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2	Socio-affective processing biases in severe alcohol use
3	disorders: Experimental and therapeutic perspectives.
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5	Running title: Socio-affective biases in alcohol use disorders.
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21 Abstract

Previous literature has consistently reported socio-affective information processing 22 impairments in patients with severe alcohol-use disorder (SAUD). Some recent studies have 23 24 also suggested that these patients might exhibit biases toward stimuli indicating social threat, such as angry or disgusted faces. Such biases have been largely documented in other 25 26 psychopathological disorders like anxiety, where they play a critical role in the emergence and 27 maintenance of the disorder. A comprehensive understanding of these biases in SAUD would 28 thus deepen the understanding of interpersonal difficulties and relapse-related factors. 29 However, to date, no study has directly explored these biases in SAUD. In order to initiate 30 efforts to address this issue, we first review preliminary evidence supporting the hypothesis of 31 biased processing of social threat in SAUD. Then, we identify possible pathways through 32 which such biases might negatively impact the course of the disorder. Finally, we provide 33 precise recommendations and available materials to develop research in this promising field, 34 and underline the related theoretical and clinical perspectives.

35 **Keywords**: Alcohol use disorder; socio-affective processing; attentional bias; interpersonal

36 functioning; relapse; eye tracking

37 **1. Introduction**

38 As social individuals, human beings have a strong need to feel included and related to others. 39 When this need is thwarted, psychological well-being (Matthews et al., 2016; Taylor et al., 40 2018) and even life expectancy (Holt-Lunstad et al., 2015; Tanskanen & Anttila, 2016) are 41 reduced. Interpersonal difficulties play an important role in severe alcohol use disorders 42 (SAUD), as defined in the DSM-5 (American Psychiatric Association, 2013). Indeed, situations 43 of social exclusion and interpersonal conflict are frequent in SAUD and influence the disease's 44 course by constituting significant relapse triggers (Marlatt, 1996; Mau et al., 2019; Witkiewitz et 45 al., 2004; Zywiak et al., 2003). Conversely, the presence of social support is a predictor of long-term abstinence (Sliedrecht et al., 2019). Therefore, it is paramount to improve our 46 47 understanding of the downstream causes that negatively affect social relationships in SAUD.

48 Several societal factors contribute to interpersonal problems in SAUD. For example, this population is at high risk of being confronted with stigma (i.e., negative attitudes and social 49 50 rejection; Pescosolido et al., 2010; Schomerus et al., 2011) and dehumanization (i.e., the 51 denial of one's human features; Fontesse et al., 2019) from the general population, which 52 underlines the need for sensitization campaigns raising awareness on this disorder. Beyond 53 these external variables, neuroscientific studies have also highlighted that intrapersonal 54 factors might negatively affect interpersonal relations in SAUD, shedding light on valuable 55 individual treatment targets. Most recently, numerous studies have documented socio-affective 56 impairments in SAUD, with facial emotion decoding and Theory of Mind (broadly defined as 57 the ability to infer other's mental state, beliefs, and feelings) abilities being most affected (Bora 58 & Zorlu, 2017; Castellano et al., 2015; Donadon & Osório, 2014; Le Berre, 2017; 2019; 59 Maurage et al., 2019) and predicting treatment dropout and relapse (Rupp et al., 2017). 60 Moreover, this line of work also suggested that patients with SAUD, like many other psychiatric 61 populations (Bantin et al., 2016; García-Blanco et al., 2017; Hommer et al., 2014; Leyman et 62 al., 2007; Mogg et al., 2000) might process socio-affective information in a biased fashion, and

particularly exhibit biases¹ towards negative or socially threatening cues. These biases are 63 64 conceptualized as transdiagnostic factors contributing to psychopathology-related social stress and exclusion (Reinhard et al., 2019). They might also underpin the above-mentioned socio-65 affective impairments: a selective processing of negative social information may prevent 66 67 patients from correctly assessing and accurately reacting to social situations. Their presence could thus have tremendous implications for the understanding of SAUD development and 68 related interpersonal problems. Surprisingly, no scientific effort has been devoted to their 69 70 direct exploration in SAUD. In this paper, we thus aim at (i) reviewing the preliminary empirical 71 evidence supporting the presence of socio-affective biases in SAUD, (ii) discussing the mechanisms through which they might negatively influence the course of SAUD, and (iii) 72 73 outlining innovative research avenues to move forward in the exploration of these biases.

74 2. Current evidence for socio-affective biases in SAUD

While socio-affective biases have never been directly measured in SAUD, several arguments
suggest that they are involved in this disorder:

77 (1) Patients with SAUD exhibit modified processing of socially threatening emotions. They are 78 less accurate and slower than controls to identify emotions conveyed by faces, as well as to 79 estimate emotional intensity (e.g., Foisy et al., 2007; Kornreich et al., 2001a;2001b;2002;2013; 80 Maurage et al., 2009; Philippot et al., 1999). However, differences across emotions remain to be clarified. In a recent meta-analysis, Bora & Zorlu (2017) underlined that patients' modified 81 82 emotion processing abilities are most evident for faces displaying anger and disgust, with only 83 small-sized effects observed for other emotions and no difference for happy faces. Therefore, 84 rather than being characterized by general socio-affective impairments, patients with SAUD

¹ Here, we define biases as the preferential allocation of cognitive resources to specific stimuli (e.g., alcohol-related stimuli or social stimuli).

might exhibit selective changes for processing anger and disgust, which are construed as
emotions signaling social threat by eliciting behavioral tendencies destined to punish moral
violators (Chapman et al., 2009; Seip et al., 2014).

88 (2) Patients with SAUD over-estimate the presence of socially threatening emotions. Beyond the reduced decoding accuracy presented above, SAUD is actually related to a confusion 89 90 between emotions, and to an over-estimation of anger and disgust. Indeed, Philippot et al. 91 (1999) evidenced a tendency to perceive negative emotions in happy faces and to misattribute 92 anger and contempt (which the authors interpreted as signals of interpersonal conflict) to faces 93 actually displaying other emotions. Frigerio et al. (2002) further showed that patients with 94 SAUD more frequently misrecognized sad faces as angry or disgusted. Foisy et al. (2007) also 95 found both a tendency to misperceive anger and disgust as sadness and to report disgust in sad faces. Later, Maurage and colleagues (2009) showed that patients overestimate the 96 97 intensity of facial stimuli presenting anger, and confirmed that they also detect anger in stimuli 98 actually presenting sadness, fear, and even neutral emotions. More recently, Freeman et al. 99 (2018) further supported previous findings by revealing specific error patterns in SAUD when 100 categorizing emotional facial expressions, with patients more often perceiving anger and disgust in other negative and neutral emotions. Altogether, these behavioral studies using 101 102 different tasks and measures support the view that people with SAUD exhibit, beyond the 103 mere reduced performance in emotion decoding, biases towards the over-estimation of socio-104 affective information signaling social threat.

(3) Patients with SAUD have modified brain activations related to social threat. Congruent with
the proposal of altered social threat processing, patients with SAUD display increased dorsal
anterior cingulate cortex (dACC) activation compared to healthy controls when processing
angry faces (Park et al., 2015). Moreover, they show greater insula and dACC activation when
confronted with social threat, namely during social exclusion (Maurage et al., 2012).
Interestingly, higher dACC activation to specific stimuli (smoking cues) is related to attentional

biases (AB) towards the same specific stimuli in smokers (Luijten et al., 2011). Additionally,
the dACC and insula are involved in the attribution of salience to and the detection and
appraisal of social threat (Heilig et al., 2016; Kawamoto et al., 2015). Therefore, this pattern of
neural activation may reflect a heightened sensitivity to stimuli signaling social threat in SAUD,
which might underlie the biased processing of these stimuli.

3. Impact of socio-affective biases in SAUD

Given the above-mentioned influence of social factors on SAUD development and
maintenance, we argue that the biased processing of social threat may act as harbingers of
relapse, via two complementary pathways:

120 (1) At short term, it may increase patients' perception of social threat and augment their vulnerability to social rejection. This proposal is supported by results among healthy 121 122 participants showing that experimentally inducing an AB social threat led to increased anxiety 123 during social exclusion (Heeren et al., 2012). Furthermore, such biases could impede their ability to regulate the negative affects resulting from social exclusion (Gerber & Wheeler, 124 125 2009), as shown by persistent brain activations related to negative emotions and social 126 exclusion even after the end of the actual exclusion episode (Maurage et al., 2012). 127 Conversely, when excluded, healthy participants typically attend to positive social information, which is viewed as an adaptive way to recover from the negative effects associated with it 128 (DeWall et al., 2009). The tendency of patients with SAUD to show biases toward social threat 129 rather than positive social signals following social exclusion might thus exacerbate its negative 130 131 consequences and deprive patients from typical emotion regulation resources, leading them to resort to alcohol as an alternative way of coping with social exclusion feelings (Fairbairn & 132 Sayette, 2014). 133

(2) In the long run, biases toward social threat may facilitate the deterioration of social 134 135 relationships and prevent the emergence of new ones, reducing social support. For instance, 136 biases toward socially threatening information might favor the interpretation of ambiguous 137 social situations as hostile, and thus lay the ground for inappropriate responses such as aggression or avoidance, lowering social bonding. In accordance with this view, studies 138 139 showed that AB towards social threat are implicated in the negative interpretation of ambiguous social signals (Haller et al., 2017; White et al., 2011). Furthermore, both the 140 141 tendency to misperceive anger in non-angry stimuli and AB towards social threat are linked 142 with the frequency of aggressive behaviors (Hall, 2006; Miller & Johnston, 2019; Penton-Voak 143 et al., 2013). Consequently, biases towards social threat in SAUD might influence the 144 interpersonal problems encountered in this population, by promoting social avoidance or 145 aggression among patients as well as a resulting desire for social distance among other 146 individuals. The resulting social seclusion would again expose patients to higher relapse risk (Sliedrecht et al., 2019). 147

4. Towards a comprehensive investigation of socio-affective biases in SAUD

150 Previous sections underscored the pertinence of studying socio-affective biases in SAUD. Here, we provide means to initiate a research program in this promising field. A crucial first 151 152 step is to ascertain the genuineness of the bias via direct experimental examination. Such a goal can be achieved by employing validated cognitive bias paradigms such as the dot-probe 153 154 task (MacLeod et al., 1986), which has been largely used in other psychopathological states to 155 measure AB. Here, we focus on AB rather than memory or interpretation biases because AB 156 may be upstream determinants of the two other biases: selectively attending to specific stimuli 157 in a scene may influence its interpretation and facilitate the encoding and recall of these stimuli 158 (Blaut et al., 2013; Bowler et al., 2017; Everaert et al., 2014; Haller et al., 2017; White et al., 159 2011). In the dot-probe task, pairs of images (one emotional, one neutral) are presented, one

image being subsequently replaced by a target that participants are instructed to characterize 160 161 as fast and accurately as possible. Faster reaction times to targets replacing the emotional 162 image are a typical AB index. This task has often been employed in SAUD to measure 163 alcohol-related AB (i.e., using pictures of alcoholic versus soft drinks; Field & Cox, 2008), but it 164 has never been used to study socio-affective material in this population. This gap can be filled 165 by using socio-affective stimuli, such as emotional faces: by showing pairs consisting of one neutral and one emotionally-loaded face of different valences (e.g., happy, sad, fearful, angry, 166 167 disgusted), one can directly test whether patients exhibit biased attentional processing of 168 certain socio-affective information and whether it is specific to socially threatening ones (as 169 predicted by previous studies). At a later stage, task specificities can be modified to draw more 170 ecologically valid conclusion by testing whether the bias persists when the stimuli of interest 171 (i.e., presenting socially threatening emotions) are paired with non-neutral emotions (e.g., non-172 socially threatening but negative emotions like sadness) rather than neutral stimuli. Its generalization towards non-socially threatening stimuli (e.g., visual scenes depicting situations 173 174 related to anger or disgust) should also be tested.

175 Reaction-time based AB indices reveal the location of attention when images disappear, but 176 fail to capture attentional deployment over time (McNally, 2019). Therefore, complementing 177 the dot-probe task with eye tracking measures is valuable to study the dynamics of attention. 178 Eye tracking is a useful tool to unfold the nature of attentional processes in alcohol-related 179 disorders (Maurage et al., 2020), and eye-movements yield more reliable AB indices than 180 reaction times (Christiansen et al., 2015). Eye tracking measures would thus track the 181 evolution of overt attention allocation over time by computing gaze indices for different time 182 windows of the trials (Schofield et al., 2012). It would also help in the characterization of the 183 biases, with initial gaze orienting or first fixation latency indices reflecting rather automatic 184 attentional capture, whereas total dwell time indexes more controlled processes (Armstrong & 185 Olatunji, 2012). This precise characterization is paramount since different mechanisms (i.e. 186 attentional, but also perceptive, memory or executive processes) might underpin the biases.

187 Especially, SAUD is characterized by neurocognitive deficits (Bühler & Mann, 2011; Stavro et 188 al., 2013), which may play a role in the proposed biases. The eye tracking indices described 189 above can shed light on the cognitive processes involved: longer dwell time on threatening 190 faces can, for example, reflect patient's inability to exert executive control over attention. The 191 implication of cognitive control deficits can be further explored by manipulating explicit instructions during the dot-probe task (e.g., "do not look at threatening faces"). In this 192 193 paradigm, the number of fixations on the threatening face indexes failures to voluntarily control 194 attention. Finally, the processes underlying AB can be further revealed through the 195 identification of neural underpinnings of the biases using neuroimaging or neuromodulation 196 techniques.

197 After evidencing socio-affective biases in SAUD, another critical step would be to investigate 198 their interpersonal and clinical impact, notably by manipulating AB. Indeed, using the eye 199 tracker, attention can be trained away from negative stimuli (or towards positive ones) through 200 gaze-contingent operant conditioning (positive/negative feedback is provided when 201 participants look at positive/negative stimuli; e.g., Sanchez et al., 2016, 2019 but see Heeren 202 et al., 2015a, 2015b for criticism of attentional bias modification procedures). We previously 203 mentioned that biases toward social threat might play a causal role in exacerbating the 204 negative consequences of social exclusion in SAUD. This can be tested by manipulating AB in 205 patients before inducing social exclusion (see Reinhard et al., 2019 for a review of social 206 exclusion studies in psychiatry) and measuring the resulting affective state. Note that this 207 protocol can be flexibly adapted to test the causal role of AB in the interpretation of ambiguous 208 social stimuli (Sanchez et al., 2017) or avoidance behaviors of social situations (Rougier et al., 209 2019). We also predicted that patients with SAUD would not display typical biases towards 210 positive social cues following exclusion, leading to the impaired regulation of the associated 211 negative feelings. Contrasting the performance of patients and controls using a dot-probe task (containing both positive and threatening social stimuli) following social exclusion, and 212 monitoring their negative affects directly after exclusion and after the dot-probe task, would 213

214 allow stating on the validity of our prediction. Importantly, if our hypotheses regarding the 215 social and clinical impact of the biases in SAUD are supported by their experimental manipulation described above, their reduction through such manipulation should lead to 216 217 positive effects in clinical contexts. Therefore, if experimental protocols prove successful in 218 modifying the biases, they could constitute a worthy intervention technique for practitioners. 219 Raising awareness on the existence and impact of the bias may also help people with SAUD 220 to develop their ability to regulate and counteract negative affects and behavioral 221 consequences (e.g., favoring reappraisal and approach of social situations rather than 222 avoidance; Bernstein & Zvielli, 2014; Zvielli et al., 2016).

5. Conclusion

224 We argued that studying socio-affective biases in SAUD constitutes an innovative and 225 promising research avenue holding critical implications. At the fundamental level, it will enrich the growing body of literature reporting socio-affective abnormalities in SAUD, and provide 226 novel mechanistic insights vis-à-vis the interpersonal difficulties characterizing this population. 227 At the clinical level, the description of cognitive biases toward social threat in SAUD can lead 228 229 to targeted interventions complementing current treatments, particularly the attentional bias 230 modification procedures that have proven to be useful in social anxiety (Lazarov et al., 2017) 231 and are transposable to SAUD.

Declaration of interest

233 None

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486 **Figure Caption**

- 487 Figure 1. Schematic representation of the postulated short and long term paths leading
- 488 from socio-affective biases towards interpersonal threat to clinical outcomes.



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