We are IntechOpen, the world's leading publisher of Open Access books Built by scientists, for scientists

4,800
Open access books available

122,000
International authors and editors

135M
Downloads

Our authors are among the

154
Countries delivered to

TOP 1%
most cited scientists

12.2%
Contributors from top 500 universities

CLARIVATE ANALYTICS BOOK CITATION INDEX INDEXED

WEB OF SCIENCE™

Selection of our books indexed in the Book Citation Index in Web of Science™ Core Collection (BKCI)

Interested in publishing with us?
Contact book.department@intechopen.com

Numbers displayed above are based on latest data collected.
For more information visit www.intechopen.com

Chapter

Addiction: Brain and Cognitive Stimulation for Better Cognitive Control and Far Beyond

Xavier Noël, Antoine Bechara, Mélanie Saeremans, Charles Kornreich, Clémence Dousset, Salvatore Campanella, Armand Chatard, Nemat Jaafari and Macha Dubuson

Abstract

Addiction behaviors are characterized by conditioned responses responsible for craving and automatic actions as well as disturbances within the supervisory network, one of the key elements of which is the inhibition of prepotent response. Interventions such as brain stimulation and cognitive training targeting this imbalanced system can potentially be a positive adjunct to treatment as usual. The relevance of several invasive and noninvasive brain stimulation techniques in the context of addiction as well as several cognitive training protocols is reviewed. By reducing cue-induced craving and modifying the pattern of action, memory associations, and attention biases, these interventions produced significant but still limited clinical effects. A new refined definition of response inhibition, including automatic inhibition of response and a more consistent approach to cue exposure capitalizing on the phase of reconsolidation of pre-activated emotional memories, all associated with brain and cognitive stimulation, opens new avenues for clinical research.

Keywords: addiction, inhibition, brain stimulation, memory reconsolidation, cue exposure

1. Introduction

Despite considerable progress in detoxification, pharmacology, and psychological interventions in addictive behaviors, clinical outcomes remain suboptimal (e.g., high relapse rate or poor quality of life) [1]. The main reason of the poor clinical outcomes is likely to be related to multiple interacting determinants of social, psychological, and biological mechanisms involved in the addiction risk and the relapse, a view that is not compatible with pure essentialism and simplistic approaches of addiction [2].

Inter-individual variations within the addiction group in respect to neurobiological mechanisms of addiction were highlighted by influential theorizations [3–9]. Indeed, addictive behaviors can be viewed as the product of an imbalance between separate, but interacting, neural systems: an impulsive, largely amygdala-striatum-dependent, neural system that promotes automatic, habitual, and salient

behaviors; a reflective, mainly prefrontal cortex-dependent, neural system for decision-making, forecasting the future consequences of a behavior, and inhibitory control; and the insula that integrates interoception states into conscious feelings and decision-making processes that are involved in uncertain risk and reward. Any imbalance in the dynamics of these systems can account for poor decision-making (i.e., prioritizing short-term consequences of a decisional option), and the lack of willpower [10–12], which heightens the risk for addiction and relapse.

As part of the "executive network" involving ventrolateral prefrontal cortex and dorsolateral prefrontal cortex, response inhibition interacts with automatic behavioral ("habit network") and motivational responses ("reward network") to produce flexible actions and adaptive choices. Indeed, the inhibition of a prepotent response has become an important element of the responsible braking system and limiting the expression of spontaneous motivation and emotion signals [13]. Indeed, successful self-regulation requires the ability to inhibit impulses that are not compatible with one's goals [14].

Importantly, psychostimulant dependence, alcohol dependence, and gambling disorders have been consistently associated with a response inhibition deficit [5]. However, the deficit in inhibition observed in addiction population is generally of low or moderate effect size [15, 16]. Nevertheless, even a small effect size can have clinically relevant effects, as evidenced by the impact of impaired response inhibition on the risk of dependence and response to treatment [9, 17–19]. Indeed, response inhibition is considered as a primary candidate for cognitive remediation that can potentially reduce the risk of addiction and the relapse [20]. As an alternative way consistent with dual-process theories, to limit these risks is to reduce the need for inhibitory control, for instance, by dampening automatic conditioned responses (e.g., craving, attentional and memory biases) triggered by contextual (e.g., the sight of a bottle of beer) or internal (e.g., negative effects) cues. In addition, more automatic forms of response inhibition could be trained in the hope of enabling individuals to generate appropriate alcohol-stop associations without too much of an effortful process [21].

In this chapter, we investigate the manner the risk associated with too limited response inhibition can be reduced by implementing multiple forms of cognitive training, invasive and noninvasive brain stimulation techniques, and neurofeedback (NF). It should be noted that an overwhelming majority of neuroscientists engaged in brain stimulation in psychopathology has truly viewed brain-based interventions as complementary interventions to clinical treatments such as cognitive-behavioral therapy and motivational enhancement intervention [22, 23]. Indeed, the beliefs, desires, emotions, and intentions of patients are essential elements to take into account [2], which can be modulated by brain- and cognitive-based interventions.

After a brief presentation of response inhibition theories and methods, we summarize cognitive training intervention in the context of addictive behaviors as well as three brain stimulation techniques (i.e., deep brain stimulation, electric and magnetic brain stimulation) and finally protocols of neurofeedback. We then develop more complex clinical and research concepts (e.g., combined cognitive training and brain stimulation along with cue exposure interventions).

2. Executive functioning, response inhibition, and self-regulation: terminological and theoretical clarifications

Numerous terms have often been used to describe similar concepts. For example, concepts such as self-regulation, inhibition, executive function, cognitive control, effortful processes, impulsivity, risk-taking, and disinhibition are sometimes clearly

delineated but sometimes are used as synonyms or closely related concepts [24]. Attempts to clarify those concepts (e.g., the degree that some of those constructs overlap) have been scarce but mostly suggest that intrinsic aspects of regulation, self-regulation, serve as an umbrella concept that encompasses top-down and bottom-up processes that mutually influence one another [24–26]. Naturally, the influence of extrinsic aspects of regulation, that is, facilitated or hindered self-regulation due to others' mind and action, is far to be negligible and should be considered to fully apprehend the determinants of dysregulated actions, such as addictive behaviors [27, 28].

2.1 Inhibition in definition

As suggested by William James, "Voluntary action, then, is at all times a resultant of the compounding of our impulsions with our inhibitions" [29]. In order to control the desire, the reason takes place as represented like Plato seeing the will as a charioteer attempting to control two horses (one of desire and one of reason) in Phaedrus. For both Hippocrates and Aristotle, the body and mind are not independent, but each influences the other. Long after, the fundamental duality between reason and emotion conferred to will the essence to control (or inhibit) action and emotion. A few decades later, Sherrington was awarded the 1932 Nobel Prize for Physiology and Medicine for his contribution to our understanding of inhibition in neurophysiology, which consolidated the concept.

Although creating a sense of comfort in theorizing, the explanation (e.g., brain structure in the frog that inhibits a spinal reflex) based on similarity to excitatory or inhibitory functions of the nervous system (i.e., neurons can serve either functions) that strong impulses can be impeded through the implementation of inhibition remains a debated matter [30].

Because of this warning, presenting an operational definition of "inhibition" remains an adventurous venture, not only because of the weight of its intuitive load (e.g., cognitive inhibition is equivalent to neural inhibition sometimes as metaphor) but also because of the phenomenon and explanation conflation or a confusion between a causal process and a functional relationship [31].

In most cases, response inhibition mainly refers to the suppression of actions that are no longer required or that are inappropriate, which supports flexible and goal-directed behavior in ever-changing environments [32]. As such, given its role in supervising ongoing thoughts and action in working memory, response inhibition has been considered as a hallmark of executive functions [33, 34]. As a form of top-down (intentional) inhibition process, prepotent response inhibition refers to deliberate inhibition operating on basic and reactive elements of action, which is essentially non-automatic and represents a cost. Intentional control depends on motivation and capacity [35]; it is subjectively deliberate, slow, and sequential; and it requires working memory and is capacity-limited.

However, a growing amount of data challenged this strictly hierarchical view [36, 37]. Indeed, executive control emerges from an interactive and competitive network generating biases in advance and is strongly influenced by personal recent and past experiences. Indeed, humans automatize as much as possible; hence apparent intentional inhibition can in fact operate automatically for particular contexts, due to context-inhibition associations made through learning. For instance, on the stop-signal task [32], when people are informed that they may have to stop a response in the near future, they typically slow down operation through altering activity in lower-level systems that are involved in stimulus detection, action selection, and action execution [38]. Put differently, instead of relying only on executive functioning, low-level and high-level systems work together for self-regulation.

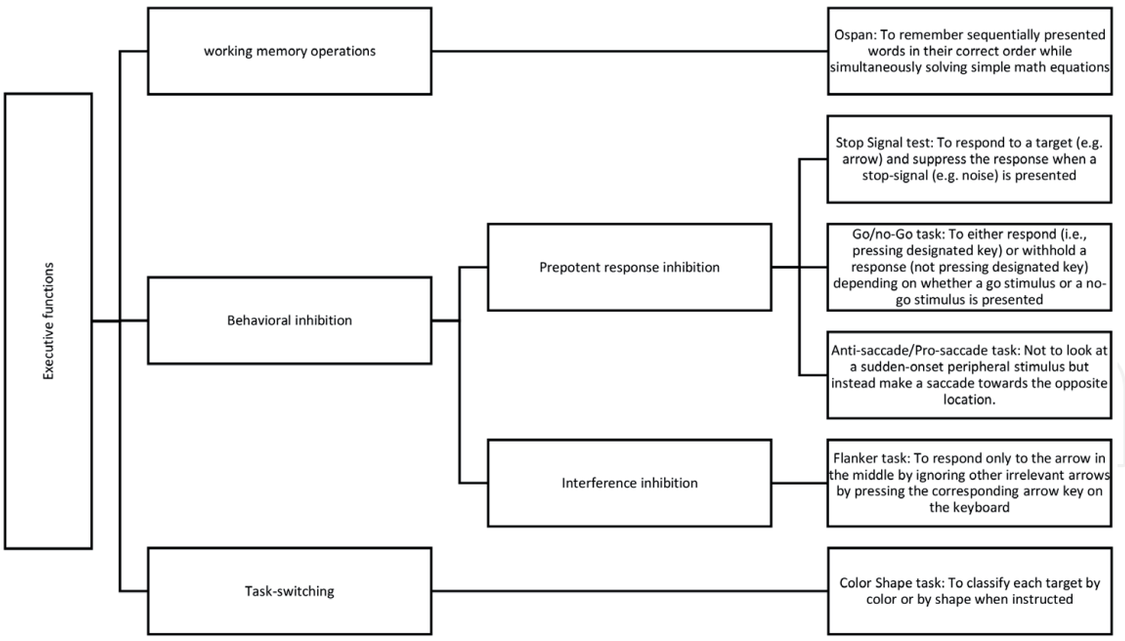

Figure 1.
Executive function classification proposed by [33].

Although closely related to executive functioning, response inhibition can be distinct from other forms of executive functions such as working memory update (i.e., the ability to replace information stored in working memory with new information) and switching (i.e., the ability to shift attention to other tasks or perceptual dimensions) [33] (see **Figure 1**).

Based on latent variable analysis, several forms of response inhibition could be distinguished [39–42]. A first distinction has been made between the inhibition of prepotent response and the resistance to distracter interference. However, the robustness of this two-factor solution remains questionable in light of low correlations between inhibition measures, when the contribution of memory processes was intentionally reduced [41]. It follows from this discussion that studies using a single laboratory paradigm for assessing or investigating inhibition do not warrant generalization beyond the specific paradigm studied.

More fine-grained forms of inhibition have been put forward across the years [39, 41]. Indeed, resistance to proactive interference consists of resisting memory intrusions from information that was previously relevant to the task but has since become irrelevant.

A second categorization relies on the degree of anticipation and preparation of response inhibition [43, 44]. Reactive inhibition (or reflexive inhibition) is a form of inhibition that one can implement without anticipation (e.g., stopping the car when an animal unexpectedly jumps on to the road). Proactive inhibition refers to the impact of inhibition preparation on the inhibitory performance (e.g., keeping one's foot close to the brake after passing a warning sign for animals on the road). Possibly because proactive form of response inhibition requires much more than just inhibition, as attested by shared brain contribution of both forms of inhibition (the right inferior frontal gyrus, supplementary motor area and striatum) and also specific engagement of working memory-related regions (i.e., dorsolateral prefrontal region) [45], proactive inhibition may be more ecologically valid than reactive inhibition [46].

Sufficient agreement can be found on the contributions of these different inhibitory control mechanisms as measured by a variety of cognitive tasks described by Friedman and Miyake [39]. The list of tasks includes the color Stroop, anti-saccade,

stop-signal, simon, global-local, and negative compatibility tasks that could share a component of inhibition of prepotent response; the letter flanker, the number Stroop, arrow flanker, and negative compatibility as well as the task assessing n-2 repetition costs tend to assess resistance to distracter interference.

3. Response inhibition and addiction

Consistent with the previous discussion, response disinhibition is an important element of modern addiction models [6, 9], and empirical data support this claim, particularly for gambling, psychostimulant, and alcohol addiction [5]. By conferring a central position to response inhibition, brain imaging and behavioral studies demonstrated abnormal functioning in individuals at risk to develop an addictive behavior, in addicted people, and in individuals who relapsed [9, 47, 48]. Indeed, a variety of response inhibition deficits are present in numerous forms of reinforcement pathologies (e.g., tobacco dependence [49, 50], alcohol disorder [51, 52] , eating disorders [53, 54], gambling disorder [55] (but see [56])). Second, those deficits can predict relapse in drug and behavioral addiction [18, 57, 58], and research suggests that recently abstinent addicts experience heightened difficulties with response inhibition [59, 60]. Thirdly, the inability to stop one's actions, due notably to early stressful life events and negative parent–child interaction [61], can influence behavioral and substance addictions later in life [17, 61].

In addition, it should be noted that impaired response inhibition has a strong impact in important aspects of decision-making. For instance, impaired prepotent response inhibition in alcoholics was associated with poorer performance on the Iowa gambling task [62], which requires participants to deal with uncertainty in a context of punishment and reward, with some choices being advantageous in the short term (high reward) but disadvantageous in the long run (higher punishment) and known for its ecological validity of decision-making [63–65]. Risk-taking could also be modulated through inhibitory control engagement, with participants being more cautious once anticipating to suppress their response [66]. Unfortunately, the benefit of this form of inhibitory training is fragile and transitory [67]. Besides, data from a sample of pathological gamblers revealed no effect of this procedure on risk-taking [68]. Finally, prepotent response inhibition can moderate the behavioral expression of implicit cognition [69]. Indeed, the impact of implicit cognitive processes on drinking behavior should be stronger in individuals with relatively weaker executive control than in individuals with relatively good executive control, as shown by using the classical Stroop interference scores [70]. Conversely, among adolescents with relatively good executive control, explicit expectancies were the best predictor of alcohol use [71].

In theory, prepotent response inhibition can directly be involved in *myopic* decision, that is, a preference for dominant sooner-smaller at the detriment of less salient larger-later decisions [72]. Steeper delay discounting rate is indubitable in individuals with addiction [73], which concurs to the risk of addiction and treatment response [74, 75]. In support of the existence of a relationship between prepotent response inhibition and short-termism, decreased gray matter volume in lateral prefrontal regions is associated with greater impatience [72, 76]. However, the level of inhibitory control, as typified by the stop-signal reaction time of the stop-signal task [32], and preference for large delayed rewards, as assessed using delay-discounting paradigms, are generally *not* correlated in both healthy participants [77] and clinical populations (e.g., in patients with attention deficit/and hyperactivity disorder) [78], which suggests that response inhibition and delay discounting are independent factors, each of them contributing to addiction.

4. Cognitive training

As mentioned earlier, several findings argued in favor of cognitive-based interventions aimed at targeting response inhibition as an assistant in preventing relapse in addicted population.

Amending those deficits is a huge endeavor and ways to achieve it is still a debated matter [79]. This section elaborates on several cognitive training interventions (CTI) that potentially impact positively on inhibition-related processes in individuals with reinforcement pathologies.

4.1 Restoring inhibitory control

Two contrasting approaches have been used to evaluate response inhibition training on substance use disorders and behavioral addiction: general stop inhibition with classical paradigms assessing prepotent response inhibition or with versions adapted to the type of addictive behaviors (e.g., *alcohol* Stroop test or *cocaine* go/no-go task).

Although there is no conclusive evidence of true increase in inhibitory control in response to extensive training with standard go/no-go or SST tasks in adults [80], training of inhibitory control reduced monetary risk-taking [66] and alcohol-seeking [81]; even this effect is small and short-lived [67, 68], which could potentially explain why some studies failed to observe far-transfer effects [82].

In contrast to some studies using formal training of working memory (e.g., [83]) to evaluate their direct impact on unhealthy behaviors (e.g., alcohol abuse), which can be positive in nonclinical samples [84], but not clinical population [85], modified versions of response inhibition tasks have served as training paradigms [79, 86–90].

During "inhibitory control training" (ICT), participants complete an inhibitory control task (go/no-go task, stop-signal task, anti-saccade task) in which the requirement to exercise inhibitory control is paired with cues related to healthy behaviors, before the effects of this training on the target behavior are measured (for reviews, see [79, 89, 91]). For example, when a group of participants in whom inhibition was paired with neutral cues was compared, participants who completed a stop-signal task in which alcohol images were paired with inhibition subsequently led to reduced ad libitum alcohol consumption in the laboratory, but not self-reported drinking in the week after training [90]. In the same vein, participants who learned to associate food images with inhibition on a go/no-go task subsequently consumed less of those foods when given access to them [88]. In contrast, training of oculomotor inhibition in the presence of alcohol-related cues led to slowed eye movements toward target cues on catch trials, but this manipulation failed to influence the proportion of inhibitory failures and had no influence on alcohol consumption in the laboratory [90]. Initial results indicated that the relationship between behavioral inhibition and alcohol intake may be causal, possibly to the ecological value of alcohol motor response inhibition paradigms (e.g., picking up a glass of alcohol beverage may be directly targeted by motor inhibition training), and training of oculomotor inhibitory control is far less convincing.

Meta-analytic approach [89, 91, 92] demonstrated that the effect of ICT on behavior was dependent on the task used. In theory, research on inhibition have led to the recognition that there are at least two types of inhibitory control: action restraint in which the decision to inhibit is made from the onset (go/no-go tasks) and action cancelation in which the decision to inhibit occurs after implementation of the prepotent response (stop-signal task) [93, 94]. However, the meta-analyses reveal that the higher the proportion of successful inhibitions of appetitive signals, the greater the magnitude of the effect of ICTs. Indeed, studies found a larger and

more statistically robust ICT effect size when go/no-go rather than stop-signal tasks are used. One reason for the superiority of training action restrain on action cancelation [95, 96] is that compared to go/no-go tasks, stop-signal tasks have a lower rate of overall stop success that ends up hindering the development of strong stimulus-stop associations [53, 95]. Instead, go/no-go tasks feature strong stimulus-stop association due to the rate of successful inhibitions reflected in the number and proportion of stop-stimulus pairings, which in turn moderate the effects of training on unhealthy behavior. It is still in debate to ascertain what repeated stop-stimulus pairings could cause: better intentional inhibitory control over impulsive action [97], facilitated automatic retrieval of stimulus-stop associations [21, 37, 98], or diminished motivational properties of target information [99–101]. The issue of which mechanisms mediate the relationship between cognitive training paradigms and behavioral changes remains highly complex for several reasons. First, the size of behavioral change is at best rather small and does not survive more than a couple of hours [67]. Besides, it remains to be seen whether the control condition used in most of the studies where participants are required to rapidly respond to appetitive stimuli as often as inhibiting responses contributes to inflated effect size of ICT [89]. Second, there is no clear consensus on theoretical constructs such as motivation, where generally there is a weak relationship between implicit and explicit measures of stimulus evaluation [102]. Indeed, whereas a majority of studies using implicit motivational measures demonstrate no effect of inhibition of cognitive training on stimulus devaluation, other studies using Likert scale or other explicit procedures [101] demonstrated devaluation effects following this sort of intervention [103–105].

To sum up, general or cue-specific inhibition training has yielded only modest clinical results, and mechanisms remain to be elucidated.

4.2 Cognitive bias modification

Cognitive bias modification consists of pairing alcohol-related content with action tendencies, classically pushing a joystick in response the alcohol-related images and pulling the same joystick in response to soft drinks [106, 107]. Cognitive and clinical effects of this procedure have been compared to sham training conditions requiring an equal number of approach and avoidance movements to both alcohol and soft drinks pictures (i.e., no stimulus-response contingency). Main original outcomes are (a) reduced alcohol approach-related biases indicated with the implicit association task and (b) reduced alcohol relapse up to 1 year after the training. As suggested, an important mediating effect was the building of an alcohol-avoidance bias [106]. The clinical efficacy of this approach regardless of patients' characteristics (age, number of prior detoxifications, etc.) has shown to be too limited to be integrated as such in clinical settings. Indeed, on a meta-analysis of 14 studies (mainly for alcohol and tobacco use problems) involving 2435 participants [22], the authors found a small, nonsignificant overall effect on cognitive bias assessed directly after the completion of the training intervention. In addition, neither smoking nor alcohol reduction was found in response to training intervention. In the same vein, a recent meta-analysis "cast serious doubts on the clinical utility of CBM interventions for addiction" [108]. In response to this assertion, influential researchers in the field, Wiers et al., argued that this analysis combined the results of laboratory and randomized controlled trials, which may underestimate CBM's actual effectiveness when incorporated into regular therapy [109].

In addition to those theoretical and methodological limitations, several moderators could hinder yet existing ICT effects. It is the case of the degree of

readiness to change, that is, the goal to gain control over harmful behaviors that make the ICT intervention more congruent with the participant's mindset, hence potentiating its effects [110]. Another source of variation in the effect of ICT could be the strength of appetitive responses to food cues [111], with the effects of ICT on behavior being proportional to the strength of appetitive responses to cues before ICT [112, 113]. Whether individual differences in attempts to limit drinking, smoking, or gambling moderate the effects of ICT on alcohol intake is a promising avenue for future research. Put together with current literature revealing substance-specific relapse (and vulnerability)-related impairments, it is recommended to investigate cognitive training programs based on a patient-tailored protocol [114].

5. Brain neurostimulation techniques

5.1 Brain stimulations: noninvasive and invasive techniques

Effects of brain stimulation of basic processes, neurochemical regulation, and cognitive and affective processes at the system level have revealed promising results when applied to addiction treatment (for reviews and meta-analyses, see [23, 115, 116]). The most used stimulation techniques include deep brain stimulation, repetitive transcranial magnetic stimulation, and transcranial direct current stimulation known for their effect on self-regulatory processes and possibly acting on several forms of response inhibition.

5.2 Invasive brain stimulations

5.2.1 Deep brain stimulation

Despite ethical concerns due to potential serious side effects [117], deep brain stimulation has expanded from successful thalamic stimulation for Parkinsonian tremor (for a review, see [118]) to psychiatric conditions including addiction [23, 115, 116]. DBS is a neurosurgical procedure involving the placement of a neurostimulator, often called "brain pacemaker," which delivers electrical impulses through implanted electrodes to specific brain regions related to abnormal functioning characterizing neurological and psychiatric conditions.

Back in the 1980s, BDS was introduced as treatment for movement disorders and became well known for treating the tremor of patients with Parkinson disease [119]. During the 2000s, it started to be applied in psychiatric disorders when the pathology is treatment-refractory: in obsessive-compulsive disorder (OCD) [120] and in major depression [121]. DBD gained interest as a means to treat addiction as soon as studies reported unintended alleviation of comorbid alcohol [115], nicotine [122], and gambling [123] addictions.

As reviewed by Luigjes et al. [124], based on a total of eight studies, bilateral high-frequency NAc stimulation in heroine dependence came with reduced craving and prolonged abstinence. In addition, animal studies have provided evidence that NAc DBS dampens impulsivity [125, 126], which represents a core aspect of addictive behaviors [127].

However, because of the absence of double-blind controlled trials in addiction, the cost and the invasiveness of the procedure, as well as the lack of consensus regarding its clinical efficacy and the encountered difficulties to recruit motivated participants [128], DBS to treat addiction could suffer from feasibility issues.

5.3 Noninvasive brain stimulations

Because they offer a safe economical way to modulate brain activity, techniques such as repetitive transcranial magnetic stimulation and transcranial direct current stimulation are growing in popularity for interventions in psychiatric disorder [129, 130]. They are so-called noninvasive to reflect the fact that the magnetic pulses are delivered from a coil placed over the scalp, without a surgical intervention (in contrast to DBS), which contributed to its popularity as techniques for modulating brain activity over the past two decades. Although recent reviews repeatedly recommended more clinical trials before firm conclusions about their efficacy could be drawn [124], their effects on key addictive-related phenomena (e.g., craving, impulsivity) are noteworthy [131].

5.3.1 Repetitive transcranial magnetic stimulation

Repetitive transcranial magnetic stimulation delivers in a time interval a magnetic pulse through the skull via a stimulating coil. The magnetic field involves a focal electrical current, depolarizing underlying cortical neurons. The intensity, duration, properties, localization, and frequency directly influence the effects. Low frequency (1–5 Hz) tends to produce inhibitory effects and fits well the intention of downregulating activity in the targeted regions [132, 133]. High frequency (10–20 Hz) tends to produce excitatory effects on the stimulated brain area. However, substantial inter-individual responses to both low- and high-frequency stimulation have been reported [134]. By using either figure-of-eight coils or H-coils known to produce highly focal stimulation in superficial cortex or deeper intracranial penetration to a more central target, respectively [135], the clinical influence of a variety of clinical phenomena has been investigated.

rTMS and addictive behaviors: The most frequently used rTMS setup has been 10 sessions of stimulation on either the right DLPFC with a high frequency or the left DLPFC with lower frequency. In nicotine addiction, frequently reported findings include reduced transitory (no longer than several weeks following the intervention) cue-induced craving for cigarette as well as lower nicotine consumption [136, 137]. Interestingly, an important placebo effect has been repeatedly found in rTMS studies. Indeed, a reduction in the daily consumption of alcohol [138] or cocaine [139] has been found in response to both active and sham stimulation. In the same vein, although a reduced attentional bias toward alcohol cues has been found in response to high-frequency left DLPFC rTMS, all participants (irrespective of their stimulation condition) reported a reduced craving [140]. The placebo response should be due to a concurrent treatment regimen, which too often is missing from these studies, and better study designs should involve participant blinding.

Regarding the clinical impact of rTMS in behavioral addiction (e.g., gambling addiction, binge eating), the insufficient number of controlled trials prevents drawing conclusion [23].

An important issue to be discussed is the potential cognitive mediators of rTMS effects in addicted subjects. In theory, a reduction in craving intensity and in substance use could be mediated by improved response inhibition or mental flexibility or a change in salience or automatization. No effects above sham stimulation were found on prepotent response inhibition evaluated by a go/no-go task [141].

Although DLPFC is critical for cognitive-executive functions, stimulation of medial regions tends to influence affective-motivational functions [142]. This region along with others such as the insula is important for the selection of long-term over short-term reward, an interplay that may be abnormal in individuals with addictive behaviors [143, 144]. Magnetic stimulation of the medial prefrontal

cortex may bias the preference for delayed, over sooner, rewards [145]. However, this encouraging view has been recently tempered by a study reporting the absence of effect of rTMS targeting the medial prefrontal cortex on impulsive choice on the delay discounting task in pathological gamblers [146].

In contrast to rTMS that requires 20–30 min of stimulation time to achieve its full effect, theta burst stimulation (TBS) protocols could achieve similar efficiency by employing protocols lasting between 20 s and 3 min that induce NMDA receptor-dependent long-term potentiation and long-term depression [147]. A recent meta-analytic review [148] that focused on healthy participants on the prefrontal cortex with theoretically linked cognitive test performance as the outcome revealed that uninterrupted train of TBS decreases performances on measures of inhibitory control, attentional control, and working memory, whereas intermittent TBS has positive effects on executive functions (but not likely ceiling effects). Future studies comparing different magnetic stimulation protocols should be conducted in the context of addictive behaviors.

5.3.2 Transcranial direct current stimulation

Transcranial direct current stimulation involves delivering low-intensity electric current (typically 0.5–2 mA) via electrodes placed on the scalp and/or upper body. Cortical excitability is modulated by a polarity-dependent shift of the neuronal membrane potential [149, 150]. On the macroscopic level, anodal stimulation enhances cortical excitability via depolarization and long-term potentiation, whereas cathodal stimulation inhibits excitability via hyperpolarization and long-term depression [149]. The density, duration, and direction of the current that comes into contact with underlying neurons determine the strength and direction of neuromodulation [149, 150]. After an initial subthreshold depolarization or hyperpolarization of neuronal membrane potentials that increases or decreases the likelihood of spontaneous neural firing, facilitation of long-term potentials or long-term depression occurs [151]. tDCS modulation of the action potentials even lasts beyond the stimulation period [149, 150], and several neuromodulation sessions could increase the duration of the effects [152].

tDCS as an intervention in addictive disorders: a recent review [23] showed that seven published studies have focused on the impact of tDCS on various measures related to substance addiction. Despite important inter-individual differences in response to tDCS [153], most preeminent effects were found on craving reduction [154]. In addition, mixed results were found with respect to executive control functions [124, 131, 155, 156]. Importantly, in healthy controls no improvement was found after tDCS stimulation of bilateral DLPFC stimulation of either right anodal/left cathodal or left anodal/right cathodal on decision-making under risk (e.g., balloon analogue task), an absence of effect possibly due to a ceiling effect [157].

The benefit from reducing cue-induced craving for clinical population could be pertinent. Indeed, pressing, urgent, and irrepressible desire to drink or to smoke has been strongly associated with *loss of control*, leading to a high relapse rate [158]. However, the mediating effect of craving variation in response to tDCS on relapse is not obvious. For instance, in a tDCS study in patients with alcohol dependence (two daily stimulations 5 consecutive days on left cathodal/right anodal over the dorsolateral prefrontal cortex), no differences with regard to changes on scores of craving were found despite an improved overall perception of quality of life and reduced relapse probability in several alcoholics [159]. In nicotine addiction, right anodal stimulation on the DLPFC reduces craving with minimal heterogeneity, whereas cathodal tDCS on this region showed the most positive effect on cue-provoked craving and smoking intake [154]. However, this craving reduction, which may be due

to increased control on cue reactivity, could be too small to positively impact cigarette use. Indeed, as compared to sham, active tDCS significantly reduced smoking craving and increased brain reactivity to smoking cues within the right posterior cingulate, as measured with a functional magnetic resonance imaging event-related paradigm, but failed to diminish the number of cigarettes smoked (see also [160]) and the exhaled carbon monoxide 1 month following the stimulation [161].

Regarding the association between tDCS and food, reduction of food craving [162–164] and calorie intake [97] in healthy subjects and reduced craving for food in overweight subjects [165] have been reported.

Mediating processes involved in brain stimulation of the PFC is likely to be more complex than previously expected. It was demonstrated that anodal tDCS applied over frontoparietal regions has previously been shown to enhance attention and executive control functions [166–168], but the effects are limited and non-lasting.

Working memory, depending on the stimulation modalities, can be a valid candidate mediator [169]. As a multicomponent system responsible for temporary storage and manipulation of information, working memory sustained emotional regulation [14]. Because many psychiatric disorders are associated with working memory impairments, it may be useful to improve the transient "online" manipulation of emotional thoughts in treatment rehabilitation.

Response inhibition is another good candidate mediator of the relationship between tDCS and clinical change. For instance, a recent study showed that tDCS over the right inferior frontal cortex made healthy participants more efficient in proactive, but not reactive, inhibition [170]. In another study, tDCS over the pre SMA during a stop-signal task increases activity in the pre SMA after anodal stimulation during stop trials and was associated with improved inhibitory control [171]. Finally, after applying tDCS over the rIFG, two studies [170, 172] observed a decrease in P3 amplitude during no-go and/or stop trials in anodal compared to inactive stimulation. The clinical value of those results in the case of addictive behaviors remains to be seen. One possibility is that a reduction of P3 amplitude during successful response inhibition on a go/no-go task in response to tDCS could be a protective factor for the risk of relapse in vulnerable alcoholics, that is, those with greater amplitude of P3 [173].

The clinical impact of tDCS on substance use can be still more subtle. For instance, in obese participants, electric brain stimulation on the DLPFC facilitated the transition between unconscious and conscious perception of appetitive stimuli, a phenomenon particularly pronounced in participants with higher body mass index [174]. Those findings could have an impact on craving regulation, via augmented awareness of implicit determinants of craving, enhancing the risk of relapse.

Although the proposed cognitive mediators presented in this section showed promising results, their clinical relevance is still tentative. Much more data is needed to achieve a better comprehension of the impact of tDCS on addictive behaviors.

5.3.3 Neurofeedback

In neurofeedback, participants learn to modulate their own brain activity through feedback. The main goal is for participants to develop effective self-regulation strategies to increase desired brain activity. Functional magnetic resonance imaging neurofeedback (fMRI-NF) and electroencephalography neurofeedback (EEG-NF) are the most developed configurations [175], each with its strengths and weaknesses [176, 177]. Higher spatial resolution and broad brain coverage characterize fMRI-NF [178], while EEG-NF has very good timing but low spatial accuracy. In EEG-NF, it is possible to modify neuronal oscillations in specific frequency

domains associated with functions such as attention or relaxation. fMRI-NF and its variant, real-time fMRI [179], provide direct feedback to modulate (increase or decrease) neuronal activity in the regions of interest [180]. With fMRI-NF, brain regions of interest are defined a priori on the basis of consensual articles describing which neurocognitive networks are altered and predictive of low use of controlled substances [181]. In EEG-NF, critical oscillations in certain frequency bands have been associated with mental states (e.g., alpha and theta frequencies for a relaxed or meditative state, beta rhythm, or sensorimotor for inhibition).

In the context of addictive behaviors, alpha-theta and the alpha-theta augmented with SMR training represent the two main protocols of EEG-NF. As pointed out by [23], only a few studies have reached a reasonable quality (only one study used a control condition matched in time) [182], which makes it difficult to determine which protocol provides the best results. However, in two studies [182, 183], a reduction in the number of false alarms (i.e., response to no-go trials) on a go/no-go task was observed in participants who received EEG-NF rather than an alternative treatment. It is interesting to note that sensorimotor interferences can be reduced in healthy participants who undergo SMR neurofeedback training, which they have learned to voluntarily increase, resulting in better cognitive performance [184].

With respect to fMRI-NF, an analysis based on eight studies [23] revealed that six of them performed on nicotine addiction showed better regulation at the level of the anterior part of the cingulate gyrus directly associated with a decrease in the desire to smoke [185]. In alcohol addiction, reduced craving was achieved by modifying activity in the ACC, PFC, and insula [186]. Further studies should explore reward (e.g., ventral striatum) and control processing before the clinical relevance in addiction could be confirmed and mediating factors (e.g., prepotent response inhibition) identified.

6. A step forward: combined interventions with retrieval-extinction techniques

Coupling brain stimulation with other pharmacological and non-pharmacological interventions may provide further knowledge about individual brain oscillation states across several montages and voltages as well as long-term structural and functional effects of brain stimulation on addicted patients [187]. These proposals will certainly make better use of brain stimulation techniques and therefore optimize their clinical effects (**Table 1**).

Here we focused more on the effects of combined interventions to improve clinical efficacy. Combined methodologies have provided positive clinical results in a variety of psychiatric conditions [188]. From a broad perspective, the use of neuromodulation techniques to promote brain plasticity [189, 190] while exerting response inhibition, extinction learning, or cognitive restructuration may help regain control over prepotent actions.

As shown in **Table 2**, only five studies used several combined approaches in the context of substance use disorders. The results are rather disappointing. Indeed, in five out of five studies, no interaction between brain stimulation and cognitive manipulation was found, indicating that tDCS did not add any clinical value to behavioral training. However, two studies have examined the combined effects of left anodal tDCS on DLPFC and cognitive-behavioral modification (CBM) in high-risk drinkers undergoing or not treatment. In the high-risk drinker sample, 1.0 mA was administered on left DLPFC during three CBM sessions for 3 to 4 days. No effect of CBM or tDCS was observed on approach bias or alcohol consumption. However, participants reported a reduced craving during a signal responsiveness task [191]. In treatment seekers, 2.0 mA over left DLPFC over the course of four

Brain stimulation and investigation techniques	
Deep brain stimulation (DBS)	A small device, similar to a pacemaker, is surgically implanted to deliver electrical stimulation to targeted areas of the brain
Transcranial direct current stimulation (tDCS) and its variant, the transcranial alternating current or random noise stimulation	Allows changes in cortical activity to be generated by inducing a direct low-intensity (1–2 mA) current in the brain
Repetitive transcranial magnetic stimulation (rTMS)	Induces repeated single magnetic pulses in the brain to modulate cortical activity
Event-related potentials (ERP)	By means of electrodes placed at various points on the scalp and amplified through an EEG machine, the ERP measures electrical potentials generated by the brain in response to specific internal or external events (e.g., sensory, cognitive, or motor stimuli)
Function magnetic resonance imagery (fMRI)	To detect regional and time-varying changes in brain metabolism and blood oxygenation
Cognitive training and related cognitive functions	
Domain-general cognitive training	A structured practice of mental abilities that are used to solve complex tasks regardless of their content (e.g., working memory)
Domain-specific cognitive training	A structured practice of mental abilities where the semantic content of the processed information is controlled (e.g., negative emotional words or alcohol-related content)
Cognitive biases	These refer generally to unidentified or inaccurately identified attitudes or stereotypes, but in the present essay, we reported attentional, memory, and action tendency biases as normal and abnormal manifestations of domain-specific processing (e.g., attentional engagement toward smoking cues in deprived smokers)
Cognitive deficits	Describes a deviation from the normal functioning of general cognitive domains (e.g., episodic memory, executive functioning)
Executive functions	Partially independent, top-down processes reflecting goal cognitive corresponding to an internal goal are involved in the control of behavior, emotions, and cognition. The updating of the relevant information, the inhibition of prepotent impulses, and the mental set shifting are core functions
Proactive control	Refers to expectancy-based activation of cognitive control (maintaining goal activation to bias responding) prior to an anticipated conflict or challenge. In contrast, reactive control refers to the activation of cognitive control after a change or conflict is detected
Working memory	The ability to hold multiple things in mind at once while mentally manipulating one or more of them (e.g., updating)
Interference control	Ignoring (inhibiting, suppressing, or deactivating) internal or external competing information to protect working memory or to focus attention on goal-relevant information
Prepotent inhibition response	Refers to the suppression of actions that are no longer required or that are inappropriate, which supports flexible and goal-directed behavior in ever-changing environments
Self-regulation	Encompasses cognitive control, emotion regulation, and top-down and bottom-up processes that alter emotion, behavior, or cognition to attempt to enhance adaptation (or to achieve an explicit or implicit goal or goal state)
Learning-related concepts	
Conditioned stimulus	A previously neutral stimulus that has been learned to predict an outcome; the presentation of the stimulus evokes the memory of the previous learning

Extinction	The presentation of a conditioned/learned stimulus now in the absence of the previously associated outcome; this results in the temporary decline of subsequent memory expression
Learning	The behavioral changes of an organism are the result of regularities in the environment of that organism
Reactivation	Re-exposure to memory reminders, which may result in destabilization of the previously learned neural representation of memory
Retrieval	A reminder results in recollection of the previously learned memory; the term encompasses the multiple processes from reactivation of the neural memory representation to behavioral expression of the memory
Reconsolidation	The active process that is necessary to restabilize a reactivated/destabilized memory; disruption of reconsolidation results in memory impairment, while new information is incorporated during reconsolidation into an updated memory
Reactivation-extinction (retrieval-extinction)	The combination of memory reactivation (usually via a reminder that results in memory retrieval) and, after a brief interval, subsequent extinction

Table 1.
Definitions and glossary of major terms as relevant in the current essay.

training sessions in 4 consecutive days was used [192]. No significant interaction effect for the full sample was found. However, in this study, there were some indications of a boosting effect of tDCS and CBM, such that relapse was lower in this group at the 1-year follow-up.

More encouraging evidence for the usefulness of a combined approach comes from research on patients with mood disorders. For instance, participants with social anxiety disorder had a significant decrease in attention bias for threatening signals during single anodal stimulation as opposed to simulated stimulation [196]. In obsessive-compulsive disorder, exposure to information aimed at generating a conditioned response (e.g., increase anxiety in response to a risk of contamination) has been tested in combination with tDCS [197] or rTMS [198]. Indeed, by using a personalized provocation of symptoms aimed at generating an appropriate level of distress, the goal was to activate the corresponding neural circuit. During brain stimulation, people were asked to think about provocation ("Please keep thinking about your dirty hands"). Positive results were found in this combined setting (brief exposure therapy + tDCS or rTMS). In the field of nicotine addiction, one study has shown that it is advantageous to use a challenge with actual exposure to tobacco signals just prior to the rTMS high-frequency stimulation treatment [199]. It should be noted that this approach requires that the interventions be individualized according to the conditioned responses involved in the addictive process.

Brain stimulation techniques could also be advantageously coupled with interventions targeting the learning process of extinction in addictive disorder. Extinction refers to the disappearance of a conditioned behavior in the absence of positive or negative reinforcement [200]. Extinction is the basis for an intervention based on exposure, a primary treatment for a variety of psychiatric conditions, including addiction [201]. Unfortunately, the extinguishing procedures did not simply wipe out the conditioned responses of the past, as shown by the return of the targeted behavior by extinction which is again apparent after the passage of time, after the presentation of the unconditioned stimulus, and when extinguished signals are encountered outside the extinction context [201]. Instead, extinction may be a new form of learning that exists with extinction memories in distinct neural

Studies	Condition	Inclusion criteria	Exclusion criteria	N	Mean age (SD)	Female/ male	Design	Experimental condition	Outcome measures	Results
den Uyl et al. [191]	Electrophysiological and behavioral effects of combined tDCS and Alcohol Approach Bias Retraining (AABR) in hazardous drinkers	Heavy drinkers want to reduce drinking Dutch-speaking 18–35 years AUDIT > 8	tDCS criteria*	78	21.8 (3.2)	51/27	2 × 2 factorial design: • Active tDCS during active training • Sham tDCS during active training • Active tDCS during sham training • Sham tDCS during sham training	Three sessions of AABR** while receiving tDCS over DLPFC (1 mA for 15 min; 35 cm^2 anode F3 and 100 cm^2 cathode over contralateral supraorbital region)	Alcohol use, craving, AAT, IAT, EEG P300 Quantity of alcohol use at month follow-up	No effects on EEG and behavioral measures of repeated CBM and/or tDCS, except for an effect of tDCS on induced craving
den Uyl et al. [191]	A clinical trial with combined tDCS and Alcohol Approach Bias Retraining in alcohol-dependent patients	Individuals with AUD under a 3-month hospital treatment	tDCS criteria*	91	47 (8.8)	30/91	Three groups in parallel design: • Active tDCS during active training • Sham tDCS during active training • Active tDCS separate from active training	Four sessions of AABR** while receiving tDCS over DLPFC (20 min, 2 mA; 35 cm^2 anode F3 and 100 m^2 cathode F4)	3-month, 1-year abstinence follow-ups, craving intensity, approach bias	No effect of repeated CBM and/or tDCS on 3 months of abstinence duration, craving, and alcohol biases, except a trend-level effect of active tDCS during active training on relapse rate at 1 year only when comparing to sham tDCS ($p = .07$)

Studies	Condition	Inclusion criteria	Exclusion criteria	N	Mean age (SD)	Female/ male	Design	Experimental condition	Outcome measures	Results
den Uyl et al. [193]	Clinical trial with combined tDCS and Attentional Bias Modification (ABM) in alcohol-dependent patients	Individuals with AUD under a 3-month hospital treatment	tDCS criteria*	83	48.6 (0.9)	21/62	2 × 2 factorial design: • Active tDCS during active ABM • Sham tDCS during active ABM • Active tDCS during sham ABM • Sham tDCS during sham training	Four sessions of ABM*** combined with tDCS (20 min, 2 mA, over DLPFC, 35 cm^2 anode F3, and 100 m^2 cathode F4)	1-year abstinence follow-up, alcohol bias, craving intensity	Stronger avoidance bias only during training session in active tDCS with active ABM ($p < 0.05$) No effects of tDCS and ABM on the bias scores, craving, or relapse
Sedgmond et al. [194]	Effect of tDCS on food consumption or food craving when combined with inhibitory control training in healthy subjects	Healthy participants	In diet to lose weight History of eating disorders Previously participated in this type of study	172	20.81 (0.26)	141/172	2 × 2 factorial design: • Active tDCS during active training • Sham tDCS during active training • Active tDCS during sham training • Sham tDCS during sham training	One session of ICT**** while receiving tDCS over DLPFC (2 mA for 20 min; 35 cm^2 anode F4 and cathode F3)	Food craving, snack buffet consumption, inhibitory control	No evidence for the effect of tDCS on food consumption or food craving with Bayesian. No effect of tDCS on inhibitory control

Studies	Condition	Inclusion criteria	Exclusion criteria	N	Mean age (SD)	Female/ male	Design	Experimental condition	Outcome measures	Results
Claus et al. [195]	Effect of combining CBM and tDCS on reduction of alcohol approach biases and alcohol consumption	At-risk alcohol drinkers AUDIT > 8	History of treatment for AUD or desire for treatment Alcohol withdrawal Brain injury Psychotropic medications Pregnancy Illicit drug use Metal in the body	79	24.5 (2.7)	Not indicated	2 × 2 factorial design: • Active tDCS during active training • Sham tDCS during active training • Active tDCS during sham training • Sham tDCS during sham training	Four sessions (of 1 h per week, 4 consecutive weeks) of AABR** while tDCS right inferior frontal gyrus (2 mA; 20 min; 11 cm^2 anode F10 and the cathode arm)	Drinks per drinking day (DDD) and percent heavy drinking days (PHDD) at baseline, the follow-up visits at 1-week and 1-month follow-ups, alcohol approach bias at baseline	Significant alcohol approach biases at baseline; neither CBM, tDCS, nor the interaction reduced the bias at the follow-up No significant effect of intervention on either DDD or PHDD

**tDCS criteria: epilepsy, multiple sclerosis or other neurological illness, previous brain injury/infection, metal in the brain, pacemaker, pregnancy, claustrophobia, recent fainting/panic attack, frequent headaches or dizziness, and eczema or other skin conditions*
***Alcohol Approach Bias Retraining: pull or push alcohol or soft drink pictures with joystick.*
****Attentional Bias Modification: dot-probe training task with alcohol, nonalcohol, or object pictures*
*****Inhibitory control training: a go/no-go training task with fatty food, healthy food, and close pictures*

Table 2.
Effect of tDCS and behavioral interventions combined in substance use disorder.

circuits [202]. Therefore, increased extinction with new approaches has been extensively studied in animals and, more recently, in humans with aversive responses (e.g., fear) and appetite disorders (e.g., addiction) [203]. The extinction of the conditioned response may be more effective if it is preceded by a brief exposure to the conditioned response, that is to say, a phase of reactivation of the memory [204–206]. This approach, often named *super-extinction*, gave rise to theories of synaptic consolidation [207], which brought a fresh look at memory processes involved in flexible actions. Briefly, once activated, conditioned responses are rendered labile and unstable that interfering intervention (e.g., propranolol administration [208], non-pharmacological manipulation [209, 210]) ensuing during the reconsolidation window could update original memory traces [204]. Reduced involvement of the inhibitory networks [211] and induced plasticity [209] during extinction following reactivation could represent some of the key mechanisms in play. Importantly, whereas in extinction amygdala's representation remains intact, the prefrontal activated reconsolidation would eliminate the necessity of such inhibition [211]. Additionally, as shown in animal studies, one factor that may initiate memory destabilization and reconsolidation is the detention of prediction errors (*surprise effect*) [212, 213]. In humans, some procedures combining prediction errors and memory reconsolidation interference have yielded interesting results in subjects with high alcohol consumption ([214, 215], p. 20; [216]). Although the clinical impact of those essays was not overwhelming, subtle changes of alcohol attractiveness have already been highlighted, such as a reduction of craving for alcohol [216] and significant reductions in verbal fluency for positive alcohol-related words [215]. In theory, conditioned stimuli could be erased with a single treatment, which could solve the compliance problems necessary to continue treatment, promoting abstinence [217]. Although promising and extremely relevant in the context of the prevention and treatment of addictive behaviors, the precise recovery conditions required to successfully destabilize memory remain unclear (e.g., role of prediction error, type of intervention post-activation, counter-conditioning, interference, extinction).

We suggest here that the *super-extinction* procedure can be implemented in combination with brain stimulation techniques and cognitive response inhibition training, for example, which may lead to stronger and more prolonged clinical effects in drug and behavioral addictions. Indeed, not only is the activation of relevant brain circuitry important before the application of brain stimulation [197–199], but it is also possible to capitalize on the lability of memory during reconsolidation. Indeed, reactivated memory becomes labile after retrieval through a process known as memory reconsolidation. Memory reconsolidation after retrieval may be used to maintain or update long-term memories, reinforcing or integrating new information into them [204–206, 209], a phenomenon that would underlie change in psychotherapy [218]. Interestingly, decreasing DLPFC activity has been observed in repeated encounters with memories (e.g., [115]), resulting in a stabilization of memory. Consistently, the stimulation of the control network via an anodal TDCS applied to the right DLPFC during repeated access to acquired information disrupts the long-term retention of these memories [219]. Based on these findings, it is likely that stimulating the control network during reconsolidation of emotional memories associated with addictive behaviors could result in disrupted storage, particularly in circumstances that generate interferences (e.g., training *alcohol-stop* associations). Future research is needed to test these hypotheses and shed new light on this theoretical reasoning.

Another promising possibility is that cognitive training works better when combined with other forms of clinical intervention aimed at enhancing motivation, self-esteem, family functioning, social support, etc. [220]. In other words, a very interesting line of research is to study the interaction between the mechanisms

involved in clinical interventions that lead to positive outcomes and the aforementioned cognitive interventions. Too often, clinical interventions have been described simply as a set of technical tools (e.g., CBT, family therapy) instead of mechanisms and processes of clinical interventions (e.g., compensatory skills, self-understanding) [221], which is a problem when we consider that each participant does not respond in the same way to a given intervention. For this reason, it may be that only the participants who benefit most in some way from a given clinical intervention are those for whom cognitive training and brain stimulation work best. It is obvious that the weakness of this hypothesis is precisely the problem encountered by research in identifying central mechanisms and methods related to psychological change in response to clinical interventions [222].

Finally, some studies have found that addicted participants have preserved automatic inhibitory resources [52]. In this study, recently detoxified alcoholics and healthy participants performed a modified stop-signal task that consisted of a training phase in which a subset of the stimuli was consistently associated with stopping or going and a test phase in which this mapping was reversed. In the training phase, stop performance improved for the consistent stop stimuli, compared with control stimuli that were not associated with going or stopping. In the test phase, go performance tended to be impaired for old stop stimuli. Combined, these findings support the automatic inhibition hypothesis. Importantly, performance was similar in both groups, which indicates that automatic inhibitory control develops normally in individuals with alcoholism. Furthermore, clinical interventions aimed at potentiating the automatic suppression of alcohol-going associations combined with procedures encouraging the automatic selection of alternative responses (e.g., intention implementation [223]). This approach has the merit to promote better inhibitory control of the action without saturating the resources of effortful self-regulation. Whether intensive addiction cues/stop associations could benefit from reactivation of craving or negative emotions is an important hypothesis to be tested in further experiments.

7. Concluding remarks

Many efforts have been made to modify the acquired motivational properties of addiction cues and to reinforce the control of prepotent responses via cognitive training, brain stimulation, and neurofeedback protocols. To date, our review has highlighted some of the promises as well as the obstacles that we need to overcome. In keeping with recent narrative critiques and the meta-analytic approach, the current state of the art appears to be like a half-empty or half-full glass. On the one side, an important limitation is the absence of a robust consensus about methods and mechanisms of brain stimulation techniques (but see for a recent consensus, article [224]) and recent findings calling into question inhibition as a psychometric construct [41]. The main consequence of this is the high level of variation between subjects in response to brain stimulation as well as a poor understanding of the precise cognitive mechanisms that mediate the efficacy of brain stimulation. On the other side, the glass could be considered half-filled because a reduction in the state of cue-induced craving is now feasible and the ongoing research on possible moderators could add important information. Indeed, the motivation for change of participants that refers to personal goals and values is a clinical target requiring specific psychological interventions before cognitive and brain enhancement can turn into robust clinical effects [109]. Clearly, the brain (e.g., using EEG or fMRI) and cognitive (e.g., impaired executive functions, exacerbated approach tendencies toward addiction cues) profiles of patients sensitive to cognitive improvement are important factors to identify [114, 225].

In this chapter, we also strongly recommend that conditioned stimuli and conditioned responses that lead to the loss and recovery of control of addictive behavior be better identified and used with retrieval-extinction techniques in combination with brain and cognitive stimulations. If ethical questions arise when unpleasant sensations are felt by people seeking care and when an intervention alters the substance of a memory, as it may disrupt a sense of self, we must remember the lack of effectiveness of contemporary clinical and experimental treatments in an intolerable situation which we have become too accustomed. We hope to have convinced the reader that in reconsolidation-based treatments, even if boundary conditions begin to be discovered [226, 227], the potential benefits may far outweigh the risks.

It is difficult to obtain better cognitive control, such as improving executive functions in adults, as shown by considerable data [80], but capitalizing on preserved automatic inhibitory resources could prove useful for promoting better inhibitory control of the action without saturating the resources of effortful self-regulation [21, 52].

In sum, these are exciting days where a number of key elements useful to change addictive behaviors have now been identified, yet their perfect fit remains to be done. What is also promising is the undeniable need to bridge the gap between experimental studies and clinical issues in taking into account motivation, relevant personal conditioned responses, acute and chronic stress, memory, response inhibition, and brain and cognitive stimulation to provide addicts with better control of their impulse and obsessions because it is often a prerequisite to return to a satisfactory quality of life.

Author details

Xavier Noël[1*], Antoine Bechara[2], Mélanie Saeremans[1], Charles Kornreich[1], Clémence Dousset[1], Salvatore Campanella[1], Armand Chatard[3], Nemat Jaafari[4] and Macha Dubuson[1]

1 Psychological Medicine Laboratory, Faculty of Medicine, Université Libre de Bruxelles, Belgium

2 Department of Psychology, Southern California University, USA

3 Faculty of Psychology, University of Poitiers, France

4 Faculty of Medicine, University of Poitiers, France

*Address all correspondence to: xnoel@ulb.ac.be

References

[1] Miller PM, Book SW, Stewart SH. Medical treatment of alcohol dependence: A systematic review. International Journal of Psychiatry in Medicine. 2011;**42**(3):227-266

[2] Borsboom D, Cramer A, Kalis A. Brain disorders? Not really... why network structures block reductionism in psychopathology research. The Behavioral and Brain Sciences. 2018;**24**:1-54

[3] Goldstein RZ, Volkow ND. Drug addiction and its underlying neurobiological basis: Neuroimaging evidence for the involvement of the frontal cortex. The American Journal of Psychiatry. 2002;**159**(10):1642-1652

[4] Goldstein RZ, Volkow ND. Dysfunction of the prefrontal cortex in addiction: Neuroimaging findings and clinical implications. Nature Reviews. Neuroscience. 2011;**12**(11):652-669

[5] Lee RSC, Hoppenbrouwers S, Franken I. A systematic meta-review of impulsivity and compulsivity in addictive behaviors. Neuropsychology Review. 2019;**29**(1):14-26

[6] Noël X, Brevers D, Bechara A. A neurocognitive approach to understanding the neurobiology of addiction. Current Opinion in Neurobiology. 2013;**23**(4):632-638

[7] Redish AD, Jensen S, Johnson A. A unified framework for addiction: Vulnerabilities in the decision process. The Behavioral and Brain Sciences. 2008;**31**(4):415-437 discussion 437-487

[8] Tang Y-Y, Posner MI, Rothbart MK, Volkow ND. Circuitry of self-control and its role in reducing addiction. Trends in Cognitive Sciences. 2015;**19**(8):439-444

[9] Zilverstand A, Huang AS, Alia-Klein N, Goldstein RZ. Neuroimaging impaired response inhibition and salience attribution in human drug addiction: A systematic review. Neuron. 2018;**98**(5):886-903

[10] Bechara A, Noel X, Crone EA. Loss of willpower: Abnormal neural mechanisms of impulse control and decision making in addiction. In: Handbook of Implicit Cognition and Addiction. Thousand Oaks, California: Sage publications, Inc., 2006. pp. 215-232

[11] Noël X, Bechara A, Brevers D, Verbanck P, Campanella S. Alcoholism and the loss of willpower: A neurocognitive perspective. Journal of Psychophysiology. 2010;**24**(4):240-248

[12] Noël X, Van Der Linden M, Bechara A. The neurocognitive mechanisms of decision-making, impulse control, and loss of willpower to resist drugs. Psychiatry (Edgmont (Pa.: Township)). 2006;**3**(5):30-41

[13] Evans JSBT. Dual-processing accounts of reasoning, judgment, and social cognition. Annual Review of Psychology. 2008;**59**:255-278

[14] Hofmann W, Schmeichel BJ, Baddeley AD. Executive functions and self-regulation. Trends in Cognitive Sciences. 2012;**16**(3):174-180

[15] Argyriou E, Davison CB, Lee TTC. Response inhibition and internet gaming disorder: A meta-analysis. Addictive Behaviors. 2017;**71**:54-60

[16] Lipszyc J, Schachar R. Inhibitory control and psychopathology: A meta-analysis of studies using the stop signal task. Journal of the International Neuropsychological Society: JINS. 2010;**16**(6):1064-1076

[17] Nigg JT, Wong MM, Martel MM, Jester JM, Puttler LI, Glass JM, et al.

Poor response inhibition as a predictor of problem drinking and illicit drug use in adolescents at risk for alcoholism and other substance use disorders. Journal of the American Academy of Child and Adolescent Psychiatry. 2006;**45**(4):468-475

[18] Noël X, Sferrazza R, Van Der Linden M, Paternot J, Verhas M, Hanak C, et al. Contribution of frontal cerebral blood flow measured by (99m)Tc-Bicisate spect and executive function deficits to predicting treatment outcome in alcohol-dependent patients. Alcohol and Alcoholism. 2002;**37**(4):347-354

[19] Whelan R, Watts R, Orr CA, Althoff RR, Artiges E, Banaschewski T, et al. Neuropsychosocial profiles of current and future adolescent alcohol misusers. Nature. 2014;**512**(7513):185-189

[20] Noël X, Brevers D, Bechara A. A triadic neurocognitive approach to addiction for clinical interventions. Frontiers in Psychiatry. 2013;**4**:179

[21] Verbruggen F, Best M, Bowditch WA, Stevens T, McLaren IPL. The inhibitory control reflex. Neuropsychologia. 2014;**65**:263-278

[22] Boffo M, Zerhouni O, Gronau QF, van Beek RJJ, Nikolaou K, Marsman M, et al. Cognitive bias modification for behavior change in alcohol and smoking addiction: Bayesian meta-analysis of individual participant data. Neuropsychology Review. 2019;**29**(1):52-78

[23] Luigjes J, Segrave R, de Joode N, Figee M, Denys D. Efficacy of invasive and non-invasive brain modulation interventions for addiction. Neuropsychology Review. 2019;**29**(1):116-138

[24] Nigg JT. Annual research review: On the relations among self-regulation, self-control, executive functioning, effortful control, cognitive control, impulsivity, risk-taking, and inhibition for developmental psychopathology. Journal of Child Psychology and Psychiatry, and Allied Disciplines. 2017;**58**(4):361-383

[25] Diamond A. Executive functions. Annual Review of Psychology. 2013;**64**:135-168

[26] Zhou Q, Chen SH, Main A. Commonalities and differences in the research on Children's effortful control and executive function: A call for an integrated model of self-regulation. Child Development Perspectives. 2012;**6**(2):112-121

[27] Fals-Stewart W, O'Farrell TJ, Hooley JM. Relapse among married or cohabiting substance-abusing patients: The role of perceived criticism. Behavior Therapy. 2001;**32**(4):787-801

[28] Sripada CS, Angstadt M, McNamara P, King AC, Phan KL. Effects of alcohol on brain responses to social signals of threat in humans. NeuroImage. 2011;**55**(1):371-380

[29] James W. Talks to Teachers on Psychology: And to Students on Some of Life's Ideals. New York: H. Holt; 1899

[30] MacLeod C, Dodd M, Sheard E, Wilson D, Bibi U. In opposition to inhibition. In: The Psychology of Learning and Motivation. Vol. 43. San Diego, CA: B.H. Ross; 2003. pp. 163-214

[31] Smith R. Inhibition: History and Meaning in the Sciences of Mind and Brain. Berkeley: University of California Press; 1992

[32] Logan GD, Cowan WB, Davis KA. On the ability to inhibit simple and choice reaction time responses: A model and a method. Journal of Experimental

Psychology. Human Perception and Performance. 1984;**10**(2):276-291

[33] Miyake A, Friedman NP, Emerson MJ, Witzki AH, Howerter A, Wager TD. The unity and diversity of executive functions and their contributions to complex "frontal lobe" tasks: A latent variable analysis. Cognitive Psychology. 2000;**41**(1):49-100

[34] Miyake A, Friedman NP. The nature and organization of individual differences in executive functions: Four general conclusions. Current Directions in Psychological Science. 2012;**21**(1):8-14

[35] Botvinick M, Braver T. Motivation and cognitive control: From behavior to neural mechanism. Annual Review of Psychology. 2015;**66**:83-113

[36] Ridderinkhof KR. Neurocognitive mechanisms of perception-action coordination: A review and theoretical integration. Neuroscience and Biobehavioral Reviews. 2014; **46**(Pt 1):3-29

[37] Verbruggen F. Executive control of actions across time and space. Current Directions in Psychological Science. 2016;**25**(6):399-404

[38] Verbruggen F, Logan GD. Proactive adjustments of response strategies in the stop-signal paradigm. Journal of Experimental Psychology. Human Perception and Performance. 2009;**35**(3):835-854

[39] Friedman NP, Miyake A. The relations among inhibition and interference control functions: A latent-variable analysis. Journal of Experimental Psychology. General. 2004;**133**(1):101-135

[40] Pettigrew C, Martin RC. Cognitive declines in healthy aging: Evidence from multiple aspects of interference resolution. Psychology and Aging. 2014;**29**(2):187-204

[41] Rey-Mermet A, Gade M, Oberauer K. Should we stop thinking about inhibition? Searching for individual and age differences in inhibition ability. Journal of Experimental Psychology. Learning, Memory, and Cognition. 2018;**44**(4):501-526

[42] Stahl C, Voss A, Schmitz F, Nuszbaum M, Tüscher O, Lieb K, et al. Behavioral components of impulsivity. Journal of Experimental Psychology. General. 2014;**143**(2):850-886

[43] Aron AR. From reactive to proactive and selective control: Developing a richer model for stopping inappropriate responses. Biological Psychiatry. 2011;**69**(12):e55-e68

[44] Braver TS. The variable nature of cognitive control: A dual mechanisms framework. Trends in Cognitive Sciences. 2012;**16**(2):106-113

[45] Zandbelt BB, Bloemendaal M, Neggers SFW, Kahn RS, Vink M. Expectations and violations: Delineating the neural network of proactive inhibitory control. Human Brain Mapping. 2013;**34**(9):2015-2024

[46] Schall JD, Godlove DC. Current advances and pressing problems in studies of stopping. Current Opinion in Neurobiology. 2012;**22**(6):1012-1021

[47] Fillmore MT, Weafer J. Behavioral inhibition and addiction. In: MacKillop J, de Wit H, editors. The Wiley-Blackwell Handbook of Addiction Psychopharmacology. Chichester, West Sussex; Malden, MA: Wiley-Blackwell; 2013. pp. 135-164

[48] Verdejo-Garcia A, Chong TT-J, Stout JC, Yücel M, London ED. Stages of dysfunctional decision-making in

addiction. Pharmacology, Biochemistry, and Behavior. 2018;**164**:99-105

[49] Billieux J, Gay P, Rochat L, Khazaal Y, Zullino D, Van der Linden M. Lack of inhibitory control predicts cigarette smoking dependence: Evidence from a non-deprived sample of light to moderate smokers. Drug and Alcohol Dependence. 2010;**112**(1-2):164-167

[50] Powell J, Dawkins L, West R, Powell J, Pickering A. Relapse to smoking during unaided cessation: Clinical, cognitive and motivational predictors. Psychopharmacology. 2010;**212**(4):537-549

[51] Noël X, Van der Linden M, Schmidt N, Sferrazza R, Hanak C, Le Bon O, et al. Supervisory attentional system in nonamnesic alcoholic men. Archives of General Psychiatry. 2001;**58**(12):1152-1158

[52] Noël X, Brevers D, Hanak C, Kornreich C, Verbanck P, Verbruggen F. On the automaticity of response inhibition in individuals with alcoholism. Journal of Behavior Therapy and Experimental Psychiatry. 2016;**51**:84-91

[53] Adams S, Mokrysz C, Attwood AS, Munafò MR. Resisting the urge to smoke: Inhibitory control training in cigarette smokers. Royal Society Open Science. 2017;**4**(8):170045

[54] Galimberti E, Martoni RM, Cavallini MC, Erzegovesi S, Bellodi L. Motor inhibition and cognitive flexibility in eating disorder subtypes. Progress in Neuro-Psychopharmacology & Biological Psychiatry. 2012;**36**(2):307-312

[55] Brevers D, Noël X. Pathological gambling and the loss of willpower: A neurocognitive perspective. Socioaffective Neuroscience & Psychology. 2013;**3**:21592

[56] Sharif-Razi M, Hodgins DC, Goghari VM. Reactive and proactive control mechanisms of response inhibition in gambling disorder. Psychiatry Research. 2019;**272**:114-121

[57] Czapla M, Simon JJ, Richter B, Kluge M, Friederich H-C, Herpertz S, et al. The impact of cognitive impairment and impulsivity on relapse of alcohol-dependent patients: Implications for psychotherapeutic treatment. Addiction Biology. 2016;**21**(4):873-884

[58] Goudriaan AE, Oosterlaan J, De Beurs E, Van Den Brink W. The role of self-reported impulsivity and reward sensitivity versus neurocognitive measures of disinhibition and decision-making in the prediction of relapse in pathological gamblers. Psychological Medicine. 2008;**38**(1):41-50

[59] Charles-Walsh K, Furlong L, Munro DG, Hester R. Inhibitory control dysfunction in nicotine dependence and the influence of short-term abstinence. Drug and Alcohol Dependence. 2014;**143**:81-86

[60] Smith JL, Mattick RP, Jamadar SD, Iredale JM. Deficits in behavioural inhibition in substance abuse and addiction: A meta-analysis. Drug and Alcohol Dependence. 2014;**145C**:1-33

[61] Otten R, Mun CJ, Shaw DS, Wilson MN, Dishion TJ. A developmental cascade model for early adolescent-onset substance use: The role of early childhood stress. Addiction. 2019;**114**(2):326-334

[62] Noël X, Bechara A, Dan B, Hanak C, Verbanck P. Response inhibition deficit is involved in poor decision making under risk in nonamnesic individuals with alcoholism. Neuropsychology. 2007;**21**(6):778-786

[63] Bechara A, Damasio H, Tranel D, Damasio AR. Deciding advantageously before knowing the advantageous strategy. Science. 1997;**275**(5304): 1293-1295

[64] Bechara A. Risky business: Emotion, decision-making, and addiction. Journal of Gambling Studies. 2003;**19**(1):23-51

[65] Bechara A. The role of emotion in decision-making: Evidence from neurological patients with orbitofrontal damage. Brain and Cognition. 2004;**55**(1):30-40

[66] Verbruggen F, Adams R, Chambers CD. Proactive motor control reduces monetary risk taking in gambling. Psychological Science. 2012;**23**(7):805-815

[67] Verbruggen F, Adams RC, van't Wout F, Stevens T, McLaren IPL, Chambers CD. Are the effects of response inhibition on gambling long-lasting? PLoS One. 2013;**8**(7):e70155

[68] Stevens T, Brevers D, Chambers CD, Lavric A, McLaren IPL, Mertens M, et al. How does response inhibition influence decision making when gambling? Journal of Experimental Psychology. Applied. 2015;**21**(1):15-36

[69] Stacy AW, Wiers RW. Implicit cognition and addiction: A tool for explaining paradoxical behavior. Annual Review of Clinical Psychology. 2010;**6**:551-575

[70] Houben K, Wiers RW. Response inhibition moderates the relationship between implicit associations and drinking behavior. Alcoholism, Clinical and Experimental Research. 2009;**33**(4):626-633

[71] Thush C, Wiers RW, Ames SL, Grenard JL, Sussman S, Stacy AW. Interactions between implicit and explicit cognition and working memory capacity in the prediction of alcohol use in at-risk adolescents. Drug and Alcohol Dependence. 2008;**94**(1-3):116-124

[72] Figner B, Knoch D, Johnson EJ, Krosch AR, Lisanby SH, Fehr E, et al. Lateral prefrontal cortex and self-control in intertemporal choice. Nature Neuroscience. 2010;**13**(5):538-539

[73] Kirby KN, Petry NM, Bickel WK. Heroin addicts have higher discount rates for delayed rewards than non-drug-using controls. Journal of Experimental Psychology. General. 1999;**128**(1):78-87

[74] Amlung M, Vedelago L, Acker J, Balodis I, MacKillop J. Steep delay discounting and addictive behavior: A meta-analysis of continuous associations. Addiction. 2017;**112**(1):51-62

[75] Bickel WK, Koffarnus MN, Moody L, Wilson AG. The behavioral- and neuro-economic process of temporal discounting: A candidate behavioral marker of addiction. Neuropharmacology. 2014; **76**(Pt B):518-527

[76] Bjork JM, Momenan R, Hommer DW. Delay discounting correlates with proportional lateral frontal cortex volumes. Biological Psychiatry. 2009;**65**(8):710-713

[77] Jauregi A, Kessler K, Hassel S. Linking cognitive measures of response inhibition and reward sensitivity to trait impulsivity. Frontiers in Psychology. 2018;**9**:2306

[78] Solanto MV, Abikoff H, Sonuga-Barke E, Schachar R, Logan GD, Wigal T, et al. The ecological validity of delay aversion and response inhibition as measures of impulsivity in AD/HD: A supplement to the NIMH multimodal treatment study of AD/HD. Journal of Abnormal Child Psychology. 2001;**29**(3):215-228

[79] Verdejo-Garcia A. Cognitive training for substance use disorders: Neuroscientific mechanisms. Neuroscience and Biobehavioral Reviews. 2016;**68**:270-281

[80] Enge S, Behnke A, Fleischhauer M, Küttler L, Kliegel M, Strobel A. No evidence for true training and transfer effects after inhibitory control training in young healthy adults. Journal of Experimental Psychology. Learning, Memory, and Cognition. 2014;**40**(4):987-1001

[81] Jones A, Guerrieri R, Fernie G, Cole J, Goudie A, Field M. The effects of priming restrained versus disinhibited behaviour on alcohol-seeking in social drinkers. Drug and Alcohol Dependence. 2011;**113**(1):55-61

[82] Redick TS, Shipstead Z, Harrison TL, Hicks KL, Fried DE, Hambrick DZ, et al. No evidence of intelligence improvement after working memory training: A randomized, placebo-controlled study. Journal of Experimental Psychology. General. 2013;**142**(2):359-379

[83] Klingberg T. Training and plasticity of working memory. Trends in Cognitive Sciences. 2010;**14**(7):317-324

[84] Houben K, Wiers RW, Jansen A. Getting a grip on drinking behavior: Training working memory to reduce alcohol abuse. Psychological Science. 2011;**22**(7):968-975

[85] Wanmaker S, Leijdesdorff SMJ, Geraerts E, van de Wetering BJM, Renkema PJ, Franken IHA. The efficacy of a working memory training in substance use patients: A randomized double-blind placebo-controlled clinical trial. Journal of Clinical and Experimental Neuropsychology. 2018;**40**(5):473-486

[86] Alcorn JL, Pike E, Stoops WS, Lile JA, Rush CR. A pilot investigation of acute inhibitory control training in cocaine users. Drug and Alcohol Dependence. 2017;**174**:145-149

[87] Houben K, Havermans RC, Nederkoorn C, Jansen A. Beer à no-go: Learning to stop responding to alcohol cues reduces alcohol intake via reduced affective associations rather than increased response inhibition. Addiction. 2012;**107**(7):1280-1287

[88] Houben K, Jansen A. Training inhibitory control. A recipe for resisting sweet temptations. Appetite. 2011;**56**(2):345-349

[89] Jones A, Di Lemma LCG, Robinson E, Christiansen P, Nolan S, Tudur-Smith C, et al. Inhibitory control training for appetitive behaviour change: A meta-analytic investigation of mechanisms of action and moderators of effectiveness. Appetite. 2016;**97**:16-28

[90] Jones A, Field M. The effects of cue-specific inhibition training on alcohol consumption in heavy social drinkers. Experimental and Clinical Psychopharmacology. 2013;**21**(1):8-16

[91] Allom V, Mullan B, Hagger M. Does inhibitory control training improve health behaviour? A meta-analysis. Health Psychology Review. 2016;**10**(2):168-186

[92] Turton R, Bruidegom K, Cardi V, Hirsch CR, Treasure J. Novel methods to help develop healthier eating habits for eating and weight disorders: A systematic review and meta-analysis. Neuroscience and Biobehavioral Reviews. 2016;**61**:132-155

[93] Eagle DM, Bari A, Robbins TW. The neuropsychopharmacology of action inhibition: Cross-species translation of the stop-signal and go/no-go tasks. Psychopharmacology. 2008;**199**(3):439-456

[94] Verbruggen F, Logan GD. Automatic and controlled response inhibition: Associative learning in the go/no-go and stop-signal paradigms. Journal of Experimental Psychology. General. 2008;**137**(4):649-672

[95] Adams RC, Lawrence NS, Verbruggen F, Chambers CD. Training response inhibition to reduce food consumption: Mechanisms, stimulus specificity and appropriate training protocols. Appetite. 2017;**109**:11-23

[96] Lawrence NS, Verbruggen F, Morrison S, Adams RC, Chambers CD. Stopping to food can reduce intake. Effects of stimulus-specificity and individual differences in dietary restraint. Appetite. 2015;**85**:91-103

[97] Lapenta OM, Sierve KD, de Macedo EC, Fregni F, Boggio PS. Transcranial direct current stimulation modulates ERP-indexed inhibitory control and reduces food consumption. Appetite. 2014;**83**:42-48

[98] Veling H, Aarts H, Papies EK. Using stop signals to inhibit chronic dieters' responses toward palatable foods. Behaviour Research and Therapy. 2011;**49**(11):771-780

[99] Hare TA, Camerer CF, Rangel A. Self-control in decision-making involves modulation of the vmPFC valuation system. Science. New York, N.Y. 2009;**324**(5927):646-648

[100] Veling H, Aarts H, Stroebe W. Stop signals decrease choices for palatable foods through decreased food evaluation. Frontiers in Psychology. 2013;**4**:875

[101] Wessel JR, O'Doherty JP, Berkebile MM, Linderman D, Aron AR. Stimulus devaluation induced by stopping action. Journal of Experimental Psychology. General. 2014;**143**(6):2316-2329

[102] Friese M, Hofmann W, Wänke M. When impulses take over: Moderated predictive validity of explicit and implicit attitude measures in predicting food choice and consumption behaviour. The British Journal of Social Psychology. 2008;**47**(Pt 3):397-419

[103] Ferrey AE, Frischen A, Fenske MJ. Hot or not: Response inhibition reduces the hedonic value and motivational incentive of sexual stimuli. Frontiers in Psychology. 2012;**3**:575

[104] Lawrence NS, O'Sullivan J, Parslow D, Javaid M, Adams RC, Chambers CD, et al. Training response inhibition to food is associated with weight loss and reduced energy intake. Appetite. 2015;**95**:17-28

[105] Veling H, Holland RW, van Knippenberg A. When approach motivation and behavioral inhibition collide: Behavior regulation through stimulus devaluation. Journal of Experimental Social Psychology. 2008;**44**(4):1013-1019

[106] Eberl C, Wiers RW, Pawelczack S, Rinck M, Becker ES, Lindenmeyer J. Approach bias modification in alcohol dependence: Do clinical effects replicate and for whom does it work best? Developmental Cognitive Neuroscience. 2013;**4**:38-51

[107] Wiers RW, Eberl C, Rinck M, Becker ES, Lindenmeyer J. Retraining automatic action tendencies changes alcoholic patients' approach bias for alcohol and improves treatment outcome. Psychological Science. 2011;**22**(4):490-497

[108] Cristea IA, Kok RN, Cuijpers P. The effectiveness of cognitive bias modification interventions for substance addictions: A meta-analysis. PLoS One. 2016;**11**(9):e0162226

[109] Wiers RW, Boffo M, Field M. What's in a trial? On the importance of distinguishing between experimental lab studies and randomized controlled trials: The case of cognitive bias modification and alcohol use disorders.

Journal of Studies on Alcohol and Drugs. 2018;**79**(3):333-343

[110] Boffo M, Pronk T, Wiers RW, Mannarini S. Combining cognitive bias modification training with motivational support in alcohol dependent outpatients: Study protocol for a randomised controlled trial. Trials. 2015;**16**:63

[111] Houben K, Havermans RC, Wiers RW. Learning to dislike alcohol: Conditioning negative implicit attitudes toward alcohol and its effect on drinking behavior. Psychopharmacology. 2010;**211**(1):79-86

[112] Freeman SM, Razhas I, Aron AR. Top-down response suppression mitigates action tendencies triggered by a motivating stimulus. Current Biology: CB. 2014;**24**(2):212-216

[113] Veling H, Aarts H, Stroebe W. Using stop signals to reduce impulsive choices for palatable unhealthy foods. British Journal of Health Psychology. 2013;**18**(2):354-368

[114] Rolland B, D'Hondt F, Montègue S, Brion M, Peyron E, D'Aviau de Ternay J, et al. A patient-tailored evidence-based approach for developing early neuropsychological training programs in addiction settings. Neuropsychology Review. 2019;**29**(1):103-115

[115] Kuhn J, Lenartz D, Huff W, Lee S, Koulousakis A, Klosterkoetter J, et al. Remission of alcohol dependency following deep brain stimulation of the nucleus accumbens: Valuable therapeutic implications? Journal of Neurology, Neurosurgery, and Psychiatry. 2007;**78**(10):1152-1153

[116] Levy D, Shabat-Simon M, Shalev U, Barnea-Ygael N, Cooper A, Zangen A. Repeated electrical stimulation of reward-related brain regions affects cocaine but not "natural" reinforcement. The Journal of Neuroscience. 2007;**27**(51):14179-14189

[117] Voges J, Waerzeggers Y, Maarouf M, Lehrke R, Koulousakis A, Lenartz D, et al. Deep-brain stimulation: Long-term analysis of complications caused by hardware and surgery—Experiences from a single centre. Journal of Neurology, Neurosurgery, and Psychiatry. 2006;**77**(7):868-872

[118] Wang TR, Moosa S, Dallapiazza RF, Elias WJ, Lynch WJ. Deep brain stimulation for the treatment of drug addiction. Neurosurgical Focus. 2018;**45**(2):E11

[119] Benabid AL, Pollak P, Louveau A, Henry S, de Rougemont J. Combined (thalamotomy and stimulation) stereotactic surgery of the VIM thalamic nucleus for bilateral Parkinson disease. Applied Neurophysiology. 1987;**50**(1-6):344-346

[120] Nuttin B, Cosyns P, Demeulemeester H, Gybels J, Meyerson B. Electrical stimulation in anterior limbs of internal capsules in patients with obsessive-compulsive disorder. The Lancet. 1999;**354**(9189):1526

[121] Mayberg HS, Lozano AM, Voon V, McNeely HE, Seminowicz D, Hamani C, et al. Deep brain stimulation for treatment-resistant depression. Neuron. 2005;**45**(5):651-660

[122] Kuhn J, Bauer R, Pohl S, Lenartz D, Huff W, Kim EH, et al. Observations on unaided smoking cessation after deep brain stimulation of the nucleus accumbens. European Addiction Research. 2009;**15**(4):196-201

[123] Ardouin C, Voon V, Worbe Y, Abouazar N, Czernecki V, Hosseini H, et al. Pathological gambling in Parkinson's disease improves on chronic subthalamic nucleus stimulation. Movement Disorders. 2006;**21**(11):1941-1946

[124] Luigjes J, Segrave R, de Joode N, Figee M, Denys D. Efficacy of invasive and non-invasive brain modulation interventions for addiction. Neuropsychology Review. 2018;**29**:116-138

[125] Sesia T, Bulthuis V, Tan S, Lim LW, Vlamings R, Blokland A, et al. Deep brain stimulation of the nucleus accumbens shell increases impulsive behavior and tissue levels of dopamine and serotonin. Experimental Neurology. 2010;**225**(2):302-309

[126] Sesia T, Temel Y, Lim LW, Blokland A, Steinbusch HWM, Visser-Vandewalle V. Deep brain stimulation of the nucleus accumbens core and shell: Opposite effects on impulsive action. Experimental Neurology. 2008;**214**(1):135-139

[127] Crews FT, Boettiger CA. Impulsivity, frontal lobes and risk for addiction. Pharmacology, Biochemistry, and Behavior. 2009;**93**(3):237-247

[128] Luigjes J, van den Brink W, Schuurman PR, Kuhn J, Denys D. Is deep brain stimulation a treatment option for addiction? Addiction. 2015;**110**(4):547-548

[129] Kekic M, Boysen E, Campbell IC, Schmidt U. A systematic review of the clinical efficacy of transcranial direct current stimulation (tDCS) in psychiatric disorders. Journal of Psychiatric Research. 2016;**74**:70-86

[130] Tortella G. Transcranial direct current stimulation in psychiatric disorders. World Journal of Psychiatry. 2015;**5**(1):88

[131] Jansen JM, Daams JG, Koeter MWJ, Veltman DJ, van den Brink W, Goudriaan AE. Effects of non-invasive neurostimulation on craving: A meta-analysis. Neuroscience & Biobehavioral Reviews. 2013;**37**(10):2472-2480

[132] Chen R, Classen J, Gerloff C, Celnik P, Wassermann EM, Hallett M, et al. Depression of motor cortex excitability by low-frequency transcranial magnetic stimulation. Neurology. 1997;**48**(5):1398-1403

[133] Siebner HR, Peller M, Willoch F, Minoshima S, Boecker H, Auer C, et al. Lasting cortical activation after repetitive TMS of the motor cortex: A glucose metabolic study. Neurology. 2000;**54**(4):956-963

[134] Maeda F, Keenan JP, Tormos JM, Topka H, Pascual-Leone A. Interindividual variability of the modulatory effects of repetitive transcranial magnetic stimulation on cortical excitability. Experimental Brain Research. 2000;**133**(4):425-430

[135] Deng Z-D, Lisanby SH, Peterchev AV. Electric field depth-focality tradeoff in transcranial magnetic stimulation: Simulation comparison of 50 coil designs. Brain Stimulation. 2013;**6**(1):1-13

[136] Amiaz R, Levy D, Vainiger D, Grunhaus L, Zangen A. Repeated high-frequency transcranial magnetic stimulation over the dorsolateral prefrontal cortex reduces cigarette craving and consumption. Addiction. 2009;**104**(4):653-660

[137] Trojak B, Meille V, Achab S, Lalanne L, Poquet H, Ponavoy E, et al. Transcranial magnetic stimulation combined with nicotine replacement therapy for smoking cessation: A randomized controlled trial. Brain Stimulation. 2015;**8**(6):1168-1174

[138] Ceccanti M, Inghilleri M, Attilia ML, Raccah R, Fiore M, Zangen A, et al. Deep TMS on alcoholics: Effects on cortisolemia and dopamine pathway modulation. A pilot study. Canadian Journal of Physiology and Pharmacology. 2015;**93**(4):283-290

[139] Bolloni C, Panella R, Pedetti M, Frascella AG, Gambelunghe C, Piccoli T, et al. Bilateral transcranial magnetic stimulation of the prefrontal cortex reduces cocaine intake: A pilot study. Frontiers in Psychiatry. 2016;**7**:133

[140] Höppner J, Broese T, Wendler L, Berger C, Thome J. Repetitive transcranial magnetic stimulation (rTMS) for treatment of alcohol dependence. The World Journal of Biological Psychiatry. 2011; **12**(Suppl 1):57-62

[141] Herremans SC, Vanderhasselt M-A, De Raedt R, Baeken C. Reduced intra-individual reaction time variability during a Go-NoGo task in detoxified alcohol-dependent patients after one right-sided dorsolateral prefrontal HF-rTMS session. Alcohol and Alcoholism (Oxford, Oxfordshire). 2013;**48**(5):552-557

[142] Steele JD, Lawrie SM. Segregation of cognitive and emotional function in the prefrontal cortex: A stereotactic meta-analysis. NeuroImage. 2004;**21**(3):868-875

[143] Naqvi NH, Rudrauf D, Damasio H, Bechara A. Damage to the insula disrupts addiction to cigarette smoking. Science. 2007;**315**(5811):531-534

[144] Volkow ND, Baler RD. NOW vs LATER brain circuits: Implications for obesity and addiction. Trends in Neurosciences. 2015;**38**(6):345-352

[145] Cho SS, Koshimori Y, Aminian K, Obeso I, Rusjan P, Lang AE, et al. Investing in the future: Stimulation of the medial prefrontal cortex reduces discounting of delayed rewards. Neuropsychopharmacology. 2015;**40**(3):546-553

[146] Zack M, Cho SS, Parlee J, Jacobs M, Li C, Boileau I, et al. Effects of high frequency repeated transcranial magnetic stimulation and continuous theta burst stimulation on gambling reinforcement, delay discounting, and stroop interference in men with pathological gambling. Brain Stimulation. 2016;**9**(6):867-875

[147] Huang Y-Z, Edwards MJ, Rounis E, Bhatia KP, Rothwell JC. Theta burst stimulation of the human motor cortex. Neuron. 2005;**45**(2):201-206

[148] Lowe CJ, Manocchio F, Safati AB, Hall PA. The effects of theta burst stimulation (TBS) targeting the prefrontal cortex on executive functioning: A systematic review and meta-analysis. Neuropsychologia. 2018;**111**:344-359

[149] Nitsche MA, Paulus W. Excitability changes induced in the human motor cortex by weak transcranial direct current stimulation. The Journal of Physiology. 2000;**527**(Pt 3):633-639

[150] Nitsche MA, Paulus W. Sustained excitability elevations induced by transcranial DC motor cortex stimulation in humans. Neurology. 2001;**57**(10):1899-1901

[151] Woods AJ, Antal A, Bikson M, Boggio PS, Brunoni AR, Celnik P, et al. A technical guide to tDCS, and related non-invasive brain stimulation tools. Clinical Neurophysiology. 2016;**127**(2):1031-1048

[152] Boggio PS, Nunes A, Rigonatti SP, Nitsche MA, Pascual-Leone A, Fregni F. Repeated sessions of noninvasive brain DC stimulation is associated with motor function improvement in stroke patients. Restorative Neurology and Neuroscience. 2007;**25**(2):123-129

[153] Strube W, Bunse T, Nitsche MA, Nikolaeva A, Palm U, Padberg F, et al. Bidirectional variability in motor cortex excitability modulation following 1 mA

transcranial direct current stimulation in healthy participants. Physiological Reports. 2016;**4**(15):e12884

[154] Kang N, Kim RK, Kim HJ. Effects of transcranial direct current stimulation on symptoms of nicotine dependence: A systematic review and meta-analysis. Addictive Behaviors. 2019;**96**:133-139

[155] Sauvaget A, Trojak B, Bulteau S, Jiménez-Murcia S, Fernández-Aranda F, Wolz I, et al. Transcranial direct current stimulation (tDCS) in behavioral and food addiction: A systematic review of efficacy, technical, and methodological issues. Frontiers in Neuroscience. 2015;**9**:349

[156] Spagnolo PA, Goldman D. Neuromodulation interventions for addictive disorders: Challenges, promise, and roadmap for future research. Brain. 2017;**140**(5):1183-1203

[157] Russo R, Twyman P, Cooper NR, Fitzgerald PB, Wallace D. When you can, scale up: Large-scale study shows no effect of tDCS in an ambiguous risk-taking task. Neuropsychologia. 2017;**104**:133-143

[158] Skinner MD, Aubin H-J. Craving's place in addiction theory: Contributions of the major models. Neuroscience and Biobehavioral Reviews. 2010;**34**(4):606-623

[159] Klauss J, Penido Pinheiro LC, Silva Merlo BL, Santos GAC, Fregni F, Nitsche MA, et al. A randomized controlled trial of targeted prefrontal cortex modulation with tDCS in patients with alcohol dependence. The International Journal of Neuropsychopharmacology. 2014;**17**(11):1793-1803

[160] Falcone M, Bernardo L, Wileyto EP, Allenby C, Burke AM, Hamilton R, et al. Lack of effect of transcranial direct current stimulation (tDCS) on short-term smoking cessation: Results of a randomized, sham-controlled clinical trial. Drug and Alcohol Dependence. 2019;**194**:244-251

[161] Mondino M, Luck D, Grot S, Januel D, Suaud-Chagny M-F, Poulet E, et al. Effects of repeated transcranial direct current stimulation on smoking, craving and brain reactivity to smoking cues. Scientific Reports. 2018;**8**(1):8724

[162] Fregni F, Orsati F, Pedrosa W, Fecteau S, Tome FAM, Nitsche MA, et al. Transcranial direct current stimulation of the prefrontal cortex modulates the desire for specific foods. Appetite. 2008;**51**(1):34-41

[163] Goldman RL, Borckardt JJ, Frohman HA, O'Neil PM, Madan A, Campbell LK, et al. Prefrontal cortex transcranial direct current stimulation (tDCS) temporarily reduces food cravings and increases the self-reported ability to resist food in adults with frequent food craving. Appetite. 2011;**56**(3):741-746

[164] Kekic M, McClelland J, Campbell I, Nestler S, Rubia K, David AS, et al. The effects of prefrontal cortex transcranial direct current stimulation (tDCS) on food craving and temporal discounting in women with frequent food cravings. Appetite. 2014;**78**:55-62

[165] Montenegro RA, Okano AH, Cunha FA, Gurgel JL, Fontes EB, Farinatti PTV. Prefrontal cortex transcranial direct current stimulation associated with aerobic exercise change aspects of appetite sensation in overweight adults. Appetite. 2012;**58**(1):333-338

[166] Keeser D, Meindl T, Bor J, Palm U, Pogarell O, Mulert C, et al. Prefrontal transcranial direct current stimulation changes connectivity

of resting-state networks during fMRI. The Journal of Neuroscience. 2011;**31**(43):15284-15293

[167] Meinzer M, Lindenberg R, Antonenko D, Flaisch T, Flöel A. Anodal transcranial direct current stimulation temporarily reverses age-associated cognitive decline and functional brain activity changes. The Journal of Neuroscience: The Official Journal of the Society for Neuroscience. 2013;**33**(30):12470-12478

[168] Nelson JT, McKinley RA, Golob EJ, Warm JS, Parasuraman R. Enhancing vigilance in operators with prefrontal cortex transcranial direct current stimulation (tDCS). NeuroImage. 2014;**85**(Pt 3):909-917

[169] Brunoni AR, Vanderhasselt M-A. Working memory improvement with non-invasive brain stimulation of the dorsolateral prefrontal cortex: A systematic review and meta-analysis. Brain and Cognition. 2014;**86**:1-9

[170] Cunillera T, Brignani D, Cucurell D, Fuentemilla L, Miniussi C. The right inferior frontal cortex in response inhibition: A tDCS-ERP co-registration study. NeuroImage. 2016;**140**:66-75

[171] Yu J, Tseng P, Hung DL, Wu S-W, Juan C-H. Brain stimulation improves cognitive control by modulating medial-frontal activity and preSMA-vmPFC functional connectivity. Human Brain Mapping. 2015;**36**(10):4004-4015

[172] Campanella S, Schroder E, Monnart A, Vanderhasselt M-A, Duprat R, Rabijns M, et al. Transcranial direct current stimulation over the right frontal inferior cortex decreases neural activity needed to achieve inhibition: A double-blind ERP study in a male population. Clinical EEG and Neuroscience. 2017;**48**(3):176-188

[173] Petit G, Cimochowska A, Kornreich C, Hanak C, Verbanck P, Campanella S. Neurophysiological correlates of response inhibition predict relapse in detoxified alcoholic patients: Some preliminary evidence from event-related potentials. Neuropsychiatric Disease and Treatment. 2014;**10**:1025-1037

[174] Osimo SA, Korb S, Aiello M. Obesity, subliminal perception and inhibition: Neuromodulation of the prefrontal cortex. Behaviour Research and Therapy. 2019;**119**:103408

[175] Dickerson KC. Upregulating brain activity using non-drug reward imagery and real-time fMRI neurofeedback—A new treatment approach for addiction? eBioMedicine. 2018;**38**:21-22

[176] Orndorff-Plunkett F, Singh F, Aragón OR, Pineda JA. Assessing the effectiveness of neurofeedback training in the context of clinical and social neuroscience. Brain Sciences. 2017;**7**(8):95

[177] Thibault RT, Lifshitz M, Raz A. The self-regulating brain and neurofeedback: Experimental science and clinical promise. Cortex. 2016;**74**:247-261

[178] Cox WM, Subramanian L, Linden DEJ, Lührs M, McNamara R, Playle R, et al. Neurofeedback training for alcohol dependence versus treatment as usual: Study protocol for a randomized controlled trial. Trials. 2016;**17**(1):480

[179] deCharms RC. Applications of real-time fMRI. Nature Reviews Neuroscience. 2008;**9**(9):720-729

[180] Hanlon CA, Hartwell KJ, Canterberry M, Li X, Owens M, LeMatty T, et al. Reduction of cue-induced craving through realtime neurofeedback in nicotine users: The role of region of interest selection and multiple visits. Psychiatry Research: Neuroimaging. 2013;**213**(1):79-81

[181] Sitaram R, Ros T, Stoeckel L, Haller S, Scharnowski F, Lewis-Peacock J, et al. Closed-loop brain training: The science of neurofeedback. Nature Reviews Neuroscience. 2017;**18**(2):86-100

[182] Scott WC, Kaiser D, Othmer S, Sideroff SI. Effects of an EEG biofeedback protocol on a mixed substance abusing population. The American Journal of Drug and Alcohol Abuse. 2005;**31**(3):455-469

[183] Keith JR, Rapgay L, Theodore D, Schwartz JM, Ross JL. An assessment of an automated EEG biofeedback system for attention deficits in a substance use disorders residential treatment setting. Psychology of Addictive Behaviors. 2015;**29**(1):17-25

[184] Kober SE, Witte M, Stangl M, Väljamäe A, Neuper C, Wood G. Shutting down sensorimotor interference unblocks the networks for stimulus processing: An SMR neurofeedback training study. Clinical Neurophysiology. 2015;**126**(1):82-95

[185] Canterberry M, Hanlon CA, Hartwell KJ, Li X, Owens M, LeMatty T, et al. Sustained reduction of nicotine craving with real-time neurofeedback: Exploring the role of severity of dependence. Nicotine & Tobacco Research: Official Journal of the Society for Research on Nicotine and Tobacco. 2013;**15**(12):2120-2124

[186] Karch S, Paolini M, Gschwendtner S, Jeanty H, Reckenfelderbäumer A, Yaseen O, et al. Real-time fMRI neurofeedback in patients with tobacco use disorder during smoking cessation: Functional differences and implications of the first training session in regard to future abstinence or relapse. Frontiers in Human Neuroscience. 2019;**13**:65

[187] Lapenta OM, Marques LM, Rego GG, Comfort WE, Boggio PS. tDCS in addiction and impulse control disorders. The Journal of ECT. 2018;**34**(3):182-192

[188] Sathappan AV, Luber BM, Lisanby SH. The dynamic duo: Combining noninvasive brain stimulation with cognitive interventions. Progress in Neuro-Psychopharmacology & Biological Psychiatry. 2019;**89**:347-360

[189] Rabey JM, Dobronevsky E, Aichenbaum S, Gonen O, Marton RG, Khaigrekht M. Repetitive transcranial magnetic stimulation combined with cognitive training is a safe and effective modality for the treatment of Alzheimer's disease: A randomized, double-blind study. Journal of Neural Transmission. 2013;**120**(5):813-819

[190] Segrave RA, Arnold S, Hoy K, Fitzgerald PB. Concurrent cognitive control training augments the antidepressant efficacy of tDCS: A pilot study. Brain Stimulation. 2014;**7**(2):325-331

[191] den Uyl TE, Gladwin TE, Wiers RW. Electrophysiological and behavioral effects of combined transcranial direct current stimulation and alcohol approach bias retraining in hazardous drinkers. Alcoholism, Clinical and Experimental Research. 2016;**40**(10):2124-2133

[192] den Uyl TE, Gladwin TE, Rinck M, Lindenmeyer J, Wiers RW. A clinical trial with combined transcranial direct current stimulation and alcohol approach bias retraining. Addiction Biology. 2017;**22**(6):1632-1640

[193] den Uyl TE, Gladwin TE, Lindenmeyer J, Wiers RW. A clinical trial with combined transcranial direct current stimulation and attentional bias modification in alcohol-dependent patients. Alcoholism, Clinical and Experimental Research. 2018;**42**(10):1961-1969

[194] Sedgmond J, Lawrence NS, Verbruggen F, Morrison S, Chambers CD, Adams RC. Prefrontal brain stimulation during food-related inhibition training: Effects on food craving, food consumption and inhibitory control. Royal Society Open Science. 2019;**6**(1):181186

[195] Claus ED, Klimaj SD, Chavez R, Martinez AD, Clark VP. A randomized trial of combined tDCS over right inferior frontal cortex and cognitive bias modification: Null effects on drinking and alcohol approach bias. Alcoholism, Clinical and Experimental Research. 2019;**43**(7):1591-1599

[196] Heeren A, Billieux J, Philippot P, De Raedt R, Baeken C, de Timary P, et al. Impact of transcranial direct current stimulation on attentional bias for threat: A proof-of-concept study among individuals with social anxiety disorder. Social Cognitive and Affective Neuroscience. 2017;**12**(2):251-260

[197] Carmi L, Tendler A, Bystritsky A, Hollander E, Blumberger DM, Daskalakis J, et al. Efficacy and safety of deep transcranial magnetic stimulation for obsessive-compulsive disorder: A prospective multicenter randomized double-blind placebo-controlled trial. The American Journal of Psychiatry. 21 May 2019

[198] Carmi L, Alyagon U, Barnea-Ygael N, Zohar J, Dar R, Zangen A. Clinical and electrophysiological outcomes of deep TMS over the medial prefrontal and anterior cingulate cortices in OCD patients. Brain Stimulation. 2018;**11**(1):158-165

[199] Dinur-Klein L, Dannon P, Hadar A, Rosenberg O, Roth Y, Kotler M, et al. Smoking cessation induced by deep repetitive transcranial magnetic stimulation of the prefrontal and insular cortices: A prospective, randomized controlled trial. Biological Psychiatry. 2014;**76**(9):742-749

[200] Pavlov I. Conditioned Reflexes. USA: Oxford University Press; 1927

[201] Conklin CA, Tiffany ST. Applying extinction research and theory to cue-exposure addiction treatments. Addiction. 2002;**97**(2):155-167

[202] Dunsmoor JE, Niv Y, Daw N, Phelps EA. Rethinking extinction. Neuron. 2015;**88**(1):47-63

[203] Milton AL, Everitt BJ. The psychological and neurochemical mechanisms of drug memory reconsolidation: Implications for the treatment of addiction. The European Journal of Neuroscience. 2010;**31**(12):2308-2319

[204] Lee JLC, Nader K, Schiller D. An update on memory reconsolidation updating. Trends in Cognitive Sciences. 2017;**21**(7):531-545

[205] Nader K, Schafe GE, Le Doux JE. Fear memories require protein synthesis in the amygdala for reconsolidation after retrieval. Nature. 2000;**406**(6797):722-726

[206] Sandrini M, Cohen LG, Censor N. Modulating reconsolidation: A link to causal systems-level dynamics of human memories. Trends in Cognitive Sciences. 2015;**19**(8):475-482

[207] McGaugh JL. Time-dependent processes in memory storage. Science (New York, N.Y.). 1966;**153**(3742):1351-1358

[208] Soeter M, Kindt M. An abrupt transformation of phobic behavior after a post-retrieval amnesic agent. Biological Psychiatry. 2015;**78**(12):880-886

[209] Monfils M-H, Cowansage KK, Klann E, LeDoux JE. Extinction-reconsolidation boundaries: Key to persistent attenuation of fear memories. Science. 2009;**324**(5929):951-955

[210] Xue Y-X, Luo Y-X, Wu P, Shi H-S, Xue L-F, Chen C, et al. A memory retrieval-extinction procedure to prevent drug craving and relapse. Science (New York, N.Y.). 2012;**336**(6078):241-245

[211] Schiller D, Kanen JW, LeDoux JE, Monfils M-H, Phelps EA. Extinction during reconsolidation of threat memory diminishes prefrontal cortex involvement. Proceedings of the National Academy of Sciences of the United States of America. 2013;**110**(50):20040-20045

[212] Pedreira ME, Pérez-Cuesta LM, Maldonado H. Mismatch between what is expected and what actually occurs triggers memory reconsolidation or extinction. Learning & Memory (Cold Spring Harbor, N.Y.). 2004;**11**(5):579-585

[213] Sevenster D, Beckers T, Kindt M. Prediction error governs pharmacologically induced amnesia for learned fear. Science. 2013;**339**(6121):830-833

[214] Das RK, Lawn W, Kamboj SK. Rewriting the valuation and salience of alcohol-related stimuli via memory reconsolidation. Translational Psychiatry. 2015;**5**:e645

[215] Hon T, Das RK, Kamboj SK. The effects of cognitive reappraisal following retrieval-procedures designed to destabilize alcohol memories in high-risk drinkers. Psychopharmacology. 2016;**233**(5):851-861

[216] Kaag AM, Goudriaan AE, De Vries TJ, Pattij T, Wiers RW. A high working memory load prior to memory retrieval reduces craving in non-treatment seeking problem drinkers. Psychopharmacology. 2018;**235**(3):695-708

[217] Everitt BJ, Giuliano C, Belin D. Addictive behaviour in experimental animals: Prospects for translation. Philosophical Transactions of the Royal Society of London. Series B, Biological Sciences. 2018;**373**:1742

[218] Lane RD, Ryan L, Nadel L, Greenberg L. Memory reconsolidation, emotional arousal, and the process of change in psychotherapy: New insights from brain science. The Behavioral and Brain Sciences. 2015;**38**:e1

[219] Marián M, Szőllősi Á, Racsmány M. Anodal transcranial direct current stimulation of the right dorsolateral prefrontal cortex impairs long-term retention of reencountered memories. Cortex; A Journal Devoted to the Study of the Nervous System and Behavior. 2018;**108**:80-91

[220] Gladwin TE, Wiers CE, Wiers RW. Interventions aimed at automatic processes in addiction: Considering necessary conditions for efficacy. Current Opinion in Behavioral Sciences. 2017;**13**:19-24

[221] Connolly Gibbons MB, Crits-Christoph P, Barber JP, Stirman SW, Gallop R, Goldstein LA, et al. Unique and common mechanisms of change across cognitive and dynamic psychotherapies. Journal of Consulting and Clinical Psychology. 2009;**77**(5):801-813

[222] Connolly Gibbons MB, Crits-Christoph P, Barber JP, Schamberger M. Insight in psychotherapy: A review of empirical literature. In: Castonguay LG, Hill C, editors. Insight in Psychotherapy. 2007. pp. 143-165

[223] Gollwitzer P, Sheeran P. Implementation intentions and goal achievement: A meta-analysis of effects and processes. In: Zanna MP, editor. Advances in Experimental Social Psychology. Vol. 38. Academic Press; 2006. pp. 69-119

[224] Ekhtiari H, Tavakoli H, Addolorato G, Baeken C, Bonci A, Campanella S, et al. Transcranial electrical and magnetic stimulation (tES and TMS) for addiction medicine: A consensus paper on the present state of the science and the road ahead. Neuroscience and Biobehavioral Reviews. 2019;**104**:118-140

[225] Campanella S, Schroder E, Kajosch H, Noel X, Kornreich C. Why cognitive event-related potentials (ERPs) should have a role in the management of alcohol disorders. Neuroscience and Biobehavioral Reviews. San Diego, California. 21 Jun 2018

[226] Dunbar AB, Taylor JR. Reconsolidation and psychopathology: Moving towards reconsolidation-based treatments. Neurobiology of Learning and Memory. 2017;**142**(Pt A):162-171

[227] Monfils MH, Holmes EA. Memory boundaries: Opening a window inspired by reconsolidation to treat anxiety, trauma-related, and addiction disorders. The Lancet. Psychiatry. 2018;**5**(12):1032-1042