or Externally-oriented thinking (e.g., Salminen et al., 1999; Parker et al., 2003; Larsen et al., 2006; Elfhag and Lundh, 2007; Moriguchi et al., 2007). The studies that found higher scores for women reported that the difference occurred for Difficulties identifying feelings (e.g., Elfhag and Lundh, 2007; Moriguchi et al., 2007).

The quasi absence of gender effects can be explained by the clinical nature of our sample. In their meta-analysis, Levant et al. (2009) found much less gender differences when clinical samples were considered (only 3 out of 13 found significant differences) as compared to non-clinical samples (18 out of 32 found significant differences). Actually, the overall mean effect size (mean *Hedges'd*) for the clinical group was .16 and the bias-corrected bootstrapped 95% confidence interval did not include zero. This indicates that the difference was not statistically significant. These findings can explain that in our sample we did not find differences for total alexithymia scores. In addition, the limited reporting of gender differences on alexithymia factors in the studies used in this meta-analysis prohibited an exploration of whether gender differences held uniformly across the three factors.

Regarding the etiology of alexithymia, Lumley and Sielky (2000) suggested that they might be different in men and women. In women, the probability for alexithymia resulting from external events such as emotional trauma is higher. It means that the frequency of secondary alexithymia should be higher in women. In men, however, it would be more the result of developmental issues (e.g., communication deficits with caregivers) that then affect the developing brain (e.g., hemispheric asymmetry and deficient interhemispheric integration).

4.6. Gender and alexithymia factors as moderators in the relation between depression and craving

In the present study, we observed important gender differences in the moderation by alexithymia factors of the relation between depression and craving. In female AD subjects with high scores on difficulties describing feelings, the relation between depression and craving was stronger than in those who did not present this difficulty. The result suggests the importance of this alexithymia factor as a moderator of stress elicited craving in women. In men, Externally-oriented thinking was shown to decrease the relation between depression and craving. A first hypothesis is that this alexithymia dimension acts as a protective factor. The protective effect of alexithymia has been already demonstrated in some studies conducted in our research's group. For instance, higher total alexithymia scores decrease interference when angry faces primes are followed by targets with a positive valence (Vermeulen et al., 2006), or limit the amount of intrusive thoughts after being

exposed to a stressful movie (Luminet et al., 2004). We also found that providing a musical cue is particularly helpful for high alexithymia scorers to better encode emotional information (Vermeulen et al., 2010), which then facilitate recall and thus counteract the systematic deficit found for recall of emotion material (Luminet et al., 2006; Vermeulen and Luminet, 2009; Dressaire et al., 2015). However, another hypothesis is that although male AD subjects – and especially those who score high on externally-oriented thinking – have the tendency for less stress elicited craving (Zywiak et al., 2003), they could still experience high craving when exposed to alcohol related cues. Future studies should thus include these two different aspects of craving into account.

4.7. Total alexithymia scores and alexithymia factor scores

A new approach has been used to examine the structure of and interrelationships among multifaceted personality and psychopathology construct, the bifactor modeling, which is a latent variable factor analytic approach. The central goal is to determine whether subscale scores provide unique information above and beyond the total score. Recently, Rodriguez et al. (2015) examined 50 studies published in psychopathology and personality supporting such approach. Some psychometric indices provided for the TAS-20 gave support for a unidimensional general factor of alexithymia, thus advocating for considering only total scores and not factor scores. But some of the indices also support the view that factors, and particularly EOT, have some specificity, which is in favor of considering them separately. Parallel conclusions were drawn by Reise et al. (2013) who stated that subscales scores of the TAS-20 “provide a relatively better indicator of subscale true score standing, and, thus, can be reported. In this case, subscale scores, indeed, are better measures of subscale true scores relative to the total score, and these results allow one to argue that it is statistically justifiable to report subscale scores for the present TAS-20 data and especially for EOT” (p.132).

In parallel to these psychometric analyses, there are also debates considering whether EOT is a central feature of the alexithymia construct or not. These debates are not grounded on theoretical considerations. Indeed, since Nemiah, Freyberger, and Sifneos (1976), the construct includes as a main component a stimulus-bound, externally-oriented cognitive style. The issue is rather that the EOT scale within the TAS-20 has demonstrated low internal consistency despite the fact that it is measured by a highest number of items (8). It is therefore an important endeavor for future research to assess it more reliably. The TSIA, an observer-rating scale for alexithymia, is however demonstrating much better psychometric indices for EOT, reaching the 0.70 threshold (Bagby et al., 2006). Interestingly, Watters et al. (2015) recently provided some rationale for the *psychometric uniqueness of EOT* within the overall alexithymia domain. Using Modularity analysis, they showed that although DIF, DDF and EOT are central components of alexithymia, EOT stands as a more distinct entity than DIF and DDF, which are highly connected.

Finally, there are three additional reasons for examining the moderating impact of each alexithymia factor separately. The first one relates to the *psychometric* analyses of the TAS-20 on a large sample of patients with alcohol addiction. Results revealed a poor fit for the one factor model, while the best fit was obtained with a three factors solution (Thorberg et al., 2010b). The second one is based on previous empirical data demonstrating that each alexithymia factor has unique relationships with the dependent variables considered. Sometimes, these relationships are even going in opposite directions (e.g. Luminet et al., 2004; Vermeulen and Luminet, 2009). In the present study, we showed that DDF and EOT act in different ways depending on the gender considered. This crucial information would have been completely missed by

considered total scores. Finally, the small existing literature that examined alexithymia factor scores in alcohol dependency showed that EOT has another type of relationship with external correlates of alcohol addiction such as attachment or craving (Thorberg et al., 2011a, 2011b). This is only a first indication and further studies are clearly needed to examine this issue. It would also be possible to investigate differences in patterns of relationships between alexithymia total and factor scores among previous studies that did not report this information but that is available.

4.8. Assessing alexithymia in alcohol dependency

Some concerns were raised about the validity of existing scales for assessing alexithymia in alcohol dependent people. Three studies shed light to this important question. Besharat (2008) confirmed the original three-factor model of the TAS-20 in a sample of 321 substance abusing patients and found acceptable internal consistency as well as test–retest reliability over a 2-week period. However, despite this acceptable fit, the author noted that the validity and reliability of the TAS-20 in this population could be improved (Besharat, 2008). Thorberg et al. (2010b) compared the TAS-20 and the OAS, an observer rating scale for alexithymia. They found acceptable internal consistency, test–retest reliability and scale homogeneity for both the OAS and TAS-20. Because the TAS-20 was more strongly associated with alcohol problems than the OAS, they concluded that it is preferable to use the TAS-20 over the OAS for this population. Finally, Thorberg et al. (2010a) investigated the factorial validity of the TAS-20 and examined several models in a group of an alcohol- dependent sample. Although the three-factor model provided a better fit across four out of five fit indices compared to the one and two-factor models, the CFI did not reach the recommended 0.90 cut-off and all models were rejected given their poor fit to the data. This means that although the TAS-20 is so far the best instrument to use for assessing alexithymia in alcohol dependent patients, improvements are still required. In addition, there is no study using the TSIA that has been conducted with alcohol dependent participants, while an observer rating scale is particularly recommended for the assessment of clinical groups.

4.9. Limitations and future directions

One limitation of the present study is that we did not examine the processes that can explain the reasons for alcohol dependent patients – and more specifically the ones scoring high on alexithymia factors – to consume more alcohol. Some recent studies provide interesting suggestions on this issue. A first one is related to alcohol outcome expectancies or beliefs like assertion, affective change or tension reduction, in which alcohol expectancies are related to higher alcohol consumption. Results supported the view that individuals with high total alexithymia scores report drinking alcohol in order to feel more outgoing, friendly and confident, and find it easier to express their feelings (Thorberg et al., 2011c). A second one is related to drinking motives, i.e. the basic psychological motivations that underlie an individual's decision to drink alcohol (Bruce et al., 2012). Regression analyses revealed that the association between total alexithymia scores and alcohol consumption was fully mediated by social ('to be sociable'), enhancement ('to get high') and coping drinking ('to forget my worries') motives, and partially mediated by conformity ('so that others won't kid me about not drinking'). The driving motivations for drinking are also dependent of people's age and duration of the addiction. For young people who started drinking recently, positive reinforcement is the main motive, while in people with a longer alcohol dependency – like our sample – negative reinforcement is at the forefront (Koob and Le Moal, 2005). This is well-supported by the strong association we found between

craving and depression. Knowing the important difference we found across gender regarding the moderating impact of alexithymia factors, it will be important to consider the possibility of very different motives for men and women, as previously suggested (Sigvardsson et al., 1982).

The present results also suggest that gender specific treatments for alcohol dependence could be recommended. For women, the moderating effect of Difficulties describing feelings acted on the behavioral dimension of craving, which is the dimension the most closely related to actual alcohol consumption. It thus seems extremely important to screen female alcohol-dependent patients who score high on Difficulties describing feelings, who need specific treatment that were already found to be efficient for high alexithymia scorers. Among them, hypnosis and relaxation exercises, affect-regulation training involving feeling-labeling or group activities from a variety of complementary psychotherapeutic approaches (cognitive, interpersonal, psychodynamic) are recommended (Cameron et al., 2014).

For men, the paradoxical result is that low Externally-oriented thinking scorers are particularly vulnerable when under depressive mood. Low Externally-oriented thinking scorers may somehow match high self-consciousness scorers where a similar relation between craving and depression was observed (de Timary et al., 2013). This means on the one hand that it will be important to screen Externally-oriented thinking in men and have a special attention for those scoring low on that factor when depression increases. On the other hand, the present results suggest that in the case of high scores in male alcohol dependent patients it might be recommended to avoid attempts to modify their cognitive style, which is externally-oriented. Any intervention to make their thinking style more internally-focused can put them at risk for craving. Thus, in some specific cases, there might be risks in teaching interoceptive skills in high alexithymia scorers.

It will be necessary in the future to examine systematically alexithymia factors by gender interactions not only for craving but also for the prediction of alcohol relapses in the long term. It will also be important to extent this search for gender by alexithymia interactions in relation with other health outcomes.

There is also a need for a more comprehensive understanding of the circumstances in which alexithymia factors can act as protective factors. Differentiating short and long-term outcomes, gender, age, or socio-economic status, together with the types of cognitive-emotional processing involved are probably a few aspects that will need to be considered in the future.

Contributors

Olivier Luminet contributed for: designing the study, running analyses, writing the paper.

Mariana Cordovil de Sousa Uva contributed for: designing the study, collecting data, analysing data.

Carole Fantini contributed for: analysing data, writing the results section.

Philippe de Timary contributed for: designing the study, writing the paper.

Conflicts of interest

None of the authors had any conflict of interest in this study.

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