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PHYSICAL ACTIVITY: A PROMISING ADJUNCTIVE TREATMENT FOR SEVERE  
ALCOHOL USE DISORDER

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## ABSTRACT

Substance use disorder develops from complex interactions between socio-environmental and neurobiological factors. A neurocognitive model of addiction, the triadic model, proposes that Alcohol Use Disorder (AUD) is the result of an imbalance between the reflective and the impulsive subcomponents along with a disruption of the regulatory subcomponent. Physical activity is considered as an emerging treatment for severe AUD (sAUD). This short review examines the efficacy and mechanisms of action of physical intervention as an adjunctive treatment in severe AUD (sAUD) within the theoretical framework of the triadic model.

Physical activity is a feasible, safe, and less stigmatizing approach than classical treatments. It improves sAUD patients' mental and physical comorbidities. The key finding of this short review is that physical activity could contribute to a rebalancing of the triadic model in sAUD patients by 1) improving neuroplasticity and cognitive functioning, 2) reducing impulsivity and urgency, and improving emotional regulation, and 3) reducing craving. This rebalancing could eventually reduce the risk of relapse. However, due to methodological issues, it remains difficult to observe an effect of physical activity on drinking outcomes. At best, a trend towards a reduction in alcohol consumption was noted. The mechanisms that could explain the benefits of physical activity in sAUD patients involve multiple physiological processes such as dopaminergic or glutamatergic transmission and signaling or neuroplasticity.

Future randomized controlled trials should include neuropsychological and impulsivity assessments, in more controlled environments. Physical activity could contribute to a personalization of sAUD treatment using each subcomponent of the triadic model as a therapeutic target. Physical exercise could be an adjunctive treatment for sAUD patients, favoring the benefit of more usual treatments such as cognitive behavioral therapies. It could also be a stand-alone intervention in less severe patients.

**KEYWORDS:** alcohol use disorder; cognitive impairments; impulsivity; craving; physical activity ; rehabilitation

## 1 **1. INTRODUCTION**

2 Alcohol Use Disorder (AUD) is a complex disease marked by a loss of control over  
3 alcohol consumption despite negative consequences (APA DSM-5 Task force, 2013; Koob &  
4 Le Moal, 2008; Volkow & Boyle, 2018 for a review). AUD involves social, psychological,  
5 behavioral and biological dysfunction such as brain alterations (Volkow & Boyle, 2018 for a  
6 review). Severe AUD (sAUD, i.e., 6 or more DSM 5 symptoms among eleven (APA DSM-5  
7 Task force, 2013) is associated with somatic and psychiatric comorbidities, as well as a  
8 frequent sedentary lifestyle (Linke & Ussher, 2015 for a review; World Health Organization  
9 et al., 2018). sAUD affects 25% of all AUD patients (Grant et al., 2015). Recovery from  
10 sAUD is often a long-term process requiring multiple episodes of outpatient or residential  
11 treatment, with a poor treatment retention and a high relapse rate (40 and 60% respectively)  
12 (National Institute on Drug Abuse (NIDA), 2012).

13 Access to standard care remains difficult for sAUD patients. A major barrier is the fear of  
14 stigmatization (Kohn et al., 2004; Probst et al., 2015). Ideally, new treatments of sAUD  
15 should have few adverse effects and improve patients' co-morbidities while promoting  
16 abstinence and preventing relapse. They should also be perceived as less stigmatizing by  
17 patients. Physical activity appears promising because it meets most of these criteria (Hallgren,  
18 Vancampfort, et al., 2018).

19 The existing literature supporting physical interventions for sAUD includes narrative and  
20 systematic reviews as well as meta-analyses. These studies explore physical functioning of  
21 sAUD patients and the short-term and long-term effects of physical activity on  
22 neuropsychiatric and cognitive measures, behavioral variables, and alcohol drinking outcomes  
23 (Ashdown-Franks et al., 2019; Giesen et al., 2015; Hallgren, Vancampfort, Giesen, et al.,  
24 2017; Stoutenberg et al., 2016 for reviews). Mechanisms underlying the impact of physical

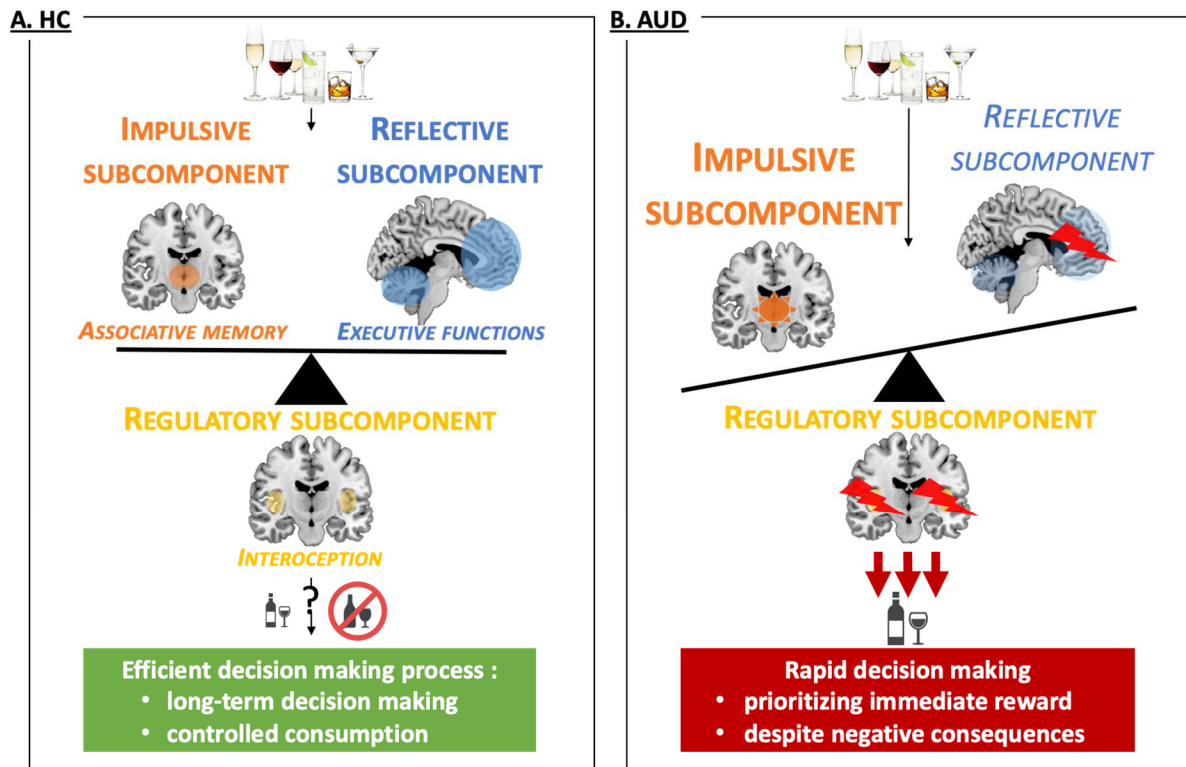
25 activity on substance use disorder, however, still need to be explored (Lynch et al., 2013 for a  
26 review).

27 The present review provides additional insight into the current literature by analyzing the  
28 efficacy and mechanisms of action of physical interventions for sAUD within the theoretical  
29 framework of the triadic model, a neurocognitive model of addiction. Its objectives are thus 1)  
30 to describe the neurobiological substrates of sAUD, 2) to examine the potential beneficial  
31 effects of physical activity in sAUD patients, and 3) to discuss the clinical and research  
32 perspectives of physical activity for sAUD and more generally for AUD patients.

33

## 34 **2. NEUROCOGNITIVE MODEL OF AUD**

35 Theoretical neurocognitive models have been proposed to better understand decision-  
36 making processes. In the dual-process model, decision-making under risk emerges from the  
37 interactions between a deliberative subcomponent underlying cognitive and analytic  
38 evaluation, and an affective subcomponent involved in an emotional evaluation (Mukherjee,  
39 2010). The first subcomponent favors controlled decisions while the second results in  
40 automatic and impulsive responses. Distinct cerebral networks underly each subcomponent: a  
41 prefrontal network for the deliberative-reflective subcomponent (prefrontal cortex, cingulum,  
42 cerebellum), and a limbic network for the affective-impulsive subcomponent (amygdala and  
43 striatum) (Mukherjee, 2010; Noël et al., 2013). This model was adapted and largely validated  
44 in AUD (Wiers et al., 2010; Noël et al., 2013). Noël et al. highlighted the role of insula and  
45 craving, and proposed a triadic model (*Figure 1A*) (Noël et al., 2013).



47

48 *Figure 1. Triadic model adapted from Noël et al. 2013. A) In healthy controls (HC), the*  
 49 *balanced interactions between the two main subcomponents result in adapted decision-*  
 50 *making due to alcohol cues. B) In sAUD patients, the weakening (⚡) of the reflective*  
 51 *subcomponent, the over-activation (★) of the impulsive subcomponent and/or the disruption (*  
 52 *⚡) of the regulatory subcomponent account for a rapid decision favoring alcohol*  
 53 *consumption.*

54 In this triadic model, sAUD is the consequence of an imbalance between the reflective and  
 55 impulsive subcomponents with a weakening of the reflective subcomponent and/or an  
 56 overactivation of the impulsive subcomponent face to alcohol and emotional stimuli (*Figure*  
 57 *1B*) (Noël et al., 2013; Wiers et al., 2010). The insula plays a regulatory role between these  
 58 two subcomponents, by translating bottom-up, interoceptive signals into subjective outputs,  
 59 such as the urge (i.e. craving) to consume alcohol (Noël et al., 2013). In response to an  
 60 alcohol cue, this imbalance accounts for rapid decision-making, prioritizing short-term reward  
 61 irrespective of the long-term consequences.

62        *Reflective subcomponent.* Chronic and excessive alcohol consumption is associated with  
63 gray matter shrinkage and altered white matter integrity affecting notably the frontocerebellar  
64 circuit involved in motor and executive abilities (Le Berre et al., 2017; Stavro et al., 2013 for  
65 reviews). Early in abstinence, these alterations result in impaired inhibition, updating and  
66 planning, flexibility and decision-making abilities with indirect consequences on  
67 metacognitive abilities, episodic memory, emotional processes and social cognition (Le Berre  
68 et al., 2017 for a review). Effective treatment requires efficient cognitive functioning in order  
69 to learn new skills and strategies to prevent relapse (Bates et al., 2013 for a review).  
70 Executive abilities are needed to achieve awareness, to resolve ambivalence towards  
71 problematic behaviors and to promote the motivation to change (Le Berre et al., 2013).  
72 Maintaining changes in behavior regarding alcohol is also a costly cognitive challenge  
73 because it requires inhibiting habits or routines as well as considering and planning new  
74 behaviors without alcohol. In a 6-month follow-up study, Czapla et al. found that deficits in  
75 response inhibition observed early in abstinence were a significant relapse predictor, in  
76 conjunction with the number of previous detoxifications (Czapla et al., 2015).

77        *Impulsive subcomponent.* Impulsivity is defined as a tendency to react rapidly or in  
78 unplanned ways to stimuli without proper regard for consequences or risks (Lejuez et al.,  
79 2010 for a review). It is viewed as a multidimensional construct related to personality traits,  
80 emotional or motivational dispositions, but also to cognitive functioning, particularly  
81 executive functions (Shin et al., 2012 for a review). Impulsivity is high in sAUD patients and  
82 increases the risk for initial use, development of dependence, and relapse (Evren et al., 2012;  
83 Lejuez et al., 2010; Shin et al., 2012 for reviews). The impulsive subcomponent is mainly  
84 associated with the amygdala and striatum (Noël et al., 2013). Decision-making deficits  
85 observed in sAUD patients may also result from impairment in emotional networks (Czapla et  
86 al., 2015; Le Berre et al., 2014). Emotional impairments, associated with alterations of the

87 limbic system, have been repeatedly reported in individuals with sAUD: alexithymia,  
88 impaired perception of emotions on faces or prosody, altered humor processing, empathy, and  
89 theory-of-mind (Le Berre, 2019; Oscar-Berman et al., 2014; Uekermann & Daum, 2008 for  
90 reviews). Moreover, sAUD patients experience increased sensitivity with higher automatic  
91 processing and attentional biases to alcohol-related cues (Field et al., 2008; Lannoy et al.,  
92 2014). Thus, when sAUD patients decide to abstain or reduce their alcohol consumption, they  
93 are confronted with habitual reflexes and alcohol-approach biases, especially in emotional  
94 contexts for which alcohol is often a coping strategy.

95 *Regulatory subcomponent.* Craving has become one of the cardinal symptoms of AUD in  
96 the most recent nosography (APA DSM-5 Task force, 2013). Craving results from a conflict  
97 between the need to drink alcohol and the desire not to do so (Naqvi et al., 2014). According  
98 to Naqvi's model, the insula is integrated with the rest of the goal-directed system, when  
99 automatic drug seeking is interrupted by a negative consequence or by the availability of a  
100 better alternative (Naqvi et al., 2014). Imaging studies show that activity of the insula  
101 correlates with subjects' rating of urge for cigarettes, cocaine, alcohol, and heroin (APA  
102 DSM-5 Task force, 2013; Noël et al., 2013).

103 Each subcomponent of the triadic model (executive functions, impulsivity/emotion,  
104 craving) is a therapeutic target in sAUD treatment. Several treatments, such as mindfulness  
105 meditation, cognitive remediation or cognitive behavioral therapy, have shown their  
106 effectiveness on some of these subcomponents (Coates et al., 2018; Garland & Howard, 2018;  
107 Rupp et al., 2012). Physical activity appears very promising since it has the potential to  
108 simultaneously target all three subcomponents.

109

### 110 3. PHYSICAL ACTIVITY IN sAUD TREATMENT

#### 111 3.1. Definition and current clinical guidelines

112 Physical activity is defined as “planned, structured, and repetitive bodily movement done  
 113 to improve or maintain one or more components of physical fitness” (Caspersen et al., 1985).  
 114 Despite promising and growing scientific data, clinical guidelines on sAUD treatment have  
 115 until now rarely mentioned physical exercise, and when they do so, it is mainly considered as  
 116 a recreational activity (*Figure 2*). For example, English, Australian and French clinical  
 117 guidelines only mention physical exercise as a “recreational group proved to be beneficial in  
 118 terms of engaging in other non-drinking-related activities”, a “simple way to relax”, and  
 119 “body-mediated activity” respectively (Haber et al., 2009; National Collaborating Centre for  
 120 Mental Health Staff, 2011; Société Française d’Alcoologie, 2015). A recent update of the  
 121 American NIDA guidelines for drug addiction treatment points out that physical activity is  
 122 increasingly being used in clinical practice for people with addictions and could be a  
 123 promising adjunctive treatment (National Institute on Drug Abuse (NIDA), 2012).

National guidelines on AUD				Exhaustive list of mentions concerning physical activity
National Institute on Drug Abuse (NIDA)		Principles of Drug Addiction Treatment: A Research-Based Guide (Third Edition)	Updated January 2018	« <u>Can exercise play a role in the treatment process?</u> Yes. <b>Exercise</b> is increasingly becoming a component of many treatment programs and has proven effective, when combined with cognitive- behavioral therapy, at helping people quit smoking. <b>Exercise</b> may exert beneficial effects by addressing psychosocial and physiological needs that nicotine replacement alone does not, by reducing negative feelings and stress, and by helping prevent weight gain following cessation. Research to determine if and how exercise programs can play a similar role in the treatment of other forms of drug abuse is under way. » p.29
U.S. Department of Health & Human Services		Facing addiction in America The Surgeon General’s Report on Alcohol, Drugs, and Health	2016	« <u>Acute Stabilization and Withdrawal Management</u> (...) Most periods of withdrawal are relatively short (3 to 5 days) and are managed with medications combined with vitamins, <b>exercise</b> , and sleep. One important exception is withdrawal from alcohol and sedatives/ tranquilizers, especially if the latter are combined with heavy alcohol use. Rapid or unmanaged withdrawal from these substances can be protracted and can produce seizures and other health complications. » p. 4.12
National Institute for Health & Clinical Excellence (NICE)		Alcohol-use disorders The nice guideline on diagnosis, assessment and management of harmful drinking and alcohol dependence	Updated August 2019	« <u>Experience of treatment setting – inpatient</u> Bacchus (1999) carried out a study about opinions on inpatient treatment for drug and alcohol dependence. (...) Recreational groups (for example, art therapy, <b>exercise</b> and cookery) also proved to be beneficial in terms of engaging in other non-drinking-related activities. » p.74
Australian Government Department of Health and Ageing		Guidelines for the Treatment of Alcohol Problems	2009	« <u>Getting through alcohol withdrawal: A guide for patients and carers</u> Everyone has simple ways to relax – watching television, videos, listening to music, warm baths, <b>light exercise</b> , reading – do whatever works for you. » p.177
Société Française d’Alcoologie (SFA)		Mésusage de l’alcool : dépistage, diagnostic et traitement Recommandation de bonne pratique <i>Alcohol abuse: screening, diagnosis and treatment Recommendation for good practice</i>	2015	« <u>What is the place of non-pharmacological and non-psychotherapeutic interventions?</u> (...) We can distinguish different types of workshops: - Body-mediated activities: <b>physical activity</b> , different methods of relaxation (...) Regular <b>physical activity</b> is often considered effective in increasing commitment to change and improving self-esteem, but there is a lack of data to support this belief. (...) The interventions that have shown the best evidence of effectiveness in reducing anxiety associated with alcohol misuse are <b>physical activity</b> , relaxation techniques and bibliotherapy. » p.48

125 *Figure 2. Comprehensive list of references to physical activity or exercise in the American,*  
126 *English, Australian and French clinical guidelines for the treatment of addictions and*  
127 *Alcohol Use Disorder (Haber et al., 2009; National Collaborating Centre for Mental Health*  
128 *Staff, 2011; National Institute on Drug Abuse (NIDA), 2012; Société Française d'Alcoologie,*  
129 *2015; Substance Abuse and Mental Health Services Administration (US) & Office of the*  
130 *Surgeon General (US), 2016).*

131 Physical activity is already being used in psychiatric disorders to improve psychiatric  
132 symptoms and physical health of patients. A recent review examined the efficacy of physical  
133 activity across numerous classes of mental disorders, including alcohol and substance use  
134 disorder (Ashdown-Franks et al., 2019). Physical activity had a significant effect on  
135 symptoms of depression, anxiety and schizophrenia with few side effects (Stubbs et al., 2018  
136 for a review).

137

## 138 **3.2. Effects of physical activity in the treatment of sAUD**

### 139 **3.2.1. Physical and mental health**

140 Most sAUD patients have a sedentary lifestyle but remain interested in physical activity,  
141 which is often preferred compared to pharmacological treatments (Abrantes et al., 2011).  
142 Several recent reviews conducted in sAUD patients indicate that moderate-to-vigorous  
143 intensity physical activity could be an adjunctive non-pharmacological treatment (Ashdown-  
144 Franks et al., 2019; Giesen et al., 2015; Hallgren, Vancampfort, Giesen, et al., 2017). Physical  
145 activity is a feasible and safe therapeutic approach in sAUD treatment. It has been related to a  
146 reduction in sedentary lifestyle and an improvement of poor physical health (Abrantes et al.,  
147 2011; Hallgren, Vancampfort, Schuch, et al., 2017). It improves sAUD patients'  
148 comorbidities such as somatic issues (metabolic syndrome, cardiovascular diseases, diabetes)  
149 or mental health problems (depression, anxiety, sleep disorder) (Giesen et al., 2015). A  
150 systematic review published by Giesen et al. included 14 controlled exercise interventions  
151 conducted in sAUD. It highlighted the beneficial effects of physical activity (aerobic exercise

152 and strength training) on physical fitness, resting heart rate, physical activity level, and  
153 strength, with no adverse events reported (Giesen et al., 2015). Hallgren et al. performed a  
154 systematic review and meta-analysis of physical activity in sAUD patients (21 studies;  
155 n=1204). Exercise programs involved moderate intensity aerobic exercise (n=13),  
156 combination of aerobic exercise and strength training (n=5) or yoga/stretching (n=3). Exercise  
157 programs were 2 to 52 weeks long, and the mean exercise session duration was 43 minutes.  
158 Most of the programs were supervised (n=17). Hallgren et al. reported a significant reduction  
159 in depressive symptoms and a significant improvement in physical fitness (Hallgren,  
160 Vancampfort, Giesen, et al., 2017). Other benefits can be expected including an improvement  
161 of social abilities, appetite and sleep, quality of life, and self-efficacy (Giesen et al., 2015;  
162 Stoutenberg et al., 2016).

163

### 164 **3.2.2. Drinking outcomes**

165 Giesen et al. reported “inconsistent effects with a slight trend toward a positive effect” on  
166 drinking behavior (abstinence rate, alcohol use frequency and total amount consumed) or  
167 craving in their systematic review (Giesen et al., 2015). Another narrative review by Manthou  
168 et al. reported that physical activity had a positive impact on alcohol consumption, abstinence  
169 rates, or the urge to drink in 6 out of the 11 studies reviewed (Manthou et al., 2016). Wang et  
170 al. performed a meta-analysis on physical activity in substance use disorder. Only 3 studies  
171 specifically examined sAUD, and 3 others focused on alcohol use in polydrug abusers (Wang  
172 et al., 2014). Results indicated that physical activity can significantly increase the abstinence  
173 rate in subjects with sAUD. Of the 21 studies included in Hallgren’s meta-analysis, only five  
174 studies adequately reported data on alcohol drinking outcomes (number of standard drinks  
175 consumed per day, or per week, number of heavy drinking days, AUDIT total score, alcohol  
176 urge/craving) (Hallgren, Vancampfort, Giesen, et al., 2017). Long-term exercise (3 studies

177 described the use of moderate intensity aerobic exercise, and 2 the use of yoga) was  
178 associated with nonsignificant reductions of alcohol consumption and of the risk level  
179 associated with alcohol consumption.

180 Three randomized controlled trials have been conducted more recently and are thus not  
181 included in the previous reviews or meta-analyses. Roessler et al (2017) examined the effects  
182 of a 6-month moderate exercise intervention in sAUD patients. The interventions were as  
183 follows: treatment as usual (TAU), TAU and supervised physical activity, TAU and  
184 individual and autonomous physical activity with only a written training program. A moderate  
185 level of physical activity was protective against excessive drinking whatever the intervention,  
186 with a “dose-response” effect. In each intervention group, participants with moderate level  
187 physical activity (using the International Physical Activity Questionnaire IPAQ categories of  
188 physical activity intensity in everyday life (Craig et al., 2003)) had better drinking outcomes  
189 than participants with low level physical activity. The amount of alcohol consumed in each  
190 intervention group decreased by 4% for each increased exercising day (Roessler et al., 2017).  
191 In a 2-arm randomized controlled trial, Georgakouli et al. (2017) investigated changes in  
192 drinking behavior and biochemical response to exercise. Eleven heavy drinkers performed an  
193 8-week supervised moderate exercise training (50-60% HRR, Heart Rate Reserve i.e. the  
194 difference between maximum heart rate and resting heart rate). The intervention resulted in a  
195 significant reduction of alcohol consumption and fitness improvement in heavy drinkers but  
196 did not significantly change hormonal responses (in particular in the hypothalamic-pituitary-  
197 adrenal axis involved in stress adaptation). Finally, Jensen et al. (2018) randomly assigned  
198 105 sAUD patients to two groups. The experimental group underwent a treatment as usual  
199 combined with running and brisk walking for 30–45 min twice a week in small supervised  
200 groups or individually. The control group consisted of a treatment as usual only. Drinking  
201 outcomes were assessed after 6 and 12 months of training. Training was estimated of

202 moderate intensity (78% HRR) with no difference between supervised groups or individual  
203 practice. A significant reduction in training frequency was observed in both groups after the  
204 first month. Alcohol intake significantly decreased (219 to 41 units of pure alcohol per 30  
205 days) for the entire sample of patients with no significant difference between groups.

206 The idea that physical activity may be an efficient strategy in sAUD treatment is not new;  
207 it has been demonstrated that physical activity is a safe and acceptable intervention with  
208 benefits on physical fitness and mental health of sAUD patients. However, the literature  
209 indicates that it remains difficult to observe changes in drinking outcomes with, at best, a  
210 trend toward a reduction in alcohol consumption. The absence of consensus regarding the  
211 effect of physical activity on drinking outcomes can be explained by several factors: the  
212 heterogeneity of the patients included in the mentioned studies, the diversity in study designs,  
213 the limited number of randomized and controlled trials, and the still imprecise criteria for  
214 personalizing physical activity for sAUD patients. A combined approach using physical  
215 activity as an adjunctive treatment, in addition to behavioral therapies and medications, is  
216 particularly pertinent for sAUD. Patients often suffer from poor physical and mental health,  
217 cognitive and emotional impairments, high impulsivity and cognitive biases, and craving, all  
218 of which require specialized intervention. Physical activity could participate in the  
219 rebalancing of the three subcomponents in the triadic model of sAUD.

220

### 221 **3.3. How can physical activity rebalance the triadic model of sAUD ?**

#### 222 **3.3.1. Reflective subcomponent**

223 Considering the pro-cognitive effect of physical activity in various adult populations  
224 (including mental disorder or regular tobacco smokers), Hallgren et al. suggested that physical  
225 activity may have a beneficial cognitive effect in sAUD patients (Hallgren, Vancampfort, et  
226 al., 2018). In their recent systematic review and meta-analysis, they point the lack of relevant

227 cognitive assessments in the studies conducted so far (Hallgren, Vancampfort, Giesen, et al.,  
228 2017). However, data from other clinical populations appear promising and highlight the  
229 potential role of physical activity programs as an adjunct to current cognitive rehabilitation  
230 strategies.

231 Studies conducted in both animals and humans suggest that physical activity has a  
232 facilitating effect on neuroplasticity and may improve cognitive functioning (Costa et al.,  
233 2019; Hötting & Röder, 2013 for reviews). Meta-analyses report a significant positive effect  
234 of regular physical training in sedentary adults, healthy older adults, or in psychiatric  
235 populations on several cognitive functions, including executive abilities, attention and  
236 processing speed, memory, and on different related cerebral networks (Firth et al., 2016;  
237 Hötting & Röder, 2013; Knöchel et al., 2012; Smith et al., 2010). In schizophrenia, a review  
238 conducted on the pro-cognitive mechanisms of physical exercise described the use of aerobic  
239 exercise using cycle ergometers or treadmills, bodyweight exercises, interactive videogames  
240 or free-weights sometimes associated with resistance-based training such as muscle  
241 strengthening (Firth et al., 2016 for a review). Exercise programs included in this meta-  
242 analysis were on the average 12,2 weeks long (ranging from 4 to 24 weeks) with 2,9 sessions  
243 per week on average (ranging from 2 to 4 sessions), of 20 to 60 minutes in duration. Control  
244 conditions were table football, occupational therapy, treatment as usual or relaxation training.  
245 Exercise was associated with improvement in global cognition, in particular for supervised  
246 interventions by physical activity professionals. Exercise significantly improved working  
247 memory functioning, social cognition, attention and vigilance, but not processing speed,  
248 verbal and visual memory, or reasoning and problem solving. In sedentary adults, exercise  
249 programs involved aerobic exercise comprising endurance programs (running, walking,  
250 cycling, or swimming), ranging from a few weeks up to one year in duration (Hötting &  
251 Röder, 2013 for a review). Control interventions were light stretching and toning programs, or

252 waiting list. Benefits were mostly observed for executive functions associated with frontal  
253 brain regions. In healthy older adults (Smith et al., 2010 for a review), exercise programs  
254 lasted between 6 weeks to 18 months and focused on moderate aerobic exercise such as brisk  
255 walking and/or jogging, combined or not with strength training intervention. Control  
256 conditions were stretching and toning, health education, relaxation, or waiting-list. Combined  
257 aerobic exercise and strength training interventions seemed to improve attention and  
258 processing speed to a greater extent than aerobic exercise alone. Longer or higher intensity  
259 programs were not associated with better improvements in neurocognition.

260 In patients with an altered reflective subcomponent, physical activity could be combined  
261 with cognitive stimulation. In effect, physical activity may “prepare” the brain to respond to  
262 cognitive stimulation. Cognitive changes induced by physical activity could thus be  
263 potentiated by this combination (Hötting & Röder, 2013 for a review). Patients with alcohol-  
264 related cognitive impairments require specific supervision because feelings of fatigue and  
265 self-defeating thoughts demand inhibitory control so that patients continue to be motivated for  
266 exercising (Costa et al., 2019 for a review). Self-selected exercise (e.g. by giving patients a  
267 choice of different types of moderate intensity group aerobic exercise) is preferable to reduce  
268 self-defeating thoughts, promote adherence to the exercise and train self-assessment abilities.  
269 Decision-making is highly mobilized to arbitrate between perceived effort, feelings, and  
270 internal conversations (Costa et al., 2019 for a review).

271

### 272 **3.3.2. Impulsive subcomponent**

273 Physical activity has been successfully used in attention deficit hyperactivity disorder  
274 (ADHD) (Christiansen et al., 2019). ADHD is characterized by symptoms of inattention,  
275 hyperactivity and impulsivity, along with deficits in executive functions, emotional regulation  
276 and motivation (APA DSM-5 Task force, 2013). ADHD is highly comorbid with sAUD

277 (Zulauf et al., 2014). Regular physical activity significantly reduced ADHD subjects'  
278 impulsivity and hyperactive behaviors (Abramovitch et al., 2013; Christiansen et al., 2019).

279 Two components of impulsivity that are particularly implicated in sAUD could be targeted  
280 by physical activity: sensation seeking and urgency, or the tendency to act rashly to regulate  
281 emotions, in particular negative emotions (Shin et al., 2012 for a review). Physical activity  
282 could be useful to decrease urgency and improve emotional regulation. Reed et al. performed  
283 a meta-analysis that examined the effect of acute aerobic exercise (such as aerobic dance,  
284 walking, jogging, running, swimming, and cycling) on self-reported positive affect (focusing  
285 on the positive subscale such as “energy” or “joy”). Dose of exercise was estimated as the  
286 product of exercise intensity (%Vo<sub>2</sub>R i.e. % of oxygen uptake reserve) and duration. Physical  
287 activity was associated with increased positive affect, which could last up to 30 minutes post-  
288 exercise, especially in individuals with low affective pre-exercise scores, and even for low to  
289 moderate doses. No threshold could be found for intensity or duration to be considered as  
290 having a significant effect on affect. Physical activity could thus be a self-regulatory strategy  
291 to improve “feelings of energy” and increase positive affect (Reed & Ones, 2006; Stoutenberg  
292 et al., 2016). It could also be considered as a safe way to activate the reward system, thus  
293 “competing” with drinking behavior (Brené et al., 2007; Lynch et al., 2013 for reviews).  
294 Finally, in a randomized counter balanced cross-over study (brisk walking i.e. moderate  
295 aerobic exercise versus 15 minutes of passive seating) conducted in 20 abstaining (at least 3  
296 days of abstinence) excessive alcohol drinkers, Taylor et al showed that a single session of  
297 exercise could reduce automatic attentional bias towards alcohol-related images and alcohol  
298 urge (Taylor et al., 2013).

299 In patients with an overactive impulsive subcomponent, it seems safer to avoid high-  
300 intensity exercise, which has been associated with negative affective states and lower pleasure  
301 during exercise in sedentary individuals, causing an increase in the dropout rate (Costa et al.,

2019 for a review). High-intensity exercise could also mimic the brain effects of alcohol drinking on the reward circuit and increase vulnerability to substance abuse and excessive exercise (Hausenblas et al., 2017; Lynch et al., 2013 for reviews). Moderate intensity exercise should be preferred, ideally in supervised but open-access exercise sessions, to avoid absenteeism and abandonment.

307

### 3.3.3. Regulatory subcomponent

Exercise has been shown to be associated with decreased craving for smoking, or marijuana use (Stoutenberg et al., 2016 for a review). In sAUD, two of the studies included in the meta-analysis of Hallgren et al. explored the acute effects of physical activity in sAUD patients (Hallgren, Vancampfort, Giesen, et al., 2017). In the first randomized trial (Ussher et al., 2004), craving intensity was significantly reduced in sAUD inpatients immediately following moderate intensity cycling lasting 10 minutes, compared to patients undergoing 10 minutes of very light intensity cycling. However, the decrease was short-lived with a significant decline in alcohol urges for the experimental condition versus control during exercise but not at any measurement point following (immediately after the exercise, and 5 and 10 minutes following exercise). In the second study (Jamurtas et al., 2014), 9 sAUD inpatients and 9 healthy controls exercised for 30 minutes at a low intensity. There was a 17%, but nonsignificant, decrease of alcohol urge in sAUD inpatients tested before and immediately after exercising. Authors pointed the very small sample size of their study and the low initial alcohol urge levels of the patients. In the Taylor et al. study, the short bout of moderate aerobic exercise (brisk walking) reduced significantly craving compared to passive seating when evaluated immediately after the exercise, and 5 and 10 minutes after (Taylor et al., 2013). In a more recent study, Brown et al described a decrease in alcohol craving in 26 patients following a 20- to 40-minute moderate intensity exercise program that was conducted

327 once a week, over 12 weeks. This decrease in craving was significantly more pronounced than  
328 the one observed in patients who received only physical activity advice (a single session of  
329 brief advice for autonomous practice) (Brown et al., 2016). Taken together, these results  
330 indicate that exercise should be at least of moderate intensity to reduce craving. It seems  
331 relevant to consider short and easily achievable sessions several times a week and early after  
332 detoxification when the control of sudden craving is targeted.

333

#### 334 **3.4. Mechanisms underlying the impact of physical activity on sAUD**

335 A better understanding of the potential numerous mechanisms of action of physical activity  
336 would help improve its effectiveness for each sAUD patient. Physical activity might be  
337 positive not only on a psychological (e.g. stress and mood regulation, self-efficacy) or social  
338 level (e.g. social reinforcement, change in lifestyle that encourages more healthy behaviors  
339 including better diet or sleep) but also on a neurobiological and neurocognitive level (Costa et  
340 al., 2019; Giesen et al., 2015; Hallgren, Vancampfort, Giesen, et al., 2017; Stoutenberg et al.,  
341 2016 for reviews).

342 Neurobiological mechanisms involved in the development of AUD include a dysregulation  
343 of the reward function via dopamine and opioid peptide deficits and increased brain stress  
344 system activity via corticotropin-releasing factor and dynorphin. It also involves a  
345 dysregulation of glutamatergic and GABAergic networks (Koob & Volkow, 2016). sAUD is  
346 associated with brain alterations and dysfunction (in particular prefrontal cortex, limbic  
347 system and cerebellum), neuroinflammation, altered neurogenesis and neuroplasticity, and  
348 abnormal neurotransmission. These abnormalities account for cognitive and emotional  
349 processing impairments (Le Berre, 2019; Oscar-Berman et al., 2014; Perry, 2016).  
350 Neurobiological mechanisms induced by physical activity in sAUD involve multiple  
351 signaling pathways and systems (Costa et al., 2019; Lynch et al., 2013). Physical activity may  
352 favor the regulation of the neurotransmission, and a protective and restorative effect against

353 the neurotoxicity of alcohol (Perry, 2016 for a review). In effect, physical activity results in  
354 neuroplasticity, possibly through a stimulation of cerebral circulation (Mandolesi et al., 2018  
355 for a review), as well as neurogenesis and synaptogenesis, possibly through an increase in  
356 neurotrophins expression (such as Brain-Derived Neurotrophic Factor BDNF) (Hötting &  
357 Röder, 2013; Perry, 2016 for reviews). Increased neurogenesis, decreased neuroinflammation  
358 and oxidative stress, and moderation of glucocorticoid release in the stress axis could  
359 compensate for the harmful effects of alcohol in sAUD (Perry et al. 2016 for review).  
360 Moriarty et al. demonstrated that the level of exercise intensity may influence prefrontal  
361 cortex oxygenation during cognitive testing using functional near infrared spectroscopy  
362 (fNIR) (Moriarty et al., 2019). The fNIR device was used to measure hemoglobin difference  
363 changes between pre-exercise baseline and post-exercise cognitive assessment. Four  
364 conditions were compared in height healthy and physically active volunteers: non-exercise  
365 control, moderate intensity aerobic exercise, high intensity aerobic interval exercise, and  
366 mind-body yoga exercise. Activation (using oxygenated/deoxygenated hemoglobin changes  
367 as an indirect marker of neural activation) was higher after moderate intensity aerobic  
368 exercise compared to high intensity, yoga or control. But prefrontal cortex activation did not  
369 correlate with cognitive performance. In addition, a negative relationship was found between  
370 cognitive abilities and exercise intensity, indicating that exhausting exercise could be  
371 cognitively prejudicial. Even though the sample size remains small and the experiment only  
372 included single exercise sessions, these findings suggest that repeated moderate activity may  
373 improve brain oxygenation and cognitive functioning.

374 Lynch et al. proposed that the efficacy of physical activity in sAUD may vary across  
375 individuals (age or sex in particular) and depend on the stage of the addiction process as well  
376 as the exercise modalities (Lynch et al., 2013 for a review). Through facilitation of  
377 dopaminergic transmission and adaptations in dopaminergic signaling, moderate physical

378 activity could prevent drug use by introducing an alternative reward. By its own reinforcing  
379 properties, physical activity could also prevent the development of addiction and reduce the  
380 risk of relapse through the normalization of glutamatergic and dopaminergic signaling or the  
381 blockage of changes in chromatin via epigenetic regulation of BDNF caused by chronic  
382 exposure to alcohol and repeated withdrawal (Costa et al., 2019; Lynch et al., 2013 for  
383 reviews).

384 Other physiological systems involved in the initiation and development of sAUD could  
385 also be impacted by both short-term and long-term physical activity : norepinephrine,  
386 serotonin, endocannabinoids (Hallgren, Vancampfort, Giesen, et al., 2017; Lynch et al., 2013;  
387 Stoutenberg et al., 2016 for reviews).

388

## 389 **4. LIMITS AND PERSPECTIVES**

### 390 **4.1. Research considerations**

391 To our knowledge, no studies evaluated the effects of physical activity on each of the 3  
392 sub-components of the triadic model simultaneously. Future protocols investigating the  
393 mechanisms explaining the efficacy of physical activity in sAUD should include repeated  
394 neuropsychological assessments and neuroimaging examinations, but also a comprehensive  
395 evaluation of impulsivity and craving.

396 It is very difficult to investigate the efficacy of physical activity in sAUD in a real-world  
397 setting since many environmental factors can interfere with the effect of exercise programs  
398 (e.g. alcohol exposure, stressors, lack of social support or resources, etc.). Stoutenberg et al.  
399 (2016) claimed that a highly controlled environment (i.e., residential treatment programs) is  
400 crucial to determine the efficacy of exercise training in sAUD and its optimal modalities  
401 (dose, frequency, intensity) before determining its effectiveness in a real-world setting  
402 (Stoutenberg et al., 2016). Exercise programs should also take the heterogeneity of sAUD

403 patients into account, in order to determine an optimal and personalized exercise intervention.  
404 The impact of demographical or clinical factors (e.g. impulsivity, craving levels, cognition,  
405 but also age, comorbidities and physical condition, gender, stage and severity of AUD, social  
406 status and skills, co-addictions, etc.) on the effectiveness of physical activity should be  
407 investigated more precisely (Lynch et al., 2013, 2017; Sari et al., 2017; Wang et al., 2014).

408 Moreover, there is only a limited number of randomized controlled trials and previous  
409 studies are very heterogeneous regarding the nature of the interventions and measurements (in  
410 particular concerning alcohol consumption), as well as limited sample sizes with a high drop-  
411 out rate. For example, in Hallgren et al meta-analysis (10 studies, 1204 participants), 40,3%  
412 of sAUD patients dropped out from physical activity programs. This dropout rate was  
413 noticeably higher than in other populations with mental illness, such as depression or  
414 schizophrenia. However, this dropout rate was not significantly different from the control  
415 conditions (Hallgren, Vancampfort, Giesen, et al., 2017). Supervision of physical activity by a  
416 qualified trainer and motivational strategies was associated with a decrease in the dropout  
417 rates (Hallgren, Vancampfort, Giesen, et al., 2017).

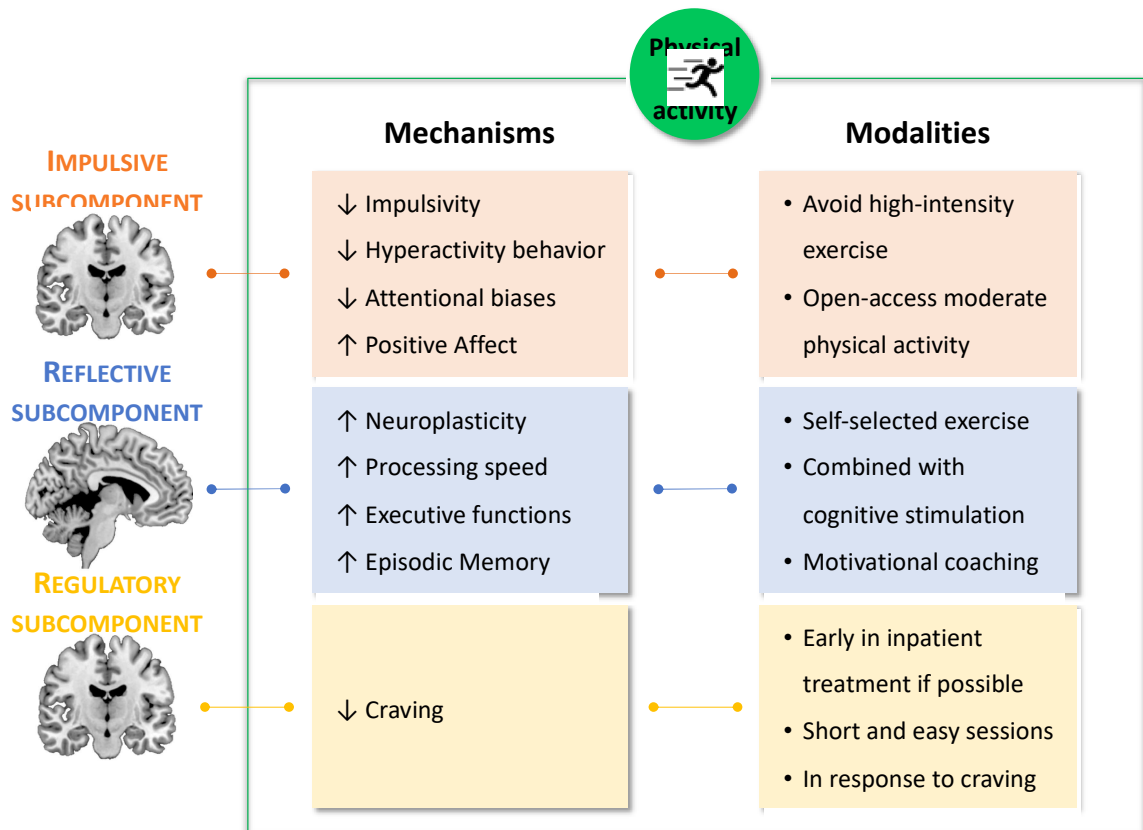
418 The implementation of physical activity in sAUD treatment programs could also enable us  
419 to deepen our understanding of this triadic neurocognitive model. The fact that each  
420 subcomponent is potentially affected in a different way by physical activity or requires  
421 specific adaptation of exercise programs reinforces their theoretical autonomy. On the  
422 contrary, a global effect of physical activity would rather suggest a direct relationship  
423 between the subcomponents, which is also suggested by the bidirectional relationship  
424 between cognitive and affective/impulsive regulation during physical activity (Costa et al.,  
425 2019 for a review). This review therefore encourages rethinking the nature of the relationships  
426 between the three subcomponents.

427

428 **4.2. Clinical considerations**

429 4.2.1. Physical activity as a personalized intervention for sAUD patients

430 Each subcomponent of the triadic model of sAUD constitutes a therapeutic target for  
431 physical activity. It might be useful to evaluate each of the three subcomponents in clinical  
432 practice. Physical activity could be adjusted with regard to each individual’s triadic  
433 subcomponent configuration (Figure 3).



434  
435  
436 *Figure 3. Potential effects and mechanisms of physical activity on each subcomponent of the*  
437 *triadic model. Suggestions of physical activity specifically targeting each subcomponent.*  
438

439 The physical activity proposed to sAUD patients could range from yoga to different kinds  
440 of aerobic or non-aerobic exercises, from low to vigorous intensity. It could be a single  
441 session or routine exercise and could be performed individually or in groups (Costa et al.,  
442 2019; Hallgren, Vancampfort, Giesen, et al., 2017). Clinical guidelines for patients with  
443 severe mental illness propose that the “intervention consists of 2-3 sessions of supervised

444 aerobic and/or aerobic and resistance training exercise a week of 45-60 minutes duration of  
445 moderate (to vigorous) intensity” (Stubbs et al., 2018 for a review). Further clinical research  
446 is required to specify the ideal modalities of physical interventions in sAUD depending on  
447 which subcomponent is especially affected, on the patients’ comorbidities or physical  
448 limitations, their lack of exercise experience, and their exercise preferences and expectations.  
449 sAUD patients expect physical exercise to improve their health, to be an accomplishment, to  
450 make them feel stronger, be physically fit, and to increase their self-confidence and their  
451 confidence in staying sober (Abrantes et al., 2011; Stoutenberg et al., 2015). However,  
452 structural (type of exercise, timing, transportation/equipment issues, cost), social (need for  
453 accountability and unsupportive relations) and emotional (fear, guilt, shame, negative affect,  
454 laziness, lack of motivation) barriers can be identified and they could result in high dropout  
455 rates in physical activity programs (Abrantes et al., 2011; Stoutenberg et al., 2015). To  
456 maximize participation, sAUD patients should be given motivational coaching, and  
457 psychosocial and cognitive support, with the goal of identifying an enjoyable physical  
458 activity. Reduction of the dropout rate is crucial and could be achieved by individualizing the  
459 physical activity proposed to each patient (Hallgren, Vancampfort, et al., 2018; Williams,  
460 2008).

461 In sum, physical exercise programs conducted in sAUD should be progressive and  
462 supervised to increase motivation and engagement, reduce failure, and improve self-efficacy  
463 and empowerment. Programs should provide diversified range of moderate intensity aerobic  
464 exercise, taking the participants’ expectancies and limitations into account. These programs  
465 should be offered early in the therapeutic program, on a long-term basis, with several sessions  
466 per week, and as a first line treatment to reduce stigma. Craving could be specifically targeted  
467 by short and easily achievable physical exercise. The French “physical activity on  
468 prescription” program is an interesting model. Enshrined in law in 2016, this free program

469 emphasizes that “As part of the care pathway for patients with chronic diseases, the attending  
470 physician may prescribe physical activity adapted to the pathology, physical abilities and  
471 mental risk of the patient”. Exercise could be incorporated into usual sAUD cares, in  
472 particular in cognitive behavioral therapy and cognitive remediation programs.

473

#### 474 4.2.2. Physical activity as an adjunctive treatment

475 With the exception of patients with severe withdrawal syndrome (e.g. delirium tremens or  
476 seizure), light and supervised physical activity could even be proposed from the very  
477 beginning of the residential treatment in order to attenuate withdrawal symptoms and ease  
478 anxiety symptoms (Hallgren, Vancampfort, Giesen, et al., 2017; Wang et al., 2014).

479 For sAUD patients, physical activity could be implemented in sedentary patients by  
480 adapting physical activities and providing specialized motivational support in medically-  
481 prescribed programs (Hallgren, Vancampfort, et al., 2018). Existing psychosocial and  
482 neurocognitive rehabilitation programs could integrate physical activity advices, or at best  
483 supervised physical activity modules including empowerment strategy.

484 We can also speculate that physical activity could improve the efficacy of the behavioral  
485 therapies recommended in sAUD treatment. First, physical activity could improve cognitive  
486 abilities (in particular episodic memory and executive functions), which would result in  
487 increased awareness of the consequences of the disease and better learning processes, abilities  
488 to project into the future and to implement relapse prevention strategy. These skills are crucial  
489 in cognitive behavioral therapy. Second, improvements in physical and mental health could  
490 increase the motivation to pursue sAUD treatment. In a motivational interview approach, the  
491 perception of short and middle-term benefits could help maintain a change in drinking  
492 behavior. A cognitive behavioral therapy approach could also encourage patients to challenge

493 their own irrational beliefs about alcohol thanks to physical activity benefits (e.g. from “ I  
494 need alcohol to feel well” to “I could exercise to feel well”).

495

#### 496 4.2.3. Physical activity as a stand-alone intervention?

497 Although this review focuses on sAUD patients, who require specific care and for whom  
498 physical activity would be an adjunctive treatment, physical activity could be seen as a less  
499 stigmatizing entry point into addiction care for mild-to-moderate AUD subjects (e.g. patient  
500 who do not require pharmacological treatment or hospital care) (Hallgren, Vancampfort, et  
501 al., 2018). In this specific context, physical activity could be used as a stand-alone  
502 intervention. This hypothesis is currently examined in a Swedish RCT that compared, in 210  
503 mild-to-moderate AUD patients, the effect of a 12-week intervention (treatment as usual ;  
504 yoga ; aerobic training) on alcohol outcomes (Hallgren, Andersson, et al., 2018). Physical  
505 activity could also be useful after a brief screening intervention in primary care settings or as  
506 a preventive measure, because craving is described at all stages of AUD, and impulsivity can  
507 be very strong, even in non-sAUD individuals. Findings from prevention studies showed that  
508 drug prevention programs that include physical activity effectively reduced rates of initiation  
509 and use of alcohol (Lynch et al., 2013 for a review).

510

511 In sum, physical activity is a promising adjunctive treatment for sAUD. The triadic model  
512 provides a theoretical framework 1) to better understand the mechanisms of physical activity  
513 efficacy, 2) to evaluate which of the three components is affected and 3) to target the  
514 subcomponent affected by adapting and personalizing exercise programs in order eventually  
515 to rebalance the triadic model of AUD.

## REFERENCES

- Abramovitch, A., Goldzweig, G., & Schweiger, A. (2013). Correlates of physical activity with intrusive thoughts, worry and impulsivity in adults with attention deficit/hyperactivity disorder: a cross-sectional pilot study. *The Israel Journal of Psychiatry and Related Sciences*, *50*(1), 47–54. PMID : 24029111
- Abrantes, A. M., Battle, C. L., Strong, D. R., Ing, E., Dubreuil, M. E., Gordon, A., & Brown, R. A. (2011). Exercise preferences of patients in substance abuse treatment. *Mental Health and Physical Activity*, *4*(2), 79–87. <https://doi.org/10.1016/j.mhpa.2011.08.002>
- APA DSM-5 Task force. (2013). *Diagnostic and Statistical Manual of mental disorders: DSM-5* (American Psychiatric Association).
- Ashdown-Franks, G., Firth, J., Carney, R., Carvalho, A. F., Hallgren, M., Koyanagi, A., Rosenbaum, S., Schuch, F. B., Smith, L., & Solmi, M. (2019). Exercise as Medicine for Mental and Substance Use Disorders: A Meta-review of the Benefits for Neuropsychiatric and Cognitive Outcomes. *Sports Medicine*, 1–20. <https://doi.org/10.1007/s40279-019-01187-6>
- Bates, M. E., Buckman, J. F., & Nguyen, T. T. (2013). A role for cognitive rehabilitation in increasing the effectiveness of treatment for alcohol use disorders. *Neuropsychology Review*, *23*(1), 27–47. <https://doi.org/10.1007/s11065-013-9228-3>
- Brené, S., Bjørnebekk, A., Åberg, E., Mathé, A. A., Olson, L., & Werme, M. (2007). Running is rewarding and antidepressive. *Physiology & Behavior*, *92*(1–2), 136–140. <https://doi.org/10.1016/j.physbeh.2007.05.015>
- Brown, R. A., Prince, M. A., Minami, H., & Abrantes, A. M. (2016). An exploratory analysis of changes in mood, anxiety and craving from pre- to post-single sessions of exercise, over 12 weeks, among patients with alcohol dependence. *Mental Health and Physical Activity*, *11*, 1–6. <https://doi.org/10.1016/j.mhpa.2016.04.002>
- Caspersen, C. J., Powell, K. E., & Christenson, G. M. (1985). Physical activity, exercise, and physical fitness: definitions and distinctions for health-related research. *Public Health Reports (Washington, D.C.: 1974)*, *100*(2), 126–131. PMID: 3920711
- Christiansen, L., Beck, M. M., Bilenberg, N., Wienecke, J., Astrup, A., & Lundbye-Jensen, J. (2019). Effects of Exercise on Cognitive Performance in Children and Adolescents with ADHD: Potential Mechanisms and Evidence-based Recommendations. *Journal of Clinical Medicine*, *8*(6), 841. <https://doi.org/10.3390/jcm8060841>
- Coates, J. M., Gullo, M. J., Feeney, G. F. X., Young, R. M., & Connor, J. P. (2018). A Randomized Trial of Personalized Cognitive-Behavior Therapy for Alcohol Use Disorder in a Public Health Clinic. *Frontiers in Psychiatry*, *9*, 297. <https://doi.org/10.3389/fpsy.2018.00297>
- Costa, K. G., Cabral, D. A., Hohl, R., & Fontes, E. B. (2019). Rewiring the Addicted Brain Through a Psychobiological Model of Physical Exercise. *Frontiers in Psychiatry*, *10*, 600. <https://doi.org/10.3389/fpsy.2019.00600>
- Craig, C. L., Marshall, A. L., Sjöström, M., Bauman, A. E., Booth, M. L., Ainsworth, B. E., Pratt, M., Ekelund, U., Yngve, A., Sallis, J. F., & Oja, P. (2003). International Physical Activity Questionnaire: 12-Country Reliability and Validity: *Medicine & Science in Sports & Exercise*, *35*(8), 1381–1395. <https://doi.org/10.1249/01.MSS.0000078924.61453.FB>
- Czapla, M., Simon, J. J., Richter, B., Kluge, M., Friederich, H.-C., Herpertz, S., Mann, K., Herpertz, S. C., & Loeber, S. (2015). The impact of cognitive impairment and impulsivity on relapse of alcohol-dependent patients: implications for psychotherapeutic treatment. *Addiction Biology*. <https://doi.org/10.1111/adb.12229>
- Evren, C., Durkaya, M., Evren, B., Dalbudak, E., & Cetin, R. (2012). Relationship of relapse

- with impulsivity, novelty seeking and craving in male alcohol-dependent inpatients. *Drug and Alcohol Review*, 31(1), 81–90. <https://doi.org/10.1111/j.1465-3362.2011.00303.x>
- Field, M., Kiernan, A., Eastwood, B., & Child, R. (2008). Rapid approach responses to alcohol cues in heavy drinkers. *Journal of Behavior Therapy and Experimental Psychiatry*, 39(3), 209–218. <https://doi.org/10.1016/j.jbtep.2007.06.001>
- Firth, J., Stubbs, B., Rosenbaum, S., Vancampfort, D., Malchow, B., Schuch, F., Elliott, R., Nuechterlein, K. H., & Yung, A. R. (2016). Aerobic Exercise Improves Cognitive Functioning in People With Schizophrenia: A Systematic Review and Meta-Analysis. *Schizophrenia Bulletin*, sbw115. <https://doi.org/10.1093/schbul/sbw115>
- Garland, E. L., & Howard, M. O. (2018). Mindfulness-based treatment of addiction: current state of the field and envisioning the next wave of research. *Addiction Science & Clinical Practice*, 13(1), 14. <https://doi.org/10.1186/s13722-018-0115-3>
- Giesen, E. S., Deimel, H., & Bloch, W. (2015). Clinical Exercise Interventions in Alcohol Use Disorders: A Systematic Review. *Journal of Substance Abuse Treatment*, 52, 1–9. <https://doi.org/10.1016/j.jsat.2014.12.001>
- Grant, B. F., Goldstein, R. B., Saha, T. D., Chou, S. P., Jung, J., Zhang, H., Pickering, R. P., Ruan, W. J., Smith, S. M., Huang, B., & Hasin, D. S. (2015). Epidemiology of DSM-5 Alcohol Use Disorder: Results From the National Epidemiologic Survey on Alcohol and Related Conditions III. *JAMA Psychiatry*, 72(8), 757. <https://doi.org/10.1001/jamapsychiatry.2015.0584>
- Haber, P., Australia, & Department of Health and Ageing. (2009). *Guidelines for the treatment of alcohol problems*. Dept. of Health and Ageing.
- Hallgren, M., Andersson, V., Ekblom, Ö., & Andréasson, S. (2018). Physical activity as treatment for alcohol use disorders (FitForChange): study protocol for a randomized controlled trial. *Trials*, 19(1), 106. <https://doi.org/10.1186/s13063-017-2435-0>
- Hallgren, M., Vancampfort, D., Giesen, E. S., Lundin, A., & Stubbs, B. (2017). Exercise as treatment for alcohol use disorders: systematic review and meta-analysis. *British Journal of Sports Medicine*, 51(14), 1058–1064. <https://doi.org/10.1136/bjsports-2016-096814>
- Hallgren, M., Vancampfort, D., Lundin, A., Andersson, V., & Andréasson, S. (2018). New steps for treating alcohol use disorder: the emerging importance of physical exercise. *Psychopharmacology*, 235(9), 2771–2773. <https://doi.org/10.1007/s00213-018-5002-9>
- Hallgren, M., Vancampfort, D., Schuch, F., Lundin, A., & Stubbs, B. (2017). More Reasons to Move: Exercise in the Treatment of Alcohol Use Disorders. *Frontiers in Psychiatry*, 8. <https://doi.org/10.3389/fpsy.2017.00160>
- Hausenblas, H. A., Schreiber, K., & Smoliga, J. M. (2017). Addiction to exercise. *BMJ*, j1745. <https://doi.org/10.1136/bmj.j1745>
- Hötting, K., & Röder, B. (2013). Beneficial effects of physical exercise on neuroplasticity and cognition. *Neuroscience & Biobehavioral Reviews*, 37(9), 2243–2257. <https://doi.org/10.1016/j.neubiorev.2013.04.005>
- Jamurtas, A. Z., Zourbanos, N., Georgakouli, K., Georgoulas, P., & Manthou, E. (2014). Beta Endorphin and Alcohol Urge Responses in Alcoholic Patients Following an Acute Bout of Exercise. *Journal of Addiction Research & Therapy*, 05(03). <https://doi.org/10.4172/2155-6105.1000194>
- Janse Van Rensburg, K., Elibero, A., Kilpatrick, M., & Drobles, D. J. (2013). Impact of aerobic exercise intensity on craving and reactivity to smoking cues. *Experimental and Clinical Psychopharmacology*, 21(3), 196–203. <https://doi.org/10.1037/a0032768>
- Jensen, K., Nielsen, C., Ekstrøm, C. T., & Roessler, K. K. (2018). Physical exercise in the treatment of alcohol use disorder (AUD) patients affects their drinking habits: A

- randomized controlled trial. *Scandinavian Journal of Public Health*, <https://doi.org/10.1177/1403494818759842>
- Knöchel, C., Oertel-Knöchel, V., O'Dwyer, L., Prvulovic, D., Alves, G., Kollmann, B., & Hampel, H. (2012). Cognitive and behavioural effects of physical exercise in psychiatric patients. *Progress in Neurobiology*, *96*(1), 46–68. <https://doi.org/10.1016/j.pneurobio.2011.11.007>
- Kohn, R., Saxena, S., Levav, I., & Saraceno, B. (2004). The treatment gap in mental health care. *Bulletin of the World Health Organization*, *82*, 858–866.
- Koob, G. F., & Le Moal, M. (2008). Addiction and the brain antireward system. *Annual Review of Psychology*, *59*, 29–53. <https://doi.org/10.1146/annurev.psych.59.103006.093548>
- Koob, G. F., & Volkow, N. D. (2016). Neurobiology of addiction: a neurocircuitry analysis. *The Lancet Psychiatry*, *3*(8), 760–773. [https://doi.org/10.1016/S2215-0366\(16\)00104-8](https://doi.org/10.1016/S2215-0366(16)00104-8)
- Lannoy, S., Billieux, J., & Maurage, P. (2014). Beyond Inhibition: A Dual-Process Perspective to Renew the Exploration of Binge Drinking. *Frontiers in Human Neuroscience*, *8*. <https://doi.org/10.3389/fnhum.2014.00405>
- Le Berre, A-P. (2019). Emotional processing and social cognition in alcohol use disorder. *Neuropsychology*, *33*(6), 808–821. <https://doi.org/10.1037/neu0000572>
- Le Berre, A-P., Fama, R., & Sullivan, E. V. (2017). Executive functions, memory, and social cognitive deficits and recovery in chronic alcoholism: a critical review to inform future research. *Alcoholism: Clinical and Experimental Research*, *41*(8), 1432–1443. <https://doi.org/10.1111/acer.13431>
- Le Berre, A-P., Rauchs, G., La Joie, R., Segobin, S., Mézenge, F., Boudehent, C., Vabret, F., Viader, F., Eustache, F., Pitel, A.-L., & Beaunieux, H. (2013). Readiness to change and brain damage in patients with chronic alcoholism. *Psychiatry Research*, *213*(3), 202–209. <https://doi.org/10.1016/j.psychresns.2013.03.009>
- Le Berre, A-P., Rauchs, G., La Joie, R., Mézenge, F., Boudehent, C., Vabret, F., Segobin, S., Viader, F., Allain, P., Eustache, F., Pitel, A.-L., & Beaunieux, H. (2014). Impaired decision-making and brain shrinkage in alcoholism. *European Psychiatry: The Journal of the Association of European Psychiatrists*, *29*(3), 125–133. <https://doi.org/10.1016/j.eurpsy.2012.10.002>
- Lejuez, C. W., Magidson, J. F., Mitchell, S. H., Sinha, R., Stevens, M. C., & de Wit, H. (2010). Behavioral and biological indicators of impulsivity in the development of alcohol use, problems, and disorders. *Alcoholism, Clinical and Experimental Research*, *34*(8), 1334–1345. <https://doi.org/10.1111/j.1530-0277.2010.01217.x>
- Linke, S. E., & Ussher, M. (2015). Exercise-based treatments for substance use disorders: evidence, theory, and practicality. *The American Journal of Drug and Alcohol Abuse*, *41*(1), 7–15. <https://doi.org/10.3109/00952990.2014.976708>
- Loprinzi, P. D., Pazirei, S., Robinson, G., Dickerson, B., Edwards, M., & Rhodes, R. E. (2020). Evaluation of a cognitive affective model of physical activity behavior. *Health Promotion Perspectives*, *10*(1), 88–93. <https://doi.org/10.15171/hpp.2020.14>
- Lynch, W. J., Abel, J., Robinson, A. M., & Smith, M. A. (2017). Exercise as a Sex-Specific Treatment for Substance Use Disorder. *Current Addiction Reports*, *4*(4), 467–481. <https://doi.org/10.1007/s40429-017-0177-4>
- Lynch, W. J., Peterson, A. B., Sanchez, V., Abel, J., & Smith, M. A. (2013). Exercise as a novel treatment for drug addiction: A neurobiological and stage-dependent hypothesis. *Neuroscience & Biobehavioral Reviews*, *37*(8), 1622–1644. <https://doi.org/10.1016/j.neubiorev.2013.06.011>
- Mandolesi, L., Polverino, A., Montuori, S., Foti, F., Ferraioli, G., Sorrentino, P., &

- Sorrentino, G. (2018). Effects of Physical Exercise on Cognitive Functioning and Wellbeing: Biological and Psychological Benefits. *Frontiers in Psychology*, 9, 509. <https://doi.org/10.3389/fpsyg.2018.00509>
- Manthou, E., Georgakouli, K., Fatouros, I. G., Gianoulakis, C., Theodorakis, Y., & Jamurtas, A. Z. (2016). Role of exercise in the treatment of alcohol use disorders. *Biomedical Reports*, 4(5), 535–545. <https://doi.org/10.3892/br.2016.626>
- Moriarty, T., Bourbeau, K., Bellovary, B., & Zuhl, M. N. (2019). Exercise Intensity Influences Prefrontal Cortex Oxygenation during Cognitive Testing. *Behavioral Sciences*, 9(8), 83. <https://doi.org/10.3390/bs9080083>
- Mukherjee, K. (2010). A dual system model of preferences under risk. *Psychological Review*, 117(1), 243–255. <https://doi.org/10.1037/a0017884>
- Naqvi, N. H., Gaznick, N., Tranel, D., & Bechara, A. (2014). The insula: a critical neural substrate for craving and drug seeking under conflict and risk: The insula: craving and drug seeking under conflict and risk. *Annals of the New York Academy of Sciences*, 1316(1), 53–70. <https://doi.org/10.1111/nyas.12415>
- National Collaborating Centre for Mental Health Staff. (2011). *Alcohol Use Disorders: The NICE Guideline on the Diagnosis, Assessment and Management of Harmful Drinking and Alcohol Dependence*. <https://www.ncbi.nlm.nih.gov/books/NBK65487>
- National Institute on Drug Abuse (NIDA). (2012). *Principles of drug addiction treatment: a research-based guide (third edition)*.
- Noël, X., Brevers, D., & Bechara, A. (2013). A Triadic Neurocognitive Approach to Addiction for Clinical Interventions. *Frontiers in Psychiatry*, 4. <https://doi.org/10.3389/fpsyg.2013.00179>
- Oscar-Berman, M., Valmas, M. M., Sawyer, K. S., Ruiz, S. M., Luhar, R. B., & Gravitz, Z. R. (2014). Profiles of impaired, spared, and recovered neuropsychologic processes in alcoholism. *Handbook of Clinical Neurology*, 125, 183–210.
- Perry, C. J. (2016). Cognitive Decline and Recovery in Alcohol Abuse. *Journal of Molecular Neuroscience*, 60(3), 383–389. <https://doi.org/10.1007/s12031-016-0798-4>
- Probst, C., Manthey, J., Martinez, A., & Rehm, J. (2015). Alcohol use disorder severity and reported reasons not to seek treatment: a cross-sectional study in European primary care practices. *Substance Abuse Treatment, Prevention, and Policy*, 10(1), 32. <https://doi.org/10.1186/s13011-015-0028-z>
- Reed, J., & Ones, D. S. (2006). The effect of acute aerobic exercise on positive activated affect: A meta-analysis. *Psychology of Sport and Exercise*, 7(5), 477–514. <https://doi.org/10.1016/j.psychsport.2005.11.003>
- Roessler, K. K., Bilberg, R., Nielsen, A. S., Jensen, K., Ekstrøm, C. T., & Sari, S. (2017). Exercise as adjunctive treatment for alcohol use disorder: A randomized controlled trial. *PLoS One*, 12(10), <https://doi.org/10.1371/journal.pone.0186076>
- Rupp, C. I., Kemmler, G., Kurz, M., Hinterhuber, H., & Fleischhacker, W. W. (2012). Cognitive remediation therapy during treatment for alcohol dependence. *Journal of Studies on Alcohol and Drugs*, 73(4), 625–634. <https://doi.org/10.15288/jsad.2012.73.625>
- Sari, S., Muller, A. E., & Roessler, K. K. (2017). Exercising alcohol patients don't lack motivation but struggle with structures, emotions and social context - a qualitative dropout study. *BMC Family Practice*, 18(1). <https://doi.org/10.1186/s12875-017-0606-4>
- Shin, S. H., Hong, H. G., & Jeon, S.-M. (2012). Personality and alcohol use: The role of impulsivity. *Addictive Behaviors*, 37(1), 102–107. <https://doi.org/10.1016/j.addbeh.2011.09.006>
- Smith, P. J., Blumenthal, J. A., Hoffman, B. M., Cooper, H., Strauman, T. A., Welsh-Bohmer,

- K., Browndyke, J. N., & Sherwood, A. (2010). Aerobic Exercise and Neurocognitive Performance: A Meta-Analytic Review of Randomized Controlled Trials: *Psychosomatic Medicine*, 72(3), 239–252. <https://doi.org/10.1097/PSY.0b013e3181d14633>
- Société Française d'Alcoologie. (2015). Mésusage de l'alcool, dépistage, diagnostic, et traitement. Recommandation de bonne pratique. *Alcoologie et Addictologie*, 37(1), 5–84.
- Stavro, K., Pelletier, J., & Potvin, S. (2013). Widespread and sustained cognitive deficits in alcoholism: a meta-analysis. *Addiction Biology*, 18(2), 203–213. <https://doi.org/10.1111/j.1369-1600.2011.00418.x>
- Stoutenberg, M., Rethorst, C. D., Lawson, O., & Read, J. P. (2016). Exercise training – A beneficial intervention in the treatment of alcohol use disorders? *Drug and Alcohol Dependence*, 160, 2–11. <https://doi.org/10.1016/j.drugalcdep.2015.11.019>
- Stoutenberg, M., Warne, J., Vidot, D., Jimenez, E., & Read, J. P. (2015). Attitudes and preferences towards exercise training in individuals with alcohol use disorders in a residential treatment setting. *Journal of Substance Abuse Treatment*, 49, 43–49. <https://doi.org/10.1016/j.jsat.2014.08.008>
- Stubbs, B., Vancampfort, D., Hallgren, M., Firth, J., Veronese, N., Solmi, M., Brand, S., Cordes, J., Malchow, B., Gerber, M., Schmitt, A., Correll, C. U., De Hert, M., Gaughran, F., Schneider, F., Kinnafick, F., Falkai, P., Möller, H.-J., & Kahl, K. G. (2018). EPA guidance on physical activity as a treatment for severe mental illness: a meta-review of the evidence and Position Statement from the European Psychiatric Association (EPA), supported by the International Organization of Physical Therapists in Mental Health (IOPTMH). *European Psychiatry: The Journal of the Association of European Psychiatrists*, 54, 124–144. <https://doi.org/10.1016/j.eurpsy.2018.07.004>
- Substance Abuse and Mental Health Services Administration (US), & Office of the Surgeon General (US). (2016). *Facing Addiction in America: The Surgeon General's Report on Alcohol, Drugs, and Health*. US Department of Health and Human Services. <http://www.ncbi.nlm.nih.gov/books/NBK424857/>
- Taylor, A. H., Oh, H., & Cullen, S. (2013). Acute effect of exercise on alcohol urges and attentional bias towards alcohol related images in high alcohol consumers. *Mental Health and Physical Activity*, 6(3), 220–226. <https://doi.org/10.1016/j.mhpa.2013.09.004>
- Uekermann, J., & Daum, I. (2008). Social cognition in alcoholism: a link to prefrontal cortex dysfunction? *Addiction*, 103(5), 726–735. <https://doi.org/10.1111/j.1360-0443.2008.02157.x>
- Ussher, M., Sampuran, A. K., Doshi, R., West, R., & Drummond, D. C. (2004). Acute effect of a brief bout of exercise on alcohol urges. *Addiction*, 99(12), 1542–1547. <https://doi.org/10.1111/j.1360-0443.2004.00919.x>
- Volkow, N. D., & Boyle, M. (2018). Neuroscience of Addiction: Relevance to Prevention and Treatment. *American Journal of Psychiatry*, 175(8), 729–740. <https://doi.org/10.1176/appi.ajp.2018.17101174>
- Wang, D., Wang, Y., Wang, Y., Li, R., & Zhou, C. (2014). Impact of physical exercise on substance use disorders: a meta-analysis. *PloS One*, 9(10). <https://doi.org/10.1371/journal.pone.0110728>
- Wiers, R. W., Ames, S. L., Hofmann, W., Krank, M., & Stacy, A. W. (2010). Impulsivity, Impulsive and Reflective Processes and the Development of Alcohol Use and Misuse in Adolescents and Young Adults. *Frontiers in Psychology*, 1. <https://doi.org/10.3389/fpsyg.2010.00144>
- Williams, D. M. (2008). Exercise, affect, and adherence: an integrated model and a case for

- self-paced exercise. *Journal of Sport & Exercise Psychology*, 30(5), 471–496. <https://doi.org/10.1123/jsep.30.5.471>
- World Health Organization, Management of Substance Abuse Team, & World Health Organization. (2018). *Global status report on alcohol and health 2018*. [http://www.who.int/substance\\_abuse/publications/global\\_alcohol\\_report/en/](http://www.who.int/substance_abuse/publications/global_alcohol_report/en/)
- Zulauf, C. A., Sprich, S. E., Safren, S. A., & Wilens, T. E. (2014). The Complicated Relationship Between Attention Deficit/Hyperactivity Disorder and Substance Use Disorders. *Current Psychiatry Reports*, 16(3), 436. <https://doi.org/10.1007/s11920-013-0436-6>