APPROACH-AVOIDANCE BEHAVIOUR IN PSYCHOPATHOLOGY

A CLINICAL NEUROPSYCHOLOGICAL PERSPECTIVE



ANKE LOIJEN

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Approach-avoidance behaviour in psychopathology

A clinical neuropsychological perspective

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Anke Loijen
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Promotoren
Prof. dr. J.I.M. Egger
Prof. dr. E.S. Becker
Prof. dr. M. Rinck

Manuscriptcommissie
Prof. dr. A.F.A. Schellekens (chair)
Prof. dr. C.T.W.M. Vissers
Prof. dr. R.W.H.J. Wiers (Universiteit van Amsterdam)

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INTRODUCTION

Introduction

Cognition and Psychopathology

A core characteristic of psychopathology is altered cognitive information processing. Neurocognitive deficits may be present in multiple cognitive domains, can be persistent in nature, have a negative impact on daily functioning, quality of life and are related to distress (Green & Harvey, 2014; Rock et al., 2014). Psychopathology-related biases in information processing refer to systematic distortions in information processing that can not be consciously controlled. These implicit or automatic biases in information processing can be observed in several cognitive domains (e.g. attentional and memory bias) as well as in relation to action tendencies (Koster et al., 2009). Action biases are the result of altered approach or avoidance responses towards stimuli that have increased valence in favour of the psychopathology-related associations, such as the automatic and relatively faster approach of alcohol-related stimuli in the presence of alcohol use disorder (AUD).

These alterations in information processing, neurocognitive impairment and cognitive biases are transdiagnostic in nature, as they are found to be present across multiple diagnostic classifications. They are associated with increased vulnerability to the development and maintenance of mental illness, as well as with reduced treatment response or heightened relapse risk in various psychopathological conditions. Based on these characteristics of cognitive alterations in psychopathology, this "C-factor" is considered to be an intrinsic component of psychopathology (Caspi et al. 2014; Abramovitch et al., 2021; East-Richard et al., 2020; Fox & Beevers, 2016;; Lavigne et al.,2024; Marteau et al., 2012; Mathews & MacLeod 2005; Wiers et al., 2007).

The nature of the bias in approach-avoidance behaviour in psychopathology as well as its modification in the presence of AUD-related cognitive impairment is studied in this thesis.

Interventions that intend to modify these cognitive biases (cognitive bias modification, CBM) could contribute to the spectrum of cognitive interventions for patients with neurocognitive impairment. This is in specific of interest for patients with cognitive disorders related to AUD for two reasons: Treatment options addressing these cognitive alterations are still limited (Hallion et al., 2024), and due to the neurocognitive deficits (such as diminished illness-insight and declarative memory impairment) they can profit less from traditional treatment such as cognitive behavioural therapy as well as compensatory cognitive training.

In order to improve the availability of cognitive interventions in the presence of cognitive alterations in psychopathology, both the feasibility of a compensatory cognitive intervention (CCTr) in a transdiagnostic patient population is studied, as well as the alcohol avoidance training (AATr) in a population with alcohol-related neurocognitive impairment (ARNI).

Approach-avoidance Tendencies in Psychopathology

The majority of humans' behavioural action tendencies are executed unconsciously and are based on associative implicit (non-declarative) learning of the relation between actions and their inferences (Solms & Friston, 2018). By means of these implicit processes we are drawn towards pleasant, appetitive stimuli or conversely we tend to withdraw from unpleasant or aversive stimuli. This basic implicit approach-avoidance behaviour based on affective evaluation of a stimuli is an important element of adaptive human behaviour (Cacioppo & Gardner, 1999; Elliot, 2006; Frijda, 1986; Lang et al., 1990).

Studies by Solarz (1960) and Chen & Bargh (1999) have shown that action tendencies can be captured by and quantified in response latencies. Reaction times increase when participants are instructed to perform an action *incongruent* with the stimulus valence compared to reaction times after *congruent* instructions. For example, approaching a negative/ aversive stimulus such as moving towards a spider will show an increased latency compared to moving away from this spider. This relative delay reflects the conflict between automatic processes (the tendency to withdraw from the spider) and cognitive control (deliberate response to the instruction to approach the spider) in approach-avoidance behaviour elicited by emotionally valenced stimuli (Strack & Deutsch, 2004).

In (the development of) psychopathology, specific stimuli (friendly faces in social anxiety or alcohol drinks in alcohol use disorder)) can gain extra valence when compared to neutral stimuli (neutral face, soda drinks). This increased valence can result in increased approach or avoidance behaviour towards the specific (psychopathology-related) stimulus: In social anxiety disorder, one may even avoid friendly faces due to fear of negative evaluations by others (Heuer et al., 2007). Or in the presence of a depressive disorder, the natural tendency to approach positive stimuli may be diminished (Trew, 2011) and finally the relatively faster approach of alcohol-related stimuli in AUD may result in relapse or increased alcohol intake.

Altered Information Processing in Alcohol Use Disorder

In the context of AUD both (major) alcohol-related neurocognitive impairment and biased action tendencies can occur. These changes in information processing and their interactions both contribute to the challenges of recovering from alcohol use disorder and achieving sustained abstinence (Bechara et al., 2006; Domínquez-Salas et al., 2016; Russell et al., 2025).

Neurocognitive Impairment in AUD

Neurocognitive impairment, especially within the executive function domain, plays a critical role in the development and maintenance of alcohol abuse and

dependency (Brion et al., 2017; Russel et al., 2025). This impairment can be caused by traumatic brain injury, given the likelihood of traumatic brain injury occurring in AUD is significantly increased. (Marceau et al., 2016; Weil et al., 2018). However also the neurotoxic effects of alcohol itself can result in the occurrence of alcohol-related neurocognitive disorders (ARNI) (Oscar-Berman & Marinkovic, 2007; Spear, 2018).) ARNI is highly prevalent as estimates of 30% to 80% arise in the screening of patients with AUD who are seeking treatment (Bates et al., 2002; Bruijnen et al., 2019). This neurocognitive impairment may be present in executive functioning, episodic memory, visuo-spatial abilities and social cognition (Bernardin et al., 2014; Le Berre et al., 2017; Stavro et al., 2013). These impairments reduce self-regulatory capacity, allowing problematic drinking patterns to persist and heightening the likelihood of relapse (Noël et al., 2002). Therefore, the recovery of cognitive impairment is a key predictor of successful and sustained abstinence of alcohol (Bates et al., 2006; Czapla et al., 2016; Melugin et al., 2021).

A small group of patients with AUD is diagnosed with *major* neurocognitive disorder or Korsakoff's Syndrome (KS). KS is a severe neuropsychiatric condition related to thiamine deficiency. Amongst other features KS is characterised by confabulation, apathy and profound anterograde and retrograde amnesia (Arts et al., 2017). Whereas declarative memory is severely impaired, the implicit memory is usually preserved. Whereas ARNI can be reversible and cognitive improvement is reported over a year of abstinence, the Korsakoff's Syndrome is a non-reversable condition usually requiring long-term specialised care and residential facilities (Arts et al. 2017; Bruijnen et al., 2021).

Biased Automatic Action Tendencies in AUD

In (the development) of AUD a relatively faster tendency to approach alcohol-related stimuli, as compared to non-alcoholic drinks and non-problematic drinkers, has been demonstrated. This alcohol-approach bias is a result of associative learning, automatic in nature and associated with increased alcohol consumption (Wiers et al., 2010). This biased action tendency has been linked to genetic vulnerability among heavily drinking men (Wiers et al., 2009) as well as specific impulsivity-related neural substrates (Martínez-Maldonado et al., 2020; Muller et al., 2024; C.E. Wiers et al., 2014). These kind of biased automatic action tendencies can help explain the difficulty refraining from alcohol when confronted with it, despite one's motivation and intention not to drink alcohol.

In order to resist impulsive automatic actions towards alcohol-related stimuli, strong cognitive control (particularly executive and memory functions) is essential: One needs to recall long term goals and disadvantages of drinking and apply goal-directed behaviour aligned with these objectives. However impaired neurocognitive functioning and increased automatic action responses hinder this

goal-directed behaviour, thereby increasing the risk of continued alcohol abuse or relapse (See Fig. 1 for the schematic overview of Wiers & Stacey, 2006).

Cognitive Interventions in Psychopathology

In the past decades several interventions have been developed to improve treatment outcome in the presence of cognitive alterations in the course of psychopathology. Whereas *Cognitive Remediation* (CR) involves treatment of neuro-cognitive impairment and aims to improve functional outcome, *Cognitive Bias Modification* (CBM) intends to alter action tendencies through repetitive contingency learning, thereby directly modifying implicit biases in information processing (Koster et al, 2009).

Cognitive Remediation

In 2005 and 2012, the Cognitive Remediation Expert Working Group provided the following definition: "Cognitive remediation is an intervention targeting cognitive deficit (attention, memory, executive function, social cognition, or meta cognition) using scientific principles of learning, with the ultimate goal of improving functional outcomes. Its effectiveness is enhanced when provided in a context

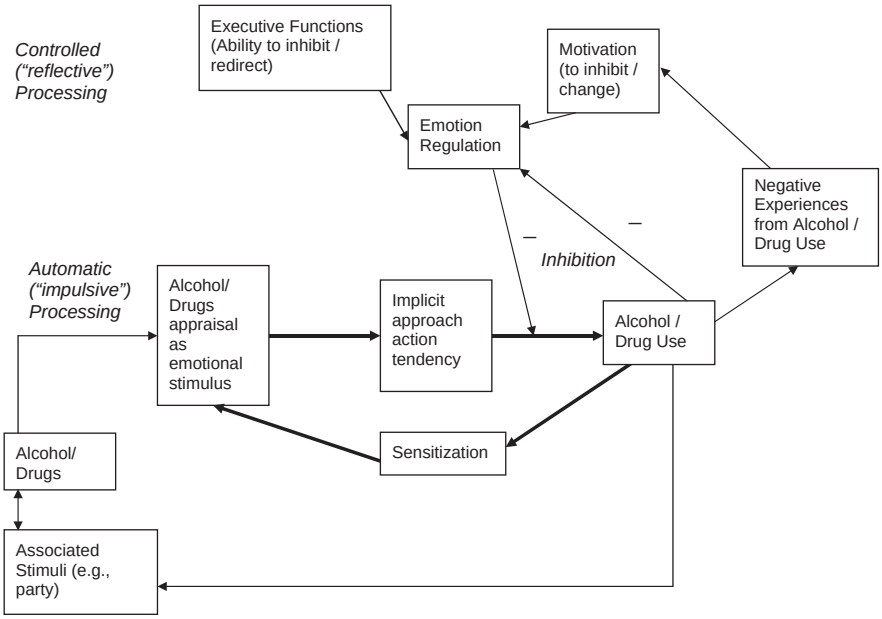


Figure 1. Schematic overview of processes involved in the development of substance use disorder. Figure by Wiers & Stacey, 2006.

(formal or informal) that provides support and opportunity for improving everyday functioning" (Bowie et al., 2020). Regarding cognitive remediation in the context of psychopathology, most of the available literature focuses on programs for patients with schizophrenia and mood disorders (Kim et al., 2018; Thérond et al., 2021). CR can encompass different methods such as psych-education, drill-and-practice and strategy-based interventions (Best & Bowie, 2017; Bowie et al., 2020). In many protocols, multiple methods are applied, and their effects have been shown to be associated with alterations in brain networks (Penadés et al., 2017).

Restorative Cognitive Training. Restorative Cognitive Training (RCTr) is a drill-and-practice computerised method to improve (restore) the cognitive function itself (Keshavan et al., 2014). This 'bottom-up approach' has so far obtained the best results when integrated in functional or vocational treatment, including therapeutic focus on the development of cognitive strategies in daily life (Cicerone et al., 2019; Hallion et al.,2024). (See for example for application of RCTr in psychotic disorders: Bowie et al., 2012; McGurk et. al 2007; Vita et al., 2021; Wykes et al., 2011; See for AUD Nardo et al., 2024; See for mood disorder: Motter et al., 2016).

Compensatory Cognitive Training. Compensatory Cognitive Training (CCTr), or 'strategy-based training' ('top-down approach'), focuses on the enhancement of coping with cognitive deficits by use of internal or external cognitive strategies. Internal strategies are for example rehearsal of the name of the person you just met, or the visualisation of what you need to remember. Examples of external strategies are setting an alarm or using an agenda, plan- and checkinglist). These strategies do not focus on improving the cognitive function itself. Most CCTr protocols include elements of psycho-education as well.

CCTr has yielded lasting results on daily functioning and well-being in severe mental illness and is related to decreased drop-out rates in substance use disorder (Allott et al., 2020; Rezapour et al., 2019; Twamley et al., 2019). There is even some evidence suggesting that this strategy-based approach may improve working memory function (Rezapour et al., 2019; Twamley et al., 2019). How this effect is established is not yet understood. Strategy use may be related to restoration of brain function by neuroplasticity (Eack et al., 2010; Penadés et al., 2013). Another hypothesis is that improved strategy use and/or working memory function enables one to engage with, and mitigate the stress caused by, cognitively challenging daily tasks. For further reference, see the combined study on Goal Management Training and mindfulness meditation in SUD by Valls-Serrano et al., 2016). Since stress / stress-vulnerability are key factors in the risk and maintenance of psychopathology (Ingram & Luxton, 2005), this rationale may help explain the effects of CCTr.

Cognitive Bias Modification

Cognitive Bias Modification (CBM) was developed based on the assumption that (the interaction between) two different cognitive processes enable adaptive behaviour: An associative, slow-learning or 'impulsive' system supporting effortless processing and a rule-based, effortful and 'reflective' system (Smith & DeCoster, 2000; Strack & Deutsch, 2004). These dual process theories provide a rationale for the understanding of the origins of cognitive biases and their relation with difficulties of controlling for these biases, especially in the presence of cognitive impairment. Directly intervening on the associative system by targeting the automatic, implicit, level of information processing (such as approach-avoidance tendencies) by means of cognitive bias modification is of interest as this intervention type complements traditional treatment strategies (Stacey & Wiers, 2010).

In the domain of alcohol-approach bias, one of the first studies by Wiers et al. (2011) demonstrated that retraining alcohol-approach tendencies could significantly influence alcohol consumption. Also, significant results have been yielded by (replicated) randomised-controlled studies involving clinical populations with AUD. These studies showed that alcohol-avoidance training as an add-on intervention in the treatment of AUD is associated with reduced relapse rates (Eberl et al., 2013; Manning et al., 2016; Rinck et al., 2018; Wiers et al., 2011). As this intervention is cost-efficient, scalable and relatively easy to implement, it holds considerable promise for prevention and treatment strategies in clinical settings (Baert et al., 2011).

To retrain alcohol-approach tendencies, interventions such as the Alcohol Avoidance Training (AATr) have been developed. The AATr, which is used in experiments included in the studies described in this thesis, is a computerised joystick task (Rinck & Becker, 2007). The participant is presented with pictures of either alcohol or soda drinks and while pushing or pulling the joystick lever, a zoom effect is present. The pictures get bigger by pulling or smaller by pushing, mimicking the approach or avoidance of the actor towards or away from the stimulus. The participant receives an indirect instruction as they are instructed to either push or pull, according to the slightly skewed picture(pull the left tilted picture, push the right tilted picture). This procedure creates both a test phase and a training phase. In the brief test phase, the contingency is psychopathology-congruent: participants are instructed to approach alcohol by pulling the lever and to push soda drinks away. Next, in the training phase psychopathology-incongruent movement-stimuli pairs are presented: Alcohol stimuli are paired with avoidance movement (pushing the lever) and soda drinks with approach movement (pulling the lever). After the training phase the test phase is repeated to measure the alcohol-approach bias and its modification.

Classification of Cognitive Interventions

As discussed before, cognitive interventions are promising in the treatment of psychopathological conditions and alcohol use disorders. However, the understanding of their working mechanisms and effects on functional outcome or relapse prevention can be improved (Hallion et al., 2024; Nardo et al., 2022, Spruyt et al., 2025). A closer examination of the characteristics of cognitive interventions could help to improve the understanding of their mechanisms of change and, consequently, improve clinical outcomes. A classic way to classify these interventions is along the bottom-up / top-down axis. By means of the bottom-up approach, the cognitive deficiency or distortion itself is addressed with the aim to be restored or modified. By means of the top-down approach, individuals learn how to cope with the neurocognitive deficit, rather than targeting the deficit itself as a direct treatment goal.

Braunstein and colleagues (2017) provided a theoretical framework to classify emotion regulation interventions into four classes, by means of two axis: The implicit-explicit axis of *the nature of the emotion regulation goal* and the automatic-controlled axis of *the nature of change process*. This framework aligns with the memory system of implicit and explicit memory systems (Schacter & Tulving, 1994; Squire 2004), and as it draws on a neuropsychological perspective, this approach could also be applied to the classification of cognitive interventions. By means of this framework, the cognitive goal of regulation and the nature of change of the cognitive intervention can be disentangled and studied.

First, with regard to RCTr the change process may be relatively more automatic, given its drill-and-practice procedure, and the fact that progress typically occurs without the individual's awareness. However, it can also be argued that the nature of the change process is more explicit in nature, since this approach is often combined with cognitive strategy training in daily living to improve generalisation (Vita et al., 2021). The regulation goal is explicit, as improving cognitive function is clearly stated in both the instructions and the treatment objectives.

Second, CCTr can be considered an explicit, controlled type of intervention type. The goal to compensate for cognitive deficits is explicit in nature, and the nature of the change process is controlled; the participant is well aware of the process, results pend on motivation, willingness to change and skills to apply and practice with cognitive strategies in daily life. Some CCTr's use elements of errorless learning procedures. In that case the intervention may fit the explicit-automatic intervention type, since the nature of the change process is based on implicit learning, while the goal is clear (e.g. improve a self-care procedure) (Rensen et al., 2019; Allott et al., 2020).

With regard to the AATr, it is hypothesised that the nature of change is automatic, since an indirect instruction has been given. Moreover, no illness-insight is needed to execute the training task, and the participant can not be aware of the presence of or change in bias. On a neural level, action-bias modification is associated with reduced salience of alcohol cues, reflected in decreased amygdala reactivity. This attenuation of cue-reactivity indicates that the intervention engages bottom-up mechanisms (Wiers & Wiers, 2017). So the nature of change process is considered to be automatic and the nature of the regulation goal implicit. As the task execution relies on a single response option (the picture does not disappear until the correct movement has been made), and involves a simple repetitive action, the AATr does not rely on higher order functioning. With these characteristics, the AATr matches the preserved implicit memory function of patients with ARNI and KS and their ability to benefit from procedural learning (Hayes et al., 2012; Kessels & Kopelman, 2012) .

Fig. 2 illustrates the cognitive interventions mentioned above, organised according to Braunstein's framework.

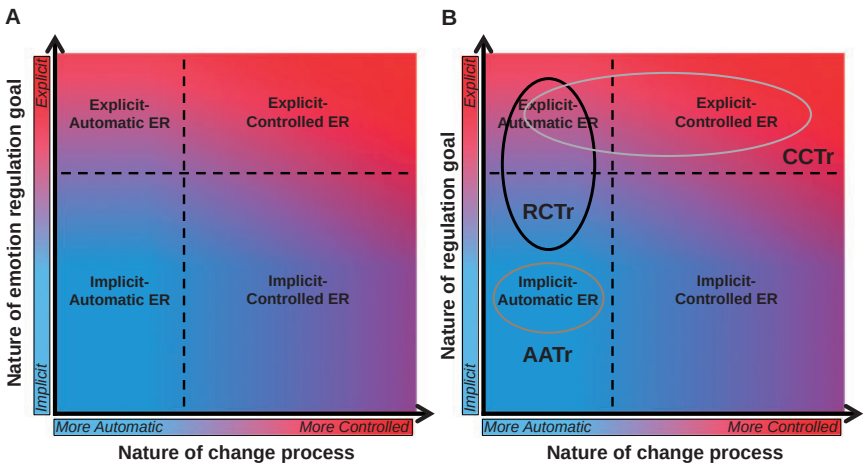


Figure 2. Classification of cognitive interventions using the multi-level framework from Braunstein et al., 2017.

Note: The brown circle represents the classification of the AATr based on the nature of the regulation goal and the nature of the change process. The black circle represents the classification of RCTr and the grey line represents CCTr.

Cognitive Intervention in Specialised Mental Health Care

The importance of implementation of effective remediation of neurocognitive deficits in clinical practice is emphasised by several research groups (Allott et al., 2025; Maurage et al., 2024; Trapp et al., 2022; Wong et al., 2024; Wykes et al, 2024) as well as for CBM (Baert et al., 2011; Vrijsen et al., 2024). In the understanding and treatment of AUD it is has been suggested to address several cognitive systems, from cognitive bias to higher-order cognitive functioning (Kwako et al., 2016; Verdejo-Garcia et. al, 2023). This neuroscientific approach could improve integrative as well as personalised treatment and is particularly relevant for the patient populations with ARNI and KS (Lohoff, 2022).

The need for large scale implementation of cognitive interventions is evident given the profound role of cognitive deficiencies in psychopathology. However, cognitive interventions are not consequently included in treatment guidelines as its inclusion in guidelines differs between countries and between specific mental illness classifications. Moreover, evidence-based protocols remain scarce in clinical practice, and further research is needed to establish their cost-effectiveness (Maurage et al. 2024; Vrijsen et al., 2024; Wong et al., 2024; Wykes et al., 2024; Wykes, 2025). Additionally, theoretical issue remain and hinder large-scale implementation. As for computerised interventions, such as the drill-and-practice methods used in RCTr and the AATr, generalisation of effects on a functional level remain limited (Hallion et al., 2024; Harvey et al., 2018; Kim et al., 2018; Boffo et al., 2019). With regard to the AATr, the theoretical focus on the associative account of the intervention leaves little room for individual differences and contextual factors that shape the complex behavioural responses to the emotional valence of stimuli in the real-world (Cousijn et al., 2014; Watson et al., 2022; Wiers et al., 2020). For CCTr, moderate effect sizes for functional outcome in severe mental illness have been established. However, *how* these effects are established have sparsely been studied yet. The relations between objective and subjective cognitive functioning and CCTr effects on proactive coping, self-efficacy need further elaboration (Allott et al., 2025).

In general, several questions regarding cognitive interventions remain unanswered, such as: how do they work, for whom are they effective, and how can training effects be transferred to functional outcomes? Nonetheless, improved management of altered cognitive information processing in the treatment of mental health disorders may contribute to improved treatment outcome, well-being and cognitive health.

Thesis outline

This thesis examines approach-avoidance behaviour in psychopathology and explores the feasibility of cognitive interventions in a neuropsychiatric patient population. The findings provide theoretical insights and inform clinical practice regarding the applicability of cognitive interventions for individuals with cognitive deficits, in particular for patients with ARNI or KS. Alcohol-approach bias modification has not yet been studied and applied before in a patient population with (major) neurocognitive disorders. The match between the AATr task characteristics and the preserved ability of implicit learning in ARNI and KS provides a unique context for research from both a clinical and a theoretical perspective. This intervention type may complement compensatory cognitive interventions for individuals with of cognitive impairment or problems.

First, a systematic review (**Chapter 2**) on the assessment and modification of (biased) approach-avoidance (AA) behaviour across various categories of psychopathology is presented. In addition to the findings on the clinical relevance of AA behaviour and its modification effects, study designs as well as methodological and statistical aspects were reviewed. This critical evaluation will contribute to both future research on AA behaviour in psychopathology as well as to the refinement of assessment and modification protocols in clinical practice.

Next, to address the need for improved treatment options for patients with neurocognitive deficiencies associated with psychopathology, the applicability of the newly developed CCTr 'Master Mind' was explored in a population with (severe) mental illness and associated neurocognitive deficiencies, with a particular focus on the relationship between (self-reported) proactive behaviour, daily satisfaction and cognitive processing capacities (**Chapter 3**).

If, as argued above, compensatory cognitive training is considered to be an explicit-controlled intervention, CBM is an interesting route of intervention since it is hypothesised that the regulation goal (cognitive bias) is implicit in nature, and the nature of change is automatic. AATr task characteristics, a variant of CBM, match with the intact implicit memory capacity of patients with ARNI and KS and their potential to benefit from procedural learning (Hayes et al., 2012). Taken together with previously reported findings on reduced relapse relates in the AUD population without neurocognitive impairment, AATr may also hold promise for patients with AUD with neurocognitive disorders. Therefore, in the next chapter the applicability of AATr in this specific patient population was studied (**Chapter 4**). To improve the understanding of the relationship between the AATr implicit tasks characteristics, mechanism of change and declarative memory function, a second study was conducted in the same patient population, examining the relationship between declarative memory function and bias reduction within AATr sessions

(**Chapter 5**). In the final chapter (**Chapter 6**), a summary of the findings will be provided along with a discussion of the theoretical and clinical impact of these findings, including a critical reflection on the strengths and limitations of the studies. Finally, recommendations for clinical practice and future research are provided.


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BIASED APPROACH-AVOIDANCE TENDENCIES IN PSYCHOPATHOLOGY: A SYSTEMATIC REVIEW OF THEIR ASSESSMENT AND MODIFICATION

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Abstract

We systematically review the literature on approach-avoidance (AA) tendencies in mental disorders, including 97 empirical studies. Most evidence for the role of biased AA tendencies was found in addictive disorders: The presence of an approach bias (ApB) for substance related stimuli in subclinical populations can be a risk factor for increased future substance use, and AA modification training given as an add-on to standard treatment has the potential to reduce intake and relapse rates reliably. In depression, reduced approach of positive stimuli and reduced avoidance of negative stimuli have been found, and modification procedures seem to have clinical potential. In anxiety disorders, an avoidance bias (AvB) for threat-related stimuli has been found frequently, but modification studies did not yield any clinical effects. In eating disorder a lack of food preferences in anorexia nervosa may be present, but relations between AA measures and clinical (outcome) measures were not established. In other disorders, the evidence was limited due to a low number of published studies. Several methodological problems are discussed: It is often difficult to compare studies to each other, control groups and control stimuli are frequently missing, and many studies suffer from insufficient statistical power due to small samples. We finally give suggestions for future research on biased AA tendencies in psychopathology.

Introduction

Approaching pleasant, positive stimuli and avoiding unpleasant, negative ones is a core element of adaptive behavior in response to important, emotionally valenced stimuli (Frijda, 1986). These action tendencies are seen as the result of two behavioral systems: The *positive* and the *negative* valence system (Lang, 1995). The positive valence system instigates approach responses to rewarding and generally positive information, whereas the negative valence system drives avoidance of aversive and generally negative information. The approach-avoidance mechanism is considered to be the core element of motivation and behavioral orientation (Elliot 2006), emphasizing the need to understand how approach-avoidance behavior originates, and how it is associated with adaptive and maladaptive human behavior.

Approach-avoidance behavior is usually seen as the result of a complex interaction of implicit and explicit information processing (Metcalfe & Mischel, 1999; Strack & Deutsch, 2004). The explicit information processing route is characterized by deliberate and reflective reasoning, it requires effort and is relatively slow. This processing system is thought to be related to functions of cognitive control and to depend on cortical frontal brain regions. On the other hand, the implicit route involves emotion-driven, fast processing of information, and it is associated with subcortical structures involved in affect processing, such as the amygdala and the ventral striatum (Ochsner & Gross, 2005; Wager, Davidson, Hughes, Lindquist, & Ochsner, 2008). A balanced and continued interaction of these two systems results in flexible and adaptive social-emotional behavior, including functional approach-avoidance (Parsons, Kruijt & Fox, 2016).

However, the attribution of valence to specific cues can be biased, and this can disrupt the balance between the explicit and the implicit system. A biased attribution of positive or negative valence to specific cues can be the result of personal factors such as learning history, traumata, or genetic predisposition. It can also be driven by characteristics of the stimuli, as in increased appetitive features of drugs and high-calorie foods, or in an increased threat value of potentially dangerous stimuli such as snakes and spiders. The increased valence then enhances fast implicit processing, which facilitates, for instance, automatic approach of attractive drugs or automatic avoidance of perceived threat. The explicit cognitive control system is supposed to regulate this in favor of adaptive behavior. However, the quality of explicit control can be diminished as well, due to impaired executive functioning (Snyder, Miyake, & Hankin, 2015), cognitive depletion (Hagger, Wood, Stiff, & Chatzisarantis, 2010; Hofmann, Gschwendner, Friese, Wiers, & Schmitt, 2008), or elevated symptom levels which decrease processing effectivity (Eysenck, Derakshan, Santos & Calvo, 2007). As a result of

the disbalance between implicit and explicit processes, biased approach-avoidance behavior patterns can occur, which are considered to be a risk factor for the development and maintenance of psychopathology (Fox & Beevers, 2016; Mathews & MacLeod, 2005; Marteau, Hollands & Fletcher, 2012).

In fact, dysfunctional approach-avoidance tendencies have been implicated in various mental disorders. For instance, in the case of anxiety disorders, Ouimet, Gawronski and Dozois (2009) proposed a multi-process model of cognitive vulnerability. According to this model, stimuli can elicit threat-related associations and thereby drive attentional engagement with the fear-provoking stimulus as well as behavioral avoidance of it. For example, socially anxious individuals will associate social encounters with being negatively evaluated by others, and therefore try to avoid social interactions. This avoidance can even extend to friendly smiling faces because they also carry the threat of evaluation (Horley, Williams, Gonsalvez & Gordon, 2004). This avoidance of potentially positive social feedback contributes to the maintenance of fear-related associations and obstructs corrective positive social experiences. As another example, depressive patients often show diminished approach tendencies. This is related to neurobiological correlates of depression, and it is thought to contribute to and maintain depressive symptomatology, as these patterns facilitate loss of reinforcement and social support (Trew, 2011).

Finally, in substance use disorders, a disbalanced interaction of implicit and explicit processing is thought to result in a response conflict. For example, in alcohol use disorder, as a result of the toxic effect of alcohol, the explicit control function (executive functioning) is impaired and the brain reward system is sensitized, resulting in enhanced influence of implicit processes on behavior in response to substance-related cues (Robinson & Berridge, 2008). This may lead to automatic approach of substance-related cues and consumption of the substance, even when one is well aware of its harmful health effects and explicitly intends to avoid it (Bechara, 2005; Field, Kiernan, Eastwood, & Child, 2008; Wiers, Gladwin, Hofmann, Salemink, & Ridderinkhof, 2013).

Given the proposed causal role of biased approach-avoidance (AA) behavior in the development and maintenance of mental disorders, the amount of experimental research on AA patterns in clinical populations has grown exponentially during the past fifteen years. However, the empirical evidence is scattered, and as far as we know, there is no systematic review of the available research on AA tendencies in psychopathology, addressing various forms of psychopathology. This in contrast to the closely related fields of attention bias and interpretation bias and their relevance for psychopathology. For these processes, the number of published reviews is striking, especially when compared to the AA literature (see Jones & Sharpe, 2017, for a review of meta-analyses). There are also a few reviews of

research on related aspects of AA tendencies (Kakoschke, Kemps, & Tiggemann, 2017; Roefs et al., 2011; Wiers et al., 2013; Wiers & Jansen, 2011), but these focus either on a single type of psychopathology, address modification studies only (excluding assessment studies), or they are not exclusive to approach-avoidance behavior. Therefore, we aim to provide a comprehensive overview of the available clinical research on AA behavior, addressing both the assessment and the modification of AA tendencies in various subclinical and clinical populations. The first goal of this review is to summarize the most important empirical findings regarding biased AA tendencies in various mental disorders. The second goal is to critically evaluate the designs and paradigms used in this domain, and to point out strengths, shortcomings and problems. Finally, we hope that the information provided here will be helpful for designing future studies of AA tendencies in psychopathology.

Since this review is focused on the relation between AA tendencies and psychopathology, only studies that included participants with subclinical or clinical levels of psychopathology were included. The level of symptom severity had to be defined a-priori and used as an inclusion criterion for selecting participants. Studies in which diagnostic groups were defined post-hoc (usually based on questionnaire scores) were excluded because this runs the risk of insufficient discrimination in symptom severity between clinical groups and control groups. Moreover, non-clinical samples have shown qualitatively different cognitive biases (including AA tendencies) from individuals with (sub-)clinical levels of symptomatology (Fox & Beevers, 2016; Koster & Bernstein, 2015; Vrijsen, van Oostrom, Speckens, Becker, & Rinck, 2013).

The studies contained in this review vary considerably in design, and they can be classified into three categories. The majority of studies are assessment studies (henceforth called 'Type 1' studies) which compared the AA tendencies of a (sub-) clinical group to a control group. In contrast, the 'Type 2' studies reviewed here involve AA tendencies as an outcome measure after an experimental intervention which intended to manipulate AA tendencies only indirectly or used AA tendencies primarily to predict clinical outcome. These studies provide insights into how AA tendencies can be affected (e.g., by treatment, mood induction, or intoxication), and they inform us about possible mechanisms of change. Finally, 'Type 3' studies involve the direct modification of AA tendencies. These studies employ modified versions of AA tasks, turning them from assessment paradigms into so-called Cognitive Bias Modification (CBM) paradigms. The direct modification of AA tendencies is seen as a clinical intervention, expected to reduce biases in AA tendencies and consequently, clinical symptoms. Differentiating between different study types is important because failure to do so leads to over-generalized conclusions (for an example, see Cristea, Kok, & Cuijpers, 2016), as pointed out by Wiers, Boffo, and Field (2018).

We also address design and other methodological and statistical aspects of the reviewed studies, because all of these influence the research outcomes and the conclusions that can be drawn from them (Christiansen, Schoenmakers & Field, 2015; Grafton, MacLeod, Rudaizky, Holmes, Salemink, Fox, & Notebaert, 2017; Rinck, 2017). Given the limited overlap of the available studies in goals, designs, populations, AA tasks, and clinical outcome variables, a meta-analysis was not feasible. We therefore decided to perform a systematic review, describing the available evidence with regard to the characteristics of AA tendencies in mental disorders. We hope that the implications of this review will facilitate the refinement of AA assessment and intervention protocols, and we will suggest aims for future research.

Methods

Inclusion Criteria

We used the following set of criteria for studies to be included in this review:
(1) Studies with adolescent and adult samples with subclinical or clinical levels of psychiatric symptomatology; (2) symptomatology had to be assessed with a validated or *best-practice* (semi)structured interview or self-report questionnaire, and when participants were recruited from the general population, a-priori conditions for (sub)clinical symptom severity had to be set. Post-hoc classifications of subclinical groups after inclusion were not included. An exception was made for papers involving nicotine and cannabis dependence: Studies on smokers from the general population were allowed because we assumed that respondents who consider themselves (cannabis) smokers will meet at least the criteria for a subclinical level of dependence. In alcohol use disorder, an exception was made for initial inclusion based on intake levels above the amount advised as 'safe' by health care services and indicating at least hazardous drinking levels. Samples were defined as *clinical* when participants were in treatment at the time of research, met DSM-IV/V criteria (American Psychiatric Association, 2010; 2013) and/or met pre-defined and validated clinical symptom levels based on self-report questionnaires. (3) Only computerized AA tasks with pictorial stimuli and recorded reaction times were included, whereas studies using a Behavioral Approach Task (BAT) did not qualify. Furthermore, since this review is focused on the clinical relevance and application of AA assessment and modification tasks in psychopathology, we excluded studies with a different research question and therefore different outcomes measures. For instance, the study by Eberl, Wiers, Pawelczack, Rinck, Becker, and Lindenmeyer (2014) was excluded because it did not address the modification of AA tendencies per se, but the variables that predict learning effects in an AA modification task. Additional selection criteria were:

Studies had to present original data (no abstracts, reviews, conference proceedings, research protocols, or dissertations not published in peer-reviewed journals), they had to be written in English, and papers had to be available online in peer-reviewed scientific journals.

Search Methods

Studies were collected through a systematic search in the PubMed and PsychINFO databases, including papers published until May 10, 2019. We used the search terms "approach avoid*", ''approach avoidance AND task OR behavior OR bias OR conflict'', "action tendency", "approach bias", "avoidance bias", "cognitive bias", ''approach behavior'' AND ''psychopathology'' (in any possible combination with various mental disorders).

Articles were selected according to the PRISMA guidelines (Moher, Liberati, Tetzlaff & Altman, 2009), and duplications were removed from the database. Next, two authors (AL, JV) made independent selections based on article title. Then all to-be-included articles were again separately assessed for eligibility by the two authors on abstract information, and then on full text, if information in the abstract was not sufficient for a decision. The final inclusion was made based on consensus between the two authors. In the case of a discrepancy in judgement between the two authors, a third author (MR) was consulted, and based on consensus, a decision was made. Next, search results were compared to eligible articles already known by the authors, and the references of all included articles were screened, to include additional articles if they fitted the inclusion criteria.

Data Abstraction and Analysis

Author AL abstracted the data following a coding system and compiled the evidence table based on the defined aspects of interest. Authors JV and MR checked the data of the evidence table. The following variables were abstracted from each included article: (1) Authors; (2) study type (including number of sessions in Type 3 studies); (3) included groups and number of participants defined as the number finally available for data analyses; (4) symptom severity (name of the psychopathology questionnaire, mean and standard deviation, and/or DSM classification); (5) characteristics of the control group, including information on whether it was matched to the clinical group in assessment studies or whether randomization was applied in intervention studies; (6) duration of abstinence, if relevant; (7) characteristics of the AA assessment task (manikin or joystick, relevant-feature or irrelevant-feature instructions, type of stimuli, and other specific features; (8) (clinical) outcome measures: presence and characteristics of AA tendencies and correlation between AA measures and psychopathology characteristics if available (e.g., symptom severity, illness duration, craving). In the evidence table, the

selected studies are structured by psychopathology classification according to the DSM, and next according to study types.

Approach-Avoidance paradigms

Two computerized paradigms have been used most frequently to assess AA tendencies. The first is a manikin task, usually called 'Stimulus-Response Compatibility Task' (SRC; De Houwer, Crombez, Baeyens, & Hermans, 2001). In this task, the participant is asked to move a small manikin on a computer screen either towards a centrally located target picture (simulating approach) or away from the picture (simulating avoidance). This is achieved by pressing the arrow keys on a keyboard or separate button box. The time from the simultaneous appearance of manikin and picture to the key press is used as the dependent variable of interest. AA tendencies are usually reported as reaction time (RT) differences between approaching versus avoiding each stimulus category, and relative tendencies are computed as so-called compatibility effects. These represent the RT difference between so-called compatible stimulus-response combinations (approach-positive and avoid-negative) and incompatible ones (approach-negative and avoid-positive), although studies vary in what is defined as compatible vs. incompatible.

The second frequently used paradigm is a computerized joystick task, the so-called 'Approach-Avoidance Task' (AAT; Rinck & Becker, 2007). It uses comparable computations for approach-avoidance tendencies and compatibility effects, but here participants respond to single pictures on a computer screen by moving a joystick towards themselves (by flexing the arm as if pulling the stimulus closer, simulating approach) or away from themselves (by stretching the arm as if pushing the stimulus away, simulating avoidance). The movement is usually combined with visual feedback involving a dynamic zoom effect: The picture grows in size when the joystick is pulled, and it shrinks when the joystick is pushed. This strengthens the subjective impression of pulling the picture closer versus pushing it away by means of pulling versus pushing the joystick. The zoom effect is intended to prevent re-categorizing of the joystick movements (Krieglmeyer & Deutsch, 2010; Phaf, Mohr, Rotteveel, & Wicherts, 2014) and to improve the validity of the measurement of approach-avoidance tendencies (Rinck & Becker, 2007).

For both the SRC and the AAT, instructions can be given in two different ways. First, the instructions can make the contents and/or the valence of the stimuli task-relevant, for instance by instructing participants to approach spider pictures and avoid butterflies (or vice versa). This task version is often referred to as a "relevant-feature task", and although the name is somewhat ambiguous, we will used the term as well. Second, the instructions can render stimulus contents and valence task-irrelevant by asking participants to respond to some unrelated

feature of the stimuli, for instance the format (landscape or portrait) or the tilt (slightly left-tilted or right-tilted). This is often called an "irrelevant-feature task", and we will also use this name.

Importantly, both paradigms can be used with both instructions for the assessment as well as for the modification of AA tendencies. The difference between assessment and modification lies solely in the contingency of stimuli and responses: In assessment task versions, all stimuli have to be approached and avoided with equal frequency. In modification tasks, however, some stimuli have to be approached (almost) all the time, while others have to be avoided (almost) all the time. This has been done most often with irrelevant-feature versions of the AAT. For instance, in the first study of this kind, Wiers, Rinck, Kordts, Houben, and Strack (2010) presented pictures of alcoholic vs. non-alcoholic drinks in landscape or portrait format, and all participants had to pull one format closer while pushing the other format away. Here, format was not independent of contents: The to-be-avoided beverage type was shown 90% of the time in the to-be-pushed format, while the to-be-approached beverage type was shown 90% of the time in the to-be-pulled format. In modification paradigms like this (the Type 3 studies below), the control versions of the training and the number of training sessions differ considerably between studies, the latter ranging from a single session to 12 sessions. Typically, before and after the modification procedure (or at the start of each session), an assessment version of the task is applied as a manipulation check.

Results

Results of the Search

Our search yielded 2028 studies that were screened on title. Thirteen additional studies known by the final author were added, and 9 studies were found when checking references. In total, 167 articles were screened full-text on the inclusion criteria (see Figure 1). The included studies covered 17 DSM-IV classifications and a total of 97 studies (see Table 1). In addition, we searched for studies including children, given the postulated role of AA in the development of psychopathology. However, we found a single study only: Deckers, Roelofs, Muris, and Rinck (2014) assessed AA tendencies in children with autism. Therefore, we restrict ourselves to findings in adolescent and adult samples. We will first discuss the disorders for which we found the largest number of studies, namely substance-related disorders.

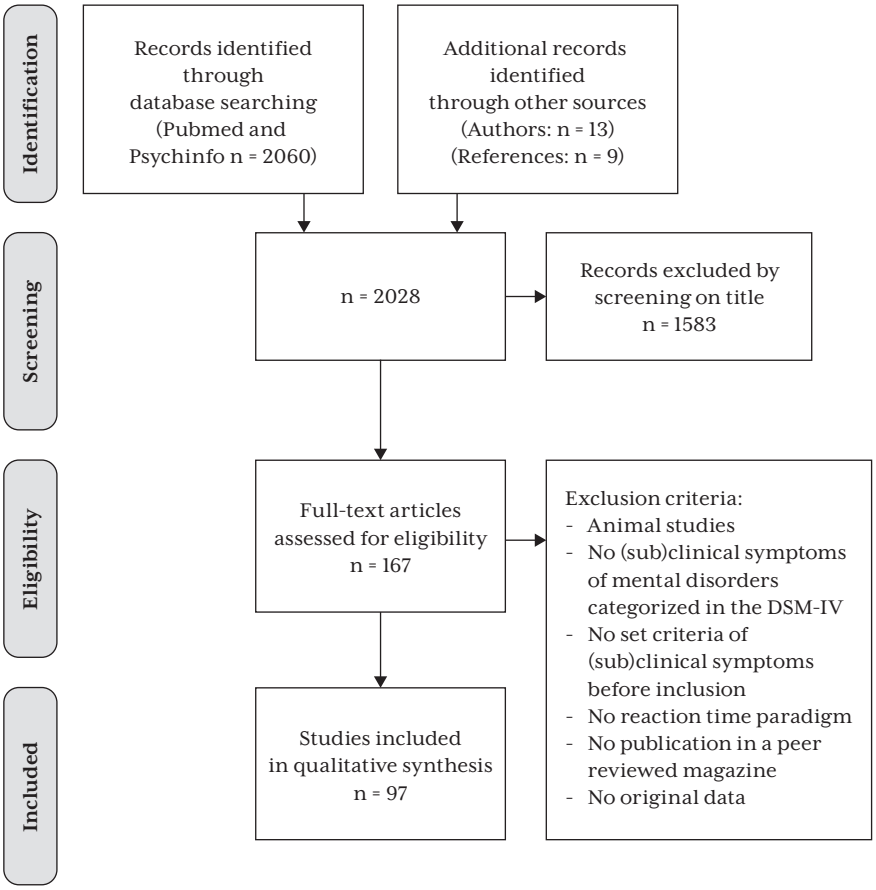


Figure 1. Flowchart.

Substance-Related Disorders

Nicotine Use Disorder (NUD). In most of the 16 studies (7 of which were Type 1 studies), an initial approach bias (ApB; faster approach than avoidance) for smoking-related stimuli was found in smokers. Moreover, even unpleasant smoking-related stimuli (e.g., ashtrays) were approached by smokers, whereas non-smokers did not show an approach tendency for smoking-related stimuli (Bradley et al., 2008). However, the ApB may be stronger in low-dependency smokers than in moderate dependency (Mogg et al., 2005; Watson et al., 2012; but see Elfeddali et al., 2016, for contrasting results). The relation between dependence and bias strength is possibly mediated by genetic vulnerability for a decreased

natural reward reactivity, due to decreased dopaminergic activity (Zlomuzica et al., 2018).

The studies in this area illustrate the importance of reporting which stimuli were used in the computation of AA bias scores, in order to improve the interpretability of individual study results and the comparability of study outcomes. For example, in the study by Machulska and colleagues (2015), the non-clinical control group showed an ApB towards smoking pictures relative to tooth-brushing pictures, but not relative to food pictures or neutral pictures. In contrast, the moderately-dependent smokers showed an ApB for smoking-related stimuli relative to all other picture types.

Next, a positive relation between urge or craving measures and ApB was present in studies using the AAT (Watson et al., 2012; Wiers, Kühn et al., 2013;). Bradley et al. (2008) did not find this correlation between urge and ApB using the SRC, which may be due to the fact that stimulus contents was task-relevant in this SRC version, while it was task-irrelevant in the two AAT studies. Thus, the study by Bradley may have tapped into more controlled responses than the other studies. Another variable affecting the presence of urge-bias correlations may be the time between the AA task and the last cigarette use. This interval was longest in the study by Bradley et al. (2008). Several studies suggest a state-dependence of ApB for smoking-related stimuli, and the ApB was shown to diminish over time after smoking cessation (C. Wiers et al., 2013).

Moreover, it was found that the AA bias for smoking-related stimuli was sensitive to priming effects. According to two included Type 2 studies (using AA tendencies as a dependent variable) just thinking of smoking a cigarette may increase the ApB: When instructed to pay attention to possible consent to smoke, or when actual smoking was allowed, the ApB increased in very-low-dependent and low-dependent samples (Thewissen et al., 2007; Watson et al., 2012). These priming effects are clinically relevant because an increased approach bias may lower the threshold for smoking.

Table 1. Characteristics of included studies, ordered by DSM-IV classification

	Authors (year)	Study type[a]	N[b]	Symptom severity[c]	Control group[d]	Duration of abstinence[e]
1	Amnestic disorders					
1.1	Loijen et al. (2018)	3 (six sessions)	46 mild neurocognitive disorder 39 major neurocognitive disorder	DSM-5 criteria for alcohol- induced neurocognitive disorder. DSM-5 criteria of alcohol dependence	X	E
	Substance-related disorders					
2	Nicotine use disorder					
2.1	Mogg et al. (2003)	1	18 smokers 21non-smokers	FTND 4.5 (0)	B	B
2.2	Bradley et al. (2004)	1	20 smokers 18 non-smokers	FTND 3.5 (1.6)	C	A
2.3	Mogg et al. (2005)	1	19 low dependence 22 moderate dependence	Moderate dependence FTND median > 3 mFTQ 4.05(1.5) (2.0 (0.0))	D	B
2.4	Bradley et al. (2008)	1	22 smokers 23 non-smokers	FTND 3.1 (1.4)	B	C
2.5	Wiers, C. et al. (2013)	1	24 smokers 20ex-smokers 20 non smokers	FTND 5.08 (1.18), (4(1.41))	A	B
2.6	Machulska et al. (2015)	1	90 smokers 49 non-smokers	FTND 3.38(2.3)	D	A
2.7	Elfeddali et al. (2016)	1	434 smokers	FTND 4.30 (2.33	X	X
2.8	Thewissen et al. (2007)	2 (SRC before and after 8 trials of consent to smoke or smoking routine without puff)	38 smokers	FTND 2.41 (1.89)	N/A	B
2.9	Watson et al. (2012)	2 (AAT before and after smoking in pause or non-smoking)	49 smokers	FTND 2.9 (2.1)	G	B/C

	Task and materials[f]	Clinical measures/outcomes
	2, 4, 5 (alcohol/soda drinks)	AvB after training with moderating effect of baseline tendency. AAT effects were related to capacity of implicit memory function and age, not to strength of executive functioning or declarative memory function. Clinical outcome measures N/A.
	1, 3 (smoking-related/ matched control stimuli)	ApB for smoking-related stimuli in smokers and non-smokers. ApB smokers > non-smokers. Corr. with clinical measures N/A.
	1, 3 (smoking-related/ matched control stimuli)	ApB for smokers. No bias present in non-smokers. Corr. with clinical measures N/A.
	1, 3 (smoking-related/ matched control stimuli)	ApB for smoking-related stimuli in low and moderate dependent group. ApB low > moderate dependence, ApB was pos. related to lower N of cig/day.
	1, 3 (smoking-related/ matched control stimuli)	ApB for smokers for unpleasant smoking-related stimuli. ApB in both groups for pleasant smoking-related stimuli. No corr. between ApB and urge, symptom severity, or time of abstinence.
	2, 4, 5 (smoking/neutral stimuli)	ApB smokers > non-smokers/ex-smokers for smoking-related stimuli. Corr. of ApB with urge, not with FTND.
	2, 4, 5 (smoking/natural rewarding/neutral stimuli)	ApB smokers for smoking-related stimuli > all other stimuli. ApB non-smokers smoking-related stimuli > tooth-brush pictures. No diff. between Ap-RT for smokers and non-smokers for nicotine stimuli. Corr. ApB and urge N/A
	Web-based, 1 +3 (smoking/ matched neutral pictures)	Heavy smokers (defined as >15 cig/day) approached smoking-related pictures more quickly than light/moderate smokers.
	1, 3 (smoking-related / matched control stimuli)	ApB in smokers at pretest. General ApB at posttest when consent to smoke, but only when instructed to attennd to the contingency. Corr. between ApB and urge N/A.
	2, 4, 5 (smoking-related/ matched control stimuli)	Higher FTND score on pretest was predictive of a smaller ApB. Corr. of urge and ApB. Smoking increased ApB to smoking-related pictures compared to the deprived group and decreased urge reports.

Table 1. Continued

	Authors (year)	Study type[a]	N[b]	Symptom severity[c]	Control group[d]	Duration of abstinence[e]
2.10	Zlomuzica et al. (2018)*	2 (effect of the Taq1B polymorphism of the DRD2 gene genotype on bias score)	90 smokers 49 non-smokers	FTND 3.4	(D)	(A)
2.11	Kong et al. (2015)	3 (4/5 sessions)	non-treatment seeking adolescents 21 Training +TAU 20 Sham + TAU	mFTQ .2.86 (1.35)	G	D
2.12	Wittekind et al. (2015)	3 (AAT pretest, unknown number of sessions; online training/control condition/ waitlist, AAT post-test after four weeks)	257 smokers: 87 AAT 85 control 85 waitlist 156 completed: 38 sAAT; 33 mAAT	FTND 4.55 (2.52) 4.67 (2.29) 4.89 (2.45)	G	N/A
2.13	Machulska et al. (2016)	3 (5 sessions)	139: 73 training 66 sham training	FTND 5.6-2 (2.10) (5.86 (2.11))	G	N/A
2.14	Baird et al. (2017)	3 (pre- post AAT every training session, four sessions,	52: 28 active CBM 21 sham training	FTND 4.5 (2.6) 4.1 (2.3)	G	N/A
2.15	Wittekind, Lüdecke et al. (2019)	3	149 smokers: 49 active training 49 sham training 49 waitlist condition	FTND+CDS-12 4.2 (2.5)+ 44.4 (7.8) 4.1 (2.6)+ 45.1 (7.1) 4.4 (2.9)+ 44.6 (8.2) FTND	A	N/A
2.16	Wittekind, Reibert et al. (2019)	3	105 smokers: 54 active training+TAU 51 sham training+TAU	5.4 (2.1) 5.7 (1.8)	A	N/A

Task and materials[f]	Clinical measures/outcomes
2,4,5 (smoking-related/ matched control/natural reward/matched neutral pictures)	In carriers of the B1 allele: Smokers showed ApB for smoking-related stimuli, and reduced approach of food-related pictures compared to non-smokers. This group also reported fewer stopping attempts thsn smokers homozygous for the B2 allele.
2, 4, 5 (smoking/matched neutral stimuli)	No difference in ApB modification between sham and training group. Participants with baseline ApB showed decreased ApB after training regardless of condition.
2 (computer mouse), 4, 5. Standard AAT/modified AAT with RT feedback after each stimulus (smoking/ neutral).	Decrease of N of cig/day and of CDS-12 scores in active standard AAT group (no difference between AAT types). No mediation analyses available.
2, 4, 5 (smoking/matched neutral stimuli)	Initial ApB for smoking in both groups. Decrease in N of cig/day in both groups from pre- to posttest. No mediation effect. Active AAT decreased N of cig/day at FU.
2, 4, 5 (smoking/positive pictures)	AvB in active CBM group after training. Neutral bias in sham training. Baseline ApB was small and not related with clinical measures. Pos. relation between bias reduction and number of days of abstinence after training.
2, 4, 5 (smoking-related/ matched control stimuli)	No change in AvB. On the long term, the conditions did not differ on cigarette consumption or dependence. All groups showed a reduction in cig/day from pre to FU. On the short term, the active training condition > waitlist reduction in cig/day. No differences on FTND or CDS-12
2, 4, 5 (smoking-related/ matched control stimuli)	No differential AvB change in ITT analyses. Both active and sham condition decreased significantly on cig/day, abstinence, dependence, CO value. No evidence for mediation.

Table 1. Continued

	Authors (year)	Study type[a]	N[b]	Symptom severity[c]	Control group[d]	Duration of abstinence[e]
3	Cannabis Use Disorder (CUD)					
3.1	Field et al. (2006)	1	23 regular cannabis users 26 non-users	C-SDS 9.48(2.27)	B	A
3.2	Cousijn et al. (2011)	1	32 heavy cannabis users 39 non-users	MINICUDIT 12.4(5.8)	A	C
3.3	Cousijn et al. (2012)	1	33 heavy cannabis users 36 low frequent users	CUDIT 12.4 (5.7) (0.0)	A	C
3.4	Cousijn et al. (2015)	1	57 treatment seeking adolescents	CUDIT 21.8 (8.3; 5–39)	N/A	N/A
3.5	Wolf et al. (2016)	1	7 heavy users 6 moderate users	CUDT 16.57(2.14) (10.90(1.52))	A	N/A
3.6	Cousijn et al. (2013)	2 (field study, in coffee shops, pre and post cannabis users were included)	40 pre-user group 44 post-user group	CUDIT Pre-use group: 13.21 (5.23) Post-use group: 14.98 (6.43	N/A Post-user group sign. older than pre-use group	C Pre-user A Post-user
3.7	Jacobus et al. (2018)	3 (pre- post training assessment, six sessions)	non-treatment seeking adolescents 43 training 37 sham	Marijuana Problem Scale, Baseline Training: 5.3 (4.3) Sham: 3.6 (3.3)	G	N/A
3.8	Sherman et al. (2018)	3 (pre- post training plus two week follow-up AA assessment; Four training sessions Experimental/ sham training condition)	39 training : 16 active 17 sham 33 including follow-up	DSM-V criteria CUD	G	C

Task and materials[f]	Clinical measures/outcomes
1, 3 (cannabis/matched neutral stimuli)	ApB for cannabis in cannabis users for cannabis-related stimuli, no comparison with control stimuli.
2, 4, 5 (cannabis/matched neutral stimuli)	ApB for cannabis users for cannabis-related pictures, compared to neutral pictures and control group. ApB was negatively related to craving-related measures, and unrelated to problem severity/level of dependence. ApB at baseline was related to 6-months FU cannabis use.
1, 3 (compatible for fMRI) (cannabis/matched neutral stimuli)	Both groups were faster to approach than avoid cannabis pictures. No comparison with control stimuli. Participants with higher DLPFC/ ACC activity during approach-cannabis trials had lower CUDIT-scores, whereas higher activity during avoid-cannabis trials was associated with increased CUDIT scores after six months. ApB activations in various fronto-limbic areas were more pronounced with increased lifetime cannabis use.
2, 4 ,5 (cannabis/ alcohol/ control (neutral/appetitive)	ApB was not present at baseline and not related with any clinical outcome measures at time of assessment or six month follow-up.
1,3 ; 2, 4	SRC: Heavy cannabis users were faster to approach cannabis than neutral stimuli. Moderate users showed no bias. No corr. of ApB and CUDIT. AAT: No interaction effect, no correlation of ApB and CUDIT.
2, 4, 5 (cannabis/tabacco/ matched neutral stimuli)	Post-use group showed stronger bias for alcohol, tobacco and cannabis, compared to pre-use group. No ApB for intending-to-use heavy user group. Craving was neg. correlated with ApB. No corr. between ApB and satiation/prior cannabis use/response inhibition.
2, 4, 5 (cannabis/ neutral)	No decrease of initial ApB, decrease of 7% at follow-up assessment of cannabis intake during the training, 10% increase of alcohol use.
2,4,5 (cannabis and neutral items)	Baseline ApB for cannabis was present and related to cue-induced craving after training. No training effects were found. Baseline ApB was not related to cannabis use during the training or at FU.

Table 1. Continued

	Authors (year)	Study type[a]	N[b]	Symptom severity[c]	Control group[d]	Duration of abstinence[e]
4	Alcohol Use Disorder (AUD)					
4.1	Wiers, R. et al. (2009)	1 (relation between genotype and AA tendencies)	84 heavy drinking without a g-allele the OPRM1 gene and 23 heavy drinking with at least one g-allele	AUDIT 85%>8, 70%>11 Median 13	E	N/A
4.2	Barkby et al. (2012)	1	61 AUD 64 light drinking	AUD diagnose inpatients LDQ 22.88 (5.66) (0.8 (1.22))	C	D
4.3	van Duijvenbode et al. (2012)	1	57: 19 light AUD 16 moderate AUD 22 high AUD 32 average IQ 16 borderline ID 9 mild ID	AUDIT 2.65(2.18) 10.67(2.80) 22,5 (8.26); IQ 96.35(7.96); 78.14(4.19) 66.43(3.69)	E	B
4.4	Sharbanee et al. (2013)	1	38 problem drinkers 40 non-problem drinkers	AUDIT 17.17(5.07) (3.45 (3.66))	N/A	E
4.5	Spruyt et al. (2013)	1	40 AUD 40 HC	DSM-IV criteria AUD (after clinical detox)	A	D
4.6	Wiers C. et al. (2014)	1	20 AUD 17 HC	AUD (inpatients) AUDIT 27.05 (7.82) 2.82 (1.67)	A	D
4.7	Ernst et al. (2014)	1	21 AUD 21 HC	DSM-IV criteria, AUD (inpatients)	A, HC AUDIT 3.86(2.29):	D
4.8	Snelleman et al. (2015)	1	50	DSM-IV criteria AUD (Outpatients receiving treatment)	A	D

Task and materials[f]	Clinical measures/outcomes
2, 4, 5 (alcohol, matched appetitive/general positive and negative stimuli)	ApB for carriers of g-allele on OPRM1: General ApB for alcohol and appetitive (soft drinks) pictures. Without this genotype, no bias for any picture type.
1, 3 (alcohol/matched neutral stimuli)	No ApB was found. Corr. between individual differences in pretreatment drinking quantity and strength of ApB in AUD group.
2, 4, 5 (alcohol/non-alcohol drinks)	No interaction effect. Neither IQ level or AUD severity was related with AA tendencies.
2, adapted for initial joystick position and response options, 4 (alcohol/non-alcohol drinks)	Sign. Interaction: Group differences for avoid-push trials were present and moderated by WMC: Problem drinkers with lower WMC showed greater ApB than those with higher WMC.
1, 3 (alcohol/matched neutral stimuli)	AvB in AUD group, ApB in control group. AvB was related to relapse measures
2, 4 compatible for fMRI (alcohol/non-alcohol drinks)	fMRI: NAcc/mPFC activated when approaching vs. avoiding alcohol cues, due to soft drink ApB of controls. No corr. with duration of abstinence. Craving correlated with approach activation in amygdala, not with self-reports.
2, 3 compatible for fMRI (alcohol/non-alcohol stimuli)	ApB for alc stimuli in patients, for soft drinks in HCs. Regulatory activity in right dorsolateral prefrontal cortex was stronger during avoiding than approaching alcohol pictures, and during approaching than avoiding nonalcohol pictures.
1, 3 (alcohol/non-alcohol drinks)	AvB present in initial session after 2 weeks abstinence, no difference between groups after 4 weeks. Neither relapse nor time to relapse was predicted by AvB.

Table 1. Continued

	Authors (year)	Study type[a]	N[b]	Symptom severity[c]	Control group[d]	Duration of abstinence[e]
4.9	Wiers, C. et al. (2017)**	1	30 AUD 15 HC	Inpatients DSM-IV criteria AUD	A	A-E
4.10	Schoenmakers et al. (2008)	2 alcohol or placebo drink before AA session	21	Heavy drinkers AUDIT Males 15.6 (5.48). Females 13.9 (5.47).	N/A	< 3 alcoholic drinks the night before each session
4.11	Houben et al. (2012)	2 SRC before and after beer go/no go training	55 heavy drinkers 26 beer go 29 beer no go	:AUDIT 13.97 (2.47)	G (go/no go condition)	N/A
4.12	Cousijn et al. (2014)	2 Emotional priming AAT	65 heavy drinkers 50 occasional drinkers	AUDIT 12.5 (3.9) (4.3 (1.9))	B	N/A
4.13	Mitchell et al. (2016)	2 Pre and post intranasal oxytocin	32	Alcohol abuse AUDIT 19.6 (6.67), DSM-IV criteria alcohol abuse, no physical dependence	G (oxytocin or placebo)	N/A
4.14	Beraha et al. (2018)	2 Mood induction at t1 and t2. Between t1 and t2 four weeks of Baclofen or placebo use	Pretest 138 Posttest Baclofen: 50 Placebo: 40	DSM-IV criteria AUD AUDIT 28.5(5.2)	B (placebo/ baclofen group)	D
4.15	Wiers, R. et al. (2010)	3 (pretest, one training session, alcohol intake, post-test)	41	Heavy drinkers AUDIT >8 pull condition 11.8 (2.6) push condition 14.0 (3.0)	G (pull/push condition)	X
4.16	Wiers, R. et al. (2011)	3 (four sessions)	102 active training 98 sham training	DSM-IV criteria AUD (inpatients) AUDIT 24.(17.7)	G	E
4.17	Eberl et al. (2013)	3 (pretest, 12 training sessions, posttest)	406 pretest 341 posttest	DSM-IV criteria AUD (inpatients)	G (CBM or treatment as usual)	E

Task and materials[f]	Clinical measures/outcomes
2, 4, 5 (alcohol/soft drinks)	No group differences on AAT. Within patient group, ApB correlated positively with attentional bias, but negatively with alcohol-approach associations. No relation with use.
1, 3 (alcohol/matched neutral stimuli)	No interaction effects, main effect of block indicative of ApB for both groups; no specific effect of intoxication. No relation with craving or ApB.
1, 3 (beer-related/ empty glass/neutral stimuli)	Generally faster responses to alcohol pictures than empty glasses in both groups and both conditions, Responses became faster over time.
2, 4, 5 (alcohol/positive negative/appetitive stimuli)	Slower avoidance of alcohol in negative context than in appetitive context in both groups. This effect was negatively related to alcohol-related problems.
2, 4, 5 (alcohol/naturel appetitive/general positive/ general negative stimuli)	No ApB at pre-test for alcohol-related pictures. Initial ApB for appetitive stimuli was present and decreased after oxytocin administration.
2, 4, 5 (alcohol/soda/ negative stimuli)	No ApB at pre-test, no difference in approach-avoidance tendencies between experimental groups using Baclofen or placebo after mood induction.
2, 4, 5 (alcohol/non-alcohol stimuli)	Successfully trained heavy drinkers in push-alc. condition drank less than participants in pull-alc. condition in taste test. Not related to prior urge.
2,3/4 (alcohol/soft drink stimuli)	After active training, the ApB for alcohol changed into an AvB. This effect generalized to untrained stimuli. Less relapse at 1-year FU after active training compared to control groups.
2, 4, 5 (alcohol/soft drink stimuli)	No bias at pretest. AvB for alcohol after active training, not after sham training. ApB for soft drinks in both groups at post-test. Higher abstinence rates after active training at 1-year FU, mediated by training effect. Age and number of previous detoxifications moderated training effects.

Table 1. Continued

	Authors (year)	Study type[a]	N[b]	Symptom severity[c]	Control group[d]	Duration of abstinence[e]
4.18	Rinck et al. (2018)	3 (six sessions)	238 active training 316 sham training 366 no training	DSM-IV criteria AUD (inpatients) AUDIT 24.(17.7)	G	E
4.19	Wiers, C. et al. (2015[b])	3 (six session)	15 active training 17 sham training	Inpatients DSM-IV criteria AUD	G (active/ sham)	D/E
4.20	Lindgren et al. (2015; Study 2)	3 (pretest, two training sessions, post-test, booster training session)	42 active training 42 sham training	At risk drinkers AUDIT > 8 13.74(4.78) (11.56(4.58))	G (experimental/ control)	N/A
4.21	Wiers, R. et al. (2015)	3 (pretest, four online sessions, posttest)	35 action tendency training (ATT) (explicit) ATT implicit 100% alc psuh 33 AAT implicit 90% alc push 24 sham training	Heavy drinkers AUDIT > 8 4 AAT conditions: 18.7/21.1/20.9/21.4 (18.7)	G (see conditions)	N/A
4.22	Wiers, C. et al. (2015[a])***	3 (fMRI AAT pre- post training, six sessions AAT (training/sham))	13 active training 13 sham training	Inpatients DSM-IV criteria AUD	G (active/ sham)/A	D/E
4.23	Manning et al. (2016)	3 (four sessions)	41 experimental training 42 Sham training	Inpatients DSM-5 criteria AUD SADQ-C 32.5 (13.6)	G (exp./sham)	D
4.24	den Uyl et al. (2017)	3 (prestest, four sessions, 1. Active tDCS during experimental CBM 2. Sham tDCS during sham CBM 3. tDCS after CBM, posttest)	1. 30 2. 30 3. 31 (Of AA bias pre-post measures 23% is missing)	Inpatients DSM5 criteria AUD	G (active/sham tDCS	D

Task and materials[f]	Clinical measures/outcomes
2, 4, 5 (alcohol/soft drink stimuli)	Less relapse at 1-year FU after active training compared to both control groups.
2, 4, 5 (alcohol/soda stimuli)	Active training yielded greater reductions in cue-evoked activation in amygdala bilaterally, and in arousal ratings of alcohol pictures, compared to sham training. Decreases in right amygdala activity correlated with decreases in craving after active, but not sham training.
2, 4, 5 (alcohol/water stimuli)	No sign. interaction; no bias at pretest.
Mouse-AAT, 3, 5/4,5	No sign. interaction for any condition. Decrease in drinking quantity, but no difference between active and sham training group.
2, 4, 5 error or reacted too slowly, a red cross appeared on the screen and feedback accuracy rates (alcohol/soft drink stimuli)	Decreases in mPFC activations correlated with pre-post training decreases of behavioural alcohol ApB in the active training group. .
2, 4, 5 plus feedback. After wrong response a red cross occurred and the trial was repeated (alcohol/non alcohol drinks stimuli)	Effect of training when four sessions were completed: abstinence 5 times more likely.
2, 4, 5 (alcohol/soft drink stimuli)	Main effect of time, no tDCS enhancement of training effects.

Table 1. Continued

	Authors (year)	Study type[a]	N[b]	Symptom severity[c]	Control group[d]	Duration of abstinence[e]
4.25	Di Lemma & Field (2017)	3 (AA pretest, one training session, AA posttest,	120, randomisation over two intervention types, sham per intervention N per group N/A	heavy drinkers > 24 or 21 units per week.	G (experimental/ control training)	N/A
5	Heroin Use Disorder (HUD)					
5.1	Zhou et al. (2012)	1	22 HUD 20 HC	DSM-IV criteria HUD	N/A	Alcohol E-F; Nicotine B.
6	Schizophrenia					
6.1	Radke et al. (2015)	1	27 patients with schizophrenia/ schizo-affective disorder 27 HC	In/outpatients PANSS 35.2(12.7)	B	X
6.2	de la Asuncion et al. (2015)	1	37 patients with schizophrenia 29 HC	DSM-IV criteria schizophrenia	A	X
6.3	Reddy et al. (2016)	1	92 patients with schizophrenia 68 HC	Ouptatients DSM-IV criteria schizophrenia	C	X
7	Mood Disorders (MD)					
7.1	Seidel et al. (2010)	11	24 depression 24 HC	Inpatients DSM-IV criteria depression BDI 27.54 (11.05) HAMD 17.35 (5.69)	A	X
7.2	Derntl et al. (2011)	11	15 depression 15 HC	Inpatients DSM IV criteria major depression BDI 25.6 (6.05)	A	X
7.3	Radke et al. (2014)	11	30 depression 20 HC	Patients DSM-IV criteria depression BDI 27.0 (11.5),	A	X

Task and materials[f]	Clinical measures/outcomes
2, 4, 5	Active training reduced ApB no more than sham training, but reduced alcohol intake after active training.
2 (56cm long lever), 3, 30 min break (heroin-related/ vehicles stimuli)	ApB for heroin in heroin user group.
2, 3 (happiness, sadness, anger, fear, disgust, neutral expression)	No interaction, generally slower RTs in patient group.
2, 3, 5 (happy/angry expressions with direct/averted gaze)	Averted happy faces: ApB in controls, AvB in patients. No effects for angry faces. Faster avoidance correlated with lower Flattened Affect (FA), faster approach with higher FA.
2, 4, 5 (happy/angry/male/ female expressions)	ApB for angry faces in patients, not in controls. Among patients, ApB was not related to any of the clinical symptoms or cognitive variables.
2, 4 (happy/angry/sad/fear expressions)	AvB in MD for angry faces, and ApB for happy male faces. No differences in HCs. In MD, several correlations of AAT biases with number of previous episodes, illness duration, and symptom severity.
2, 4 compatible for fMRI (happy, neutral, angry expressions)	No interactions.
2, 3, 5 (angry, happy, neutral expressions with indirect/direct gaze)	HCs approached happy faces more quickly than angry faces, depressed patients not.

Table 1. Continued

	Authors (year)	Study type[a]	N[b]	Symptom severity[c]	Control group[d]	Duration of abstinence[e]
7.4	Bartoszek & Winer (2015)	1 (Zooming AAT (Z-AAT)/ Duration Time AAT (DT-AAT))	Z-AAT: 23 depressive symtoms 50 spider fearful 47 HC DT-AAT 18 depressive symptoms 46 spider fearful 41 HC	BDI Depressed: 29.04(6.87) Spider fearful: 11.22(10.33) FSQ Depressed 44.22(35.59) Spiderfearful 102.52(15.83) (HC BDI:4.7(3.38)/ FSQ 11.30(13.12))	A	X
7.5	Struijs et al. (2017)	1	877 remitted depressive patients 217 currently anxious 154 depressed 154 comorbid patients. 405 HC	DSM-IV criteria major depression and anxiety disorders.	X	X
7.6	Fleurkens et al. (2018)	2 (AAT after mood induction)	209 39: LaLa genotype + No childhood Trauma. 15 LaLa genotype + Childhood trauma 94: S/Lg-carriers + No childhood trauma 61: S/Lg-carriers + Childhood trauma	DSM-IV remitted depression	B	X
7.7	Becker et al. (2016; Study 2)	3 Pre-test AAT (T1), post test after mood induction (T2), training AAT (experimental and sham training; one session) and post training assessment AAT (T3), booster training session.	36 dysphoric 25 non-dysphoric	Student sample SDS ≥ 40	B	X

Task and materials[f]	Clinical measures/outcomes
Z-AAT 2, 4, 5; DT-AAT: 2, 3, participants were instructed to imagine zoom effects positive/ neutral/negative stimuli (half spiders)	Zoom-AAT: SP showed AvB for negative pictures and spider pictures, no differences in depressed an HCs. DT-AAT: HCs showed ApB for positive pictures, compared to depressed patients and neutral pictures.
2, 4, 5 (angry, happy, neutral, disgusted expressions, checkerboards)	No sign. group differences.
2, 4, 5 (angry, sad, happy, neutral expression/ chessboard)	Stronger AvB for sad faces in remitted depressed patients with the LaLa genotype who had not experienced childhood trauma, compared to LaLa-homozygotes with childhood trauma. No AvB for angry faces.
2, 4, 5 (positive/negative stimuli)	Both groups showed initial ApB for positive pictures. ApB was increased by active training more than by sham training. Training had no effect on mood reports.

Table 1. Continued

	Authors (year)	Study type[a]	N[b]	Symptom severity[c]	Control group[d]	Duration of abstinence[e]
7.8	Vrijsen et al. (2018)	3 (four sessions, active/control condition)	121	DSM-IV criteria depression	G (active/ control)	X
7.9	Becker et al. (2019)	3 (four sessions, active/control condition)	240 mental disorders	Inpatients (minus substance use and eating disorders). ICD diagnosis	G	X
	Anxiety disorders					
8	Obsessive Compulsive Disorder (OCD) and related					
8.1	Najmi et al. (2010)	1	20 high level of symptoms Contamination Fear (CF) 21 low level of symptoms (HC)	Contamination-related obsessive-compulsive symptoms OCI-R total 25,00(7.99) OCI-R washing 5.85 (2.16). OCI-R total 7.57(5.00) OCI-R Washing 1.05(1.16)	A	X
8.2	Amir et al. (2013)	3 (active approach condition/ control condition)	44 high contamination-related obsessive-compulsive symptoms	MOCI 14.07 (4.13) subscale cleaning 6.32 (1.79)	G (active approach/ control)	X
8.3	Schuck et al. (2012)	1	26 skin picking disorder (SPD) 49 HC	Patients SPS 9.48(3.49) (1.76 (1.76))	A	X (imaginary spot rubbing before and during the task)
8.4	Cludius et al. (2017)	1	63 OCD 30 HC	DSM-IV criteria OCD Y-BOCS 22.25 (6.32)	A	X
8.5	Maas et al. (2018[a])	1	54 hair pulling disorder (HPD) (pretest)	Outpatients DSM-IV criteria HPD	X	(Before AAT invitation to touch their hair.)

Task and materials[f]	Clinical measures/outcomes
2, 4, 5 (positive/neutral stimuli)	Active training reduced symptom severity more than sham training, this effect was not mediated by change in positivity bias.
2, 4, 5 (positive, neutral)	Active training increased relative ApB in patients high on depressive symptoms only. Depressive symptoms decreased more in the active compared to sham training. No evidence for mediation.s
2, 4, 5 (contamination-related/ matched neutral stimuli)	CF pulled contamination pictures more slowly than neutral pictures, but did not push them away more quickly than HC.
2, 4, 5 (contamination-related, neutral stimuli)	No bias at baseline. After active training, ApB at post-test. No difference after control training. More completed steps on the BAT after active training.
2, 4 (skin irregularities/ healthy skin/control stimuli)	ApB in SPD, no bias in HCs.
2, 4, 5 (pictures and words: checking-related/ contamination-related/ neutral)	Patients with checking-related symptoms of OCD were faster at pulling than pushing checking-related stimuli
2, 4, 5 (pictures and words of hair pulling or resistance/neutral pictures and words unrelated to hair pulling)	Patients pushed and pulled hair-pulling-related words faster, while they pushed and pulled hair-pulling-related pictures more slowly. The latter effect was associated with higher symptom severity.

Table 1. Continued

	Authors (year)	Study type[a]	N[b]	Symptom severity[c]	Control group[d]	Duration of abstinence[e]
8.6	Maas et al. (2018[b])	3 (six sessions, active condition, sham condition)	HPD: 25 active condition 27 sham condition	Outpatients DSM-IV criteria HPD	G	(Before AAT invit touch their hair.)
9	Posttraumatic Stress Disorder (PTSD)					
9.1	Fleurkens et al. (2014)	1	15 PTSD (sexual trauma) 23 HC	DSM-V criteria PTSD	A	X
10	Specific Phobia (Spider Phobia, SP)					
10.1	Rinck, & Becker (2007) (Study 1)	1	25 SP 22 HC	DSM-IV criteria A t/m D	A	X
10.2	Rinck, & Becker (2007) (Study 3)	1	21 SP 24 HC	DSM-IV criteria A t/m D	A	X
10.3	Reinecke et al. (2012)	2 (AA pretest, after CBT post-test AA)	25 SP	DSM-IV criteria A t/m D	A	X
11	Social Anxiety Disorder (SAD)					
11.1	Heuer et al. (2007)	1	43 HSA 43 HC	LSAS 37.8(8.3) (7.1(4.6))	A	X
11.2	Lange et al. (2008)	1	25 HSA 30 HC	LSAS 35,6 (7.1), ((9.0(2.6))	A	X
11.3	Roelofs et al. (2010)	1	20 HSA 19 LSA	LSAS 56.1 (11.5) (15.1 (7.5))	A	X
11.4	Roelofs et al. (2009)	2 (AAT before/ after social stress task; ten cortisol measures during assessment)	18 SAD: 17 PTSD 22 HC	SAD SPAI 156(7.7) PTSD SPAI 131(7.9) HC SPAI 89 (7.0)	B	X
11.5	Voncken et al. (2012)	2 (AAT before and after face turning AAT)	24 HSA 22 LSA	SIAS 38.2(11.0) (12.2 (4.3)) LSAS 32.6(9.9) (14.8 (5.5))	A	X

	Task and materials[f]	Clinical measures/outcomes
ation to	2, 4, 5 (pictures and words of hair pulling or resistance/neutral pictures and words unrelated to hair pulling/empty frames)	AAT training prior to CBT did not result in enhanced symptom reduction or reduced relapse after CBT.
	2, 4 (high-threat sexual, non-threat sexual, high-threat accident, positive stimuli)	AvB for high-threat sexual pictures in PTSD, compared to control group. Self-reported arousal predicted AvB.
	2, 3, 5 (spiders/neutral stimuli)	AvB for spiders in SPs, no bias in HCs.
	2, 4, 5 (spiders/neutral pictures)	Compared to HCs, SFs showed AvB for spiders
	2, 4, 5 (spiders/butterflies stimuli)	AvB for spiders decreased after CBT, this reduction was positively correlated with reduction in subjective spider fear.
	2, 3 (angry/happy/neutral expressions/puzzles)	HSA showed AvB for angry and smiling faces. HCs did not show any bias.
	2 (crowd AAT), 4 (neutral-angry/happy-angry expressions)	HSA showed overall AvB, irrespectively of intensity ratio, for angry-happy crowds. HSA showed increasing AvB for neutral–angry crowds when the number of angry faces in the crowd increased.
	2, 4, 5, (neutral/happy/sad expressions; direct/averted gaze)	HSA showed AvB for angry faces with direct gaze, more than LSA. HSA showed AvB of happy faces, irrespectively of gaze direction. Neutral faces elicited no AA tendencies.
	Affective Evaluation Task, (happy/angry expressions)	At baseline, no differences between SAD, PTSD and HC. After stress induction, increased cortisol in SAD was associated with increased AvB for angry faces.
	2, 4, 5 (neutral/friendly expressions/PC monitor stimuli)	Neutral condition: Decreased ApB for faces in HSA compared to LSA. After anticipation: Increased ApB for faces in HSA compared to LSA.

Table 1. Continued

	Authors (year)	Study type[a]	N[b]	Symptom severity[c]	Control group[d]	Duration of abstinence[e]
11.6	Rinck et al. (2013)	2 (approach faces condition, avoid faces condition, one training session followed by Face-Turn AAT, see Voncken et al. 2012)	HSA 16 approach-smile condition, 16 avoid-smile condition	LSAS approach-smile condition 30.8 (11.1), avoid-smile condition 34.7 (8.6)	G	X
11.7	Enter et al. (2016)	2 (placebo/ testosterone administration, AAT)	17	DSM-IV criteria SAD, female outpatients LSAS>60 (No HC in this experiment)	G	X
11.8	Taylor & Amir (2012)	3 (pretest, one session, post-test social interaction test)	20 approach positive AAT 24 sham AAT	LSAS Approach positive AAT 53.75 (29.03) Control AAT 52.79 (18.05)	G	X
11.9	Asnaani et al. (2014)	3 (three sessions, pre/post assessment every session, BAT before session one and after session three)	21 active condition 22 sham swcontrol	DSM-IV diagnostic criteria for SAD LSAS Training condition 66.1 (14.0) Control condition 74.6 (14.8)	G At baseline control group patients reported higher levels of SAD on the SPIN.	X
	Seksual disorder					
12	Paraphilias					
	Weidacker et al (2018)	1	38 pedophiles 27 controls	ICD-10 criteria for pedophilia	A	X
13	Eating Disorders					
13.1	Veenstra et al. (2011)	1	89 AN(-like) 76 healthy controls	Patients DSM-IV diagnostic criteria of AN (-like) disorder. EDE-Q 3.31 (1.36) (0.93 (0.84))	A	Time since last ea covariate

	Task and materials[f]	Clinical measures/outcomes
	2, 4, 5 (smiling expressions/ checkerboards stimuli)	No bias at pre-test. At post-test, ApB for smiling faces after approach-smile training, and AvB after avoid-smile training. Reduced social stress vulnerability after approach-smile training.
	2, 4, 5 (happy, angry, and neutral facial expressions)	Significant interaction; significant increase of approach tendencies toward angry faces after testosterone administration in SAD participants.
	Pull-sideway AAT, 4, 5 (neutral/disgust/positive faces AAT assessment; positive pictures/neutral faces in experimental manipulation)	ApB for positive pictures after positive training, ApB was related to better subsequent interaction. No direct effect of training on subjective anxiety ratings.
	2, 4, 5 (smiling expressions/ checkerboard stimuli)	No specific training effects were found. The group as a whole improved on self-reports of anxiety. Unclear, if the trainings effects mediated this effect.
	2, 5 (women, men, (pre-) pubescent boys, (pre-) pubescent girls)	ApB for sexual preferences
ting as a	Affective Simon Task 1, 4 (high-fat food/ low-fat food/ neutral)	Control group participants showed stronger error effects for HC-food and LC-food than the group of AN-like patient when avoiding food stimuli. Both groups showed stronger ApB towards LC-food compared to neutral objects. ApB for high-fat food was negatively correlated with weight.

Table 1. Continued

	Authors (year)	Study type[a]	N[b]	Symptom severity[c]	Control group[d]	Duration of abstinence[e]
13.2	Khan et al. (2015)	1 (2)	54 ED 41 'at-risk' 23 HC	Diagnosed of Eating disorder EDE-Q > 4	B unbalanced ethnic distribution	X
13.3	Paslakis et al. (2016)	1	41 AN 42 HC	Inpatients DSM 5 criteria AN	A	X (≤ 4 hours meal experiment)
13.4	Paslakis et al. (2017)	1	24 obesity + BED 32 obesity 25 HC	In- and outpattients DSM-5 criteria of BED	B	X
13.5	Leins et al. (2018)	1	55 disordered eating behaviour 45 without disordered eating behaviour	> 2.3 on EDE-Q	A	X
13.6	Neimeijer et al. (2015)	2	152 AN(-like) 76 follow-up	Patients DSM-IV diagnostic criteria of AN (-like) disorder. EDE-Q 3.62 (1.20)	X	X
13.7	Brockmeyer et al. (2015)	3 (pre-test. 10 sessions, post-test)	30 subclinical bulimic eating disorder	1 SD> Mean on loss of conrol subscale of the FCQ-T EDE-Q 2.5 (1.17) DSM IV criteria (SCID)	X	X
13.8	Brockmeyer et al. (2019)	3	56 BN/BED 28 active training 28 sham training		A	B
14	Pathological gambling					
14.1	Boffo et al. (2018)	1	22 moderate-to- high-risk gamblers 26 non-problem gamblers	Moderate-to-high-risk gamblers ≥ 3 on PGSI Low risk < 3 on PGSI SOGS	C	N/A
14.2	Wittekind et al. (2019)	3	141 gamblers 66 active condition 65 sham condition	10.0 (3.3) 10.3 (3.3)	A	N/A

	Task and materials[f]	Clinical measures/outcomes
	2, 4, 5, (keys instead of joystick; high-fat food/ low-fat food/ neutral)	No ApB/AvB present and no predictive value of the AAT measures for ED was found.
before	Mouse-AAT, 4, 5 (high/low calorie food stimuli)	HCs showed an ApB for food in general, this effect was not present in AN.
	2 .(computer mouse), 4, 5, (high/low calorie food stimuli)	Obese BED group pushed LC-food away more quickly than HC-food. This bias was absent in obese subjects, but also present in HCs. In contrast, the obese pulled LC-food closer more quickly than HC-food. This bias was absent in the obese BED group, but also present in HCs.
	2,4,5 (thin/normal weight stimuli)	Faster pushing than pulling independent of group or picture content.
	Affective Simon Task 1, 4 (high-fat food/ low-fat food/ neutral)	Stronger error effects in patient group for LC-food, but not for HC-food, follow-up (1-year) ApB for both HC- and LC-food. Change in ApB or baseline ApB was not related with clinical measures.
	2, 4, 5 (food/marched non-food stimuli)	ApB at baseline, AvB after training. Reduced craving, improved eating habits. No control group.
	2, 4, 5 (food/marched non-food stimuli)	No ApB at baseline or after training. No differential training effect on binge eating episodes- or days; both conditions showed a decrease. No significant diffential decrease in EDE, craving or food cue reactivity- or intake.
	2 (key press), 4 (gambling-related cues tailored to individual gambling habits; neutral control stimuli)	ApB for gambling stimuli in moderate-to-high-risk gamblers. ApB predicts the frequency and total duration of gambling episodes over 6-months.
	2, 4, 5 (slot-machine gambling/neutral stimuli)	Both conditions decreased on the PG-YBOCS (pathological gambling) with do differences between conditions. Days of training did not correlate with symptom reduction.

Table 1. Continued

	Authors (year)	Study type[a]	N[b]	Symptom severity[c]	Control group[d]	Duration of abstinence[e]
15	Psychogenic/Non Epileptic Sseizures (PNES)					
15.1	Bakvis et al. (2011)	2 (AAT pre and post stress-induction task)	12 PNES 20 HC	Outpatients with PNES	B	X
	Personality disorders					
16	Psychopathy					
16.1	von Borries et al. (2012)	1	17 Psychopathy 15 HC	Inpatients PCL-r ≥ 26	N/A	X
17	Borderline personality disorder					
17.1	Kobeleva et al. (2014)	1	25 BPD 25 HC	Inpatients DSM criteria BPD	B	X
17.2	Sleuwaegen et al. (2018)	1	144 31=Low Anxiety 34=Inhibited 15=High Self-control 66=Emotional/ Disinhibited	DSM-IV criteria BPD	F	X

Note: Abbreviations: Diagnostic and Statistical Manual of Mental Disorders, Fourth Edition (DSM-IV); Approach-Avoidance Task (AAT); Avoidance Bias (AvB); Fagerström Test for Nicotine Dependence (FTND); Approach Bias (ApB); Correlation (corr.); modified Fagerström Tolerance Questionnaire (mFTQ), Reaction Time (RT); Stimulus-Response Compatibility (SRC); Follow-Up (FU), Cannabis Severity of Dependence Scale (C-SDS); Cannabis Use Disorder Identification Test (CUDIT), dorsolateral prefrontal cortex (DLPC), anterior cingulate cortex (ACC), Healthy Controls (HC), Alcohol Use Disorders Identification Test (AUDIT); Leeds Dependence Questionnaire (LDQ); Intelligence Quotient (IQ); Working Memory Capacity (WMC); medial prefrontal cortex (mPFC); Severity of Alcohol Dependence Questionnaire (SADQ); transcranial direct current stimulation (tDCS); Positive and Negative Syndrome Scale (PANSS); Beck Depression Inventory (BDI); Hamilton Depression Rating Scale (HAMD); Fear of Spiders Questionnaire (FSQ); Zung Self-Rating Depression Scale (SDS); Obsessive-Compulsive Inventory (OCI -R); Picking Scale (SPS); Maudsley Obsessional Compulsive Inventory (MOCI), Behavioral Assessment Test (BAT); Cognitive Behavioral Therapy (CBT); High Socially Anxious (HSA); Liebowitz Social Anxiety Scale (LSAS); Low Socially Anxious (LSA); Social Phobia and Anxiety Inventory (SPAI); Social Interaction Anxiety Scale (SIAS); Social Phobia Inventory (SPIN); Anorexia Nervosa (AN); Binge Eating Disorder (BED); High calory food (HC-food); Low calory food (LC-food); Eating Disorder Examination-Questionnaire (EDE-Q); Eating Disorder (ED); Food Cravings Questionnaire-Trait (FCQ-T); Problem Gambling Severity Index (PGSI); Psychopathy Checklist (PCL-R); Borderline Personality Disorder (BPD);

Task and materials[f]	Clinical measures/outcomes
Affective Evaluation Task, (angry/happy expressions)	Baseline ApB correlated with baseline cortisol levels across both groups. PNES patients showed slower approach of angry faces. No difference in HCs. No interaction effect for happy faces.
2, 3 (happy/angry/neutral expressions)	Patients did not show avoidance of angry faces whereas HC did. Diminished avoidance of angry direct-gaze faces was related to instrumental aggression and perceived distress.
2, 4 (sad/anger/fear/neutral expressions)	No sign. interaction.
2, 3 (happy/angry expressions with male/female, direct/averted stimuli)	No sign. differences between the four BPD subtypes. Self-reported effortful control was positively related to general approach-avoidance tendencies to faces in direct gaze stimuli.

* Self-report and behavioral measures were obtained from participants in the Machulska et al. (2015) study.
** Data from a subset of patients have previously been reported (Wiers C. et al., 2015a, 2015b).
*** Pre-training neuroimaging data of the first 20 patients were reported previously in Wiers C. et al. (2014) and effects of CBM on a passive alcohol cue reactivity task were reported in Wiers C. et al. (2015[b]).
[a] 1 Assessment, 2. AA outcome variable after intervention, 3. Modification; [b] Total N available for analysis: (Sub)clinical sample (Healthy Controls, HC); [c] Symptom severity (M(SD)) of experimental and control group; [5] Participant group/training groups are matched on/did not differ on: A= Age, gender, education /IQ, B= Age, gender, C= Age, D= Gender, E= Age and education, F= Gender and education, G= Within group randomization, X= no control group; [5] Abstinence: A= <1 h before the experiment abstinent, B= 1-5 hours, C= 5-24 hours/day of testing, D= ≤ 1 month, E= 1 month to 1 year, F= ≤ 10 years, G= ≥ 10 years, X= not relevant; [6] Task and Materials: 1= SRC, 2= AAT, 3= Relevant feature, 4= Irrelevant feature, 5= Zoom function, (Stimulus categories).

Finally, six Type 3 modification studies were found for nicotine use disorder. In a training study including adolescents (Kong et al., 2018), no difference between the active training group and the sham training group was present, both groups showed a decreased approach bias after training. Wittekind et al. (2015) applied a stand-alone web-based AA training, using the computer mouse instead of a joystick. They reported a decrease of cigarette use and symptom severity in the active modification group after four weeks. However, mediation analyses were not reported, there was no sham-training condition, and it was unknown how many training sessions the participants actually completed. In a later study (Wittekind, Lüdecke et al., 2019), these limitations were not present, and the authors found that compared to sham-training, active web-based nicotine-avoidance training reduced daily cigarette consumption directly after training, but not at 6-months follow-up. Machulska et al. (2016) included a clinical sample of psychiatric inpatients with moderate-to-high nicotine dependence who participated in a smoking cessation program. No effect of the active add-on AAT training on AA tendencies was found. Nevertheless, 3 months later, this group reported fewer cigarettes smoked per day than the sham-training control group. In the study by Baird et al. (2017), a similar outcome was reported: The degree of bias reduction across four sessions of active nicotine-avoidance training predicted the number of abstinent days after training, in a group of smokers motivated to quit. Wittekind, Reibert et al. (2019) also investigated nicotine-avoidance training as add-on to a standard smoking cessation intervention. They found that participants receiving the intervention plus active training did not show a significantly greater reduction of daily cigarette consumption at follow-up than those receiving the intervention plus sham-training. Taking the findings of these 5 modification studies together, the behavioral outcome results suggest that AA training may have positive clinical effects, but the results are far from clear-cut.

Cannabis Use Disorder (CUD). In this category, 8 studies could be included, 5 of which were Type 1 assessment studies. In a group of treatment-seeking adolescents, no ApB for cannabis stimuli was found (Cousijn et al., 2015). Wolf et al. (2016) did not find an ApB in a small group of moderate users either, but they did detect an ApB in a small *heavy*-user group. However, note the very small sample of this study (n = 7). Field and colleagues (2006) used an SRC task, and they reported an ApB for cannabis users at risk for CUD. However, the cannabis-related AA tendencies were not compared to the tendencies for control stimuli. In the fMRI study by Cousijn et al. (2012), the ApB for cannabis-related stimuli predicted increased drug use six months later. Interestingly, increased activity in reflective control-related brain areas during *approach* responses predicted *lower* follow-up severity of CUD, and increased activity in these areas when *avoiding* cannabis-related stimuli predicted *increased* CUD severity. In the 2011 study by Cousijn and

others, it was found that an initial ApB (present in cannabis smokers, not in healthy controls) predicted the amount of cannabis use 6 months later, but did not predict problem severity. These two studies support the idea that biased AA tendencies may be related to diminished reflective control, and that an increased ApB can be a possible indicator of risk for increased cannabis use.

The single Type 2 study in this area, published by Cousijn et al. (2013), suggests that the ApB for cannabis may be increased directly after cannabis intoxication. Finally, two Type 3 modification studies could be included (Jacobus et al., 2018; Sherman et al., 2018). Both studies found no training effects on AA tendencies, and they could not relate ApB scores at baseline to amount of cannabis use. However, the results by Sherman et al. (2018) are based on a small sample, lacking sufficient statistical power. In the study by Jacobus et al. (2018), a non-treatment-seeking adolescent sample was included, and training was offered as a 'stand-alone' intervention. More research with larger samples and ABM as an add-on intervention to treatment-as-usual is needed.

Alcohol Use Disorder (AUD). For AUD, most studies were found, involving 9 Type 1 assessment studies, 5 Type 2 studies, and 11 Type 3 modification studies. With regard to Type 1 studies, the approach bias in AUD towards alcohol-related cues was found to be related to a genetic predisposition (Wiers et al., 2009) and to the quality of explicit control (Sharbanee et al., 2013). The influence of (pretreatment) drinking quantity might be another predictor of AA tendencies (Barkby et al., 2008), whereas severity of AUD itself was not found to be related (van Duijvenbode et al., 2012).

Spruyt et al. (2013) found a positive correlation between the presence of an avoidance bias (AvB; instead of the ApB one might have expected) and relapse in AUD, whereas Snelleman and colleagues (2015) did not find a correlation between the presence of an AvB and clinical measures. Moreover, Snelleman et al. (2015) found that the AvB decreased after prolonged abstinence. In these two studies, patients were either just discharged from a detox clinic or were at the end of clinical treatment, and a relevant-feature task was used, tapping into more controlled processes. It could be reasoned that actively controlling the tendency away from alcohol-related stimuli reflects an explicit coping mechanism that is present during or directly after detoxification. This may be a process that differs from the ones addressed by, for example, irrelevant-feature tasks. The potential effect of cognitive control on alcohol-related AA tendencies could be substantiated by two Type 1 studies that used fMRI measures: Ernst et al. (2014) found the 'reflective control' brain system to be more active when avoiding alcohol cues, using a relevant feature task. C. Wiers et al. (2014) found that in AUD, the brain's reward system is more active when approaching alcohol cues, and that increased approach tendencies were related to increased craving-related activity in the amygdala.

Several Type 2 studies showed little moderation of AA tendencies. Neither the administration of oxytocin or baclofen nor the dose of alcohol administration influenced AA tendencies (Beraha et al., 2008; Mitchell et al., 2016; Schoenmakers et al., 2008). Neither did Houben et al. (2012) find an effect of a Go/NoGo training on AA tendencies. Finally, Cousijn et al. (2014) found that increased AUD severity was related to diminished influence of negative emotional priming on AA tendencies.

The earliest Type 3 study in this area, conducted by Wiers et al. (2010), found that when AA tendencies were successfully manipulated, the amount of alcohol intake in a taste test was affected. Later modification studies with abstinent alcohol-dependent patients consistently showed that active alcohol-avoidance training resulted in decreased relapse rates (Eberl et al., 2013; Manning et al., 2016; Rinck et al., 2018; Wiers et al., 2011). Only the studies by Di Lemma and Field (2017) and Lindgren et al. (2015) did not show effects of the training on AA tendencies. However, in these studies only subclinical samples were included, and the training was not applied in a treatment setting as an add-on intervention. Moreover, only one or two training sessions were applied, while the results reported by Eberl et al. (2014) suggest that repeated sessions (6 to 12) will yield better results. The fMRI studies by C. Wiers and colleagues (2014; 2015a, 2015b) suggest that decreased cue-reactivity may be the working mechanism of successful ApB modification in AUD: After active training (compared to sham-training), activity in the amygdala and activity in frontal brain regions involved in reward attribution of alcohol-related pictures were decreased, and mPFC activations correlated with pre-post training decreases of behavioral alcohol ApB in the active training group.

Collectively, the results of the Type 3 studies indicate that joystick-based AAT training in clinical AUD populations is an effective intervention which contributes to decreased cue-reactivity and decreased relapse rates. However, online training (Wiers et al., 2015) might not be as effective, and neuromodulation does not seem to strengthen the training effect (den Uyl et al., 2017).

Heroin Use Disorder (HUD). One study assessed AA tendencies in heroin dependence (Zhou et al., 2012). An ApB was found in long-term abstinent inpatients, compared to students who had never used heroin.

Mood Disorders

Five Type 1 assessment studies were included. Two of them indicated a relative lack of ApB for positive stimuli in subclinical samples (Bartoszek & Winer, 2015; Radke et al., 2014). Seidel et al. (2010) found an AvB for angry faces, whereas neither Derntl et al. (2011) nor Struijs et al. (2017) found a differential ApB in clinical samples.

A single Type 2 study involving a mood induction was included: Fleurkens et al. (2018) showed the possible influence of genetic variations and childhood trauma on AA tendencies for emotional faces in a remitted depressed sample.

While almost all of the Type 1 and Type 2 studies reviewed above employed emotional facial expressions, the three Type 3 studies in this area used a wide variety of valenced pictures to modify AA tendencies. Becker et al. (2016, Study 2) first induced a negative mood in dysphoric students, then attempted to modify the so-called positivity bias (approach vs. avoidance of diverse positive vs. negative stimuli, respectively). It was found feasible to modify the positivity bias, but no clinical effects were obtained in this low-symptomatology sample using a single training session only. In contrast, in the two modification studies by Vrijsen et al. (2018) and Becker et al. (2019), decreases in depressive symptoms were found in clinically depressed samples after multiple sessions of active positivity-training, compared to sham-training conditions. However, no evidence for mediation of the effect of training on symptom change by positivity bias change was found.

In conclusion, depression may be characterized by diminished approach of positive stimuli and diminished avoidance of negative stimuli. While the evidence regarding AvB and ApB regarding emotional facial expressions is still inconsistent and incomplete, the evidence regarding positive and negative stimuli in general suggests that more severe depressive symptomatology is related to reduced approach-avoidance responses. Moreover, AA training that strengthens approach of positive stimuli and avoidance of negative ones seems to reduce depressive symptoms when given as an add-on to treatment-as-usual (TAU).

Anxiety-Related Disorders

Obsessive Compulsive Disorder (OCD) and related disorders. Three studies (two assessment and one modification) have examined AA tendencies in OCD. Participants with subclinical levels of the contamination-related OCD subtype showed an AvB: They were slower to approach contamination-related pictures than healthy controls (Najmi et al., 2010). A sample with clinical symptom levels of the checking-related OCD symptomatology was faster at pulling than pushing checking-related stimuli (Cludius et al., 2017), indicative of an ApB in this subtype. Amir et al. (2013) modified AA tendencies in a contamination-related OCD sample. The active approach training successfully strengthened approach responses towards contamination-related stimuli and yielded increased overt approach in a behavioral approach task. Moreover, the effect on the behavioral task was mediated by the strength of the AA tendency at post-test.

Only one assessment study has been conducted in skin picking disorder (Schuck et al., 2013). The results showed an ApB for stimuli depicting skin irregularities, which was absent in healthy controls.

For hair pulling disorder (HPD), one Type 1 study and one Type 3 study were included. In the assessment study, pictures and words were presented in the AAT paradigm (Maas et al., 2018). The words included pulling-related as well as resistance-related terms. The HPD patients showed generally slower reactions for hair-pulling-related pictures, and faster reactions for hair-pulling-related words, irrelevant of movement direction. The modification study (Maas et al., 2018b) did not yield a change in bias, neither did it enhance regular treatment effects. Based on the few studies reported so far, AA tendencies do not seem to be an especially relevant feature of HPD. However, as discussed by Maas and colleagues, the stimuli employed in the two studies might not have provoked enough arousal to elicit AA biases.

Taken together, these results suggest that OCD-related AA patterns can be detected. Moreover, a first AA modification study yielded promising effects: The modification of AA tendencies resulted in increased overt approach of feared stimuli. In sum, very few studies have been conducted in OCD and related disorders, but the results so far are promising.

Posttraumatic Stress Disorder (PTSD). Only one Type 1 study (Fleurkens et al., 2014) assessed AA tendencies in patients with PTSD. This study yielded an AvB for trauma-related pictures with an irrelevant-feature AAT. The strength and width of this bias was related to the disease burden, including depressive symptomatology, and the AvB correlated with self-reported arousal level. Obviously, more research is needed to replicate and extend the research on AA tendencies in PTSD.

Specific Phobias. All 3 included studies focused on spider phobia (Rinck & Becker, 2007, Studies 1 and 3; Reinecke et al., 2012), and all studies found an AvB for spider pictures in spider-phobic participants. The study by Reinecke et al. (2012) is also a Type 2 study: It was found that the initial AvB decreased after regular cognitive behavior therapy (CBT). This is an interesting finding because the AvB itself was not directly modified. This could indicate a transfer effect from behavioral exposure interventions to the level of more automatic approach-avoidance. No Type 3 modification studies were found, but this could be an interesting field of research, given the consistent finding that an AvB exists.

Social Anxiety Disorder (SAD). In total, 9 studies were included, 2 of which used adapted AA joystick tasks: A so-called "Crowd AAT" assessed AA tendencies in response to matrices of pictures depicting 12 faces, with the matrices differing in the ratio of neutral-angry and happy-angry faces (Lange et al., 2008). Another study (Voncken et al., 2012) assessed manipulation effects on AA tendencies after participants had completed a 'Face-Turning AAT'. This version of the AAT is unusual in that it employs sideway views of heads. Upon pulling or pushing the joystick, the head turned around to a frontal view of the face or a view of the back of the head, respectively.

Three Type 1 assessment studies could be included. Heuer et al. (2007) and Roelofs et al. (2010) found an AvB for both happy and angry single faces in subclinical SAD, compared to healthy control groups. Roelofs et al. (2010) also found that happy faces elicited avoidance tendencies even when the gaze was averted. Similar results were reported by Lange et al. (2008) for "crowds" of 12 faces and by Voncken et al. (2012) for faces that turned around to face the participant. In summary, both angry and happy faces seem to elicit avoidance tendencies in (subclinical) SAD. The study by Voncken et al. (2012) also qualifies as a Type 2 study, showing that the avoidance tendency was affected by the anticipation of a social interaction. Interestingly, another Type 2 study showed increased approach of angry faces in SAD after testosterone administration (Enter et al., 2016).

Turning to Type 3 studies, Rinck et al. (2013) found that the manipulation of AA tendencies in subclinical SAD was feasible, and that the approach-smiling-faces training resulted in reduced anxiety after social stress. This finding coincides with the studies reported by Taylor and Amir (2012; subclinical SAD) and Asnaani et al. (2014; clinical SAD). In both studies, participants were randomly assigned to the active training or a sham control training. Taylor and Amir (2012) found approach-smiling-faces training to be successful, leading to improved quality of subsequent social interactions. However, no effect on subjective anxiety was found. Asnaani and colleagues (2014), in contrast, did not find modified AA tendencies in a small sample of clinical SAD patients. These two studies differed in several aspects, including possible AAT response options, stimuli and statistical power, all of which may have contributed to the different results. Given the results in (subclinical) SAD, further research on clinical effects of approach-smiling-faces training seems promising.

Sexual Disorders

Paraphilia. In this category, one study was found: Weidacker et al. (2018) assessed AA tendencies in pedophilia and found congruent ApB for sexual preferences according to gender and degree of maturity, using a relevant-feature AAT.

Eating Disorders

Five Type 1 studies met our inclusion criteria. Two studies assessed AA tendencies in samples diagnosed with anorexia nervosa (AN; Veenstra and de Jong, 2011; Paslakis et al., 2016). Both studies applied an irrelevant-feature task and found an approach tendency for food in the healthy control groups, whereas the patient groups did not show this tendency. It can be hypothesized that healthy controls experience food as positive and approach it automatically, whereas patients with AN lack this tendency. Next, for binge eating disorder (Paslakis et al., 2017) and for

two samples with "disordered eating behavior" (Khan et al 2015; Leins et al., 2018), no clear AA patterns were found. In binge eating disorder, AA tendencies could be state-dependent, and thus more pronounced when one is feeling depressed or stressed, coping with the urge to eat. Mood induction paradigms could be of interest for further research on this matter.

Next, two studies (both including adolescents) aimed to predict the development of psychopathology by measuring AA tendencies (Khan and Petróczi, 2015; Neimeijer et al., 2015). However, neither study found relations between AA tendencies and clinical measures at time of assessment or at follow-up.

In a Type 3 feasibility study by Brockmeyer et al. (2015), an initial food-ApB was modified into an AvB in subclinical bulimic eating disorder sample. However, no sham-training control group was present in this proof-of-principle study. Such a group was added in the randomized controlled trial reported by Brockmeyer et al. (2019). Here, patients suffering from bulimia nervosa or binge eating disorder received 10 sessions of active or sham food-avoidance training using the AAT. The results were mixed: Active training tended to result in greater reductions of eating disorder symptoms, whereas other variables showed comparable changes in both groups (e.g., binge eating) or no changes in either group (e.g., food intake).

In sum, the studies available in this area suggest that it would be worthwhile to conduct further studies to assess and modify AA tendencies in eating disorders. Here, attention should be paid to trait-like AA characteristics of different eating disorder diagnoses, and to state-dependent AA tendencies.

Pathological Gambling

A Type 1 assessment study and a Type 3 modification study of pathological gambling behavior were included. Boffo et al. (2018) applied an AAT with individualized gambling-related and neutral stimuli in a moderate-to-high-risk sample of gamblers. They found an ApB in the at-risk group, and this bias predicted duration and frequency of gambling periods in a six-months follow-up. Wittekind, Bierbrodt et al. (2019) compared web-based active training to sham-training, using slot-machine related pictures and neutral pictures. They found similar reductions in gambling-related symptoms in the two groups.

Schizophrenia

Three Type 1 studies assessed AA tendencies in response to emotional facial expressions in patients with schizophrenia. De la Asuncion et al. (2015) found that patients avoided happy faces with an averted gaze, whereas healthy controls approached these faces. Radke et al. (2015) found no specific pathology-related AA tendencies, however, they did not use relative bias scores. Finally, Reddy et al. (2016) found an approach bias for angry faces in schizophrenic patients, compared

to other emotions and healthy controls. Given the low number of studies in this area and their methodological differences, it is difficult to draw general conclusions about AA tendencies in schizophrenia.

Somatoform Disorders

Non-epileptic seizures. In patients diagnosed with non-epileptic seizures, an AvB for angry faces was found in a relevant-feature task (Bakvis et al., 2011). The patients showed a relatively slower approach of angry faces than healthy controls, after stress induction this effect disappeared. In addition, baseline AvB was associated with cortisol levels.

Personality Disorders

Psychopathy. Von Borries et al. (2012) found a lack of avoidance of angry faces in offenders with psychopathy, whereas the healthy control group did show the expected avoidance of angry faces. Interestingly, the strength of the offenders' bias was related to higher levels of instrumental aggression and to difficulties in perceiving distress in others.

Borderline personality disorder. Two Type 1 assessment studies (Kobeleva et al., 2014; Sleuwaegen et al., 2018) compared patients with borderline personality disorder (BPD) to healthy controls. Neither study found clear AA patterns in BPD patients. Biases in AA tendencies may be less pronounced in BPD because it includes a very heterogeneous symptomatology.

Delirium, dementia, amnestic, and other cognitive disorders

Amnestic disorders. One Type 3 modification study was conducted in a clinical patient group with alcohol-related neurocognitive disorders (Loijen et al., 2018). The applied alcohol-avoidance training was found to be feasible in amnestic disorders; across 6 training sessions patients developed an AvB for alcohol-related stimuli. However, since it was a feasibility study, no control group was included and no clinical outcome measures were obtained.

Discussion

The aim of this systematic review was to provide an overview of the available evidence for (biased) approach-avoidance (AA) tendencies in different mental disorders. We discriminated between three types of studies: Type 1 assessment studies mainly probed the existence of biased AA tendencies for disorder-related stimuli in patients, Type 2 studies assessed whether the tendencies were sensitive to the influence of other variables such as mood inductions, treatment, or priming,

and Type 3 modification studies involved the direct manipulation of the AA tendencies by computerized training procedures.

Substance use disorders

The available evidence suggests that substance use disorders are characterized by dysfunctional approach of substance-related stimuli, compared to generally appetitive and neutral stimuli. AA tendencies have been studied most often in smokers, cannabis users, and alcohol-addicted individuals. In these addictions, the collective results indicate that the approach bias (ApB) may be stronger in low dependency (as in early at-risk users) than in moderate or strong dependency (as in long-term addictions) and may be related to a genetic predisposition. Moreover, priming effects due to available substance-related cues, or the actual smoking of nicotine or cannabis, seem to increase the ApB. This may have negative consequences by lowering the threshold for substance use: A stronger ApB was found to predict increased use over time. According to these findings, the presence of an ApB in subclinical populations can be a possible indicator of risk for increased future use. In the case of continued and increased substance use, the ApB may decrease, which is in accordance with current theories of addiction. These state that over the course of the illness, behavior becomes more driven by the cue-elicited 'wanting system' based on incentive salience, and less driven by the expected pleasantness of a reward in the 'liking system' (Berridge & Robinson, 2016).

A very promising result of the research on AA tendencies in addictions is the development of computerized substance-avoidance trainings. The Type 3 modification studies reviewed here indicate that AA training given as an add-on to standard treatment has the potential to reduce consumption and relapse rates reliably. This important clinical effect has been reported most consistently in AUD. Moreover, the results reported by Loijen et al. (2018) suggest that this training may even be feasible in patients with severe alcohol-induced cognitive disorders; patients for whom few other treatment options are available. In contrast, nicotine-avoidance trainings have yielded much more mixed results. This may be due to a number of differences between the studies and substances: The trainings were delivered offline vs. online, as add-on to TAU versus as stand-alone, and with relapse prevention vs. reduced consumption as treatment goals. All of these may be important moderators of efficiency.

The reviewed fMRI studies in AUD suggest a possible working mechanism of AA modification: It contributes to a reduction of stimulus-provoked activity in specific frontal brain structures and the amygdala. Cue-related activity in exactly these specific frontal brain regions is related to an increased risk for relapse (Beck et al., 2012), therefore the reduction of this activity by AA modification could

explain the positive results in clinical samples. Based on the replicated positive findings in AUD, it has been argued that modification procedures such as the alcohol-avoidance training are ready to be included in regular treatment guidelines for alcohol addiction, especially when one considers the low cost and easy implementation of these interventions (Mann et al., 2016).

Mood disorders

The studies on AA tendencies in depression reviewed here illustrate the need to differentiate between patient samples and non-clinical controls. Without this differentiation, an important finding might have gone unnoticed: According to the studies reviewed here, depression is not so much characterized by a specific AA bias, but by the reduction or complete lack of the "healthy bias" shown by controls: the automatic approach of positive stimuli and avoidance of negative ones. The potential clinical relevance of this bias is illustrated by two modification studies which applied a so-called positivity training: Both Vrijsen et al. (2018) and Becker et al. (2019) showed a reduction in depressive symptoms after active positivity training, given as an add-on to TAU, and compared to sham-training. Further research in this area is therefore encouraged, it should be determined whether AA modification can serve as a beneficial add-on to cognitive therapy of depression.

Anxiety-related disorders

The avoidance bias (AvB) found in anxiety disorders usually corresponds to self-reports: Not surprisingly, patients show an AvB for the stimuli they report to find threatening. An interesting exception was repeatedly found in SAD: Individuals suffering from SAD symptoms show an AvB for both angry and smiling faces, despite rating the former as negative and the latter as positive. This has been taken to suggest that in SAD, smiling faces are automatically perceived as threatening (because they may signal the need for social interaction), despite knowing that the intentions of the smiling person are friendly. In studies with clinical populations, this AvB was less evident. However, these studies did not include a non-anxious control group because they were modification studies. Therefore, the lack of an initial AvB cannot be interpreted; the anxious individuals' tendencies have to be compared to those of healthy controls. Finally, the modification of this specific AvB of smiling faces has been found to be feasible, but positive clinical effects have not been established yet.

For the other anxiety disorders that were reviewed, an initial AvB of feared stimuli was found rather consistently when compared to neutral or positive stimuli, and compared to healthy controls. These biases are all in line with the self-reports and the overt avoidance behavior of the patients: An AvB of

spider-related pictures in spider phobia, of trauma-related stimuli in PTSD, and of contamination-related pictures in contamination-related OCD. In line with this, in the checking-related OCD type, an ApB was found, consistent with the need to approach in compulsive behaviour. Although this can been interpreted as a validation of the AA construct, one might wonder what the added value of assessing these tendencies is, over and above simply giving a questionnaire or conducting a diagnostic interview. So far, a definite answer to this question has not been given yet, but it has been speculated that the strength of pre-treatment AA tendencies may predict treatment success (as in attention biases; Amir, Taylor, & Donohue, 2011), or that AA biases which remain after treatment may predict relapse. These speculations await empirical testing.

Finally, modification studies involving pathologies in the anxiety spectrum (including samples with sub-clinical symptomatology) are still rather scarce. The few published SAD modification studies did not reveal convincing reductions of anxiety symptoms yet. The OCD modification study by Amir et al. (2013) did yield encouraging results, but it has not been replicated yet. All in all, the lack of published AvB modification studies is surprising in light of the extensive evidence for the existence of an AvB in anxiety disorders. This may hint at the existence of unpublished studies that failed to modify the AvB or to find clinical effects of the modification. Generally, it may be the case that a dysfunctional ApB (as in addictions) is easier to modify with positive clinical effects than the dysfunctional AvB of anxiety disorders.

Eating disorders

With regard to eating disorders, we believe that it will be necessary to differentiate between different disorders (e.g., anorexia nervosa vs. binge eating), and between disorders vs. dysfunctional eating behavior (e.g., unhealthy food choices, obesitas). A recent review of AA modification studies in dysfunctional eating behavior came to positive conclusions (Kakoschke et al., 2017). However, almost none of the studies reviewed there involved patients with diagnosed eating disorders, therefore, further research involving clinical samples is needed. Anorexia Nervosa (AN) may be a good candidate for these clinical studies: The lack of a natural food-approach tendency found in at least one AN study resembles the lack of positivity-approach found in depression, therefore a food-approach training for AN resembling the positivity-approach training for depression may be a promising candidate. In Binge Eating Disorder/ Bulimic Eating Disorder, more state-dependent features of AA mechanism are of interest.

Other disorders

For all other disorders, only a few studies could be included for each disorder. Therefore, only very tentative conclusions can be drawn from them. In pathological gambling, for instance, only two studies were included. However, in line with the findings in substance use disorders (SUD), an ApB in an at-risk group was found, and this bias predicted the duration and frequency of gambling periods six months later. Given the overlap of this disorder with SUD, the positive results of AA modification studies in SUD suggest that further research into AA tendencies in pathological gambling will be highly interesting, as evidenced by the pilot study reported by Wittekind, Bierbrodt et al. (2019).

For the remaining disorders reviewed here, too few studies were available to draw firm conclusions. It seems that biased AA tendencies may exist in pedophilia, psychopathy and in patients diagnosed with non-epileptic seizures. In contrast, the available studies do not provide clear evidence for or against biased AA tendencies in schizophrenia, borderline personality disorder, skin-picking disorder, or hair-pulling disorder.

Methodological issues

Several methodological issues became obvious during our inspection of the reviewed studies. A general problem which most of the studies have in common is the small sample size which seriously limits the statistical power of the studies. As has been pointed out many times, in underpowered small-sample studies, even true medium-sized effects will not reach statistical significance, and only large effects - which are almost certainly larger than in reality - will be statistically significant (Rinck, 2017). Together with the existing publication bias in favor of statistically significant results, this facilitates the selective reporting of inflated effects and false positives. For the studies that we reviewed here, we have to suspect that some of the reported AA tendencies, correlations with other variables, and changes due to modification attempts are actually not as large as they were reported. Moreover, we have to expect that similar studies with non-significant effects exist, and that we could not review them because they ended up unpublished in the infamous “file drawer”.

Other methodological issues are not problems per se, but create methodological differences between the studies, which make it difficult to compare their results. We only list the most obvious ones here. First, with regard to the handling of reaction times (RTs), many different ways of computing the critical bias scores have been used. Different computations may affect the interpretation of the outcomes, and a direct comparisons of studies becomes more difficult. For instance, many studies compute bias scores as differences between approach RTs vs. avoidance RTs for the same stimuli, whereas others compare RTs for different

stimuli for the same movement. A potential solution for this issue would be open raw data storage, to allow for re-analyses with other computations.

Another issue around the interpretation of bias scores is related to their relative nature. For instance, in the joystick task (but to some degree also in the manikin task), the mere finding that some stimuli are moved more quickly into one direction than into the other does not indicate an approach or avoidance tendency. The difference may simply be due to the fact that the movement is shorter in one direction than in the other. Therefore, the observed RT difference has to be compared to the corresponding difference for control stimuli, yielding a difference of differences as the bias score. This leads to another source of variation: Different studies may use different control stimuli, for instance, when angry faces are compared to neutral faces vs. to non-facial stimuli. Moreover, in Type 1 studies, we can only speak of biased AA tendencies in patients if we compare them to control groups, in addition to comparing the disorder-related stimuli to control stimuli. For instance, we would not speak of a bias when SAD patients show avoidance of angry faces that is comparable to the avoidance tendency exhibited by non-anxious controls. Instead, the lack of a similar avoidance tendency found in psychopaths would be considered a biased response.

Other potentially critical differences between the studies reviewed here stem from the tasks and instructions used. Regarding tasks, both the joystick task and the manikin task have been applied, but we do not know of any direct comparisons in patient samples, so we cannot be sure that biases found with one task will replicate with the other task. Regarding instructions, the reviewed studies differ in whether they employed instructions that made the meaning and valence of the stimuli task-relevant or task-irrelevant. Both approaches have their advantages and disadvantages. For instance, with instructions that make stimulus valence task-relevant, compatibility effects are usually larger (Krieglmeyer & Deutsch, 2010; Kersbergen, Woud & Field, 2015; Lender, Meule, Rinck, Brockmeyer, & Blechert, 2018; Rinck & Becker, 2007). However, they are also more prone to social desirability, and the task becomes more complex, which may be undesirable for patient samples. In any case, whatever the choice, it is not clear whether effects found with one type of instruction can be compared to effects found with the other type. This is particularly obvious for assessment studies, but may also be relevant for modification studies. Moreover, with regard to assessment versus modification of AA tendencies, we cannot simply assume that any given task is suitable for both. For instance, there is reason to assume that the manikin task yields more reliable RT data in assessment studies of Type 1 and 2 (Krieglmeyer & Deutsch, 2010), whereas the joystick task may be more suitable for the modification of AA tendencies. In the future, it will also be necessary to develop new AA paradigms for smartphones and tablet computers as well as gamified approaches

and virtual reality tasks, given that computer keyboards are used less and less, and that joysticks are almost extinct.

Regarding Type 3 modification studies, fortunately there is wide agreement that effects of AA trainings can only be interpreted when patients are randomly assigned to the active training versus a control sham-training. However, the reviewed studies differ in their choices of the control condition, and it is not clear what the best control training version is. For instance, it has been suggested that the most widely used control condition - which is essentially an extended assessment procedure - may be inappropriate (Blackwell, Woud, & MacLeod, 2017), and may affect AA tendencies as well (Becker, Jostmann, & Holland, 2018). Another critical aspect of modification studies is the question whether the biased AA tendency has indeed been changed as intended (Grafton et al., 2017; MacLeod, Koster & Fox 2009;), and whether bias change mediates symptom reduction. Again, the studies reviewed here vary greatly in whether this was the case or not, and whether it was reported at all. Finally, the modification studies also differ in whether the AA training was administered as a stand-alone intervention, or as an add-on to treatment-as-usual.

Limitations of the current review

As we limited ourselves to AA tendencies in psychopathology, we excluded samples with symptom levels not reaching subclinical levels. However, the cut-off levels could be arbitrary, and the consequent application of our inclusion criteria could have caused us to exclude relevant studies from the review. Another important limitation of the current review is the publication bias described above. We cannot estimate the size of this bias, but it most certainly exists, and it will affect the conclusions that can be drawn from the published studies. Since our review is based on peer-published papers, we must have missed relevant unpublished studies and null findings.

Implications and suggestions for future research

As explained above, biased AA tendencies were found in several mental disorders. These biases can occur as dysfunctional avoidance (as in anxiety disorders), as dysfunctional approach (as in addictions), or even as a dysfunctional lack of tendencies (as in depression, anorexia nervosa, or psychopathy). Moreover, several of these biases have been found to be malleable, and some cognitive bias modification trainings have been able to reduce both the targeted bias and clinical symptoms. All of these findings underscore the relevance of biased AA tendencies in mental disorders, and they warrant further research.

Given the paucity of studies in many disorders, our first suggestion for future research is obvious: We need more of it. In addition, these studies should have

good statistical power. Without a sufficient number of well-powered assessment studies, we cannot determine whether and how AA tendencies are biased in the different disorders. Currently, most studies addressed addictive disorders, but even in this area, the empirical picture is far from complete. And for many other disorders, hardly any studies are available. For future assessment studies, it will also be important to increase the reliability of the assessment procedures because now, it is often disappointingly low (Rinck & Becker 2007). Reliable assessment procedures are also important for modification studies because without them, it is impossible to determine whether the to-be-modified tendency does indeed change. To find out whether this is the case, and whether changes in bias are accompanied by symptom reductions, we will need more well-powered modification studies. Currently, there are many promising attempts, but reliable and replicated clinical effects are still scarce. And even in the one area where AA modification has already found its way into standard treatment guidelines, namely relapse prevention in currently abstinent alcohol-dependent patients, many questions remain unanswered, and we are left with much room for improvement. Finally, future cognitive bias modification studies should also address new training procedures. Given the rise of smartphones, tablets, virtual reality, and internet-based applications, and the concurrent disappearance of keyboards and joysticks, it will be absolutely necessary to develop and validate new procedures to assess and modify AA tendencies via these new media. We hope that this work will be undertaken because the evidence reviewed here suggests that in various mental disorders, the patients may benefit from the assessment and modification of their biased AA tendencies.


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MASTER MIND: A COMPENSATORY COGNITIVE TRAINING FOR PSYCHOPATHOLOGY-RELATED COGNITIVE DEFICITS: IMPACT ON PROACTIVE COPING AND DAILY LIFE SATISFACTION

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Abstract

Objective: Cognitive deficits are prevalent across various mental health disorders. Compensatory cognitive training learns individuals how to manage and compensate for these deficits in daily life. Since few integrative compensatory cognitive training programs in mental health care treatment are available, Master Mind was developed. The acceptability and feasibility of the intervention in a transdiagnostic sample of patients with predominantly severe mental illness were studied, and an initial exploration of its effects on proactive coping and quality of life was conducted. **Method**: To measure the acceptability of the training, Session Rating Scales were completed by the participants. Next, the impact on proactive coping behavior and daily life satisfaction over time was studied. Also the relation between the level of proactive coping and cognitive resources was tested with linear mixed models. **Results**: Forty-four patients (age ranging from 22 to 68 years) with severe mental illness (affective and psychotic disorders) as well as developmental disorders participated. Present findings suggest a good acceptability of the compensatory cognitive training given the positive participant evaluation. Thirty-three participants completed both the baseline and posttraining measure, and 18 participants completed the follow-up measure. Preliminary results showed a significant improvement in proactive coping level from baseline to posttraining. Cognitive processing capacities were not found to be related to proactive coping. Proactive coping was found to predict an increase in daily life satisfaction at 4-month follow-up. **Conclusions and Implications for Practice**: Master Mind shows good acceptability in a transdiagnostic sample. The intervention may enhance proactive coping, regardless of the quality of actual cognitive resources.

Introduction

Cognitive deficits are rather the rule than the exception in psychopathology, and this "C factor" is to be considered as a transdiagnostic feature (Abramovitch et al., 2021; Caspi et al., 2014; Chavez-Baldini et al., 2023; East-Richard et al., 2019). They are associated with an increased risk of development, maintenance, and relapse of mental illnesses and typically manifest in the mood disorder and psychotic disorder spectra (Bora et al., 2013; Martínez-Arán et al., 2004; Martino et al., 2008; McIntyre et al., 2013; Robinson et al., 2006; Thompson et al., 2005; Zuckerman et al., 2018). Cognitive deficits have significant impact on participation level and quality of life (Green & Harvey, 2014; Papakostas, 2014; Rock et al., 2014; Sanchez-Moreno et al., 2009).

Indeed, patients report substantial burdens due to these cognitive deficits (Kitchen et al., 2012). In treatment of psychopathology-related cognitive dysfunction (cognitive remediation), two different approaches can be distinguished, the restorative and the compensatory approach. Restorative training intents to restore the cognitive deficit itself. Restorative training procedures have yielded some improvements on the level of specific cognitive tasks by drill and practice exercises. However the generalization of these task effects to "real-world benefits" remains limited (Hallion et al., 2024). Best results have been established when programs were integrated in other psychological or vocational interventions (Bowie et al., 2017; Wykes et al., 2011). Compensatory cognitive training (CCTr) involves developing strategies that help individuals manage and compensate for cognitive deficits in their daily lives (Bowie et al., 2017; Martínez-Arán et al., 2011). CCTr can improve functioning in patients with severe mental illness: Positive effects are reported on outcome factors such as medication, adherence, employment rates, and overall functioning and wellbeing (Allott et al., 2020; Twamley et al., 2019; Velligan et al., 2002). The CCTr approach aligns well with the current opinion on indicators of personal recovery from mental illness, shifting from severity of symptoms to well-being or life satisfaction (Correll et al., 2025).

The underlying mechanisms through which CCTr may exert its effects on functional outcomes are poorly understood as yet (Allott et al., 2020; Douglas et al., 2020; Lee et al., 2013; Lejeune et al., 2021; Twamley et al., 2019). The "C-factor" construct identifies several potential factors, such as affective state, perceived cognitive ability, and motivational factors such as perceived self-efficacy, that affect cognitive resources (Abramovitch et al., 2021). In line with this reasoning, CCTr effects were indeed found to be related to the perceived ability to manage cognitively demanding daily tasks among participants with severe mental illness (Bowie et al., 2017). Moreover, defeatist beliefs on one's cognitive functioning were found to mediate the level of functional outcome and negative symptoms (Grant &

Beck, 2009). These findings are consistent with theoretical models that associate reduced cognitive resources with increased stress perception, negative task appraisal, and negative affective state (Eysenck et al., 2007; Staal, 2004). This theory relates cognitive depletion in psychopathology to stress and affective burden, which can help explain the mechanism of change by CCTr.

One potential mechanism by which CCTr could lead to improved functioning and well-being could be proactive coping (PrC). PrC coping is defined as the capacity to anticipate and manage future stressors through goal-directed behavior (Greenglass, 2002). Research in healthy populations has shown that PrC is related to positive affect, well-being, and life satisfaction (Greenglass & Fiksenbaum, 2009; Stanojevíc et al., 2014). Studies on somatic health conditions with comorbid cognitive disorders such as stroke, Parkinson's disease, and diabetes have also indicated PrC to be positively related to quality of life and effective disease management (de Graaf et al., 2022; Hurt et al., 2012; Thoolen et al., 2009; Tielemans et al., 2014, 2015).

This capacity to respond proactively to potential stressors is related with the quality of executive functioning (such as working memory, cognitive flexibility, and inhibitory control; Hofmann et al., 2012). Executive functioning in turn is sensitive to the effects of elevated stress levels (Garrison & Schmeichel, 2022; Shields et al., 2016) and associated with the vulnerability to the development of psychopathology (Zelazo, 2020). This highlights the complex and reciprocal relationship between cognitive processing resources and the use of PrC strategies in psychopathology (Allott et al., 2015; Matthews & Campbell, 2010; Nieto et al., 2020). CCTr may facilitate a more proactive approach to cognitively demanding daily tasks. This could in turn lead to reduced stress and symptoms, as well as improved functional outcome in psychopathology (Fredrick et al., 2015; Morris et al., 2015; Torrent et al., 2013; Twamley et al., 2019).

Despite the considerable evidence highlighting the prevalence, persistence, and burden of cognitive deficits in psychopathology, there still remains a significant gap in clinical practice treatment approaches (Wong et al., 2024). Several calls have been made for the development of integrative treatments that include CCTr, both for depressive disorders and bipolar disorders, as well as schizophrenia (Douglas et al., 2020; Kaser et al., 2017; Miskowiak et al., 2018; Solé et al., 2017).

A transdiagnostic CCTr program for psychiatric conditions in general is not yet available in specialized mental health care (in the Netherlands). Therefore Master Mind, based on evidence-based cognitive strategy interventions studied in medical rehabilitation settings, has been developed by the authors (Anke Loijen, Ellen Wingbermühle, Wouter Oomens, and Jos Egger) at the Centre of Excellence for Neuropsychiatry, Vincent van Gogh Institute for Psychiatry, Venray, The Netherlands.

The training addresses several cognitive domains (processing speed and attention, memory, executive functioning, and social cognition), as well as limited load capacity and negative thinking patterns with regard to cognitive functioning. Eight group sessions once every 2 weeks were alternated with individual online feedback; the program was supported by an e-health application. In all sessions, extensive psychoeducation is provided, and several strategies are introduced and practiced. Personal goals related to problems arising in daily life are set, and a neuropsychological assessment at start of the training is conducted to select appropriate strategies. A significant other is involved during the training, During training, the presence of cognitive deficiencies associated with psychopathology is normalized, whereas therapists encourage a proactive encounter to compensate for these restraints. The therapists provide active support on the generalization of strategies to cognitive challenges in daily life.

The primary objective of this initial study is to study the feasibility of a transdiagnostic application of the Master Mind CCTr intervention. To answer the question whether the training is feasible and acceptable for the intended patients, at every training session, participants' subjective evaluations of the sessions are assessed. Furthermore a potential mechanism of change by CCTr, the level of PrC, is studied over time and related with cognitive resources, as well as satisfaction with daily life. It is expected that PrC will increase over the course of the training, which may have a positive effect on satisfaction with daily life. We hope that the findings of this exploratory study will provide further insight into the feasibility of the CCTr "Master Mind" for patients with various forms of mental illness and into the relationship between CCTr, PrC, and cognitive resources.

Method

Participants

In the period between 2016 and 2021, 44 outpatients were referred by their specialized mental health caregivers or general practitioner for Master Mind treatment, which was offered by the Vincent van Gogh Centre of Excellence for Neuropsychiatry in Venray, the Netherlands, and participated in this study. All have cognitive complaints related to their psychiatric condition and receive mental health care. The psychiatric classification by referral was accepted as such. A cognitive assessment was part of the treatment and was conducted (unless a recent assessment was available). The main inclusion criterion was that participants experienced limitations in their daily lives as a result of subjective cognitive complaints (related to psychopathology) and wanted to learn how to cope with

these limitations and participate in a group. No strict exclusion criterion was set. No other psychotherapeutic treatment asides pharmacotherapeutic treatment or home support took place during the Master Mind training.

Material

Master Mind. Master Mind developed at the Centre of Excellence for Neuropsychiatry is a blended treatment, with face-to-face group sessions combined with an e-health application for providing information, exercises, and feedback. The treatment is given by two health care psychologists who are supervised by a clinical neuropsychologist. Before the start of the group sessions, individual neuropsychological tests are applied by a psychologist, in order to gain insight into the participants' personal cognitive profile. This profile is used in order to set individual goals for specific cognitive strategies. Goals are set in the individual session following assessment based on the personal cognitive profile. Goals are set on a behaviour level and should be as specific, measurable, achievable, relevant, and time-bound (SMART) as possible. Each group session is started with the Master Mind worksheet: On this overview, the specific problem occurring in which situation and what strategy could help to cope with this problem within this situation is filled in and evaluated in either the group session itself or at the individual online feedback moment. Treatment consists of eight group sessions (consisting of four to 8 participants), with a duration of 90 min plus a 15-min break. In each session, a separate cognitive domain is addressed. By the use of the online learning environment ("health space"), psychoeducation on that specific cognitive (dys) function is provided, and the different cognitive strategies to cope with those deficits are discussed in the group. Group sessions take place once every 2 week. These sessions are alternated by personalized online feedback by the trainers on the progress of strategy application in daily life via the message functionality of the online learning environment. Halfway and at the end of training, individual goals are evaluated with the trainer, participant, and a significant other of the participant. Paper–pencil material remains available for those who are not able to make use of the online learning environment due to either lacking personal computer skills or the limited accessibility to a technical device. All participants are strongly encouraged to involve a significant other, who may be a mental health care worker. This buddy can be involved in goal setting, evaluation, and exercises/homework. Involving a significant other can contribute to understanding and support.

The treatment itself builds on extensive evidence-based neuropsychological treatment protocols (Ponds et al., 2010). These protocols are condensed into the Master Mind treatment protocol. The following cognitive deficits are covered, and every group session addresses one cognitive domain: (a) attention and decreased

processing speed (Winkens & Fasotti, 2010), (b) memory deficits (van Kessel et al., 2010), (c) executive dysfunction (Boelen et al., 2012; Levine et al., 2000), and (d) social cognitive deficits. Besides these cognitive modules, the treatment is complemented by a fifth module focusing on how to cope with limited mental capacity (Zedlitz & Fasotti, 2010) and a final module (6) on dysfunctional thoughts concerning ones subjective cognitive deficits. During treatment, the trainers keep attention to individual learning goals, accentuating the domains most relevant for one's individual goals. An introduction session in which goals are set, as well as the final "Reminder" session in which all individual goals and strategies are rehearsed and future use is discussed, completes the training.

To illustrate a participant's goals, process, and evaluation, a case report of an individual with psychotic vulnerability and a mood disorder is presented: The neuropsychological assessment revealed executive dysfunction and impaired processing speed, providing clarification of memory complaints in daily life. Due to these cognitive problems, this participant spends a disproportionate amount of time on daily household activities. This prevents her from being able to relax and causes her to think more and more negatively about her functioning, resulting in a decreased mood. The goals as set in the online treatment environment were making structural use of an agenda, starting photographing again, and improving balance between physically and mentally demanding activities. The participant hopes these goals will result in improved perceived control over cognitive and daily functioning. During the training, she explored the use of various strategies in different domains. In the groups session, different strategies for each domain are discussed and tips were shared. A single strategy was chosen each session to practice in the following 2 weeks. This participant learned how to make and use step-by-step plans and how to (structurally) use an agenda. She learned to structurally apply a thought defusion exercise. Her significant other gained insight in the cognitive deficiencies as well and helped her to cope with her cognitive problems. A better balance between (cognitive) strenuous and relaxing activities enabled her to be more active in her leisure time. All these strategies led to better control over her (cognitive) functioning and stabilized mood.

Questionnaires. In order to evaluate the acceptability of Master Mind, Likert scales regarding general well-being (one question of the Outcome Session Rating Scale), relationships, approach and methods, goals and subjects, and the overall evaluation of the session (Session Rating Scales; SRS) were assessed at each session (except the introduction and final session; Hafkenscheid et al., 2010).

The level of PrC over time was measured using the Utrecht's Proactive Coping Competence List. This questionnaire consists of 21 items measuring the level of PrC from 1 = not very competent, 2 = hardly competent, 3 = competent, and 4 = very

competent. Higher scores on the questionnaire represent higher levels of experienced capacity to anticipate on and to cope with health issues.The reliability of this questionnaire has been rated as good (Cronbach's α = .83–.95; Bode et al., 2008). In the current sample, Cronbach's αs are .92 TP1, .92 TP2, and .92 TP3.

Participation was measured by the Utrecht Scale for Evaluation of Rehabilitation Participation ("Schaal voor Evaluatie van Revalidatie Participatie," USER-P; van der Zee et al., 2010). The first part of the questionnaire quantifies the frequency (four questions) and the amount of time one spends in daily life on work (seven questions), study, and household and activities such as leisure, sports, visiting others. Part two contains eleven questions on experienced limitations in daily living due to health issues (level of restriction), and part three assesses with 10 questions on satisfaction with one's daily life. This third part of "satisfaction with daily living" (SDL) has five response options for each question: very dissatisfied, dissatisfied, neutral, satisfied, and very satisfied. Scaled scores are used (percentage of maximum score for each subscale). Higher scores represent a higher participation level (Subscale 1), fewer participation restrictions (Subscale 2), and higher satisfaction (Subscale 3) with regard to the participation in daily living. The questionnaire gives three separate scores, and no total score is available. Its internal consistency in a mixed sample of rehabilitation outpatients, Cronbach's α, ranges from 0.70 to 0.91 (Post et al., 2012; n = 395, Dutch sample). In the sample of this present study, Cronbach's α ranges from .71 at TP1, .86 at TP2, and .60 at TP3.

Neuropsychological Screening. Part of the treatment program is a neuropsychological assessment in order to increase insight in one's cognitive strengths and weaknesses and to discuss participants' (negative) attributions regarding their cognitive functioning. From this assessment, the Working Memory Index (WMI; n = 38) and Processing Speed Index (PSI; n = 39) of the DutchWechsler Adult Intelligence Scale (Wechsler, 2008, 2012) are used as measures of cognitive processing resources to relate to PrC.

Design and Procedure

This study has a noncontrolled exploratory study design with a 4-month follow-up evaluation. The study was performed in accordance with the Declaration of Helsinki and was approved by the Vincent van Gogh Institutional Review Board (Nr. 2018.00.18), and all participants gave their consent to participate. Participants completed questionnaires at the first and in the final sessions of Master Mind. SRS were administered each session as part of the training.

Participants were contacted 4 months after treatment for a follow-up measurement of the questionnaires. In order to increase the response rate at all timepoints, participants

were asked if they would like assistance in completing the lists, either at an on-site appointment or by telephone with the research assistant. Alternatively, they could return the completed lists by post. The TP response does not equate to attendance or training drop-out. Not all participants succeeded in completing all the TP measures. Number and reasons of drop-out have not been logged.

Data Analysis

For the assessment of the acceptability of the training, the mean rating per session on the rating scale was calculated for each session, including the number of respondents for each session and scale. Because of several missing TPs and the within-subject design, linear mixed modeling was used (SPSS Version 28.0) to analyze the level of PrC over training and the impact on general well-being. For each model, the timepoints TP1, TP2, and TP3 were entered as a repeated measures factor (without intercept). The ARH(1) covariance matrix was used, allowing variances to differ over time: It is hypothesized that the last TP3 (4 months after training) is less strongly correlated to TP1 then TP2 to TP1. PrC was entered as a fixed factor. Next, subjects were included as random factors including intercepts accounting for the unique variability across different subjects (the level of PrC can differ between individuals from the start of training).

Maximum likelihood method was used, and Type III tests with Satterthwaite-adjusted degrees of freedom (default option of SPSS) were used to test the significance of the fixed effects of PrC. Bonferonni-corrected pairwise comparisons were run for post hoc tests. Effect sizes for significant post hoc comparisons were calculated using Cohen's d, with pooled standard deviations derived from the reported standard errors and sample size. First a model was fitted with PrC as a dependent variable (Model 1). Next, it was tested whether either WMI or PSI accounted for differences in PrC over time of training (Models 2 and 3). Another Model (4) with SDL as dependent variable was fitted, and PrC was added as a covariate in this Model (5). Likert scales of the Sessions Rating Scales were visualized and means were reported.

Results

Demographic Information

The sample consisted of 20 males and 24 females. The study population was characterized by limited ethnic diversity, with the majority of participants identifying as White and ethnically Dutch. The mean age of the sample was 50 years (ranging from 22 to 68 years). Educational levels were recorded as follows: primary education n = 2, prolonged primary education n = 6, lower level secondary

education n = 4, higher level secondary education n = 18, and preuniversity/higher education professional education n = 13 (of one participant, the educational level was unknown).

Classifications of psychopathology according to the Diagnostic and Statistical Manual of Mental Disorders, fifth edition, text revision at the time of referral showed that 31 participants (31 out of 44) were classified with a mood disorder (American Psychiatric Association, 2022). Within this group of participants with mood disorders, 20 individuals suffered from a comorbid disorder: Neurological disorders were present in 11 cases, psychotic disorder in two cases, developmental disorder in five cases, and personality disorder in two cases. Besides the group of mood disorders, nine participants were diagnosed with psychotic disorder (both first psychotic episodes and schizophrenia classifications were present). Besides mood disorder and psychotic disorder, in two cases, the primary diagnosis was a developmental disorder, one of them complicated with neurological disorder. At last, in one case anxiety disorder was reported and in one case the diagnostic classification was unknown. The mean Wechsler scores and standard deviations were 90 (SD =15) for the WMI and 85 (SD = 17) for the PSI.

Acceptability

In order to assess the acceptability of the training at every training session, participants' subjective evaluations of the program were assessed by scores on the SRS (ranging from 0 to 100). Outcomes indicate good evaluations of the therapeutic alliance (SRS1: 77.6), goals and subjects of training (SRS2: 77.6), general approach and method (SRS3: 76.0), and overall evaluation of the session (SRS4: 74.2). General sense of well-being according to the outcome rating scale showed a general mean of 74.2. See Table 1 for all the mean ratings for each session and scale.

Explorative Analyses on PrC and Quality of Life

The total number of respondents for TP1 was n = 42 (42 out of 44); for TP2 n = 34 (34 out of 44); and for TP3 n = 18 (18 out of 27). See Table 2 for the descriptives of each questionnaire on every timepoint.

See Table 3 for an overview of the number of participants and their completed timepoints.

Tables 4 and 5 present the outcomes of the linear mixed models. Table 4 shows the estimated marginal means and standard errors for the questionnaire measures, while Table 5 summarizes the results of the tested models.

Table 1. Mean rating per scale and session, number of respondents for each sessions and scale.

Session	ORS	n	SRS 1	N	SRS 2	n	SRS3	n	SRS4	n
1	71.5	41	73.2	42	73.7	42	71.5	42	73.3	42
2	72.8	41	73.3	42	76.2	42	76.8	42	72.9	42
3	74.8	36	80.0	37	80.7	37	76.5	37	76.1	37
4	75.5	35	80.2	36	78.2	36	76.6	36	71.1	36
5	76.4	32	78.4	32	75.8	33	76.4	33	73.3	32
6	74.1	30	80.2	31	80.7	31	77.9	31	78.2	31
Total	74.2	215	77.6	220	77.6	221	76.0	221	74.2	220

Note. Session 1: 'Time & Attention' ; Session 2: Memory; Session 3: 'Plan Better' ; Sessions 4: Limited Load Capacity; Sessions 5: 'View on Emotions'; Session 6: 'The Power of Thoughts'. Outcome Rating Scale (ORS) = General sense of well-being; Session Rating Scale 1 = Therapeutic alliance; Session Rating Scale 2 = Goals & subjects of training; Session Rating Scale 3 = General approach & method; Session Rating Scale 4 = Overall evaluation of the session.

Table 2. Descriptives Questionnaires at each Timepoint

Measure	TP	*N*	*M*	*SD*
SDL	1	42	53.2	20.8
	2	34	57.0	20.6
	3	18	60.0	13.4
PrC	1	42	53.4	9.0
	2	32	56.7	8.0
	3	18	54.9	9.3

Note. TP= Timepoint; SDL = Satisfaction with Daily Living (part three of the "Schaal voor Evaluatie van Revalidatie Participatie", USER-P); PrC = total sore on the Utrecht's Proactive Coping Competence List; *N* = number of respondents.

Table 3. Frequency of Completed Timepoints

Completed Timepoints	*N*
TP1 + TP2 + TP3	14
TP1 + TP2	19
TP2 + TP3	1
TP1 + TP3	3
TP1	6
TP2	1
Total	44

Note. TP= Timepoint; TP1= baseline, TP2= posttraining, TP3= follow-up; *N*= Number of Subjects

Table 4. Estimated Marginal Means and Standard Error PrC en SDL

Timepoint (TP)	Proactive Coping (PrC)[1]	Satisfaction with Daily Living (SDL)[2]
1	53.1 (1.3)	53.3 (3.1)
2	56.3 (1.3)	56.5 (3.3)
3	55.6 (1.4)	61.4 (2.6)

Note. [1] Total mean (standard error); [2] Percentage of maximum score for the scale.

Table 5. Linear Mixed Model: Fixed-effects and Post-Hoc Pairwise Comparisons

Model	Effect	Mean difference	Std Error	df	F	p	n
Model 1	PrC dependent variable						44
	Time			(3, 25.90)	F= 771.21	< .001	
Post-hoc[1]	TP2-TP1	3.2	1.1	36.21		.023	
Model 2	PrC dependent variable; PSI covariate						39
	Time			(3, 20.05)	F = 19.02	< .001	
	PSI			(1, 38.74)	F = 1.55	.220	
Post-Hoc							
Model 3	PrC dependent variable; WMI covariate						38
	Time			(3, 18.01)	F = 66.56	< .001	
	WMI			(1, 37.17)	F = .002	.968	
Post-Hoc							
Model 4	SDL dependent variable						44
	Time			(3, 34.95)	F= 215.03	< .001	
Post-Hoc	TP3-TP1	8.1	3.1	25.37		.041	
Model 5	SDL dependent variable; PrC covariate						44
	Time			(3,36.32)	F= 1.63	.199	
	PrC			(1, 43.15)	F= 18.03	< .001	
Post Hoc							

Note. SE = standard error; PrC = proactive coping; TP = timepoint; TP1 = baseline; TP2 = posttraining; PSI = Processing Speed Index WAIS-IV; SDL = satisfaction with daily living; WMI = Working Memory Index, WAIS-IV; WAIS-IV = Dutch Wechsler Adult Intelligence Scale. [a] Post hoc results for significant findings are reported.

The first model is run to answer the research question of whether PrC increases over time of training. Second, it is tested whether cognitive processing resources (PSI or WMI) account for the level of PrC over time (Model 2 and Model 3). Next, model four is run to test whether SDL changes over time. The fifth model adjusts the change in SDL in relation to PrC. A significant increase of PrC over time of training (between TP1 and TP2) was found: After training, PrC was significantly higher ($p = .023$), and this effect remained stable over time at follow-up. The corresponding effect size was small to medium, Cohen's $d = 0.38$. Controlling for cognitive processing resources did not change this outcome: Neither working memory capacity nor processing speed accounted for the differences in PrC over time. Next, a significant difference (between TP1 and TP3) in SDL was found: SDL was significantly higher at follow-up compared to the start of the treatment ($p = .041$) with a small-to-medium effect size (Cohen's $d = 0.43$). However when PrC was added as a covariate in the model, the former significant differences vanished. This suggests that this effect of time can be attributed to differences in PrC: Participants with higher PrC showed higher SDL at follow-up.

Additionally, the actual level of participation and perceived restrictions (part one and part two of the Utrecht Scale for Evaluation of Rehabilitation Participation) were explored. The scores were entered as fixed effects in separate models. Significant effects were present; however post hoc analysis did not show significant differences between timepoints. This indicates that the differences between the estimated means were too small.

Discussion

By means of this initial exploratory study, the feasibility and acceptability of Master Mind, applied in a transdiagnostic sample of patients with severe mental illness and/or developmental disorder, were studied. The level of PrC behavior and daily life satisfaction over time (baseline, posttraining, and follow-up) was studied, as well as the relation between cognitive processing capacities and PrC. Master Mind was applied in a specialized mental health care outpatient setting. A wide range of psychiatric classifications was represented among the participants, including affective disorders, psychotic disorders, and developmental disorders. The training was well evaluated by its participants; the training content, used methods, and therapeutical factors received good evaluations. These positive ratings were consistently present over the sessions. Moreover, preliminary findings are indicative of an improvement in PrC during the training period and stabilization at the follow-up phase. A significant increase in satisfaction with daily living was observed over time, between the first assessment and the follow-up

assessment. PrC was found to be associated with this effect. The increase in PrC did not change when controlling for cognitive processing resources (working memory capacity or speed of information processing). Finally, no significant differences between the three timepoints were observed with regard to the actual level of participation and perceived restrictions.

To the best of our knowledge, this is the first evaluation of a CCTr in the Netherlands applied within groups of patients with various forms of mental illness, including developmental disorders, adapting a transdiagnostic approach. The current findings suggest that Master Mind meets the needs of individuals with severe mental health conditions and neurocognitive deficiencies, supporting improvement in PrC skills and satisfaction with daily life. The significant difference in PrCover time of training alignswith previous research that indicates that CCTr enhances more adaptive coping mechanisms (Paans et al., 2018). Being able to cope with these persistent cognitive constraints actively may help to reduce the stressors related to cognitive tasks encountered in daily life (De Raedt & Hooley, 2016). This relation is of interest as improvements in self-efficacy and stress resilience after CCTr may result in a decrease of psychopathology-related symptoms (Allott et al., 2026; Burton & Twamley, 2015; Twamley et al., 2019).

In line with current findings, previous research has also reported an absence of association between cognitive processing resources and PrC (MacAulay & Cohen, 2013). Furthermore, it has been found that individuals with lower cognitive capacity may also benefit from CCTr (Lejeune et al., 2021). Taken together, these findings could substantiate the finding that the effect of Master Mind on enhanced PrC is not necessarily limited by cognitive resources.

However, replication in a larger sample, allowing the inclusion of an interaction effect, can improve insight in the relation between cognitive resources and coping style over time of training. In future research, the quality of memory consolidation and retrieval is also of interest to relate to PrC, in addition to working memory and processing speed. Additionally, the diversity of psychiatric classifications in the current sample, including developmental disorders, may have introduced heterogeneity in treatment response.

Future studies could therefore examine treatment effects separately for individuals with developmental disorders. More insight in the relation between PrC and the ability to apply cognitive strategies is of interest as well. Therefore future studies could include personalized measures of the perceived ability to cope with cognitive challenges specific to each participant, as well as ecological valid outcome measures such as the Oxford digital multiple errands test (Webb et al., 2022). Finally, the level of restriction experienced in daily life due to mental illness remained stable throughout the training period for the current sample. This lack of association between PrC and the level of restriction experienced has

also been found in other studies involving patients with chronic health condition (Tielemans et al., 2015; Weldam et al., 2013).

Several limitations should be acknowledged. First, the interpretation of the acceptability and feasibility of the training would have been strengthened if attendance rates and reasons for dropping out had been systematically recorded. In addition, information on whether a significant other was involved, as well as the recording of the nature of the participant's relationship to this person (e.g., partner, family member, friend, or mental health worker), would have provided more contextual insight. In future research, this variable should be included. Finally, future research should investigate whether the present findings replicate in samples with greater cultural and ethnic diversity, as the current sample was largely homogeneous. The methodological limitations of the nonexperimental design should be considered when interpreting the findings: The absence of a control group clearly limits the ability to uniquely attribute effects to the Master Mind intervention: The incremental contribution of Master Mind (considering its specific focus on elaborate psychoeducation and personalized strategy use in daily life) in addition to generic treatment factors or placebo effects remains unclear, and external factors may have influenced the results. Finally the relatively small sample size, particularly at the third timepoint (TP3), raises concerns about statistical power and potential response bias. In order to retain as many data points as possible, linear mixed modeling was applied. But it is plausible that responders differ systematically from nonresponders, possibly in their level of PrC or overall well-being, as well as level of cognitive restraints. To address this, replication in a larger sample with consistent response rates over time is needed. A next step to clarify the specific effects of Master Mind is to include a control group and increase inclusion. Therefore a randomized controlled trial and a multicenter study are needed. An increasingly preferred method for studying the effects of CCTr is the use of single-case experimental designs and/or idiosyncratic systems of evaluation (Allott et al., 2026). Given the substantial variability in participants' individual goals and recovery needs, these designs may offer valuable insights into personal treatment trajectories and recovery. Single-case experimental designs prioritize the evaluation of change at the individual level, focusing on how participants themselves perceive and report their progress in domains relevant to their daily functioning and quality of life. These measures may also include the evaluation of significant others on participants' goal progress.

In conclusion, the transdiagnostic application of Master Mind in groups of patients with various forms of psychopathology, as well as developmental disorders, is found to be feasible. The training was well accepted given the positive participants' ratings and the observed enhanced PrC. Moreover, this observed effect on PrC was not related to cognitive resources and may (partially) account

for improved satisfaction of daily life. Future research, including a control group (or using a single-case experimental design) and incorporating measures of PrC, subjective cognitive complains, perceived burden, and measures of functional outcome would be of interest. The aim of this initial evaluation of Master Mind is to make personalized, integrated treatment for cognitive deficiencies more accessible to individuals with severe mental health conditions.


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MODIFICATION OF AUTOMATIC ALCOHOL-APPROACH TENDENCIES IN ALCOHOL-DEPENDENT PATIENTS WITH MILD OR MAJOR NEUROCOGNITIVE DISORDER

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Abstract

Background: To examine the applicability of an alcohol-avoidance training procedure in patients with alcohol dependence and alcohol-induced neurocognitive disorders (NDs), we trained 2 groups that differed in the degree of cognitive impairment: One group fulfilled the DSM-5 criteria for Alcohol-Induced Mild ND, and one group was diagnosed with Korsakoff's syndrome (Alcohol-Induced Major ND, confabulatory/amnesic subtype; DSM-5). The intervention is assumed to match the preserved cognitive capacity for implicit learning in both groups. **Methods**: Fifty-five inpatients with a mild neurocognitive disorder and 54 inpatients with Korsakoff's syndrome were trained. Six training sessions (including pre- and posttests) of a computerized implicit alcohol approach-avoidance task were applied. Neurocognitive variables were available from the standard assessment procedure of the clinic. **Results**: Training of alcohol-avoidance tendencies is feasible in a population with alcohol-related neurocognitive disorders. The alcohol-approach bias decreased for both groups in each session. Better learning results over time were obtained in participants with a larger baseline alcohol-approach tendency. Learning effects were positively related to age and implicit (non-declarative) memory functioning. No relation between training effects and executive or explicit memory functions were found. **Conclusions**: Training of an alcohol avoidance tendency can be successfully applied in patients with alcohol-dependence including those with alcohol-induced neurocognitive disorders.

Introduction

Alcohol-induced neurocognitive impairment is a significant factor to take into account in the treatment of alcohol dependency. The presence of neurocognitive disorders (NDs) is related to poor treatment outcome (Bates et. al., 2013) and it increases the risk of relapse in alcohol use (Noël et al., 2002). Regular treatment procedures often aim to improve self-control and are highly dependent on reflective and explicit memory capacities. However especially executive functioning and episodic memory are impaired in patients with alcohol-induced NDs (Duka et al., 2011; Fein and McGillivray 2007; Moselhy et al., 2001, Walvoort et al., 2016). In that particular population, patients with Korsakoff's syndrome (KS) can be typically differentiated from those with non-Korsakoff related alcohol–induced neurocognitive dysfunctions (NKS), based on the severity of their memory disorder (Wester et al., 2013). KS is a major neurocognitive disorder and is, other than NKS, characterized by a unique profound anterograde and retrograde amnesia (Kopelman, 1995; Kopelman et al., 2009; Pitel et al., 2008). Still, a generally well-preserved cognitive ability, present in both groups, is the non-declarative memory function (Oudman et al., 2011), including implicit motor learning skills (Hayes et al., 2012; Van Tilborg et al., 2011). For these reasons, cognitive bias modification procedures (CBM) targeting automatic, implicit processes might be promising intervention methods for patients diagnosed with alcohol-induced neurocognitive disorders.

These automatic, implicit processes interact with reflective, rational processes, and this complex interaction contributes to adaptive behavior (Strack & Deutsch, 2004). In psychopathology, implicit processes are biased in concordance with psychopathology-related schemas (Beck, 1991). One example is the approach-avoidance bias: Cues are evaluated as overly positive (appetitive) or negative (aversive), resulting in automatic approach (or avoidance) action tendencies towards or away from these cues (Chen and Bargh, 1999). These automatic action tendencies are known in several psychiatric disorders, such as anxiety (Lange et al., 2008; Reinecke et al., 2012) depression (Radke et al., 2014; Trew, 2011), obsessive-compulsive disorder (Najmi et al., 2010), skin picking (Schuck et al., 2012), and psychopathy (Von Borries et al., 2012). In alcohol use disorder (AUD), an automatic approach tendency for alcohol-related cues has been shown in several studies (Wiers, et al., 2009; 2010; 2014). This tendency is the result of a repeated association of incentive salience with the substance use and alcohol-related cues (Robinson and Berridge, 1993). These cues elicit automatic approach tendencies accompanied by increased craving (Field et al., 2005) and subsequent alcohol consumption (Christiansen et al., 2012; Wiers et al., 2010).

As this biased implicit information processing plays a substantial role in (the maintenance of) AUD (Brion, 2017), methods to directly modify these implicit processes have gained great interest in research and clinical practice over the past decade. One of these methods is the approach-avoidance training (AAT), a computerized joystick training, developed to modify approach-avoidance behavior: Participants repeatedly push pictures of alcohol-related stimuli away and pull neutral pictures towards themselves. In a student population at risk for AUD, alcohol intake decreased after one training session compared to a control group (Wiers et al., 2010). In a clinical population, the trained group displayed more than 10% lower relapse rates 1 year after training, compared to a sham training condition (Wiers et al., 2011). Here, soda pictures and alcohol pictures were presented during four 15-minute training sessions. In those studies, the AAT was executed using an optical zoom effect: The size of the presented picture increases or decreases according to the movements of the joystick. For example, while one pushes the joystick away, the picture size decreases. This zoom effect optimizes the impression of moving away from the stimulus, as the distance seems to increase between oneself and the stimulus. This was done to prevent recategorizing of the approach-avoidance movements and to improve the validity of the approach-avoidance tendency measurement (Rinck & Becker, 2007). Moreover, the training usually employs indirect instructions: Participants are asked to pull or push the joystick depending on a surface feature that is unrelated to picture contents, for instance according to the slight tilt with which the pictures are presented (push right-tilted pictures and pull left-tilted). Manning and colleagues (2016) as well as Eberl and colleagues (2013) replicated the decrease in relapse rates as shown in the study by Wiers and colleagues (2011). Eberl and colleagues (2013) additionally reported that the change in alcohol-approach tendencies mediated the training's positive effect on treatment outcome. However, there are contradicting reports of the relation between alcohol approach bias and drinking behavior: While Martin Braunstein and colleagues (2016) reported that stronger alcohol-approach tendencies predicted more drinking, Field and colleagues (2017) as well as Spruyt and colleagues (2013) found the opposite relation. The latter 2 studies question the usefulness of alcohol-avoidance training, while the relapse-preventive effect of such a training reported by Wiers and colleagues (2011) and Eberl and colleagues (2013) seems to support it. Systematic reviews of approach-avoidance modification paradigms also differ in their conclusions about the effectiveness of this intervention (Cristea et al., 2016; Kakoschke et al., 2017). This emphasizes how important it is to take into account possible moderators of CBM effects, the influence of methodological characteristics (such as how bias scores are calculated, and whether relevant or irrelevant features are used for instructions), study designs, sample sizes, problem severity

of the samples, and statistical approaches (see the online commentaries of Wiers [2016] and Field [2016]).

Of particular relevance for the aforementioned patient population with alcohol-induced NDs is that implicit processes are known to be powerful predictors of alcohol use when effortful control processes are relatively weak (Stacy and Wiers, 2010). These effortful control processes, also described as executive functioning, comprise three different cognitive processes: Interference control (IC), working memory and mental flexibility (Miyake et al., 2000). The first two were frequently studied as moderators of the relation between implicit processes and psychopathology.

IC is mostly operationalized by variations of the classical Stroop paradigm (MacLeod, 1991). When IC is relatively weak, implicit processes are stronger and contribute more to psychopathological behavior (Peeters et al., 2012; Houben & Wiers 2009; Wiers et al., 2009). Therefore, this factor is of interest as a predictor of successful modification, since one can hypothesize that people with lower IC may profit more from implicit process modification procedures than from traditional methods. Salemink and Wiers (2012) indeed reported IC as a moderator of modification effects in a sample with anxiety problems. However, Eberl and colleagues (2013) could not replicate this moderation effect in an alcohol-dependent patient population.

As to working memory capacity (WMC), low levels possibly predict the influence of implicit processes (Sharbanee et al., 2013) and the amount of drugs or alcohol intake as well (Grenard et al., 2008; Thush et al., 2008).

Besides IC and WMC, in the study by Eberl and colleagues (2013), age and the size of the alcohol-approach tendency at pretest moderated AAT training outcome: A larger bias before training and being older were related to better training outcome. The positive relation between magnitude of bias at pretest and clinical outcome measures is in line with other bias modification studies such as Amir and colleagues (2011) and Salemink and Wiers (2012), both in populations with anxiety-related problems.

In summary, the applicability of alcohol-avoidance training procedures is of high interest for patients diagnosed with alcohol-induced NDs, for several reasons. First, impaired executive functioning (a profound characteristic of this patient population) is associated with a stronger influence of implicit processes on drinking behavior, and it is a possible moderator of CBM. Second, in contrast to traditional treatments, for CBM, illness insight on behalf of the patients is not a prerequisite. Third, alcohol-approach modification is assumed to match the patients' preserved implicit learning capacity. Based on these characteristics, CBM could be an important additional treatment method for this specific population.

The aim of our study was twofold: First, we studied the applicability of an alcohol-avoidance training in patients with alcohol-induced neurocognitive disorders. Since this type of training has never been used in this population, we deemed it necessary to conduct a feasibility study before conducting a randomized controlled trial. We investigated the difference in trainability between 2 groups of patients who markedly differed in the degree of cognitive impairment: One group fulfilled the DSM-5 criteria for alcohol-induced mild ND, and the other group was diagnosed with Korsakoff's syndrome (alcohol induced major ND, confabulatory/ amnesic subtype according to the DSM-5 (American Psychiatric Association, 2013). We hypothesized that the training procedure is applicable in both groups, because CBM is supposed not to rely on declarative memory processes which are (severely) impaired in this sample. This should be reflected in a decrease of the alcohol-approach tendency in both groups with ongoing learning over sessions. Therefore, extending the studies by Wiers and colleagues (2011) and Eberl and colleagues (2013), we applied 6 training sessions for each patient to enhance learning. All training sessions were accompanied by craving questionnaires before and after training for 2 reasons: First, to monitor potential induced craving due to alcohol-related cue exposure; second, successful modification may be related to reduced craving reports.

Second, we studied how intelligence and neurocognitive factors such as attentional capacity comprising IC, (working) memory and planning skills, were related to bias at pretest and AAT modification effects. Based on former studies it was hypothesized that diminished interference control and lower working memory capacity are related to a larger baseline approach bias and enlarged AAT learning effects. Since age (higher in age) and the size of bias at baseline (larger baseline bias) are known to be related with relatively larger learning effects as well, these variables were also included.

As this study is the first to apply this method in a population with (major) NDs, our prior interest is the applicability and a better understanding of for whom this treatment procedure works best. Besides these clinically relevant issues, this study design can contribute to the understanding of the exact working mechanisms of implicit processes (De Houwer et al., 2009) and cognitive bias modification procedures, as it remains uncertain which specific (and/ or level of) cognitive capacities are required for successful training (Eberl et al., 2013).

Materials and Methods

Participants

In total, 105 inpatients from the Centre of Excellence for Korsakoff and Alcohol-Related Cognitive Disorders at Vincent van Gogh Institute for Psychiatry in Venray, the Netherlands, were included in this study. All patients had a history of alcohol dependency and had persistent cognitive disorders. The sample consisted of two groups which were differentiated based on the severity of cognitive impairment: In the presence of a profound anterograde amnesia, patients were diagnosed with Korsakoff's syndrome (in terms of the DSM-5: alcohol induced major ND, confabulatory/amnesic subtype major ND). In 54 patients, these criteria were met. The second group was formed by 51 patients who fulfilled the DSM-5 criteria of mild ND. Diagnoses were based on clinical observation, extensive neuropsychological assessment, psychiatric and neurological examination (including neuroradiological evidence), and were the result of multidisciplinary consultation.

The following patient characteristics were collected: age, sex, education level, estimated average alcohol intake per day prior to admission to the clinic, estimated duration of AUD in years, duration of abstinence in weeks. All patients were abstinent for at least 6 weeks at the time of testing and participation. None of the baseline variables differed significantly between the 2 patient groups.

Materials

Alcohol AAT. The Alcohol Approach-Avoidance re-training task was used, a variant of the assessment AAT developed by Rinck and Becker (2007). This modification procedure was first administered in a study by Wiers and colleagues (2010) and furthermore in studies by Wiers and colleagues (2011) and Eberl and colleagues (2013). Participants were presented with single pictures on a computer screen, namely, 10 different pictures of alcoholic drinks (of common Dutch brands) and 10 different non-alcoholic drinks (e.g., fruit juices, soda). They were asked to use a joystick to either push these pictures away or pull them towards themselves. An indirect instruction was given; participants were asked to pull the joystick towards themselves when a picture was rotated slightly to the left (by 3 degrees) and to push the joystick when it was rotated slightly to the right (by 3 degrees). The response was accompanied by a dynamic zooming effect, such that the picture increased in size when the joystick was pulled, whereas it decreased in size when the joystick was pushed. This created the impression of increased (or decreased) distance between the participant and the stimulus; strengthening the impression of approach (pull) or avoidance (push) of the stimulus. Furthermore, pictures only disappeared after the correct movement was fully executed. Each of the 6 training sessions started with a number of practice trials (26 in Session 1, 2 in all subsequent

sessions) with common household objects. This was followed by a pretest of 40 trials in which both alcohol and non-alcoholic drinks were both pulled and pushed (10 trials each). An extended training phase followed in which patients had to push away 100 alcohol pictures and pull closer 100 nonalcoholic pictures (each individual picture 10 times). Each session ended with a posttest which was identical to the pretest. Within the pretest, training phase, and posttest, the order of the trials was pseudo-random with the restriction that no more than 4 consecutive trials of the same picture type or the same response were allowed. Each session took about 20 minutes, including a short break halfway through.

Craving questionnaires. The Dutch translation of Bohn's Alcohol Urge Questionnaire (AUQ) (Bohn et al., 1995) and of the Obsessive-Compulsive Drinking and Drug Use Scale of the Measurements in Addictions for Triage and Evaluation (MATE-nl 2.1, OCDS-50 (Schippers et al., 2010) were used to measure state and trait craving, respectively.

Neuropsychological assessment. The following tasks and subtests were used to predict training effects. Intelligence: Full-Scale IQ (FSIQ) using the WAIS-III or WAIS-IV (Wechsler, 2005; 2012). Working memory: the Working Memory Index of the WAIS-III/IV. Attention capacities: the d2 concentration performance score was included (Brickenkamp and Oosterveld, 2014) to measure concentration ability. Interference control was measured by calculating the difference in reaction times on Card 2 and Card 3 of the Stroop task (Hammes, 1971). Executive functioning: Tower of London (ToL; Lezak et al., 2012) was used to measure planning. In addition, the immediate free recall score of the California Verbal Learning test (CVLT) (Dutch Version) (Mulder et al., 1996) and the Fragmented Pictures Test from the Implicit Memory task (IMT)(Sopena et al., 2005) were used to measure explicit and implicit memory function, respectively.

Procedure

All participants were provided with written and verbal information about the study, they provided written informed consent, and they could withdraw at any time for any reason without consequences for their treatment. The study was performed in accordance with the Declaration of Helsinki and approved by the Institutional Review Board of Vincent van Gogh Institute for Psychiatry (Nr. U12.054). The standard neuropsychological assessment after six weeks of abstinence (Walvoort et al., 2013) was followed by the baseline assessment including (in a fixed order) state and trait craving questionnaires, as well as the IMT. These instruments were administered again after completion of the training. During the 3 weeks after baseline assessment, six 20-minute AAT administrations

(2 sessions equally distributed over a week) were performed, each was preceded and followed by state craving questionnaires. During all administrations, a trained professional was present in order to answer questions, repeat instructions when needed due to memory problems, and supervise the process.

Data preparation and analyses

In order to assess training effects, the reaction times (RTs) of full correct movements during pretest and posttest were analyzed. Median RTs were computed from the raw data after excluding outliers (fastest 1% and slowest 1% of the data). Due to practical issues, in three cases a single AAT training session was missing. In order not to lose all data of these participants, we replaced the missing data by the data of the previous session (last observation carried forward method). This conservative variant of imputation was used to assume neither improvement nor decline over sessions. After inspection of the average AAT data per pre- and posttest, additionally all data of 1 participant were excluded from analyses because he was a multivariate outlier.

Per session, a pretest *alcohol approach-avoidance tendency* was calculated from the median RTs of the pretest: (RT approach alcohol pictures + RT avoid soda pictures) - (RT avoid alcohol pictures + RT approach alcohol pictures). A negative score indicates a relative alcohol-approach tendency, whereas a positive score indicates a relative alcohol-avoidance tendency. The alcohol-approach tendency at the pretest of Session 1 was the *baseline tendency* (BT). The same tendencies were computed for the posttests, yielding 12 scores for each patient (a pretest score and a posttest score for each session The internal consistency of these 12 scores was quite high for a reaction time task, particularly in this population, yielding Cronbach's alpha values between 0.27 and 0.70, with a mean value of 0.49. Importantly, the BT already yielded a Cronbach's alpha of 0.50. From these scores, we also computed each patient's *Mean Training Effect* (MTE) per session by averaging the 6 pre-/postdifferences in approach tendencies.

Group differences in approach tendencies were tested with repeated-measures analyses with Diagnosis as between-subjects factor (mild vs. major ND) and the two within-subject factors Time (6 sessions) and Test (pre- vs. posttest). This analysis was repeated for a sub-group of participants, that is, only those who showed a baseline alcohol-approach tendency. Finally, correlations between neurocognitive variables and training measures were computed to study the relation between cognitive abilities and training effects.

Results

Applicability

Acceptability and Compliance. In addition to the participant who was excluded for being a multivariate outlier (11 out of 12 test measures were significantly higher than the scores of the other participants), 19 of the remaining participants dropped out. Significantly more participants with major ND than participants with mild ND dropped out, $X^2(1)= 5.495$, p =.019; n =15 (27.8%) against n =5 (9.8%). Eight of the dropouts were too severely cognitively impaired, being unable to fully understand the instructions and to proceed. Seven patients dropped out after computing the pretest due to motivational problems. Three patients dropped out because of premature discharge from the clinic and/ or relapse during the procedure. One patient finished all training sessions, but could not perform the posttest assessments due to premature discharge. Among the remaining participants, attendance rates were high, and according to the training supervisors, the acceptability of the task was high. Training fidelity was ensured by by having a trained supervisor present during task execution, and by using standardised (verbal and written) instructions. Significant differences in cognitive abilities between dropouts and completers were present for FSIQ, $F(1,92) = 6.367$, $p= 0.013$ (note that only one patient with an IQ under 60 was able to complete the training), Working Memory Index, $F(1,91) = 4.99$, $p = 0.028$, d2 concentration performance, $F(1,86) = 9.34$, $p = 0.003$, Stroop interference, $F(1,91) = 14.44$, $p < 0.001$, implicit (non-declarative) memory function, $F(1,63) = 4.49$, $p = 0.038$, and CVLT delayed recall, $F(1,97) = 4.59$, p =0.035. Only performance on the ToL, $F(1,63) = 1.92$, CVLT encoding, $F(1,97) = 3.69$, $p = 0.058$, and CVLT immediate recall, $F(1,97) = 3.64$, did not differ between dropouts and completers.

Among the completers, we also tested for differences between the two patient groups. No significant differences with respect to demographics or illness characteristics were found (see Table 1).

AAT Alcohol-approach Tendencies and Training Effects

To analyze how the 2 groups' alcohol-approach tendencies changed over time in the pre- and post-tests, a repeated-measures analysis with Diagnosis as between-subjects factor (Mild vs. Major ND) and Session (7 sessions) and Test (pre- vs. post-test) as within-subjects factors was computed. The resulting means and standard deviations are shown in Table 2. The factor Test was significant, $F(1,82) = 17.72$, $p < 0.001$, η_p^2=.18, indicating that in general, the tendencies were more positive (i.e., more alcohol-avoidance) in the post-tests than in the pre-tests. The main effect of Diagnosis was also significant, $F(1,82) = 6.93$, $p = 0.01$, η_p^2=.08, because on average, patients with Major ND showed a stronger alcohol-avoidance

Table 1. Characteristics of the Participants Who Completed the Procedure (Means and Standard Deviations)

Characteristics	Mild neurocognitive disorder (ND) (*N* = 46)	Major ND (*N* = 39)	*P*
Age	51.4 (15.0)	52.3 (16.2)	*0.796*
Sex (percentage male)	71.1%	79.5%	*0.265*
Educational level (percentage)			*0.713*
<6 years education	2.2	2.6	
Primary education	4.4	2.6	
Prolonged primary education	22.2	20.5	
Lower level secondary education	24.4	38.5	
Higher level secondary education	28.9	20.5	
Preuniversity education and/or Higher professional education	15.6	7.7	
University	2.2	5.1	
Average intake per day (standard units)	18.1 (10)	17.3 (8.7)	*0.721*
Duration of abstinence (weeks)	12.5 (8.2)	15.5 (8.4)	*0.458*
Duration of AUD (years)			0.473
≤5	13.3	15.4	
5 to10	26.7	12.8	
10 to 15	17.8	20.5	
15 to 20	8.9	17.9	
20 to 25	4.4	10.3	
> 25	24.4	20.5	

tendency than those with Mild MD. In contrast, neither the main effect of Session, $F(5,78) = 1.03$, $p = 0.406$, $\eta_p^2 = .06$, nor any interaction effects were significant. Additional trend analyses of the pretest data revealed a significant linear trend for the Session main effect in the pretests, $F(1,82) = 8.48$, $p = 0.005$, $\eta_p^2 = .09$, suggesting that across all patients, the pretest avoidance tendency increased linearly from Session 1 to Session 6, as shown in Figure 1. In contrast, there was no significant trend in the posttest values, $F(1,82) = .07$, $p = 0.796$, as illustrated by the flat line shown in Fig 1.

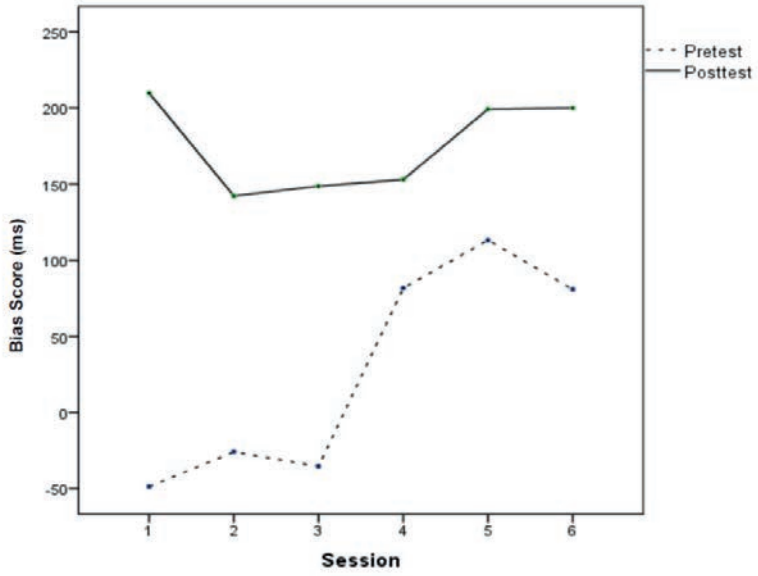


Figure 1. Approach-avoidance Tendencies per Session (1-6) and Test (pre vs. post), for All Patients.

Table 2. AAT alcohol approach tendencies (negative values indicate alcohol-approach), means and standard deviations per group, session, and test time, in ms.

	Mild neurocognitive disorder (ND)		Major ND	
Session	**Mean**	**SD**	**Mean**	**SD**
Session 1, Pretest	-162	455	65	507
Session 1, Posttest	148	399	272	552
Session 2, Pretest	-48	330	-4.1	568
Session 2, Posttest	33	484	252	543
Session 3, Pretest	-55	531	-16	391
Session 3, Posttest	160	290	138	290
Session 4, Pretest	8	287	156	436
Session 4, Posttest	92	480	214	506
Session 5, Pretest	100	358	126	425
Session 5, Posttest	60	497	338	741
Session 6, Pretest	49	281	112	241
Session 6, Posttest	177	486	112	241

Next, AAT effects were analyzed with the same repeated-measures analysis of variance as before, but now only participants who displayed an alcohol approach tendency at baseline (BT ≤ 0; n = 51) were included, because this subgroup should show the largest learning effects (decrease of the difference between pre- and posttest) and profit from multiple sessions.

Indeed, the predicted interaction of Test and Session was significant, $F(5,46)$ = 7.40, p < 0.001, η_p^2= 0.446, indicating that the training effect within sessions decreased over time because the to-be-modified alcohol-approach tendency at pretest decreased over time (Fig. 2). This 2-way interaction was not significant in the group that did not display an approach bias at pretest (BT > 0, n = 33; $F(5,28)$ = 1.64, p =1.81, η_p^2=.227. Next, the training effect was analysed in all participants by adding the size of the BT as a covariate in an analyses of covariance with Session (6 sessions) and Test (pre- vs. post-test) as within-subjects factors. A 3-way interaction effect was present, $F(5,78)$ = 8.65, p < 0.001, η_p^2 = 0.357, confirming that learning effects increased with an increasing baseline alcohol-approach tendency.

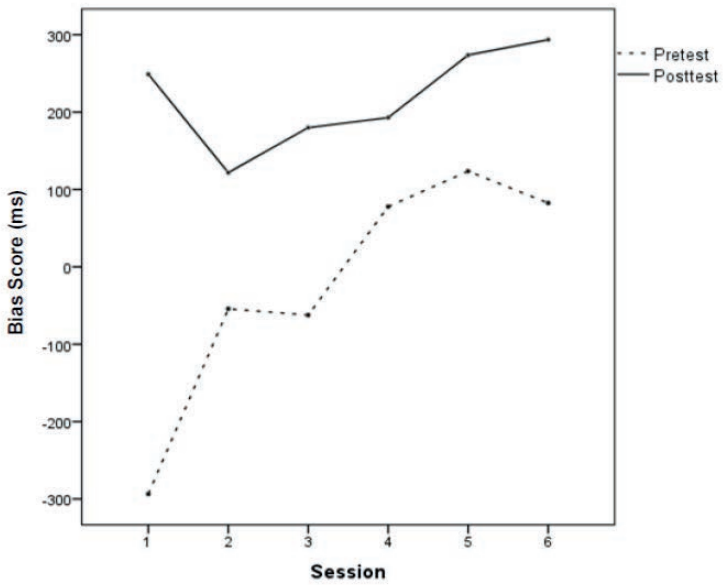


Figure 2. Approach-avoidance Tendencies per Session (1-6) and Test (pre vs. post) for Participants with a Baseline Alcohol-approach Tendency

Training Effects on Craving

State craving reports on the AUQ decreased significantly, $t(82) = 3.77$, $p < 0.001$, over the course of the training (mean pretest score of Session 1: 12.9; SD =7.9; mean posttest score of Session 6: 10.3; SD=4.4). Within sessions, however, the MTE was unrelated to the AUQ difference scores (posttest minus pretest score) (r=-.097, p =.40). When state craving reports were analysed per group, a significant decrease of the AUQ score was found in the patients with Major ND, $t(38)$=3.56, p=.001, but not in the patients with Mild ND, t(43)=1.67, p=.103. A paired-samples t-test comparing the OCDS-5 scores before training to those after training revealed no significant difference in trait craving, $t(87)$=.11, p = 0.91.

(Neurocognitive) Predictors of AAT Effects

Table 3 shows the correlations of the participants' MTE and their BT)with the predictor variables, including neurocognitive variables and age. The Implicit Memory task was added later to the procedure, therefore the first 25 participants did not perform this task, and the correlations are based on a smaller sample.

A negative correlation was found between MTE and BT. This is to be expected because the more positive the tendency is at pretest already, the less it can improve from pre- to posttest. A positive correlation was present between MTE and age, indicating that older participants showed a larger improvement. Moreover, patients with better implicit memory capacity showed better training results (note that a relatively lower score on the IMT indicates better performance, therefore the negative correlation). No significant correlations were found with any of the explicit memory variables.

Table 3. Correlations between (Neurocognitive) Predictors and AAT Measures.

	FSIQ	WMI	d2 (CP)	Stroop interference	ToL	Implicit Memory Task	CVLT (encoding)	CVLT (immediate recall)	CVLT (delayed recall)	BT	Age
MTE	0.037	-0.080	-0.137	0.185	-0.041	-0.291*	-0.050	-0.113	-0.039	-0.416[b]	0.243[a]
BT	0.046	0.086	0.028	-0.070	0.098	-0.013	-0.103	-0.122	-0.137	-	-0.012

FSIQ, Full Scale Intelligence Quotient (WAIS); WMI, Working Memory Index (WAIS;, d2, Concentration Performance score; ToL, Tower of London; CVLT, California Verbal Learning Test; MTE, Mean Training Effect; BT= Baseline Tendency

[a]Correlation is significant at the 0.01 level (2-tailed).

[b]Correlation is significant at the 0.05 level (2-tailed).

Discussion

The main goal of this study was to examine the applicability of the alcohol-avoidance training in patients with (severe) alcohol-induced NDs. Our results indeed show that, after training, an alcohol-avoidance bias was found, suggesting that the training was successful in creating an automatic alcohol-avoidance tendency in both patients with Mild and Major ND. Drop-outs, however, were more prevalent in patients with Major ND. Based on clinical observations, we noticed an impaired awareness of illness (*anosognosia)* to be a risk factor for treatment compliance. This factor is a well-known problem in traditional treatment procedures as well, and it corroborates reports on the need to assess level of insight before treatment (Walvoort et al., 2016). Additionally, we suggest to use a FSIQ below 60 as an exclusion criterion due to the risk of drop-out. This quantification may be related to a sufficient level of illness insight as well as to the minimum level of attentional capacity which is needed to execute the task. Next, visual inspection of the data (Fig. 1) shows that after 6 sessions, further improvement may still be possible (see also Eberl et al. 2014). Although after 4 sessions, no alcohol-approach bias was visible anymore, the retained alcohol-avoidance tendencies at pretests remained weaker than the corresponding tendencies at posttest. In future studies, additional sessions should be added to assess the continuation of the learning curve and treatment enhancement over time.

Our next research question relates to for whom AAT works best, addressing neurocognitive abilities, age, and size of pretest approach bias. We found age and non-declarative memory function to be related to a larger overall AAT learning effect: Older patients and patients with stronger implicit memory function showed a larger training effect. Interference control and working memory capacity, however, were unrelated to baseline bias or learning effects. Moreover, none of the neurocognitive variables were related to the size of pretest approach bias. This is in contrast to earlier findings in non-clinical populations by Peeters and colleagues (2012) and Sharbanee and colleagues (2013) who did find that interference control and working memory capacity were related to approach-avoidance tendencies. It can be hypothesized that instead of being a stable predictor, cognitive control plays a more dynamic role in the enhancement of CBM effects (Clarke et al., 2014; Sharbanee et al., 2014) or is even an outcome of CBM (Chen et al., 2015), and increased activity in brain areas involved in cognitive control may stimulate CBM effects. Our results, however, replicate findings of Eberl and colleagues (2013) who trained a clinical population as well, and who (i) did not find a relation of training effects with these cognitive measures either, and (ii) did find that older participants show larger training effects. This suggests important differences between clinical and nonclinical samples.

Implicit memory function was also related to larger general training effects, whereas a relation between training effects and executive functioning was not found. This pattern of results is in line with the notion that implicit, automatic rather than explicit, controlled processing may underlie the working mechanism of the AAT. Also, more severe encoding disorders did not hamper learning effects, and they did not predict drop-out. We may conclude that the AAT indeed matched the patients' preserved implicit (nondeclarative) learning capacities.

Finally, a significant interaction of Session and Test was found: The tendencies at pretest became increasingly positive, showing that with every session, more and more of the trained alcohol-avoidance tendency was retained between sessions. In contrast, the tendencies at posttest were strongly positive (indicating an alcohol avoidance bias) from the first session on, showing that the training was suitable for these patients. Moreover, a moderating effect of the BT was found. Thus, our study revealed strong training effects within sessions, as well as increasing session-to-session retention effects, and the latter were larger for patients who started with a larger alcohol-approach bias at baseline. In previous studies, a larger implicit bias at baseline also appeared to be a predictor for larger therapeutic effects of training, as well as for increased problem severity when no training was offered (Amir et al., 2011; Eberl et al., 2013; Salemink & Wiers, 2012; Schuck et al., 2012). Due to the nature of our current study, no control group was included. Obviously, this is a major limitation as no conclusions about therapeutic effects can be drawn. Based on the results of our study, we can say that this particular patient population can be trained, even those patients who did not have any explicit memory of having performed the AAT before when they started a consecutive session. However, we do not know whether the effects generalize to behavioural outcomes; we can only say that explicit craving reports did not increase. This is an important task for future research: To include a control group and additional behavioural outcome measures in this particular patient population. A behavioural outcome measure is needed to exclude the possibility of simple habituation to the presented stimuli. Also, statistical effects such as regression to the mean should be taken into account. However, as extreme outliers were removed from the analyses and post-test tendencies remained more or less stable over the six sessions, these effects cannot fully explain the observed effects. As this study is the first to employ pre- and posttests of alcohol-approach tendencies in every session, it is difficult to compare the observed learning patterns to those of other studies.

The studies by Wiers and colleagues (2011) and Eberl and colleagues (2013) included variables of clinical outcome, such as relapse rates one year after training, and they showed that after active alcohol-avoidance training, relapse rates were lower than after sham training or after no training at all. One might fear that the repeated and extensive exposure to alcohol-related stimuli during the AAT may

result in potentially harmful side effects such as an induced craving. However, our results clearly show that craving reports were stable or even decreased over the course of the training. In particular, patients with Major ND reported decreased craving. Whether this decrease in craving reports is an effect of AAT training cannot be answered at this point: As our current interest focused on the feasibility and the working mechanism of the AAT, no sham training control group was included. In further research, it should be tested whether the active training is also clinically beneficial in patients with Mild or Major ND, and more so than a sham training. See and colleagues (2017) for a discussion of the difficulties in this research area when it comes to finding appropriate neutral control conditions, as in a sham condition, modification effects are possibly present as well.

In conclusion, alcohol-avoidance training is applicable in patient populations with alcohol-induced NDs. Better training results were obtained in participants with a relatively stronger baseline alcohol-approach tendency, in older participants, and in those with stronger nondeclarative memory function. Executive functions and explicit memory were not related to drop-out nor were they predictive of the training results, corroborating the implicit nature of the training. With regard to acceptability and compliance, we saw that more patients with Major ND were at risk to drop out compared to those with Mild ND, but most patients were able to successfully complete the training and to learn over time. Further research, particularly a randomized controlled trial with a sham training control group and clinical outcome measures, is recommended for further establishing the efficacy and effectiveness of this intervention. Given the present findings and the generally modest results of treatments that solely rely on illness insight and self-reflection, training of automatic processes may be an important step forward in the treatment of patients with alcohol-related NDs.


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A NEUROCOGNITIVE VIEW ON ALCOHOL AVOIDANCE TRAINING: THE RELATION BETWEEN DECLARATIVE MEMORY FUNCTIONING AND MODIFICATION OF ALCOHOL-APPROACH TENDENCIES

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Abstract

Objective: Alcohol-avoidance training (AATr) targets the cognitive-affective (implicit) level of information processing in alcohol use disorder (AUD). AATr has shown to be a successful intervention reducing relapse. Since AATr is assumed to rely predominantly on implicit learning, this intervention is of special interest for AUD patients with alcohol-related memory disorders. This study investigates whether within-session reduction in alcohol-approach bias during AATr can be explained by declarative memory functioning and training duration. Results can contribute to a better understanding of the implicit nature of AATr and thereby personalized training protocols. ***Method*:** Reaction time data of a 12-session AATr of 64 participants diagnosed with AUD was analyzed. Thirty-one participants met the diagnostic criteria of alcohol-related neurocognitive disorders, of whom five were diagnosed with Korsakoff's syndrome. Multilevel Modelling was used to analyze if within-session bias reduction could be explained by the number of (planned) sessions and/ or declarative memory function and their interaction effect. ***Results*:** A significant effect of declarative memory on bias reduction was present as well as an interaction effect of declarative memory and training duration over time of training: In the presence of better declarative memory function fewer sessions were needed. Conversely, when declarative memory is decreased additional sessions are needed to obtain bias reduction. ***Conclusions***: These findings suggest that bias reduction is related to either more explicit learning or implicit learning mechanisms driven by declarative memory capacity. Neuropsychological evaluations are essential for tailoring AATr protocols to individual neurocognitive profiles. This study advances the theoretical understanding of AATr mechanisms.

Introduction

Most established therapeutic interventions target the conscious (explicit) level of cognitive reappraisal and behavioural modulation (Braunstein 2017; Ochsner, 2012). In the last decade, these more traditional interventions have been complemented by cognitive bias modification (CBM). CBM was developed as an add-on intervention, aiming to directly target the cognitive-affective (implicit) level of information processing (Marteau et al., 2012).

CBM is aimed to modify biased information processing in psychopathology. These biases can be present in several cognitive domains and are considered to be an important factor in the development, maintenance and relapse of psychopathology (Fox & Beevers, 2016; Marteau et al., 2012; Mathews & MacLeod, 2005). Several CBM procedures contribute to treatment success in various forms of psychopathology (Grafton et al., 2017: Loijen et al., 2020; Vrijsen et al., 2024).

In the presence of alcohol use disorder (AUD) patients are often relatively faster in approaching alcohol-related stimuli, compared to other stimuli and compared to individuals without AUD (C. E. Wiers et al., 2014; R. W. Wiers et al., 2009, 2010). This automatic alcohol approach bias is related to alterations in impulsivity-linked neural substrates (Martínez-Maldonado et al., 2020; Muller et al., 2024; C. E. Wiers et al., 2014) and substantiate impulsivity traits in AUD (Verdejo-Garcia & Albein-Urios, 2021). It has repeatedly been found that alcohol-avoidance training (AATr) improves behavioural inhibition in AUD by modifying the automatic tendency to approach alcohol-related cues: AATr significantly reduces relapse rates as long as one year later (Eberl et al., 2013; Manning et al., 2016; 2022; Rinck et al., 2018; R. W. Wiers et al., 2011) and may on a neural level affect cue-reactivity (C. E. Wiers et al., 2015).

The alcohol approach bias is modified by the use of a joystick computer task: Participants are presented with pictures of alcohol and soda beverages, which they either pull towards themselves or push away in response to the tilt of the pictures (indirect instruction). In the training phase, alcohol pictures are consistently pushed away. These reaction times(RTs) and its changes are measured in milliseconds, so any conscious awareness of the magnitude of the behavioural bias itself, or of its changes, in response to the images over the course of training, is impossible. So not only the *aim* of AATr (bias reduction on an affective-implicit level) also the *process of change* has a considerable implicit nature. According to the intervention framework of Braunstein et al. (2017), the AATr fits the class of implicit-automatic interventions.

The characteristics of the AATr correspond with the intact ability of implicit learning in patients with AUD and alcohol-related declarative memory disorders (Rensen et al., 2018). Impaired declarative memory function in AUD is often

overlooked but has a substantial prevalence (Cabé et al., 2016; Bates & Pawlak, 2006; Bates et al., 2013; Maillard et al., 2020). Considering the positive results of AATr on relapse rates in the general AUD population, this add-on intervention is of particular interest for patients with AUD and impaired declarative memory function.

AATr was indeed found to be feasible in a population of patients suffering from alcohol-related neurocognitive disorders (Loijen et al., 2018). In that study, implicit memory was positively related to bias reduction, whereas declarative memory was not related to the initial bias or the mean training effect. These results indicate that the process of bias modification is related to implicit learning. However, declarative memory processes are also involved in implicit learning and their interaction is known to affect learning. For example, in skill learning and perceptual-motor learning (Keisler & Shadmehr 2010; Maresch et al., 2021; Sun et al., 2005). Little is known yet about the characteristics of the relation between declarative memory and AATr within-session bias reduction.

In the presence of impaired declarative memory (or explicit memory) one could profit from procedural or associative learning, which may be the case in AATr for this population. At first, AATr might rely more of episodic memory. However, with repetition, the AATr becomes proceduralized, meaning that the responses become more automatic. As with errorless learning training (Oudman et al., 2015; Rensen et al., 2017), patients (with declarative memory deficits) might not be able to recall (the details of the) learning sessions, however, their improved performance shows that they have, implicitly, learned new skills.

The objective of this study is to improve the understanding of how declarative memory and training duration are related to AATr within-session bias reduction. It is hypothesized that when bias modification relies relatively stronger on implicit learning, it is expected that declarative memory is not a predictor of within-session bias reduction whereas number of completed sessions is. The results may at first contribute to personalization and optimization of training protocols (e.g., the number of training sessions; Boffo et al., 2019; Bolt et al., 2022; Eberl et. al., 2013) and contribute to AATr theory (R. W. Wiers et al., 2023) Second, these insights can improve treatment options for patients with alcohol-related cognitive disorders.

This question is studied in a population of patients with AUD and different degrees of alcohol-related neurocognitive disorders (varying from no cognitive disorders to Korsakoff's Syndrome). Participants attended a 12-session AATr (two sessions a week). Multilevel modeling (MLM) was used with declarative memory function and number of completed sessions as predictors. MLM was used for the analysis instead of the initially planned repeated measures analysis given its better methodological fit.

Method

Participants

All participants were inpatients of the Centre of Excellence for Korsakoff and Alcohol-Related Cognitive Disorders at Vincent van Gogh Institute for Psychiatry in Venray, the Netherlands. Part of the standard treatment there is the computerized alcohol-avoidance training (AATr). Data from 2018 till 2020 were used in this study, collected from 64 participants in total. From 61 participants, data were sufficiently complete for analyses (see *data preparation*). All participants had a history of alcohol dependency. After detoxification and at least 6 weeks of abstinence, neuropsychological assessment took place.

Of the total of 61 participants, 25 of them did not have cognitive disorders, 26 participants were diagnosed with mild alcohol-related neurocognitive disorder, 5 participants with major alcohol-related neurocognitive disorder, confabulatory/amnesic subtype (e.g., Korsakoff's Syndrome) and five participants were classified with neurocognitive disorders not related to alcohol abuse. The participants' average age was 61 years (*SD* = 7.80, range 34-72), most of them were male (47 males, 14 females). Level of education was measured within the Dutch educational system using a 7-point rating scale, ranging from 1 (*less than primary education*) to 7 (*university degree*). The patients had a median education level of 4 (higher level secondary education; range 1-7).

Materials

Alcohol AATr. The same alcohol-avoidance training task was applied as in Loijen et al. (2018). Images of 10 alcoholic beverages and 10 non-alcoholic beverages were used. In each trial of the task, a single image was depicted on the computer screen, and participants were instructed to pull or push a joystick to either pull the image towards themselves or push the image away from themselves. The joystick movement was accompanied by a dynamic zoom effect, such that the image increased in size when the joystick was pulled and it decreased in size when the joystick was pushed. This creates the subjective impression of pulling the image closer (approach) or pushing it away (avoidance). Indirect instructions were used. Participants were asked to pull images closer if they were rotated slightly to the left (by 3 degrees) and to push them away if they were rotated slightly to the right (by 3 degrees). The images only disappeared after the correct movement was fully executed (Figure 1).

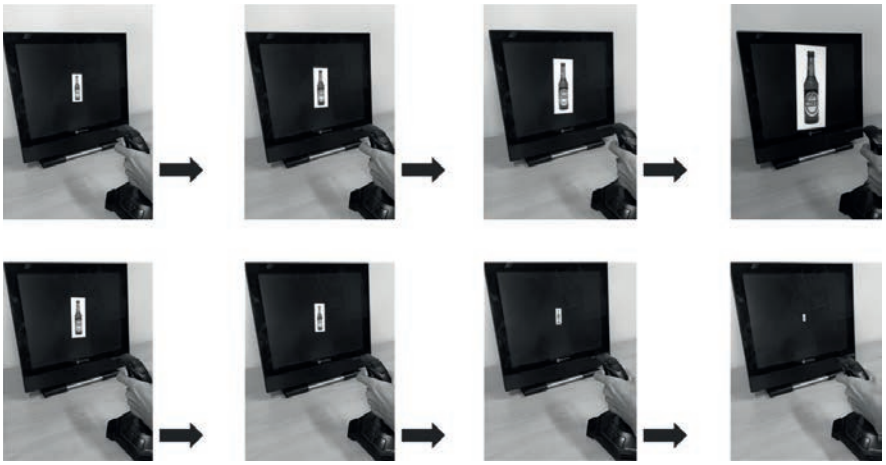


Figure 1. Illustration of Pull Trials and Push Trials of the AATr.

Note. Top row, left to right: Pulling the joystick increases the picture size. Bottom row: Pushing the joystick decreases the picture size. AATr: Alcohol-avoidance training.

All sessions started with a number of practice trials using pictures of household objects. Session 1 contained 26 practice trials, all following sessions only 2 practice trials. The practice items were followed by a pretest of 40 trials in which both alcohol and non-alcoholic beverages had to be pulled and pushed (10 trials each in this 2x2 design). In the subsequent training phase, 100 alcohol images had to be pushed away and 100 nonalcohol images had to be pulled closer (each individual image occurred 10 times). Each session ended with a posttest which was identical to the pretest. In each session's three phases, trial order was pseudo-randomized, ensuring no more than four consecutive trials of the same stimulus type or action movement.. Each session took about 20 minutes, including a short break in the middle. Sessions were performed in small groups with a maximum of four participants. A trained professional was present in order to answer questions, to repeat instructions when needed due to memory problems, and to supervise the process.

Neurocognitive measures. The neurocognitive data were obtained from the regular administration of a standardized neuropsychological assessment battery. Not all patients completed all measures. Intelligence (Full-Scale Intelligence Quotient; FSIQ) was assessed with the WAIS-IV (Wechsler, 2005, 2012); Mean FSIQ= 85.4 (SD 12.8), *n*= 51. Working memory was measured with the Working Memory Index of the WAIS-IV; Mean WMI= 87.6(14.8), *n*= 52. Declarative memory was assessed in this battery with two tests, namely the Dutch version of the

California Verbal Learning Test (CVLT; Mulder et al., 1996); and the total encoding error score of the Dutch version of the Revised Location Learning Task (LLT-R; Kessels et al. 2012). Of the LLT, most of the data were available in this AATr sample: LLT *n*= 58; CVLT *n*= 49. The modified LLT is a sensitive and valid tool for detecting spatial memory impairments and correlates significantly with verbal memory encoding (Kessels et al., 2006). We selected the LLT because extensive data are available, and it aligns well with the visual cues and visual-motor learning components of the AATr.

Therefore, LLT scores were chosen as a measure for declarative memory in further analyses.

The mean LLT Total encoding error score was 46.3 (29.9). To illustrate this score and the variability within the sample in clinical terms: For a 61-year-old male (mean age and gender of the sample), these results correspond to the 14th percentile (Kessels et al., 2012) and can be defined as a low-average score (Guilmette et al., 2020). The standard deviation corresponds to normative scores within a range from the 2nd percentile (below average) to the 66th percentile (average). This demonstrates the variability in memory impairment among participants, according to the diagnostic classifications ranging from no cognitive disorders to severe conditions such as Korsakoff's syndrome.

Procedure

The study was performed in accordance with the Declaration of Helsinki and in compliance with APA ethical standards and was approved by the Institutional Review Board of Vincent van Gogh Institute for Psychiatry (Nr. U12.054).

After six weeks of abstinence from alcohol standard neuropsychological assessment was performed. AATr is a standard neurorehabilitation intervention in this clinical setting. A 12-session AATr, was scheduled twice a week, with intervals of two to three days between sessions. Not all participants completed all 12 AATr sessions due to various reasons, most commonly relapse, clinical drop-out, or planning errors (e.g., conflicting appointments at the time of training). Missed training sessions could be caught up at the next planned session. The maximum number of appointments needed to complete 12 sessions was 21. Table 1 shows the average number of sessions missed, completed and spread of the sessions. Tables 2 and 3 provide more detailed information on the frequency and spread of either missed or completed sessions.

Table 1. Characteristics of the Sample (n= 61) in Terms of Training and Neurocognition Parameters.

Adherence rates	*M*	*SD*	*N*
Number of missed sessions	2.6	2.6	61
Number of sessions completed	8.9	3.5	61
Temporal spreading of completed sessions*	11.5	4.7	61

[a] Number of planned sessions, twice a week.

Table 2. Frequency of Missed Sessions.

Session Number	%	N
0	23.0	14
1	21.3	13
2	18.0	11
3	8.2	5
4	8.2	5
5	11.5	7
6	3.3	2
9	3.3	2
10	1.6	1
11	1.6	1

Table 3. Completed Sessions and Number of Participants.

Total completed sessions	N
2	4
3	2
4	3
5	4
6	4
7	5
8	1
9	4
10	5
11	4
12	23
13	2

Data Preparation and Analyses

Data exclusion. From all pre- and post-test data individual responses with an incorrect full first movement were excluded and RT's below 200ms and from 290,000ms. Subsequently, single outliers among the RTs were identified. Based on the mean and standard deviation of scores within subject (and assuming a normal distribution) for each RT-value, the expected probability of a value more extreme than that value was calculated. This probability was multiplied by the sample size to produce an expected frequency. Based on this frequency, RT values with low (< 1.5) expected frequency were considered as outliers and excluded. After all these steps were taken (removing subjects and individual RT outliers), 53 subjects and 509 records remained. Data are not made publicly available but are available upon request.

Variables. The number of predictors in the model was limited due to the sample size.

The total LLT encoding error score was used as a measure of the quality of Explicit Memory Encoding Score(EMES), N=53. A higher *EMES* represents more explicit (declarative) memory encoding difficulties.

The variable Time was operationalized in two ways: (a) TimeA-Duration of training: *TimeA* represents the used number of planned appointments including the time intervals of missed appointments resulting in 1 to 22 data points. (b) TimeB-Total number of completed training sessions: *TimeB* represents the total number of completed sessions (minimum of 1 and maximum of 12). For example, when a participant completed six sessions and missed two appointments, TimeB datapoints are 1,2,3,4,5,6. Due to two missed appointments the datapoints for TimeA for this same participant are 1,2,3,5,6,8 (missing appointments 4 and 7). TimeB is informative on the number of actually performed training sessions, whereas TimeA represents duration of total training, incorporating possible learning processes related to training such as maturation or extinction between sessions.

As a measure of alcohol-approach bias, compatibility scores (CS) were computed from the reaction times of the pretests (T1) and posttests (T2) of completed training sessions. For each pretest and each posttest of each session, a CS score was calculated (from the mean outlier-corrected RTs) by subtracting the mean RTs of the two training-compatible conditions from those of the two training-incompatible conditions: CS = (AlcPull + SodPush) - (AlcPush + SodPull). A higher CS score represents a smaller alcohol-approach bias. Finally, the Compatibility Difference Score (CDS) was computed by subtracting CS of T2 from the CS of T1 for each session. CDS is therefore a measure of change in CS per session, with higher scores reflecting larger training effects, that is, an increase in alcohol-avoidance bias.

Multilevel Modeling. The actual research question and applied analyzes differ from the preregistration with number 73265 at aspredicted.org. MultiLevel Modeling was chosen instead of variance analyzes for two reasons. First, data points are not independent due to the hierarchical structure of the data, with subjects at Level 2 and sessions at Level 1. Second, in a repeated-measures analysis of variance, too many subjects would have to be excluded due to missing values when a participant missed a training session.

To answer the research question of whether Time (TimeA and TimeB were analyzed separately) EMES (higher scores indicate poorer encoding), and their interaction can explain CDS, MLM analyses were conducted (using MLWiN 3.06).

This results in the following conceptual model: $CDS_{t,s} = a * Time_{t,s} + b * EMES_{.,s} + d * \{Time_{t,s} * EMES_{.,s}\} + Intercept_{.,.} + Usubjects_{.,s} + Usesssion_{t,s}$ (t = time; s = subject).

Results

Two separate models were analyzed: One (=ModelA) with predictor TimeA and one (=ModelB) with predictor TimeB as operationalization for Time. Both models included EMES and the interaction with the used variable for Time. See Table 4 for the results of both models.

Table 4. MLM Analysis Results of ModelA and ModelB

Parameters	Model 0	Full model	t-value
	Fixed Effects		
Intercept	*7.15(17.52)*		
ModelA		*69.88(53.35)*	*1.31*
ModelB		*89.24(52.30)*	*1.71*
Time			
ModelA		*-3.83(9.71)*	*-0.39 (df= 505)*
ModelB		*-6.820(7.37)*	*-0.93(df= 505)*
EMES			
ModelA		*-2.00(0.94)*	*-2.13* (df=49)*
ModelB		*-2.26(0.94)*	*-2.41* (df=49)*
Interaction			
ModelA		*0.23(0.16)*	*1.38 (df= 505)*
ModelB		*0.23(0.13)*	*1.78 (df= 505)*
	Variance components		
Intercept between subjects	*3231.28(3164.66)*		
ModelA		*2384.90(2972.44)*	
ModelB		*2573.00(3006.08)*	
Intercept within Subject	*122910.86(8113.09)*		
ModelA			
ModelB		*121912.1328(8045.06)*	
		121691.68(8031.054)	
	Model summary		
Fit[a]	*7421.40 (n=509)*		
ModelA		*7414.47 (n=509)*	
ModelB		*7414.22 (n=509)*	

Note. Parameter estimate standard errors listed in parentheses. MLM = Multilevel Modeling; EMES: Explicit Memory Encoding Score. [a] Using the Restricted Iterative Generalized Least Suare algorithm. * $p < .05$

There was no significant difference in fit between the null and the full model, deviance in fit=742.40-7414.21= 7.18 (df = 3), $p \leq 0.07$.

Model A: In Model A, the most important and significant predictor of CDS was EMES, b = [-2.26, 0.94], t = - 2.41, $p \leq .01$). Neither the predictor TimeA (negative effect) nor the interaction effect of TimeA and EMES were significant.

This means there was no significant increase in fit of the model when both predictors were included, whereas higher EMES scores where related to a negative change in CS when TimeA was zero. However, the total effect of TimeA became positive with an EMES of 30 or higher (at about planned Session 10, given this sample size), and with an EMES of 63 or higher, the interaction effect became significant. (See Table 4 for a summary of MLM results.)

These results implicate that initially, for participants with relatively more encoding difficulties (high EMES scores represent decreased declarative memory function) no bias reduction is present. However, over time of training an interaction effect is observed. This means that these participants do benefit from and need more sessions to obtain bias reduction. For participants with more intact declarative memory (represented by low EMES scores), more training sessions are not necessarily beneficial.

Using these estimates as well as the subjects' residuals (residuals were calculated with Mlwin, following Goldstein, 2003; Rasbash et al., 2020), predictions of the regressions were made, combining the variables TimeA, EMES and the interaction effect of both (Figure 2).

In 66% of the cases, a positive regression coefficient (RC) was present. A positive RC indicates a positive CDS (indicative of AA bias reduction) over time, either a change from a negative to a positive effect or a less negative effect, and it is represented by a rising line in Figure 2. When the 26 cases with a positive RC were analyzed, on average at the sixth completed session (SD 2.4) the effect of TimeA resulted in a positive CDS (see Figure 2).

These results implicate that only in the presence of decreased declarative memory functioning, training duration (predictor TimeA; total training duration including intervals of missed sessions) contributed to the reduction of alcohol-approach bias and this effect was on average present at the sixth session.

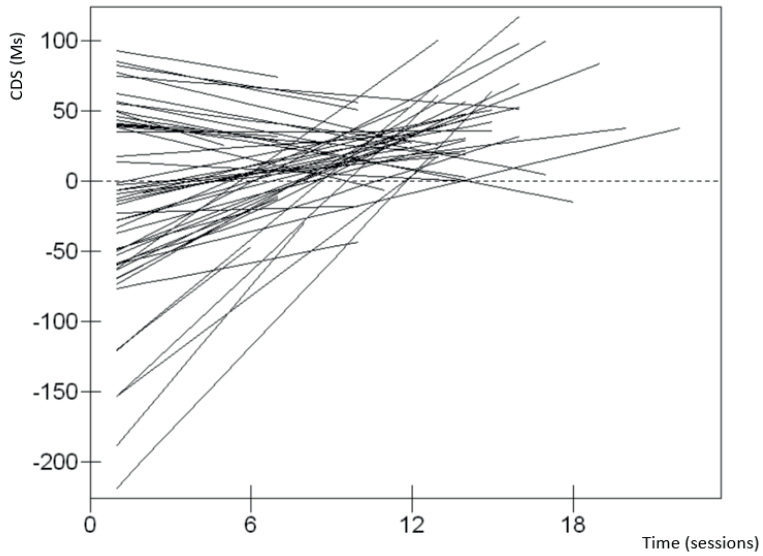


Figure 2. Predictions of Regression Lines per Subject Over TimeA for Predictor EMES and the Interaction of TimeA and EMES.

Note. EMES: Explicit Memory Encoding Score, CDS = Compatibility Difference Score.

Model B. The change in model fit between the null model and the full model, which included the predictors TimeB and EMES, was tested and found to be non-significant (deviance in fit = 7421.40 -7414.47 = 6.92; *df*=4; $p \leq 0.1$). Again, EMES was the only significant (negative) predictor of CDS: *b* = [-1.9998, 0.94], *t* = -2.127447, $p \leq 0.05$. The (negative) predictor TimeB and the interaction effect of TimeB and EMES were nonsignificant in the full model. In this model, the total effect of TimeB became positive from an EMES of 18. For an EMES of 63 and higher, the total effect of TimeB became significant. So also with TimeB, the total number of completed sessions, in the presence of decreased declarative memory bias, reduction was present over time of training: Only for those with more decreased memory function more completed sessions contributed to bias reduction, whereas for those with more intact declarative memory more sessions do not necessarily contribute to bias reduction.

Together, these findings indicate that initially a stronger declarative memory function is beneficial to reduce alcohol-approach bias in AATr. However, in subsequent sessions this effect reverses and a decline in declarative memory function actually becomes beneficial: The total effect of Time (either operationalized as duration of training duration or total number of completed training

sessions) became positive only in the presence of decreased memory function (indicated by a higher EMES). Thus patients with impaired declarative memory function need more training sessions, whereas this may not be beneficial for those with relatively intact declarative memory function.

Discussion

In this study, the relation between declarative memory function and alcohol-approach bias reduction by AATr was examined in a clinical sample of inpatients with AUD and alcohol-related neurocognitive disorders. It was found that initially stronger declarative memory was beneficial for reducing alcohol-approach bias. However, over time of training (in this sample after an average of six sessions, see Figure 2), a reduction in alcohol-approach bias was present *only* for those with decreased declarative memory.

Together these results indicate that more AATr sessions are not always beneficial for those with less decreased or intact declarative memory, whereas when declarative memory is impaired, more sessions are needed to obtain bias reduction. This finding complements our previous study with a similar patient population (Loijen et al., 2018), and it further substantiates that AATr can be applied in this specific population with (severe) alcohol-related neurocognitive disorders.

The fact that participants with decreased declarative memory need a relatively larger number of training sessions is indicative of implicit (procedural) learning, which is known to be preserved in this population, while declarative memory can be severely impaired (Hayes et al, 2012). However, for those with relatively intact declarative memory, more sessions did not always contribute to the reduction of alcohol-approach bias. This finding is indicative of the involvement of explicit (conscious) learning in this subgroup of participants. Thus, according to the intervention classification of Braunstein et al. (2017), the AATr moves from the implicit-automatic to the implicit-controlled class as a result of the quality of the declarative memory function.

The current results indicate that differences in patterns of AATr bias modification are related to the quality of declarative memory. These findings complement the recent discussion on the mechanisms underlying AATr. A change in theoretical view is presented in the literature supporting inferential reasoning to account for AATr bias modification rather than an associative stimulus-response mechanism (Van Dessel et al., 2019; Wiers et al., 2020; 2023). The inferential account emphasizes the role of predictive reasoning and contextual factors. In contrast, the associative account suggests that AATr acts directly on automatic, stimulus-driven responses,

bypassing the need for explicit memory processes. For individuals with more intact declarative memory function, the current findings do not fully align with the associative account, as the reduction in alcohol approach tendencies cannot be attributed to training duration (e.g., changes can occur within a single session, which is inconsistent with associative learning). One possible explanation for this finding is that increased awareness of the task goal contributed to bias modification, as previously observed in bias modification studies (Van Dessel et al., 2016; Zerhouni et al., 2019) as well as in cognitive learning research (Musfeld et al., 2023).

This study has some obvious methodological limitations because an experimental design was not applied. Data from regular treatment was used and no control group (neither a placebo/sham or a non-training group) was present. The specific patient population involved in this study is a strength but also it also limits generalizability to other populations. The sample size was small and due to the clinical setting there were many missing data points. This was caused by low adherence rates in some cases (common in clinical practice for this patient group). In order to retain as many data points as possible, MLM was applied. Moreover, given hierarchy in the RT data and the resulting intraclass correlation, MLM has a better statistical fit when compared to more standardly used analyses of variance. With regard to the large number of missed appointments (planned twice a week), two operationalizations of time were analyzed. However, it was not possible to control the intervals between (missed) sessions with greater precision. This resulted in varying intervals between sessions (which were measured as well as possible in TimeA). Little is yet known about the predictors of the number of sessions required in AATr (Eberl et al., 2014) to achieve optimal learning effects. In experimental learning and memory research, the spacing of sessions, the number of repetitions within a session and contingency awareness are among the factors that influence knowledge acquisition and retention (Musfeld et al., 2023; Walsh et al., 2023). It is therefore possible that more rigorous or dense AATr training protocols and a lower incidence of missed sessions may have had different effects on CDS (Walsh et al., 2023). Although spatial and verbal declarative memory are known to be correlated, it is interesting to include a measure of verbal memory as well in a subsequent study.

Finally, behavioural outcome measures were not included as this clinical study focused on the relationship between declarative memory and alcohol-approach bias reduction. As the results suggest that different AATr learning processes may be associated with alcohol bias modification, it is important to test whether the positive findings on relapse in a less cognitively impaired AUD population (Eberl et al., 2013; Manning et al., 2016; 2022; Rinck et al., 2018; Wiers et

al., 2011) can be replicated in a population of patients with AUD and cognitive impairment. Based on the extensive knowledge from experimental and patient studies in the field of memory and learning, several suggestions for further research to improve AATr learning can be considered. For example, in the presence of impaired declarative memory errorless learning paradigms are known to be beneficial for skill learning (Rensen et al., 2018). Therefore, it would be of interest to investigate adaptations of the AATr to prevent errors (the execution of incorrect movements), for example, by preventing the option to pull when confronted with an alcohol-related stimulus in the training phase. Also, as mentioned before, it would be very interesting to study the effect of session interval, including booster sessions, on the consolidation process of AATr learning effects over time (Bolt et al., 2022). Finally, it would be an improvement if clinicians could have direct insight into each patient's learning curve in order to give personalized advice on the number of sessions needed to reach a plateau effect.

Conclusion

In conclusion, for participants with decreased declarative memory function more sessions are needed to obtain within-session change in alcohol-approach bias. AATr should be standard available for this population as an add-on treatment of AUD. Also, standard individual neuropsychological evaluation is highly recommended in the AUD patient population since cognitive dysfunction is often overlooked and standard treatment protocols (including the AATr) need adaptation in the presence of neurocognitive disorders (Bates et al., 2013; Maurage et al., 2023). Finally, this neuropsychological perspective provided valuable insights into the process of action bias modification, supporting recent theory on CBM (R.W. Wiers et al., 2023). The application of a neuropsychological perspective can help improve interventions on the modulation of behavioural inhibition in psychopathology.


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MAIN FINDINGS & DISCUSSION

The main objective of this thesis was to contribute to the understanding of approach-avoidance (AA) behaviour in psychopathology and to study the feasibility of two different cognitive interventions in a neuropsychiatric population. The feasibility and acceptability of a compensatory cognitive training (CCTr) was explored in a neuropsychiatric patient population with various diagnostic classifications. Furthermore, the feasibility of an alcohol-avoidance training (AATr) was studied in a patient population with alcohol-related neurocognitive impairment (ARNI) or Korsakoff's syndrome (KS). This implicit-automatic intervention type could complement standard treatment procedures as it relies on the generally preserved cognitive ability of implicit learning of patients diagnosed with ARNI or KS. These clinical studies could contribute to improved treatment for patients with neuropsychiatric health conditions and in particular for these patients with ARNI and KS.

Main findings will be summarised, followed by a discussion of the theoretical and clinical implications of these findings. Both the AATr and a compensatory cognitive intervention (CCTr) will be discussed with regard to their (potential) mechanism of change and their applicability in a neuropsychiatric population. Finally, the strengths and limitations of the studies in this thesis are discussed, and recommendations for future research and clinical practice will be provided, along with an overall conclusion.

Summary and Main Findings

First, an extensive systematic review on AA behaviour in psychopathology was conducted, following the PRISMA guidelines (**Chapter 2**). This resulted in the inclusion of 97 studies covering 17 DSM-IV classifications. Most studies were found in the domain of substance abuse. A stronger approach bias was found in subclinical populations and an increased approach bias can be a risk factor for increased future substance use. Results showed that a dysfunctional approach tendency towards alcohol-related stimuli is a key feature of AUD, related to a genetic predisposition. Its clinical relevance was further underpinned by means of the replicated finding that successful modification of this alcohol-approach bias in clinical AUD patients shows a reduction in relapse rates. Therefore, it is argued that alcohol-approach bias modification procedures should be included in the regular treatment for alcohol addiction.

Beyond the clinical effects in AUD, evidence for clinical benefits of AA bias modification was only found in depressive disorders: successful modification of the lack of a natural approach tendency towards positive stimuli, by means of a positivity training, yielded a reduction in depressive symptoms. In anxiety disorders, a consistent avoidance bias of threatening stimuli was reached, however this

modification did not yet yield significant clinical results. Overall, the modification of an approach bias, or the lack of a natural approach bias, may be more eligible then the modification of an avoidance bias.

In order to contribute to the integrative treatment of cognitive deficiencies, two different cognitive interventions were evaluated: A 'top-down' CCTr in a mixed neuropsychiatric patient sample (**Chapter 3**), and the applicability of a 'bottom-up' approach by means of the AATr in a population with AUD related neurocognitive impairment including KS (**Chapter 4**). For both interventions, the applicability as well as the mechanisms of change were explored.

The applicability of the newly developed CCTr 'Master Mind' was studied in **Chapter 3** including 44 patients with various types of psychopathology. Proactive coping and satisfaction with daily life were measured at three time points: baseline, post-training, and four-month follow-up. No control group was included. The training set-up in patient samples with various mental health conditions, was found to be feasible according to the positive outcomes of the session rating scales. Participants reported stable positive ratings on all sessions on behalf of the training content and the methods used, as well as therapeutical factors such as the therapeutical alliance. Linear mixed modelling was applied for an initial exploration of the mechanisms of change by this CCTr. Preliminary results indicated an increase of proactive coping over training and this effect accounted for an increase in satisfaction of daily life measured at follow-up. No relation between cognitive resources (processing speed and working memory capacity) and proactive coping was found. These findings illustrate a good feasibility and acceptability of this tailored CCTr in a transdiagnostic sample of patients with cognitive deficiencies in psychopathology.

In **Chapter 4** the AATr was applied in a population with alcohol-related neurocognitive disorders. The AATr is a promising intervention for this population, as its implicit-automatic task characteristics match the generally preserved implicit memory and procedural learning ability of these patients. In this study, a six-session AATr was applied in a patient population with minor (ARNI; n= 51) and major neurocognitive disorders (KS; n= 54). It was found that alcohol approach bias could be successfully reduced. This reduction in bias was accompanied by a reduction of craving in patients diagnosed with major neurocognitive disorder. For a better understanding of the relationship between declarative memory function and AATr-related bias modification, a second study was conducted in the same patient population (**Chapter 5**). In this study, 64 patients were included of whom 31 met the criteria of ARNI and five participants were diagnosed with KS. Thirty-six patients were diagnosed with AUD without neurocognitive impairment. Here, an extended AATr was used with 12 sessions. Findings underpinned our previous findings of chapter 4: bias reduction can be

obtained by AATr in a patient sample with (severe) neurocognitive disorders. Moreover, when declarative memory capacity was impaired, more than six sessions were required to achieve sufficient within-session bias modification. This effect was not found for participants with relatively intact declarative memory function; for them the number of sessions was not related with bias reduction. Since repetition was needed for those with impaired declarative memory function, procedural (implicit) learning is likely to account for the observed results. In contrast, when declarative memory is more preserved, inferential learning processes may underlie AATr effects.

Discussion

By means of application of the framework of Braunstein et al (2017), the nature of treatment goal (**Chapter 2**) and the process of change by cognitive interventions (**Chapters 3, 4 and 5**) will be disentangled and discussed. Following this theoretical approach, the clinical applicability of cognitive interventions in psychopathology in general will be discussed as well.

The Nature of Cognitive Alterations in Psychopathology

With regard to approach-avoidance bias, as previously mentioned, the modification of an approach bias or the stimulation of an approach bias in cases where a natural approach tendency is lacking (e.g., in depressive disorders or anorexia nervosa), may be more feasible than the modification of an avoidance tendency. The difference between effects on approach or avoidance behaviour may further be explored by means of the RDoC framework (Cuthbert & Insel, 2013). The RDoC framework distinguishes seven different constructs underlying neurobehavioural functioning. Among these constructs are the *positive* valence system and the *negative* valence system. The positive valence system involves learning processes such as reward responsiveness, reinforcement learning and reward valuation, for example through the assignment of incentive salience to stimuli. Given the positive results of the AATr in changing the approach tendency, the AATr could potentially act upon this positive valence system. It may alter the association between stimulus and outcome value, thereby influencing reward valuation. The avoidance bias may be related to the negative valence system, which encompasses other constructs like fear, threat, loss and frustrative non-reward. Based on the current results, it may be reasoned that dysfunctional approach tendencies linked to the positive valence system could be particularly responsive to bias modification via AATr.

The Process of Change by Cognitive Interventions

Preliminary findings from **Chapter 3** suggested that CCTr may enhance proactive coping and, subsequently, satisfaction with daily life. Based on these findings, it can be hypothesised that improvements in proactive coping mediate the effects of CCTr on related outcomes, such as perceived burden, self-efficacy, and general well-being (Allott et al., 2025). This reasoning aligns with previous findings indicating that CCTr is associated with improvements in functional outcomes and symptom severity, which may be partly mediated by therapeutic and personal factors (Allott et al., 2024; Taylor et al., 2025; Wiers et al., 2018; Wong et al., 2024; Wykes et al., 2011).

Moreover, the capacity of cognitive processing resources was found to be unrelated to change in proactive coping. This finding suggests that individuals with impaired cognitive functioning may also benefit from this intervention. This pattern has been demonstrated in other studies as well, since patients with lower baseline cognitive functioning also benefitted from CCTr (Twamley et al., 2011).

The process of change by the AATr is generally conceptualised as an automatic, bottom-up process, aiming to directly modify cognitive biases through repetitive pairings of approach or avoidance movements with specific stimuli (e.g., pushing alcohol away, pulling non-alcoholic drinks) (Rinck & Becker, 2007). This mechanism is assumed to operate on an implicit level, reflecting procedural learning. However, findings from **Chapter 5** suggest that the nature of cognitive change depends on the quality of declarative memory: When declarative memory was relatively intact, additional AATr sessions did not lead to further reductions in alcohol-approach bias. This aligns as well with previous findings form Eberl et al. (2014) and Boffo et al (2019), who identified a fast process of modification change at the start of training. This steep decline predicted better outcomes, possibly reflecting the involvement of inferential learning rather than a purely procedural learning process. Conversely, when declarative memory was impaired, more sessions were needed, indicating reliance on implicit procedural learning, which depends on repetition (Keisler & Shadmehr, 2010); López et al., 2016; Smith & DeCoster, 2000). A capacity-dependent mechanism may therefore underlie AA modification via AATr: When declarative memory is intact, inferential processes can drive relatively rapid change with minimal repetition. When declarative memory or encoding is compromised, associative mechanisms predominate, requiring more training sessions to achieve comparable bias reduction. This reasoning is consistent with prior research showing that propositional learning requires cognitive resources (Gebauer & Mackintosh, 2007; Yang & Li, 2012; Zhan et al., 2018), and that resource depletion can hamper encoding (Pleyers et al., 2009). Moreover, research in other domains of learning, such as skill acquisition, motor learning and evaluative conditioning (EC), also distinguishes procedural and propositional learning processes. The interaction between these two processes is found to affect learning

results (Gawronksi & Bodenhausen, 2018; Hütter, 2022; Maresch et al., 2021; McLaren et al, 2014; Smith & DeCoster, 2000; Sun et al., 2005). Therefore it is of interest to study this interaction in AA learning as well.

In the related domain of EC, Gast (2018) proposed the Declarative Memory Model (DMM), which posits that EC effects occur when a declarative memory trace links the conditioned stimulus (CS) to the valence of the unconditioned stimulus (US), and a conscious retrieval of this trace is required. Applied to AA bias modification, the CS could be alcohol-related stimuli that elicit approach tendencies due to attributed positive valence, while the US could involve the affective evaluation derived from avoidance movements intended to correct this maladaptive association. From the perspective of the DMM, EC effects can be established by procedural learning, but only if the CS-US relation can be consciously detected by the participant. This aligns with the finding that contingency awareness may moderate AA learning in a healthy population (Van Dessel et al., 2016) and recent findings were indicative of inferential learning processes as well in bias modification procedures (Van Dessel et al., 2019; Wiers et al., 2020; 2023).

Integrating findings with the DMM and the multilevel framework of interventions by Braunstein et al. (2017), the AATr may shift from the implicit-automatic to the implicit-controlled quadrant under the influence of declarative memory quality. Furthermore, when the cognitive regulation goal is explicated, as in the consequence-based AA training as proposed by Van Dessel et al (2018), the nature of cognitive change of this intervention may shift towards the explicit-controlled quadrant (See Figure 3).

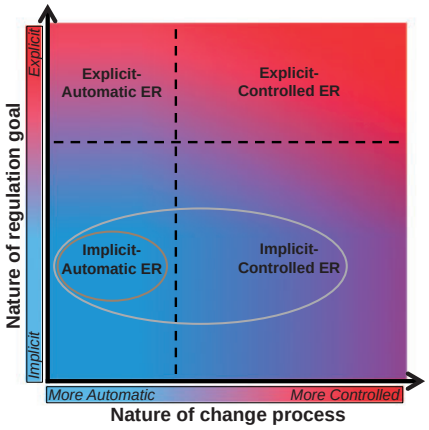


Figure 3. Classification of AATr using the multi-level framework of Braunstein et al., 2017.

Note: The brown circle represents the first classification of the AATr, the gray circle represents the AATr process of change related to declarative memory functioning.

Applicability of Cognitive Interventions in Psychopathology

The acceptability of a transdiagnostic application of CCTr in groups with various mental illnesses was studied in **Chapter 3**. This is a quite unique approach, as to the best of our knowledge only a few other CCTr studies have been conducted in mixed diagnose groups (Thomas et al, 2017; Twamley et al., 2019). Participant ratings showed good acceptability, as reflected by the session evaluations. The training goals, methods, session topics as well as the therapeutical alliance received good reports. This indicates participants felt accepted and and believed they were working on the right tasks in the right way. These initial results pave the way for a transdiagnostic application of CCTr, improving access of integrative cognitive treatment in specialised mental health care (Allott et al., 2025; Wong et al., 2024). The good acceptability of the training, together with evidence that cognitive functioning was unrelated to improvements in proactive coping, indicates that neither (the degree of) cognitive impairment or the nature of the mental illness should necessarily be used as exclusion criteria. Together, these findings together may contribute to improved availability and scalability of CCTr in mental healthcare.

With regard to alcohol-approach bias modification, the application of the AATr has been found to be feasible in an AUD population with ARNI or KS (**Chapters 4 and 5**). It is advised to apply more than six (six to 12) AATr sessions in this population with declarative memory deficits. For patients with KS it was found that the training contributed to decrease of craving, however this finding should be interpreted with caution given the lack of a control group that did not receive CBM or a sham training condition. The fact that AATr also requires (minor) adaptation in the presence of cognitive impairment reinforces the recommendation for standard cognitive assessment in AUD, in order to personalise treatment given the high prevalence of cognitive dysfunction (Kwako et al., 2016). Moreover, since another learning process seems to be present when declarative memory is impaired, it is yet unclear whether effects on relapse prevention found in general AUD can be replicated for this population.

Strengths and Limitations

As mentioned before, the inclusion of a follow-up measure on relapse rates or the use of control groups was beyond the scope of this thesis. This clearly limits the ability to draw firm conclusions regarding the effects of the intervention studies. Furthermore, conducting research in clinical practice with this very specific neuropsychiatric patient population posed challenges for participant inclusion and attendance. Nevertheless, the deliberate inclusion of this population, characterised

by severe mental illness and cognitive deficits, represents a significant strength of this thesis, as this population is often excluded from research and treatment programs.

Characteristics of the Patient Samples and Inclusion Criteria

Building on the aforementioned methodological considerations, it is important to reflect on the inclusion criteria applied across studies related to their specific research aims.

To improve understanding of the relevance of approach-avoidance bias in psychopathology, a strict criterion requiring (sub)clinical samples was applied in the systematic review (**Chapter 2**). This ensured that findings on approach–avoidance behaviour were relevant to psychopathology and minimised the risk of misinterpretation that can occur when comparing clinical and healthy populations (Boffo et al., 2019; Wiers et al., 2018).

Patients with severe mental illness and neurocognitive deficits are often excluded from research and treatment programs due to the complexity of their conditions. The studies in **Chapters 4 and 5** deliberately included individuals with ARNI and KS and the study in Chapter 5 also included AUD patients without neurocognitive impairment. This approach enabled the study of the feasibility of the AATr intervention for patients with a various degree of declarative memory impairment and the process of bias modification. This inclusion strategy yielded both theoretical and clinical insights by enabling the study of bias modification mechanisms in a population typically underrepresented in scientific evaluation.

For the CCTr intervention study (**Chapter 3**), inclusion was based on subjective cognitive complaints and motivation to learn compensatory strategies, rather than diagnostic classification or severity of cognitive impairment. Traditionally, each psychiatric classification (e.g., depressive disorder, bipolar disorder, psychotic disorder) is treated with a disorder-specific cognitive intervention. However, removing these boundaries proved feasible: the application of our CCTr 'Master Mind' in a mixed sample of patients with neuropsychiatric disorders demonstrated good acceptability. This transdiagnostic approach could enhance access to cognitive interventions in specialised mental health care.

Inclusion Number and Attendance Rates

While the importance of recognising cognitive impairment in the treatment of psychopathology is widely acknowledged, consistent referral for cognitive remediation continues to lag behind in clinical practice (Wong et al. 2024; Maurage et al. 2024). With regard to the newly introduced Master Mind intervention program (**Chapter 3**) continued extensive recruitment for referral was needed. Moreover, COVID-19 pandemic restrictions posed another challenge to maintain a consistent flow of referrals and temporarily affected group attendance rates.

The response rate for the follow-up measure was especially relatively low, despite the guidance provided. This obviously limits conclusions on long-term effects of this CCTr, as there may have been a response bias. For example, non-responders may differ from responders in coping behaviour, cognitive capacities or quality of life. Given the small sample size and in order to retain as many datapoints as possible, Linear Mixed Modeling was applied (Hox & McNeish, 2020).

With regard to the two AATr studies of this thesis (**Chapters 4 and 5**) a steady patient enrolment was achieved. The Centre of Excellence for Korsakoff and Alcohol-Related Cognitive Disorders of the Vincent van Gogh Institute of Psychiatry systematically facilitates and conducts academic research to improve clinical care for this specific group of patients with ARNI or KS. This resulted in considerable total sample sizes of inpatients with alcohol-related neurocognitive disorders in both AATr studies (Chapter 4: N= 105; Chapter 5: N= 64). However, these sample sizes still warrant statistical caution (Rinck, 2017).

Treatment dropout and irregular attendance remain major challenges in the continuation of inpatient treatment for AUD (Mladenovic et al., 2025), especially when cognitive impairments are present (Sømhovd et al., 2019; Domínguez-Salas et al., 2016). Despite the highly structured clinical setting and motivational guidance, these issues arose in our studies as well, constraining the interpretability of the findings. In **Chapter 5,** for example more frequent training might have resulted in different effects. In order to correct for differences in interval between training sessions within participants due to missed sessions, the factor Time was included and computed in two different ways. The first one incorporated the spacing between the attended sessions, and the second included only the sessions actually attended, without accounting for spacing. Furthermore, by means of Linear Mixed Modelling all available observations were retained, reducing bias and preserving statistical power compared to listwise deletion. Finally, given the efforts made in this highly structured clinical setting to enhance attendance rates, achieving higher rates will be difficult. Therefore, the findings of the two AATr studies (**Chapters 4 and 5**) can be considered ecologically valid, as they reflect the realistic results of clinical practice.

In conclusion, while the specific characteristics of the ARNI and KS patient groups limit the generalisability of the current findings to other clinical groups, our studies have demonstrated the value of including patients with illness-specific characteristics, such as cognitive impairment. Doing so contributes to personalised care and deepens the understanding of the mechanisms of change underlying cognitive interventions.

Recommendations for Future Research and Clinical Practice

The findings of the studies in this thesis, which applied a clinical neuropsychological perspective to AA behaviour, contribute to our understanding of the impact of cognitive alterations in psychopathology and support the development of targeted cognitive interventions. Specifically, a continued clinical neuropsychological perspective on AA modification in psychopathology is recommended. More generally, cognitive interventions tailored to an individual's cognitive strengths and weaknesses can contribute to recovery from mental illness and AUD. Personalised evaluation strategies, such as single-case experimental designs (SCEDs) or idiographic methods (Piccirillo & Rodebaugh, 2019), can be used to evaluate these interventions scientifically.

To optimise AATr effects, it is recommended that the interaction between procedural and inferential learning processes is further explored, as this could enhance the understanding of bias modification processes.

A neuropsychological perspective can also be used to systematically address the different phases of learning (encoding, consolidation, and retrieval) in bias modification procedures. Variables such as training density, spaced learning and booster sessions, as well as contextual factors such as craving and cognitive depletion, should be taken into account (Gast, 2018; Ghilardi et al., 2009; Musfeld et al., 2023; Walsh et al., 2023; Yücel et al., 2019).

With regard to the assessment and modification of approach-avoidance behaviour in psychopathology in general, it could be valuable to align future study hypotheses and findings with the RDoC framework. Relating the nature of biased AA behaviour to either the positive or the negative valence system could improve the development of cognitive bias modification procedures. For example, it may be valuable to investigate strategies that enhance natural approach tendencies related to the positive valence system, as they were found to be reduced in disorders such as depression and anorexia nervosa.

Regarding the application of cognitive interventions for patients with cognitive deficits in clinical practice, it is recommended to implement the AATr in AUD treatment, particularly for patients with ARNI and KS. This intervention complements cognitive rehabilitation interventions for AUD (Kwako et al., 2016; Maurage et al., 2024; Verdejo-Garcia et al., 2023; Wiers et al., 2023).

For individuals with impaired declarative memory extended training, typically six to 12 sessions are recommended. Moreover, the adaptation of the AATr to an errorless learning protocol (preventing incorrect movements in the training phase) may improve procedural learning in case of declarative memory impairment (Kessels & Haan, 2003; Rensen et al., 2019; Twamley., 2016). Finally, the effects of AATr on alcohol relapse prevention in this specific population require further investigation.

Finally, the study on Master Mind demonstrated that a transdiagnostic approach is feasible and acceptable. This approach offers a scalable strategy for implementation in specialised mental health care. Future research on proactive coping as a potential mediation variable accounting for CCTr effects is of interest.

Conclusion

Adopting a neuopsychological perspective on AA behaviour in psychopathology was found to be beneficial in both clinical and theoretical terms. The presence of an approach bias for substance related stimuli in subclinical populations can be a risk factor for increased future substance use. Clinical effects of approach bias modification were mainly found and replicated in AUD. These approach tendencies may be linked to the positive valence system and be more responsive to modification then avoidance tendencies. Furthermore, both the application of the AATr and the CCTr 'Master Mind' proved to be feasible in a neuropsychiatric patient population. Study results also yielded some insights in the potential mechanisms of these cognitive interventions. With regard to the AATr: if declarative memory is impaired, procedural learning processes may account for bias change. For those patients, extra sessions were needed to obtain bias modification effects. However, when declarative memory is relatively spared, inferential learning processes may account for bias modification effects, as the number of sessions was not related to change in bias for these participants.

With regard to Master Mind preliminary results suggest that this CCTr enhances proactive coping and this effect was associated with improved satisfaction with daily life, independent of cognitive resources.

Future research should maintain a clinical neuropsychological perspective when examining approach–avoidance behaviour in psychopathology and the mechanisms of change by cognitive interventions in mental health conditions. Embedding neuropsychological principles in cognitive bias modification development can optimise treatment protocols. A transdiagnostic application of compensatory cognitive interventions may increase accessibility and scalability.

Advancing research on the mechanisms of change by cognitive interventions is essential to bridge the gap between the C-factor, a key feature of psychopathology, and the availability of integrative cognitive treatment strategies in specialised mental health care.


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References

Abramovitch, A., Short, T., & Schweiger, A. (2021). The C Factor: Cognitive dysfunction as a transdiagnostic dimension in psychopathology. *Clinical Psychology Review*, *86*, 102007. https://doi.org/10.1016/j.cpr.2021.102007

Allott, K., Bryce, S., Douglas, K., Stainton, A., Wood, S. J., & Bowie, C. R. (2025). Formulating Cognitive Functioning to Guide Personalised Treatment for People Diagnosed With Mental Disorders. *Acta Psychiatrica Scandinavica*. https://doi.org/10.1111/acps.13811

Allott, K., El, K., Bryce, S., Parrish, E. M., McGurk, S. R., Hetrick, S., Bowie, C. R., Kidd, S., Hamilton, M., Killackey, E., & Velligan, D. (2020). Compensatory Interventions for Cognitive Impairments in Psychosis: A Systematic Review and Meta-Analysis. *Schizophrenia Bulletin*, *46*(4), 869-883. https://doi.org/10.1093/schbul/sbz134

Allott, K. A., Rapado-Castro, M., Proffitt, T.-M., Bendall, S., Garner, B., Butselaar, F., Markulev, C., Phassouliotis, C., McGorry, P. D., Wood, S. J., Cotton, S. M., & Phillips, L. J. (2015). The impact of neuropsychological functioning and coping style on perceived stress in individuals with first-episode psychosis and healthy controls. *Psychiatry Research*, *226*(1), 128–135. https://doi.org/10.1016/j.psychres.2014.12.032

American Psychiatric Association & American Psychiatric Association (Red.). (2000). *Diagnostic and statistical manual of mental disorders: DSM-IV-TR* (4. ed., text rev., 13. print). American Psychiatric Assoc.

American Psychiatric Association. (2022). *Diagnostic and statistical manual of mental disorders, Text Revision (DSM-5-TRTM)*. American Psychiatric Pub. https://doi.org/10.1176/appi.books.9780890425787

Amir, N., Kuckertz, J. M., & Najmi, S. (2013). The effect of modifying automatic action tendencies on overt avoidance behaviors. *Emotion*, *13*(3), 478-484.

Amir, N., Taylor, C. T., & Donohue, M. C. (2011). Predictors of response to an attention modification program in generalized social phobia. *Journal of consulting and clinical psychology*, *79*(4), 533-541. doi:10.1037/a0023808.

Arts, N. J., Walvoort, S. J., & Kessels, R. P. (2017). Korsakoff's syndrome: A critical review. *Neuropsychiatric Disease and Treatment*, *13*, 2875-2890. https://doi.org/10.2147/NDT.S130078

Asnaani, A., Rinck, M., Becker, E., & Hofmann, S. G. (2014). The effects of approach–avoidance modification on social anxiety disorder: A pilot study. *Cognitive therapy and research*, *38*(2), 226-238. doi:10.1007/s10608-013-9580-x.

Baert, S., Koster, E. H., & De Raedt, R. (2011). Modification of information-processing biases in emotional disorders: Clinically relevant developments in experimental psychopathology. *International Journal of Cognitive Therapy*, *4*(2), 208-222.

Baird, S. O., Rinck, M., Rosenfield, D., Davis, M. L., Fisher, J. R., Becker, E. S., Powers, M. B., & Smits, J. A. (2017). Reducing approach bias to achieve smoking cessation: A pilot randomized placebo-controlled trial. *Cognitive Therapy and Research*, *41*(4), 662-670. . https://doi.org/10.1007/s10608-017-9835-z

Bakvis, P., Spinhoven, P., Zitman, F. G., & Roelofs, K. (2011). Automatic avoidance tendencies in patients with psychogenic non epileptic seizures. *Seizure*, *20*(8), 628-634. https://doi.org/10.1016/j.seizure.2011.06.006

Barkby, H., Dickson, J. M., Roper, L., & Field, M. (2012). To approach or avoid alcohol? Automatic and self-reported motivational tendencies in alcohol dependence. *Alcoholism: Clinical and Experimental Research*, *36*(2), 361-368. DOI: 10.1111/j.1530-0277.2011.01620.x

Bartoszek, G., & Winer, E. S. (2015). Spider-fearful individuals hesitantly approach threat, whereas depressed individuals do not persistently approach reward. *Journal of behavior therapy and experimental psychiatry*, *46*, 1-7. doi: 10.1016/j.jbtep.2014.07.012

Bates, M. E., Bowden, S. C., & Barry, D. (2002). Neurocognitive impairment associated with alcohol use disorders: Implications for treatment. *Experimental and Clinical Psychopharmacology*, *10*(3), 193-212. https://doi.org/10.1037//1064-1297.10.3.193

Bates, M. E., Pawlak, A. P., Tonigan, J. S., & Buckman, J. F. (2006). Cognitive impairment influences drinking outcome by altering therapeutic mechanisms of change. *Psychology of Addictive Behaviors: Journal of the Society of Psychologists in Addictive Behaviors*, *20*(3), 241-253. https://doi.org/10.1037/0893-164X.20.3.241

Bates, M. E., Buckman, J. F., & Nguyen, T. T. (2013). A role for cognitive rehabilitation in increasing the effectiveness of treatment for alcohol use disorders. *Neuropsychology review*, *23*(1), 27-47. https://doi.org/10.1007/s11065-013-9228-3

Bechara, A. (2005). Decision making, impulse control and loss of willpower to resist drugs: A neurocognitive perspective. *Nature neuroscience*, *8*(11), 1458-1463. https://doi.org/10.1038/nn1584

Bechara, A., & Noel, X. (2006). Decision Making in Addiction. *Handbook of implicit cognition and addiction*, 215.

Beck, A. T. (1991). Cognitive therapy: A 30-year retrospective. *American psychologist*, *46*(4), 368. https://psycnet.apa.org/doi/10.1037/0003-066X.46.4.368

Beck, A., Wüstenberg, T., Genauck, A., Wrase, J., Schlagenhauf, F., Smolka, M. N., Mann, K., & Heinz, A. (2012). Effect of brain structure, brain function, and brain connectivity on relapse in alcohol-dependent patients. *Archives of general psychiatry*, *69*(8), 842-852. doi:10.1001/archgenpsychiatry.2011.2026

Becker, D., Jostmann, N. B., & Holland, R. W. (2018). Does approach bias modification really work in the eating domain? A commentary on Kakoschke et al. (2017). *Addictive Behaviors*, *77*, 293-294. https://doi.org/10.1016/j.addbeh.2017.02.025

Becker, E. S., Barth, A., Smits, J. A., Beisel, S., Lindenmeyer, J., & Rinck, M. (2019). Positivity-approach training for depressive symptoms: A randomized controlled trial. *Journal of affective disorders*, *245*, 297-304. doi:10.1016/j.jad.2018.11.042

Becker, E. S., Ferentzi, H., Ferrari, G., Möbius, M., Brugman, S., Custers, J., Geurtzen, N., Wouters, J., & Rinck, M. (2016). Always approach the bright side of life: A general positivity training reduces stress reactions in vulnerable individuals. *Cognitive Therapy and Research*, *40*(1), 57-71. doi:10.1007/s10608-015-9716-2

Beraha, E. M., Salemink, E., Krediet, E., & Wiers, R. W. (2018). Can baclofen change alcohol-related cognitive biases and what is the role of anxiety herein? *Journal of Psychopharmacology*, *32*(8), 867-875. https://doi.org/10.1177/0269881118780010

Bernardin, F., Maheut-Bosser, A., & Paille, F. (2014). Cognitive Impairments in Alcohol-Dependent Subjects. *Frontiers in Psychiatry*, *5*, 78. https://doi.org/10.3389/fpsyt.2014.00078

Best, M. W., & Bowie, C. R. (2017). A review of cognitive remediation approaches for schizophrenia: from top-down to bottom-up, brain training to psychotherapy. *Expert Review of Neurotherapeutics*, *17*(7), 713-723. https://doi.org/10.1080/14737175.2017.1331128

Blackwell, S. E., Woud, M. L., & MacLeod, C. (2017). A Question of Control? Examining the Role of Control Conditions in Experimental Psychopathology using the Example of Cognitive Bias Modification Research. *The Spanish Journal of Psychology*, *20*, E54. https://doi.org/10.1017/sjp.2017.41

Bode, C., Thoolen, B., & de Ridder, D. (2008). Measuring proactive coping. Psychometric characteristics of the Utrecht Proactive Coping Competence scale (UPCC). *Psychologie & Gezondheid*, *36*(2), 81–91. https://doi.org/10.1016/j.apmr.2013.11.010

Boelen, D. H. E., Spikman, J. M., Lamberts, K. F., Brouwer, W. H., & Fasotti, L. (2012). *Protocol dysexecutief syndroom* [Protocol for dysexecutive syndrome]. Boom Publishers.

Boffo, M., Smits, R., Salmon, J. P., Cowie, M. E., De Jong, D. T. H. A., Salemink, E., Collins, P., Stewart, S. H., & Wiers, R. W. (2018). Luck, come here! Automatic approach tendencies toward gambling cues in moderate- to high-risk gamblers. *Addiction*, *113*(2), 289-298. https://doi.org/10.1111/add.14071

Boffo, M., Zerhouni, O., Gronau, Q. F., Beek, R. J., Nikolaou, K., Marsman, M., & Wiers, R. W. (2019). Cognitive bias modification for behavior change in alcohol and smoking addiction: Bayesian meta-analysis of individual participant data. *Neuropsychology review*, *29*(1), 52-78. https://doi.org/10.1007/s11065-018-9386-4

Bohn, M. J., Krahn, D. D., & Staehler, B. A. (1995). Development and initial validation of a measure of drinking urges in abstinent alcoholics. *Alcoholism: clinical and experimental research*, *19*(3), 600-606. https://doi.org/10.1111/j.1530-0277.1995.tb01554.x

Bolt, G. L., Piercy, H., Barnett, A., & Manning, V. (2022). 'A circuit breaker' - Interrupting the alcohol autopilot: A qualitative exploration of participants' experiences of a personalised mHealth approach bias modification intervention for alcohol use. *Addictive Behaviors Reports*, *16*, 100471. https://doi.org/10.1016/j.abrep.2022.100471

Bora, E., Harrison, B. J., Yücel, M., & Pantelis, C. (2013). Cognitive impairment in euthymic major depressive disorder: A meta-analysis. *Psychological Medicine*, *43*(10), 2017–2026. https://doi.org/10.1017/s0033291712002085

Borries, A. K. L. V., Volman, I., De Bruijn, E. R. A., Bulten, B. H., Verkes, R. J., & Roelofs, K. (2012). Psychopaths lack the automatic avoidance of social threat: Relation to instrumental aggression. *Psychiatry Research*, *200*(2-3), 761-766. https://doi.org/10.1016/j.psychres.2012.06.026

Bowie, C. R., Bell, M. D., Fiszdon, J. M., Johannesen, J. K., Lindenmayer, J.-P., McGurk, S. R., Medalia, A. A., Penadés, R., Saperstein, A. M., Twamley, E. W., Ueland, T., & Wykes, T. (2020). Cognitive remediation for schizophrenia: An expert working group white paper on core techniques. *Schizophrenia Research*, *215*, 49-53. https://doi.org/10.1016/j.schres.2019.10.047

Bowie, C. R., Grossman, M., Gupta, M., Holshausen, K., & Best, M. W. (2017). Action-based cognitive remediation for individuals with serious mental illnesses: Effects of real-world simulations and goal setting on functional and vocational outcomes. Psychiatric Rehabilitation Journal, 40(1), 53–60. https://doi.org/10.1037/prj0000189

Bowie, C. R., McGurk, S. R., Mausbach, B., Patterson, T. L., & Harvey, P. D. (2012). Combined Cognitive Remediation and Functional Skills Training for Schizophrenia: Effects on Cognition, Functional Competence, and Real-World Behavior. *American Journal of Psychiatry*, *169*(7), 710-718. https://doi.org/10.1176/appi.ajp.2012.11091337

Bradley, B., Field, M., Mogg, K., & De Houwer, J. (2004). Attentional and evaluative biases for smoking cues in nicotine dependence: Component processes of biases in visual orienting. *Behavioural pharmacology*, *15*(1), 29-36.. doi:10.1097/00008877-200402000-00004.

Bradley, B. P., Field, M., Healy, H., & Mogg, K. (2008). Do the affective properties of smoking-related cues influence attentional and approach biases in cigarette smokers? *Journal of Psychopharmacology*, *22*(7), 737-745. doi:10.1177/0269881107083844.

Braunstein, L. M., Gross, J. J., & Ochsner, K. N. (2017). Explicit and implicit emotion regulation: A multi-level framework. *Social Cognitive and Affective Neuroscience*, *12*(10), 1545-1557. https://doi.org/10.1093/scan/nsx096

Brickenkamp, R., & Oosterveld, P. (2014). *D2: Aandachts-en concentratietest. Box*. Hogrefe.

Brion, M. (2017). *A dual-process model exploration of executive and emotional dysfunctions in alcohol-dependence and Korsakoff syndrome*. Catholic University of Leuven.

Brion, M., D'Hondt, F., Pitel, A.-L., Lecomte, B., Ferauge, M., Timary, P., & Maurage, P. (2017). Executive functions in alcohol-dependence: A theoretically grounded and integrative exploration. *Drug and Alcohol Dependence*, *177*, 39-47. https://doi.org/10.1016/j.drugalcdep.2017.03.018

Brockmeyer, T., Friederich, H.-C., Küppers, C., Chowdhury, S., Harms, L., Simmonds, J., Gordon, G., Potterton, R., & Schmidt, U. (2019). Approach bias modification training in bulimia nervosa and binge-eating disorder: A pilot randomized controlled trial. *International Journal of Eating Disorders*, *52*(5), 520-529. doi: 10.1002/eat.23024

Brockmeyer, T., Hahn, C., Reetz, C., Schmidt, U., & Friederich, H.-C. (2015). Approach bias modification in food craving—A proof-of-concept study. *European Eating Disorders Review*, *23*(5), 352-360. doi:10.1002/erv.2382

Bruijnen, C. J. W. H., Dijkstra, B. A. G., Walvoort, S. J. W., Markus, W., VanDerNagel, J. E. L., Kessels, R. P. C., & De Jong, C. A. J. (2019). Prevalence of cognitive impairment in patients with substance use disorder. *Drug and Alcohol Review*, *38*(4), 435-442. https://doi.org/10.1111/dar.12922

Bruijnen, C. J. W. H., Walvoort, S. J. W., Dijkstra, B., Jong, C., & Kessels, R. P. C. (2021). The Course of Cognitive Performance during Inpatient Treatment in Patients with Alcohol Use Disorder with No, Mild or Major Neurocognitive Disorders. *Oxfordshire)*, *56*(1), 89-100. https://doi.org/10.1093/alcalc/agaa100

Burton, C. Z., & Twamley, E. W. (2015). Neurocognitive insight, treatment utilization, and cognitive training outcomes in schizophrenia. Schizophrenia Research, 161(2–3), 399–402. https://doi.org/10.1016/j.schres.2014.12.002

Cabé, N., Laniepce, A., Ritz, L., Lannuzel, C., Boudehent, C., Vabret, F., Eustache, F., Beaunieux, H., & Pitel, A.-L. (2016). [Cognitive impairments in alcohol dependence: From screening to treatment improvements]. *L'Encephale*, *42*(1), 74-81. https://doi.org/10.1016/j.encep.2015.12.012

Cacioppo, J. T., & Gardner, W. L. (1999). EMOTION. *Annual Review of Psychology, 50*(Volume 50, 1999), 191-214. https://doi.org/10.1146/annurev.psych.50.1.191

Caspi, A., Houts, R. M., Belsky, D. W., Goldman-Mellor, S. J., Harrington, H., Israel, S., Meier, M. H., Ramrakha, S., Shalev, I., Poulton, R., & Moffitt, T. E. (2014). *The p Factor: One General Psychopathology Factor in the Structure of Psychiatric Disorders? Clinical Psychological Science: A Journal of the Association for Psychological Science, 2(2), 119-137.* https://doi.org/10.1177/2167702613497473

Chavez-Baldini, U., Nieman, D. H., Keestra, A., Lok, A., Mocking, R. J. T., de Koning, P., Krzhizhanovskaya, V. V., Bockting, C. L. H., van Rooijen, G., Smit, D. J. A., Sutterland, A. L., Verweij, K. J. H., van Wingen, G., Wigman, J. T. W., Vulink, N. C., & Denys, D. (2023). The relationship between cognitive functioning and psychopathology in patients with psychiatric disorders: A transdiagnostic network analysis. *Psychological Medicine, 53*(2), 476–485. https://doi.org/10.1017/s0033291721001781

Chen, M., & Bargh, J. A. (1999). Consequences of automatic evaluation: Immediate behavioral predispositions to approach or avoid the stimulus. *Personality and social psychology bulletin*, *25*(2), 215-224. https://doi.org/10.1177/0146167299025002007

Chen, N. T., Clarke, P. J., Watson, T. L., MacLeod, C., & Guastella, A. J. (2015). Attentional bias modification facilitates attentional control mechanisms: Evidence from eye tracking. *Biological Psychology*, *104*, 139-146. doi: 10.1016/j.biopsycho.2014.12.002

Christiansen, P., Cole, J. C., Goudie, A. J., & Field, M. (2012). Components of behavioural impulsivity and automatic cue approach predict unique variance in hazardous drinking. *Psychopharmacology*, *219*(2), 501-510. doi: 10.1007/s00213-011-2396-z.

Christiansen, P., Schoenmakers, T. M., & Field, M. (2015). Less than meets the eye: Reappraising the clinical relevance of attentional bias in addiction. *Addictive behaviors*, *44*, 43-50. doi:10.1016/j.addbeh.2014.10.005

Cicerone, K. D., Goldin, Y., Ganci, K., Rosenbaum, A., Wethe, J. V., Langenbahn, D. M., ... & Harley, J. P. (2019). Evidence-based cognitive rehabilitation: systematic review of the literature from 2009 through 2014. *Archives of physical medicine and rehabilitation*, *100*(8), 1515-1533. https://doi.org/10.1016/j.apmr.2019.02.011

Clarke, P. J., Browning, M., Hammond, G., Notebaert, L., & MacLeod, C. (2014). The causal role of the dorsolateral prefrontal cortex in the modification of attentional bias: Evidence from transcranial direct current stimulation. *Biological psychiatry*, *76*(12), 946-952. doi:10.1016/j.biopsych.2014.03.003

Cludius, B., Külz, A. K., Landmann, S., Moritz, S., & Wittekind, C. E. (2017). Implicit approach and avoidance in patients with obsessive-compulsive disorder. *Journal of Abnormal Psychology*, *126*(6), 761. doi:10.1037/abn0000269.

Correll, C. U., Cortese, S., Solmi, M., Boldrini, T., Demyttenaere, K., Domschke, K., Fusar-Poli, P., Gorwood, P., Harvey, P. D., Keefe, R. S. E., Knaevelsrud, C., Kotov, R., Nohr, L., Rhee, T. G., Roe, D., Rose, M., Schneider, L. S., Slade, M., Stein, D. J., ... McIntyre, R. S. (2025). Beyond symptom improvement: Transdiagnostic and disorder-specific ways to assess functional and quality of life outcomes across mental disorders in adults. *World Psychiatry, 24*(3), 296–318. https://doi.org/10.1002/wps.21338

Cousijn, J., Goudriaan, A. E., Ridderinkhof, K. R., van den Brink, W., Veltman, D. J., & Wiers, R. W. (2012). Approach-bias predicts development of cannabis problem severity in heavy cannabis users: results from a prospective FMRI study. *PloS one*, *7*(9), e42394. https://doi.org/10.1371/journal.pone.0042394

Cousijn, J., Goudriaan, A. E., & Wiers, R. W. (2011). Reaching out towards cannabis: Approach-bias in heavy cannabis users predicts changes in cannabis use. *Addiction*, *106*(9), 1667-1674. doi: 10.1111/j.1360-0443.2011.03475.x.

Cousijn, J., Luijten, M., & Wiers, R. W. (2014a). Mechanisms underlying alcohol-approach action tendencies: The role of emotional primes and drinking motives. *Frontiers in psychiatry*, *5*, 44. doi: 10.3389/fpsyt.2014.00044.

Cousijn, J., Luijten, M., & Wiers, R. W. (2014b). Mechanisms Underlying Alcohol-Approach Action Tendencies: The Role of Emotional Primes and Drinking Motives. *Frontiers in Psychiatry*, *5*. https://doi.org/10.3389/fpsyt.2014.00044

Cousijn, J., Snoek, R. W., & Wiers, R. W. (2013). Cannabis intoxication inhibits avoidance action tendencies: A field study in the Amsterdam coffee shops. *Psychopharmacology, 229*(1), 167-176. doi: 10.1007/s00213-013-3097-6.

Cousijn, J., van Benthem, P., van der Schee, E., & Spijkerman, R. (2015). Motivational and control mechanisms underlying adolescent cannabis use disorders: A prospective study. *Developmental Cognitive Neuroscience, 16*, 36-45. doi:10.1016/j.dcn.2015.04.001

Cristea, I. A., Kok, R. N., & Cuijpers, P. (2016). The effectiveness of cognitive bias modification interventions for substance addictions: A meta-analysis. *PloS one, 11*(9), e0162226. https://doi.org/10.1371/journal.pone.0162226

Cuthbert, B. N., & Insel, T. R. (2013). Toward the future of psychiatric diagnosis: The seven pillars of RDoC. *BMC medicine, 11*(1), 126. doi:10.1186/1741-7015-11-126.

Czapla, M., Simon, J. J., Richter, B., Kluge, M., Friederich, H.-C., Herpertz, S., Mann, K., Herpertz, S. C., & Loeber, S. (2016). The impact of cognitive impairment and impulsivity on relapse of alcohol-dependent patients: Implications for psychotherapeutic treatment. *Addiction Biology, 21*(4), 873-884. https://doi.org/10.1111/adb.12229

de Graaf, J. A., Schepers, V. P. M., Nijsse, B., van Heugten, C. M., Post, M. W. M., & Visser-Meily, J. M. A. (2022). The influence of psychological factors and mood on the course of participation up to four years after stroke. *Disability and Rehabilitation, 44*(10), 1855–1862. https://doi.org/10.1080/09638288.2020.1808089

De Raedt, R., & Hooley, J. M. (2016). The role of expectancy and proactive control in stress regulation: A neurocognitive framework for regulation expectation. *Clinical Psychology Review, 45*, 45–55. https://doi.org/10.1016/j.cpr.2016.03.005

De Houwer, J., Crombez, G., Baeyens, F., & Hermans, D. (2001). On the generality of the affective Simon effect. *Cognition & Emotion, 15*(2), 189-206. DOI:10.1080/0269993004200051

De Houwer, J., Teige-Mocigemba, S., Spruyt, A., & Moors, A. (2009). Implicit measures: A normative analysis and review. *Psychological bulletin, 135*(3), 347. DOI:10.1037/a0014211

de la Asuncion, J., Docx, L., Sabbe, B., Morrens, M., & De Bruijn, E. R. (2015). Converging evidence of social avoidant behavior in schizophrenia from two approach-avoidance tasks. *Journal of Psychiatric Research, 69*, 135-141. doi:10.1016/j.jpsychires.2015.08.008

Deckers, A., Roelofs, J., Muris, P., & Rinck, M. (2014). Desire for social interaction in children with autism spectrum disorders. *Research in Autism Spectrum Disorders, 8*(4), 449-453. https://doi.org/10.1016/j.rasd.2013.12.019

den Uyl, T. E., Gladwin, T. E., Rinck, M., Lindenmeyer, J., & Wiers, R. W. (2017). A clinical trial with combined transcranial direct current stimulation and alcohol approach bias retraining. *Addiction biology, 22*(6), 1632-1640. https://doi.org/10.1111/adb.12463

Derntl, B., Seidel, E.-M., Eickhoff, S. B., Kellermann, T., Gur, R. C., Schneider, F., & Habel, U. (2011). Neural correlates of social approach and withdrawal in patients with major depression. *Social neuroscience, 6*(5-6), 482-501. doi:10.1080/17470919.2011.579800

Di Lemma, L. C., & Field, M. (2017). Cue avoidance training and inhibitory control training for the reduction of alcohol consumption: A comparison of effectiveness and investigation of their mechanisms of action. *Psychopharmacology, 234*(16), 2489-2498. doi:10.1007/s00213-017-4639-0.

Domínguez-Salas, S., Díaz-Batanero, C., Lozano-Rojas, O. M., & Verdejo-García, A. (2016). Impact of general cognition and executive function deficits on addiction treatment outcomes: Systematic review and discussion of neurocognitive pathways. *Neuroscience & Biobehavioral Reviews, 71*, 772-801. https://doi.org/10.1016/j.neubiorev.2016.09.030

Douglas, K. M., Milanovic, M., Porter, R. J.,& Bowie, C. R. (2020). Clinical and methodological considerations for psychological treatment of cognitive impairment in major depressive disorder. *BJPsych Open, 6*(4), Article e67. https://doi.org/10.1192/bjo.2020.53

Duka, T., Trick, L., Nikolaou, K., Gray, M. A., Kempton, M. J., Williams, H., Williams, S. C., Critchley, H. D., & Stephens, D. N. (2011). Unique brain areas associated with abstinence control are damaged in multiply detoxified alcoholics. *Biological psychiatry, 70*(6), 545-552. doi: 10.1016/j.biopsych.2011.04.006

Eack, S. M., Hogarty, G. E., Cho, R. Y., Prasad, K. M., Greenwald, D. P., Hogarty, S. S., & Keshavan, M. S. (2010). Neuroprotective effects of cognitive enhancement therapy against gray matter loss in early schizophrenia: Results from a 2-year randomized controlled trial. *Archives of general psychiatry*, *67*(7), 674–682. doi:10.1001/archgenpsychiatry.2010.63.

East-Richard, C., Mercier, A., Nadeau, D., & Cellard, C. (2020). Transdiagnostic neurocognitive deficits in psychiatry: A review of meta-analyses. *Canadian Psychology / Psychologie Canadienne*, *61*(3), 190-214. https://doi.org/10.1037/cap0000196

Eberl, C., Wiers, R. W., Pawelczack, S., Rinck, M., Becker, E. S., & Lindenmeyer, J. (2013). Approach bias modification in alcohol dependence: Do clinical effects replicate and for whom does it work best? *Developmental Cognitive Neuroscience*, *4*, 38-51. https://doi.org/10.1016/j.dcn.2012.11.002

Eberl, C., Wiers, R. W., Pawelczack, S., Rinck, M., Becker, E. S., & Lindenmeyer, J. (2014). Implementation of approach bias re-training in alcoholism-how many sessions are needed? *Alcoholism, Clinical and Experimental Research*, *38*(2), 587-594. https://doi.org/10.1111/acer.12281

Elfeddali, I., de Vries, H., Bolman, C., Pronk, T., & Wiers, R. W. (2016). A randomized controlled trial of Web-based Attentional Bias Modification to help smokers quit. *Health Psychology*, *35*(8), 870. doi: 10.1037/hea0000346.

Elliot, A.J. The Hierarchical Model of Approach-Avoidance Motivation. *Motiv Emot* **30**, 111–116 (2006). https://doi.org/10.1007/s11031-006-9028-7

Enter, D., Spinhoven, P., & Roelofs, K. (2016). Dare to approach: Single dose testosterone administration promotes threat approach in patients with social anxiety disorder. *Clinical Psychological Science*, *4*(6), 1073-1079. DOI: 10.1177/2167702616631499

Ernst, L. H., Plichta, M. M., Dresler, T., Zesewitz, A. K., Tupak, S. V., Haeussinger, F. B., Fischer, M., Polak, T., Fallgatter, A. J., & Ehlis, A.-C. (2014). Prefrontal correlates of approach preferences for alcohol stimuli in alcohol dependence. *Addiction biology*, *19*(3), 497-508. https://doi.org/10.1111/adb.12005

Eysenck, M. W., Derakshan, N., Santos, R., & Calvo, M. G. (2007). Anxiety and cognitive performance: Attentional control theory. *Emotion*, *7*(2), 336-353.

Fein, G., & McGillivray, S. (2007). Cognitive performance in long-term abstinent elderly alcoholics. *Alcoholism: Clinical and Experimental Research*, *31*(11), 1788-1799. https://doi.org/10.1111/j.1530-0277.2007.00481.x

Field, M., Di Lemma, L., Christiansen, P., & Dickson, J. (2017). Automatic avoidance tendencies for alcohol cues predict drinking after detoxification treatment in alcohol dependence. *Psychology of Addictive Behaviors*, *31*(2), 171. doi: 10.1037/adb0000232.

Field, M., Eastwood, B., Bradley, B. P., & Mogg, K. (2006). Selective processing of cannabis cues in regular cannabis users. *Drug and alcohol dependence*, *85*(1), 75–82. doi:10.1016/j.drugalcdep.2006.03.018

Field, M., Jones, A., & Christiansen, P. (2016). Questionable classification of studies and choice of outcome measures. *PLoS One*, *11*, e0162226.

Field, M., Kiernan, A., Eastwood, B., & Child, R. (2008). Rapid approach responses to alcohol cues in heavy drinkers. *Journal of behavior therapy and experimental psychiatry*, *39*(3), 209-218. https://doi.org/10.1016/j.jbtep.2007.06.001

Field, M., Mogg, K., & Bradley, B. P. (2005). Craving and cognitive biases for alcohol cues in social drinkers. *Alcohol and alcoholism*, *40*(6), 504–510. doi:10.1093/alcalc/agh213.

Fleurkens, P., Rinck, M., & Van Minnen, A. (2014). Implicit and explicit avoidance in sexual trauma victims suffering from posttraumatic stress disorder: A pilot study. *European Journal of Psychotraumatology*, *5*(1), 21359. https://doi.org/10.3402/ejpt.v5.21359

Fleurkens, P., Van Minnen, A., Becker, E. S., Van Oostrom, I., Speckens, A., Rinck, M., & Vrijsen, J. N. (2018). Automatic approach-avoidance tendencies as a candidate intermediate phenotype for depression: Associations with childhood trauma and the 5-HTTLPR transporter polymorphism. *PLOS ONE*, *13*(3), e0193787. https://doi.org/10.1371/journal.pone.0193787

Fox, E., & Beevers, C. G. (2016). Differential sensitivity to the environment: Contribution of cognitive biases and genes to psychological wellbeing. *Molecular Psychiatry*, *21*(12), 1657-1662. https://doi.org/10.1038/mp.2016.114

Fredrick, M. M., Mintz, J., Roberts, D. L., Maples, N. J., Sarkar, S., Li, X., & Velligan, D. I. (2015). Is cognitive adaptation training (CAT) compensatory, restorative, or both? Schizophrenia Research, 166(1–3), 290–296. https://doi.org/10.1016/j.schres.2015.06.003

Frijda, N. H. (1986). *The emotions*. Cambridge University Press. Garrison, K. E., & Schmeichel, B. J. (2022). Getting over it: Working memory

Garrison, K. E., & Schmeichel, B. J. (2022). Getting over it: Working memorycapacity and affective responses to stressful events in daily life. *Emotion, 22(*3),

418–429. https://doi.org/10.1037/emo0000755

Gast, A. (2018). A declarative memory model of evaluative conditioning. *Social Psychological Bulletin*, *13*(3), 1-23. https://doi.org/10.5964/spb.v13i3.28590

Ghilardi, M. F., Moisello, C., Silvestri, G., Ghez, C., & Krakauer, J. W. (2009). Learning of a sequential motor skill comprises explicit and implicit components that consolidate differently. *Journal of neurophysiology*, *101*(5), 2218-2229. doi:10.1152/jn.01138.2007

Goldstein, H., & Goldstein, H. (2003). *Multilevel statistical models* (3. ed). Arnold [u.a.].

Grafton, B., MacLeod, C., Rudaizky, D., Holmes, E. A., Salemink, E., Fox, E., & Notebaert, L. (2017). Confusing procedures with process when appraising the impact of cognitive bias modification on emotional vulnerability†. *The British Journal of Psychiatry: The Journal of Mental Science*, *211*(5), 266-271. https://doi.org/10.1192/bjp.bp.115.176123

Grant, P. M., & Beck, A. T. (2009). Defeatist beliefs as a mediator of cognitive impairment, negative symptoms, and functioning in schizophrenia. *Schizophrenia Bulletin, 35*(4), 798–806. https://doi.org/10.1093/schbul/sbn008

Green, M. F., & Harvey, P. D. (2014). Cognition in schizophrenia: Past, present, and future. *Schizophrenia Research: Cognition*, *1*(1), e1-e9. https://doi.org/10.1016/j.scog.2014.02.001

Greenglass, E. (2002). Proactive coping. In E. Frydenberg (Ed.), *Beyond coping: Meeting goals, vision, and challenges* (pp. 37–62). Oxford University Press.

https://doi.org/10.1093/med:psych/9780198508144.003.0003

Greenglass, E. R., & Fiksenbaum, L. (2009). Proactive coping, positive affect, and well-being. *European Psychologist, 14*(1), 29–39. https://doi.org/10.1027/1016-9040.14.1.29

Grenard, J. L., Ames, S. L., Wiers, R. W., Thush, C., Sussman, S., & Stacy, A. W. (2008). Working memory capacity moderates the predictive effects of drug-related associations on substance use. *Psychology of addictive behaviors*, *22*(3), 426. doi:10.1037/0893-164X.22.3.426.

Guilmette, T. J., Sweet, J. J., Hebben, N., Koltai, D., Mahone, E. M., Spiegler, B. J., Stucky, K., Westerveld, M., & Conference Participants. (2020). American Academy of Clinical Neuropsychology consensus conference statement on uniform labeling of performance test scores. *The Clinical Neuropsychologist*, *34*(3), 437-453. https://doi.org/10.1080/13854046.2020.1722244

Hafkenscheid, A., Duncan, B. L., & Miller, S. D. (2010). The Outcome and Session Rating Scales: A cross-cultural examination of the psychometric properties of the Dutch translation. *Journal of Brief Therapy, 7*(1 & 2). https://api.semanticscholar.org/CorpusID:31950167

Hagger, M. S., Wood, C., Stiff, C., & Chatzisarantis, N. L. (2010). Ego depletion and the strength model of self-control: A meta-analysis. *Psychological bulletin*, *136*(4), 495. doi:10.1037/a0019486

Hallion, L. S., Hsu, K. J., & Schleider, J. L. (2024). Cognitive training for mental health problems. *Nature Mental Health*, *2*(1), 17-24. https://doi.org/10.31234/osf.io/w2dpk

Hammes, J. (1971). *De stroop kleur-woord test: Handleiding*. Swets & Zeitlinger.

Harvey, P. D., McGurk, S. R., Mahncke, H., & Wykes, T. (2018). Controversies in computerized cognitive training. *Biological Psychiatry: Cognitive Neuroscience and Neuroimaging*, *3*(11), 907-915. https://doi.org/10.1016/j.bpsc.2018.06.008

Hayes, S. M., Fortier, C. B., Levine, A., Milberg, W. P., & McGlinchey, R. (2012b). Implicit memory in Korsakoff's syndrome: A review of procedural learning and priming studies. *Neuropsychology review*, *22*(2), 132-153. https://doi.org/10.1007/s11065-012-9204-3

Heuer, K., Rinck, M., & Becker, E. S. (2007). Avoidance of emotional facial expressions in social anxiety: The approach-avoidance task. *Behaviour research and therapy*, *45*(12), 2990-3001. https://doi.org/10.1016/j.brat.2007.08.010

Hofmann, W., Gschwendner, T., Friese, M., Wiers, R. W., & Schmitt, M. (2008). Working memory capacity and self-regulatory behavior: Toward an individual differences perspective on behavior determination by automatic versus controlled processes. *Journal of personality and social psychology*, *95*(4), 962-977. doi:10.1037/a0012705

Hofmann, W., Schmeichel, B. J., & Baddeley, A. D. (2012). Executive functions and self-regulation. *Trends in Cognitive Sciences, 16*(3), 174–180. https://doi.org/10.1016/j.tics.2012.01.006

Horley, K., Williams, L. M., Gonsalvez, C., & Gordon, E. (2004a). Face to face: Visual scanpath evidence for abnormal processing of facial expressions in social phobia. *Psychiatry Research, 127*(1), 43-53. https://doi.org/10.1016/j.psychres.2004.02.016

Horley, K., Williams, L. M., Gonsalvez, C., & Gordon, E. (2004b). Face to face: Visual scanpath evidence for abnormal processing of facial expressions in social phobia. *Psychiatry research, 127*(1-2), 43-53. https://doi.org/10.1016/j.psychres.2004.02.016

Houben, K., Havermans, R. C., Nederkoorn, C., & Jansen, A. (2012). Beer à No-Go: Learning to stop responding to alcohol cues reduces alcohol intake via reduced affective associations rather than increased response inhibition. *Addiction, 107*(7), 1280-1287. https://doi.org/10.1111/j.1360-0443.2012.03827.

Houben, K., & Wiers, R. W. (2009). Response inhibition moderates the relationship between implicit associations and drinking behavior. *Alcoholism: Clinical and Experimental Research, 33*(4), 626-633. https://doi.org/10.1111/j.1530-0277.2008.00877.

Hox, J., & McNeish, D. (2020). Small samples in multilevel modelling. *Small Sample Size Solutions*, 215-225.

Hurt, C. S., Landau, S., Burn, D. J., Hindle, J. V., Samuel, M., Wilson, K., & Brown, R. G. (2012). Cognition, coping, and outcome in Parkinson's disease. International Psychogeriatrics, 24(10), 1656–1663. https://doi.org/10.1017/s1041610212000749

Ingram, R. E., & Luxton, D. D. (2005). *Vulnerability-Stress Models*. https://doi.org/10.4135/9781452231655.n2

Jacobus, J., Taylor, C. T., Gray, K. M., Meredith, L. R., Porter, A. M., Li, I., Castro, N., & Squeglia, L. M. (2018). A multi-site proof-of-concept investigation of computerized approach-avoidance training in adolescent cannabis users. *Drug and Alcohol Dependence, 187*, 195-204. doi:10.1016/j.drugalcdep.2018.03.007.

Jones, E. B., & Sharpe, L. (2017). Cognitive bias modification: A review of meta-analyses. *Journal of affective disorders, 223*, 175-183. https://doi.org/10.1016/j.jad.2017.07.034

Kakoschke, N., Kemps, E., & Tiggemann, M. (2017a). Approach bias modification training and consumption: A review of the literature. *Addictive behaviors, 64*, 21-28. DOI: 10.1016/j.addbeh.2016.08.007

Kakoschke, N., Kemps, E., & Tiggemann, M. (2017b). What is the appropriate control condition for approach bias modification? A response to commentary by Becker et al. (2017). *Addictive Behaviors, [Epub ahead of print]*. https://doi.org/10.1016/j.addbeh.2017.02.024 disease. International Psychogeriatrics, 24(10), 1656–1663. https://doi.org/10.1017/s1041610212000749

Kaser, M., Zaman, R., & Sahakian, B. J. (2017). Cognition as a treatment target in depression. *Psychological Medicine, 47*(6), 987–989. https://doi.org/10.1017/s0033291716003123

Keisler, A., & Shadmehr, R. (2010a). A Shared Resource between Declarative Memory and Motor Memory. *The Journal of Neuroscience, 30*(44), 14817-14823. https://doi.org/10.1523/JNEUROSCI.4160-10.2010

Kersbergen, I., Woud, M. L., & Field, M. (2015). The validity of different measures of automatic alcohol action tendencies. *Psychology of Addictive Behaviors, 29*(1), 225. http://dx.doi.org/10.1037/adb0000009

Keshavan, M. S., Vinogradov, S., Rumsey, J., Sherrill, J., & Wagner, A. (2014). Cognitive training in mental disorders: Update and future directions. *American Journal of Psychiatry, 171*(5), 510-522. https://doi.org/10.1176/appi.ajp.2013.13081075

Kessels, R. P. C., Bucks, R. S., Willison, J. R., & Byrne, L. M. T. (2012). *Location learning Test- Herziene Uitgave* (Herziene uitgave). Hogrefe Uitgevers.

Kessels, R. P. C., Nys, G. M. S., Brands, A. M. A., van den Berg, E., & Van Zandvoort, M. J. E. (2006). The modified Location Learning Test: Norms for the assessment of spatial memory function in neuropsychological patients. *Archives of Clinical Neuropsychology: The Official Journal of the National Academy of Neuropsychologists, 21*(8), 841-846. https://doi.org/10.1016/j.acn.2006.06.015

Kessels, R. P., & Haan, E. H. (2003). Implicit learning in memory rehabilitation: A meta-analysis on errorless learning and vanishing cues methods. *Journal of clinical and experimental neuropsychology, 25*(6), 805-814. https://doi.org/10.1076/jcen.25.6.805.16474

Kessels, R. P., & Kopelman, M. D. (2012). Context memory in Korsakoff's syndrome. *Neuropsychology Review, 22*(2), 117-131. DOI 10.1007/s11065-012-9202-5

Khan, S., & Petróczi, A. (2015). Stimulus-response compatibility tests of implicit preference for food and body image to identify people at risk for disordered eating: A validation study. *Eating behaviors, 16*, 54-63. https://doi.org/10.1016/j.eatbeh.2014.10.015

Kim, E. J., Bahk, Y.-C., Oh, H., Lee, W.-H., Lee, J.-S., & Choi, K.-H. (2018). Current Status of Cognitive Remediation for Psychiatric Disorders: A Review. *Frontiers in Psychiatry*, *9*, 461. https://doi.org/10.3389/fpsyt.2018.00461

Kitchen, H., Rofail, D., Heron, L., & Sacco, P. (2012). Cognitive impairment associated with schizophrenia: A review of the humanistic burden. *Advances in Therapy, 29*(2), 148–162. https://doi.org/10.1007/s12325-012-0001-4

Kobeleva, X., Seidel, E.-M., Kohler, C., Schneider, F., Habel, U., & Derntl, B. (2014). Dissociation of explicit and implicit measures of the behavioral inhibition and activation system in borderline personality disorder. *Psychiatry research*, *218*(1-2), 134-142. http://dx.doi.org/10.1016/j.psychres.2014.04.027.

Kong, G., Larsen, H., Cavallo, D. A., Becker, D., Cousijn, J., Salemink, E., Collot D'Escury-Koenigs, A. L., Morean, M. E., Wiers, R. W., & Krishnan-Sarin, S. (2015). Re-training automatic action tendencies to approach cigarettes among adolescent smokers: A pilot study. *The American journal of drug and alcohol abuse*, *41*(5), 425-432. https://doi.org/10.3109/00952990.2015.1049492

Kopelman, M. D. (1995). The Korsakoff Syndrome. *British Journal of Psychiatry*, *166*(2), 154–173. doi:10.1192/bjp.166.2.154

Kopelman, M. D., Thomson, A. D., Guerrini, I., & Marshall, E. J. (2009a). The Korsakoff syndrome: Clinical aspects, psychology and treatment. *Alcohol & Alcoholism*, *44*(2), 148-154. https://doi.org/10.1093/alcalc/agn118

Kopelman, M. D., Thomson, A. D., Guerrini, I., & Marshall, E. J. (2009b). The Korsakoff syndrome: Clinical aspects, psychology and treatment. *Alcohol and Alcoholism (Oxford, Oxfordshire)*, *44*(2), 148-154. https://doi.org/10.1093/alcalc/agn118

Koster, E. H., & Bernstein, A. (2015). Introduction to the special issue on cognitive bias modification: Taking a step back to move forward? *Journal of behavior therapy and experimental psychiatry, 49*, 1-4. https://doi.org/10.1016/j.jbtep.2015.05.006

Koster, E. H. W., Fox, E., & MacLeod, C. (2009). Introduction to the special section on cognitive bias modification in emotional disorders. *Journal of Abnormal Psychology, 118*(1), 1-4. https://doi.org/10.1037/a0014379

Krieglmeyer, R., & Deutsch, R. (2010). Comparing measures of approach–avoidance behaviour: The manikin task vs. Two versions of the joystick task. *Cognition and emotion*, *24*(5), 810-828. https://doi.org/10.1080/02699930903047298

Kwako, L. E., Momenan, R., Litten, R. Z., Koob, G. F., & Goldman, D. (2016). Addictions neuroclinical assessment: A neuroscience-based framework for addictive disorders. *Biological psychiatry*, *80*(3), 179-189. doi:10.1016/j.biopsych.2015.10.024

Lang, P. J. (1995). The emotion probe: Studies of motivation and attention. *American psychologist*, *50*(5), 372-385. https://psycnet.apa.org/doi/10.1037/0003-066X.50.5.372

Lang, P. J., Bradley, M. M., & Cuthbert, B. N. (1990). Emotion, attention, and the startle reflex. *Psychological review*, *97*(3), 377.

Lange, W.-G., Keijsers, G., Becker, E. S., & Rinck, M. (2008b). Social anxiety and evaluation of social crowds: Explicit and implicit measures. *Behaviour research and therapy*, *46*(8), 932-943. doi:10.1016/j.brat.2008.04.008

Lavigne, K. M., Deng, J., Raucher-Chéné, D., Hotte-Meunier, A., Voyer, C., Sarraf, L., Lepage, M., & Sauvé, G. (2024). Transdiagnostic cognitive biases in psychiatric disorders: A systematic review and network meta-analysis. *Progress in Neuro-Psychopharmacology & Biological Psychiatry*, *129*, 110894. https://doi.org/10.1016/j.pnpbp.2023.110894

Le Berre, A. P., Fama, R., & Sullivan, E. V. (2017). Executive functions, memory, and social cognitive deficits and recovery in chronic alcoholism: A critical review to inform future research. *Alcoholism: Clinical and Experimental Research*, *41*(8), 1432-1443. . doi:10.1111/acer.13431.

Lee, R. S. C., Redoblado-Hodge, M. A., Naismith, S. L., Hermens, D. F., Porter, M. A., & Hickie, I. B. (2013). Cognitive remediation improves memory and psychosocial functioning in first-episode psychiatric outpatients. *Psychological Medicine, 43*(6), 1161–1173. https://doi.org/10.1017/s0033291712002127

Leins, J., Waldorf, M., Kollei, I., Rinck, M., & Steins-Loeber, S. (2018). Approach and avoidance: Relations with the thin body ideal in women with disordered eating behavior. *Psychiatry Research*, *269*, 286-292. https://doi.org/10.1016/j.psychres.2018.08.029

Lejeune, J. A., Northrop, A., & Kurtz, M. M. (2021). A meta-analysis of cognitive remediation for schizophrenia: Efficacy and the role of participant and treatment factors. *Schizophrenia Bulletin*, *47*(4), 997-1006. https://doi.org/10.1016/j.psychres.2018.08.029

Lender, A., Meule, A., Rinck, M., Brockmeyer, T., & Blechert, J. (2018). Measurement of food-related approach–avoidance biases: Larger biases when food stimuli are task relevant. *Appetite*, *125*, 42-47. https://doi.org/10.1016/j.appet.2018.01.032

Levine, B., Robertson, I. H., Clare, L., Carter, G., Hong, J., Wilson, B. A., Duncan, J., & Stuss, D. T. (2000). Rehabilitation of executive functioning: An experimental-clinical validation of goal management training. *Journal of the International Neuropsychological Society, 6*(3), 299–312. https://doi.org/10.1017/s1355617700633052

Lezak, M. D. (2004). *Neuropsychological assessment*. Oxford University Press, USA.

Lindgren, K. P., Wiers, R. W., Teachman, B. A., Gasser, M. L., Westgate, E. C., Cousijn, J., Enkema, M. C., & Neighbors, C. (2015). Attempted training of alcohol approach and drinking identity associations in US undergraduate drinkers: Null results from two studies. *PloS one*, *10*(8), e0134642. doi:10.1371/journal.pone.0134642

Lohoff, F. W. (2022). Targeting unmet clinical needs in the treatment of alcohol use disorder. *Frontiers in psychiatry*, *13*, 767506. https://doi.org/10.3389/fpsyt.2022.767506

Loijen, A., Rinck, M., Walvoort, S. J., Kessels, R. P., Becker, E. S., & Egger, J. I. (2018). Modification of automatic alcohol-approach tendencies in alcohol-dependent patients with mild or major neurocognitive disorder. *Alcoholism: Clinical and Experimental Research*, *42*(1), 153-161. https://doi.org/10.1111/acer.13529

Loijen, A., Vrijsen, J. N., Egger, J. I. M., Becker, E. S., & Rinck, M. (2020). Biased approach-avoidance tendencies in psychopathology: A systematic review of their assessment and modification. *Clinical Psychology Review*, *77*, 101825. https://doi.org/10.1016/j.cpr.2020.101825

Maas, J., Keijsers, G. P., Rinck, M., & Becker, E. S. (2018a). Approach-avoidance, attentional and evaluation biases in hair pulling disorder and their relationship with symptom severity. *Journal of Cognitive Psychology*, *30*(7), 743-753.

Maas, J., Keijsers, G. P., Rinck, M., & Becker, E. S. (2018b). Does cognitive bias modification prior to standard brief cognitive behavior therapy reduce relapse rates in hair pulling disorder? A double-blind randomized controlled trial. *Journal of Social and Clinical Psychology*, *37*(6), 453-479. https://doi.org/10.1080/20445911.2018.1503278

MacAulay, R., & Cohen, A. S. (2013). Affecting coping: Does neurocognition predict approach and avoidant coping strategies within schizophrenia spectrum disorders? *Psychiatry Research, 209*(2), 136–141. https://doi.org/10.1016/j.psychres.2013.04.004

Machulska, A., Zlomuzica, A., Adolph, D., Rinck, M., & Margraf, J. (2015). "A cigarette a day keeps the goodies away": Smokers show automatic approach tendencies for smoking—But not for food-related stimuli. *PloS one*, *10*(2), e0116464. doi:10.1371/journal.pone.0116464

Machulska, A., Zlomuzica, A., Rinck, M., Assion, H.-J., & Margraf, J. (2016). Approach bias modification in inpatient psychiatric smokers. *Journal of psychiatric research*, *76*, 44-51. https://doi.org/10.1016/j.jpsychires.2015.11.015

MacLeod, C., Koster, E. H., & Fox, E. (2009). Whither cognitive bias modification research? Commentary on the special section articles. *Journal of abnormal psychology*, *118*(1), 89-99. DOI: 10.1037/a0014878.

MacLeod, C. M. (1991). Half a century of research on the Stroop effect: An integrative review. *Psychological bulletin*, *109*(2), 163.

Maillard, A., Cabé, N., Viader, F., & Pitel, A. L. (2020). Neuropsychological deficits in alcohol use disorder: Impact on treatment. In A. Verdejo-Garcia (Red.), *Cognition and addiction: A researcher's guide from mechanisms towards interventions*. AP, Academic Press, an imprint of Elsevier.

Mann, K., Hoch, E., Batra, A., Bonnet, U., Günthner, A., Reymann, G., Soyka, M., Wodarz, N., & Schäfer, M. (2016). Leitlinienorientierte Behandlung alkoholbezogener Störungen. *Der Nervenarzt*, *87*(1), 13-25. DOI 10.1007/s00115-015-0022-8

Manning, V., Garfield, J. B. B., Reynolds, J., Staiger, P. K., Piercy, H., Bonomo, Y., Lloyd-Jones, M., Jacka, D., Wiers, R. W., Verdejo-Garcia, A., & Lubman, D. I. (2022). Alcohol use in the year following approach

bias modification during inpatient withdrawal: Secondary outcomes from a double-blind, multi-site randomized controlled trial. *Addiction (Abingdon, England)*, *117*(11), 2837-2846. https://doi.org/10.1111/add.15989

Manning, V., Staiger, P. K., Hall, K., Garfield, J. B., Flaks, G., Leung, D., Hughes, L. K., Lum, J. A., Lubman, D. I., & Verdejo-Garcia, A. (2016). Cognitive bias modification training during inpatient alcohol detoxification reduces early relapse: A randomized controlled trial. *Alcoholism: Clinical and Experimental Research*, *40*(9), 2011-2019. https://doi.org/10.1111/acer.13163

Marceau, E. M., Lunn, J., Berry, J., Kelly, P. J., & Solowij, N. (2016). The Montreal Cognitive Assessment (MoCA) is sensitive to head injury and cognitive impairment in a residential alcohol and other drug therapeutic community. *Journal of substance abuse treatment*, *66*, 30-36.

Maresch, J., Werner, S., & Donchin, O. (2021). Methods matter: Your measures of explicit and implicit processes in visuomotor adaptation affect your results. *The European Journal of Neuroscience*, *53*(2), 504-518. https://doi.org/10.1111/ejn.14945

Marteau, T. M., Hollands, G. J., & Fletcher, P. C. (2012). Changing human behavior to prevent disease: The importance of targeting automatic processes. *Science (New York, N.Y.)*, *337*(6101), 1492-1495. https://doi.org/10.1126/science.1226918

Martin Braunstein, L., Kuerbis, A., Ochsner, K., & Morgenstern, J. (2016). Implicit alcohol approach and avoidance tendencies predict future drinking in problem drinkers. *Alcoholism: clinical and experimental research*, *40*(9), 1945-1952. doi:10.1111/acer.13151

Martínez-Arán, A., Torrent, C., Solé, B., Bonnín, C. M., Rosa, A. R., Sánchez-Moreno, J., & Vieta, E. (2011). Functional remediation for bipolar disorder. *Clinical Practice and Epidemiology in Mental Health: CP& EMH*, *7*, 112–116. http://dx.doi.org/10.2174/1745017901107010112

Martínez-Arán, A., Vieta, E., Reinares, M., Colom, F., Torrent, C., Sánchez-Moreno, J., Benabarre, A., Goikolea, J. M., Comes, M., & Salamero, M. (2004). Cognitive function across manic or hypomanic, depressed, and euthymic states in bipolar disorder. *The American Journal of Psychiatry*, *161*(2), 262–270. https://doi.org/10.1176/appi.ajp.161.2.262

Martínez-Maldonado, A., Jurado-Barba, R., Sion, A., Domínguez-Centeno, I., Castillo-Parra, G., Prieto-Montalvo, J., & Rubio, G. (2020). Brain functional connectivity after cognitive-bias modification and behavioral changes in abstinent alcohol-use disorder patients. *International Journal of Psychophysiology*, *154*, 46-58. https://doi.org/10.1016/j.ijpsycho.2019.10.004

Martínez-Maldonado, A., Rubio, G., Sion, A., Domínguez-Centeno, I., & Jurado-Barba, R. (2020). Stop! - The automatic tendency of action, inhibition and frontal activation in individuals with alcohol-use disorder in abstinence. *International Journal of Psychophysiology: Official Journal of the International Organization of Psychophysiology*, *158*, 123-135. https://doi.org/10.1016/j.ijpsycho.2020.08.013

Martino, D. J., Strejilevich, S. A., Scápola, M., Igoa, A., Marengo, E., Ais, E. D., & Perinot, L. (2008). Heterogeneity in cognitive functioning among patients with bipolar disorder. *Journal of Affective Disorders*, *109*(1–2), 149–156. https://doi.org/10.1016/j.jad.2007.12.232

Matthews, G., & Campbell, S. E. (2010). Dynamic relationships between stress states and working memory. *Cognition and Emotion*, *24*(2), 357–373. https://doi.org/10.1080/02699930903378719

Mathews, A., & MacLeod, C. (2005). Cognitive vulnerability to emotional disorders. *Annual Review of Clinical Psychology*, *1*, 167-195. https://doi.org/10.1146/annurev.clinpsy.1.102803.143916

Maurage, P., Rolland, B., Pitel, A.-L., & D'Hondt, F. (2024). Five Challenges in Implementing Cognitive Remediation for Patients with Substance Use Disorders in Clinical Settings. *Neuropsychology Review*, *34*(3), 974-984. https://doi.org/10.1007/s11065-023-09623-1

McIntyre, R. S., Cha, D. S., Soczynska, J. K., Woldeyohannes, H. O., Gallaugher, L. A., Kudlow, P., Alsuwaidan, M., & Baskaran, A. (2013). Cognitive deficits and functional outcomes in major depressive disorder: Determinants, substrates, and treatment interventions. *Depression and Anxiety*, *30*(6), 515–527. https://doi.org/10.1002/da.22063

Melugin, P. R., Nolan, S. O., & Siciliano, C. A. (2021). Bidirectional causality between addiction and cognitive deficits. *International review of neurobiology*, *157*, 371-407. . doi:10.1016/bs.irn.2020.11.001.

Metcalfe, J., & Mischel, W. (1999). A hot/cool-system analysis of delay of gratification: Dynamics of willpower. *Psychological review*, *106*(1), 3-19.

Miskowiak, K. W., Burdick, K. E., Martínez-Arán, A., Bonnin, C. M., Bowie, C. R., Carvalho, A. F., Gallagher, P., Lafer, B., López-Jaramillo, C., Sumiyoshi, T., McIntyre, R. S., Schaffer, A., Porter, R. J., Purdon, S., Torres, I. J., Yatham, L. N., Young, A. H., Kessing, L. V., & Vieta, E.
(2018). Assessing and addressing cognitive impairment in bipolar disorder: The international society for bipolar disorders targeting cognition task force recommendations for clinicians. *Bipolar Disorders, 20*(3), 184–194. https://doi.org/10.1111/bdi.12595

Mitchell, J. M., Arcuni, P. A., Weinstein, D., & Woolley, J. D. (2016). Intranasal oxytocin selectively modulates social perception, craving, and approach behavior in subjects with alcohol use disorder. *Journal of addiction medicine*, *10*(3), 182-189. DOI: 10.1097/ADM.0000000000000213

Miyake, A., Friedman, N. P., Emerson, M. J., Witzki, A. H., Howerter, A., & Wager, T. D. (2000). The unity and diversity of executive functions and their contributions to complex "frontal lobe" tasks: A latent variable analysis. *Cognitive psychology*, *41*(1), 49-100. https://doi.org/10.1006/cogp.1999.0734

Mladenovic, I., & Perunicic-Mladenovic, I. (2025). Clinical and background risk factors affecting dropouts from alcohol use disorder treatment: A 25-year retrospective study. *International Journal of Mental Health and Addiction*, *23*(3), 1775-1787. https://doi.org/10.1007/s11469-023-01196-7

Mogg, K., Bradley, B. P., Field, M., & De Houwer, J. (2003). Eye movements to smoking-related pictures in smokers: Relationship between attentional biases and implicit and explicit measures of stimulus valence. *Addiction*, *98*(6), 825-836. https://doi.org/10.1046/j.1360-0443.2003.00392.

Mogg, K., Field, M., & Bradley, B. P. (2005). Attentional and approach biases for smoking cues in smokers: An investigation of competing theoretical views of addiction. *Psychopharmacology*, *180*(2), 333-341. https://doi.org/10.1007/s00213-005-2158-x

Moher, D., Liberati, A., Tetzlaff, J., Altman, D. G., & PRISMA Group. (2009). Preferred reporting items for systematic reviews and meta-analyses: The PRISMA statement. *PLoS Medicine*, *6*(7), e1000097. https://doi.org/10.1371/journal.pmed.1000097

Morris, M. C., Evans, L. D., Rao, U.,&Garber, J. (2015). Executive function moderates the relation between coping and depressive symptoms. *Anxiety, Stress, and Coping*, *28*(1), 31–49. https://doi.org/10.1080/10615806.2014

Moselhy, H. F., Georgiou, G., & Kahn, A. (2001). Frontal lobe changes in alcoholism: A review of the literature. *Alcohol and alcoholism*, *36*(5), 357-368. https://doi.org/10.1093/alcalc/36.5.357

Motter, J. N., Pimontel, M. A., Rindskopf, D., Devanand, D. P., Doraiswamy, P. M., & Sneed, J. R. (2016). Computerized cognitive training and functional recovery in major depressive disorder: A meta-analysis. *Journal of affective disorders*, *189*, 184-191. https://doi.org/10.1016/j.jad.2015.09.022

Mulder, J. L., Dekker, M. J. A., & Dekker, P. H. (1996). *Verbale leer en geheugen test [Dutch Version of California Verbal Learning Test]*. Swets Test Services (STS).

Muller, A. M., Manning, V., Wong, C. Y., & Pennington, D. L. (2024). The neural correlates of alcohol approach bias–New insights from a whole-brain network analysis perspective. medRxiv. https://doi.org/10.1101/2024.09.26.24314399

Musfeld, P., Souza, A. S., & Oberauer, K. (2023). Repetition learning is neither a continuous nor an implicit process. *Proceedings of the National Academy of Sciences*, *120*(16), e2218042120. https://doi.org/10.1073/pnas.2218042120

Najmi, S., Kuckertz, J. M., & Amir, N. (2010). Automatic avoidance tendencies in individuals with contamination-related obsessive-compulsive symptoms. *Behaviour research and therapy*, *48*(10), 1058-1062. https://doi.org/10.1016/j.brat.2010.06.007

Nardo, T., Batchelor, J., Berry, J., Francis, H., Jafar, D., & Borchard, T. (2022). Cognitive remediation as an adjunct treatment for substance use disorders: A systematic review. *Neuropsychology Review*, *32*(1), 161-191. https://doi.org/10.1007/s11065-021-09506-3

Nardo, T., Berry, J., Barker, D., Assareh, H., Lunn, J., Sedwell, A., Batchelor, J., Shakeshaft, A., Kelly, P. J., Sarrami, P., Russell, S., & James, M. (2024). Cognitive remediation in residential substance use treatment: A randomized stepped-wedge trial. *Neuropsychological Rehabilitation*, *34*(10), 1378-1403. https://doi.org/10.1080/09602011.2024.2314879

Neimeijer, R. A., de Jong, P. J., & Roefs, A. (2015). Automatic approach/avoidance tendencies towards food and the course of anorexia nervosa. *Appetite*, *91*, 28-34. https://doi.org/10.1016/j.appet.2015.03.018

Nieto, M., Romero, D., Ros, L., Zabala, C., Martínez, M., Ricarte, J. J., Serrano, J. P., & Latorre, J. M. (2020). Differences in coping strategies between young and older adults: The role of executive functions. *International Journal of Aging & Human Development, 90*(1), 28–49. https://doi.org/10.1177/0091415018822040

Noël, X., Sferrazza, R., Der Linden, M., Paternot, J., Verhas, M., Hanak, C., Pelc, I., & Verbanck, P. (2002). Contribution of frontal cerebral blood flow measured by (99m)Tc-Bicisate spect and executive function deficits to predicting treatment outcome in alcohol-dependent patients. *Oxfordshire), 37*(4), 347-354. https://doi.org/10.1093/alcalc/37.4.347

Noël, X., Sferrazza, R., Van der Linden, M., Paternot, J., Verhas, M., Hanak, C., Pelc, I., & Verbanck, P. (2002). Contribution of frontal cerebral blood flow measured by 99mTc-Bicisate SPECT and executive function deficits to predicting treatment outcome in alcohol-dependent patients. *Alcohol and alcoholism*, *37*(4), 347-354. https://doi.org/10.1093/alcalc/37.4.347

Ochsner, K. N., & Gross, J. J. (2005). The cognitive control of emotion. *Trends in cognitive sciences*, *9*(5), 242-249. https://doi.org/10.1016/j.tics.2005.03.010

Ochsner, K. N., Silvers, J. A., & Buhle, J. T. (2012). Functional imaging studies of emotion regulation: A synthetic review and evolving model of the cognitive control of emotion. *Annals of the New York Academy of Sciences*, *1251*(1). https://doi.org/10.1111/j.1749-6632.2012.06751.x

O'Keeffe, J., Conway, R., & McGuire, B. (2017). A systematic review examining factors predicting favourable outcome in cognitive behavioural interventions for psychosis. *Schizophrenia Research*, *183*, 22-30. https://doi.org/10.1016/j.schres.2016.11.021

Oscar-Berman, M. (2007). Alcohol: Effects on Neurobehavioral Functions and the Brain. *Neuropsychology Review*, *17*(3), 239-257. https://doi.org/10.1007/s11065-007-9038-6

Oudman, E., Nijboer, T. C. W., Postma, A., Wijnia, J. W., & Van Der Stigchel, S. (2015). Procedural Learning and Memory Rehabilitation in Korsakoff's Syndrome—A Review of the Literature. *Neuropsychology Review*, *25*(2), 134-148. https://doi.org/10.1007/s11065-015-9288-7

Oudman, E., Van der Stigchel, S., Wester, A. J., Kessels, R. P., & Postma, A. (2011). Intact memory for implicit contextual information in Korsakoff's amnesia. *Neuropsychologia*, *49*(10), 2848-2855. https://doi.org/10.1016/j.neuropsychologia.2011.06.010

Ouimet, A. J., Gawronski, B., & Dozois, D. J. (2009). Cognitive vulnerability to anxiety: A review and an integrative model. *Clinical psychology review*, *29*(6), 459-470. https://doi.org/10.1016/j.cpr.2009.05.004

Paans, N. P. G., Dols, A., Comijs, H. C., Stek, M. L.,& Schouws, S. N. T. M.(2018). Associations between cognitive functioning, mood symptoms and coping styles in older age bipolar disorder. *Journal of Affective Disorders, 235*, 357–361. https://doi.org/10.1016/j.jad.2018.04.052

Papakostas, G. I. (2014). Cognitive symptoms in patients with major depressive disorder and their implications for clinical practice. *The Journal of Clinical Psychiatry, 75*(1), 8–14. https://doi.org/10.4088/jcp.13r08710

Parsons, S., Kruijt, A.-W., & Fox, E. (2016). A cognitive model of psychological resilience. *Journal of Experimental Psychopathology*, *7*(3), 296-310. https://doi.org/10.5127/jep.053415

Paslakis, G., Kühn, S., Grunert, S., & Erim, Y. (2017). Explicit and implicit approach vs. Avoidance tendencies towards high vs. Low calorie food cues in patients with obesity and active binge eating disorder. *Nutrients*, *9*(10), 1068. https://doi.org/10.3390/nu9101068

Paslakis, G., Kühn, S., Schaubschläger, A., Schieber, K., Röder, K., Rauh, E., & Erim, Y. (2016). Explicit and implicit approach vs. Avoidance tendencies towards high vs. Low calorie food cues in patients with anorexia nervosa and healthy controls. *Appetite*, *107*, 171-179. https://doi.org/10.1016/j.appet.2016.08.001

Peeters, M., Wiers, R. W., Monshouwer, K., van de Schoot, R., Janssen, T., & Vollebergh, W. A. (2012). Automatic processes in at-risk adolescents: The role of alcohol-approach tendencies and response inhibitionindrinkingbehavior.*Addiction*,*107*(11),1939-1946.https://doi.org/10.1111/j.1360-0443.2012.03948.x

Penadés, R., González-Rodríguez, A., Catalán, R., Segura, B., Bernardo, M., & Junqué, C. (2017). Neuroimaging studies of cognitive remediation in schizophrenia: A systematic and critical review. *World Journal of Psychiatry*, *7*(1), 34-43. https://doi.org/10.5498/wjp.v7.i1.34

Penadés, R., Pujol, N., Catalán, R., Massana, G., Rametti, G., García-Rizo, C., Bargalló, N., Gastó, C., Bernardo, M., & Junqué, C. (2013). Brain effects of cognitive remediation therapy in schizophrenia: A structural and functional neuroimaging study. *Biological Psychiatry*, *73*(10), 1015-1023. https://doi.org/10.1016/j.biopsych.2013.01.017

Phaf, R. H., Mohr, S. E., Rotteveel, M., & Wicherts, J. M. (2014). Approach, avoidance, and affect: A meta-analysis of approach-avoidance tendencies in manual reaction time tasks. *Frontiers in psychology*, *5*, 378. https://doi.org/10.3389/fpsyg.2014.00378

Piccirillo, M. L., & Rodebaugh, T. L. (2019). Foundations of idiographic methods in psychology and applications for psychotherapy. *Clinical psychology review*, *71*, 90-100. https://doi.org/10.1016/j.cpr.2019.01.002

Pitel, A. L., Beaunieux, H., Witkowski, T., Vabret, F., De La Sayette, V., Viader, F., Desgranges, B., & Eustache, F. (2008). Episodic and working memory deficits in alcoholic Korsakoff patients: The continuity theory revisited. *Alcoholism: Clinical and Experimental Research*, *32*(7), 1229-1241. https://doi.org/10.1111/j.1530-0277.2008.00677.x

Ponds, R. W. H. M., van Heugten, C. M., Fasotti, L., & Wekking, E. M. (2010). *Neuropsychologische behandeling* [Neuropsychological treatment]. Boom Publishers.

Post, M. W. M., van der Zee, C. H., Hennink, J., Schafrat, C. G., Visser-Meily, J. M. A., & van Berlekom, S. B. (2012). Validity of the Utrecht scale for evaluation of rehabilitation-participation. *Disability and Rehabilitation*, *34*(6), 478–485. https://doi.org/10.3109/09638288.2011.608148

Radke, S., Güths, F., André, J. A., Müller, B. W., & de Bruijn, E. R. (2014). In action or inaction? Social approach-avoidance tendencies in major depression. *Psychiatry research*, *219*(3), 513-517. https://doi.org/10.1016/j.psychres.2014.07.011

Radke, S., Pfersmann, V., & Derntl, B. (2015). The impact of emotional faces on social motivation in schizophrenia. *European archives of psychiatry and clinical neuroscience*, *265*(7), 613-622. https://doi.org/10.1007/s00406-015-0589-x

Rasbash, J., Charlton, C., & Browne, W. (2020). MLwiN Version 2.02. 2005. *Institute of Education: London*.

Reddy, L. F., Green, M. F., Wynn, J. K., Rinck, M., & Horan, W. P. (2016). Approaching anger in schizophrenia: What an implicit task tells you that self-report does not. *Schizophrenia research*, *176*(2-3), 514-519. https://doi.org/10.1016/j.schres.2016.05.018

Reinecke, A., Soltau, C., Hoyer, J., Becker, E. S., & Rinck, M. (2012). Treatment sensitivity of implicit threat evaluation, avoidance tendency and visual working memory bias in specific phobia. *Journal of Anxiety Disorders*, *26*(2), 321-328. https://doi.org/10.1016/j.janxdis.2011.12.010

Rensen, Y. C. M., Egger, J. I. M., Westhoff, J., Walvoort, S. J. W., & Kessels, R. P. C. (2019). Errorless (re) learning of everyday activities in patients with Korsakoff's syndrome: A feasibility study. *Neuropsychological Rehabilitation*, *29*(8), 1211–1225. https://doi.org/10.1080/09602011.2017.1379419

Rensen, Y. C. M., Beaunieux, H., Eustache, F., & Pitel, A.-L. (2018). Application of errorless learning in alcohol-related cognitive disorders. In C. Haslam & R. P. C. Kessels (Red.), *Errorless Learning in Neuropsychological Rehabilitation* (1ste dr., pp. 133-147). Routledge. https://doi.org/10.4324/9781315660738-9

Rezapour, T., Hatami, J., Farhoudian, A., Sofuoglu, M., Noroozi, A., Daneshmand, R., & Ekhtiari, H. (2019). Cognitive rehabilitation for individuals with opioid use disorder: A randomized controlled trial. *Neuropsychological rehabilitation*, *29*(8), 1273-1289. https://doi.org/10.1080/09602011.2017.1391103

Rinck, M. (2017). CBM research needs more power: Commentary on the special issue on cognitive bias modification. *Journal of Behavior Therapy and Experimental Psychiatry*, *57*, 215. https://doi.org/10.1016/j.jbtep.2016.03.001

Rinck, M., & Becker, E. S. (2007). Approach and avoidance in fear of spiders. *Journal of Behavior Therapy and Experimental Psychiatry*, *38*(2), 105-120. https://doi.org/10.1016/j.jbtep.2006.10.001

Rinck, M., Telli, S., Kampmann, I. L., Woud, M. L., Kerstholt, M., Te Velthuis, S., Wittkowski, M., & Becker, E. S. (2013). Training approach-avoidance of smiling faces affects emotional vulnerability in socially anxious individuals. *Frontiers in Human Neuroscience*, *7*, 481. https://doi.org/10.3389/fnhum.2013.00481

Rinck, M., Wiers, R. W., Becker, E. S., & Lindenmeyer, J. (2018). Relapse prevention in abstinent alcoholics by cognitive bias modification: Clinical effects of combining approach bias modification and attention bias modification. *Journal of Consulting and Clinical Psychology*, *86*(12), 1005-1016. https://doi.org/10.1037/ccp0000321

Robinson, T. E., & Berridge, K. C. (2008). The incentive sensitization theory of addiction: Some current issues. *Philosophical Transactions of the Royal Society B: Biological Sciences*, *363*(1507), 3137-3146. https://doi.org/10.1098/rstb.2008.0093

Robinson T. E., & Berridge, K. C. (1993). The neural basis of drug craving: An incentive-sensitization theory of addiction. *Brain Res Brain Res Rev.*, *18*, 247-291. https://doi.org/10.1016/0165-0173(93)90013-P

Robinson, L. J., Thompson, J. M., Gallagher, P., Goswami, U., Young, A. H., Ferrier, I. N., & Moore, P. B. (2006). A meta-analysis of cognitive deficits in euthymic patients with bipolar disorder. *Journal of Affective Disorders*, *93*(1–3), 105–115. https://doi.org/10.1016/j.jad.2006.02.016

Rock, P. L., Roiser, J. P., Riedel, W. J., & Blackwell, A. D. (2014). Cognitive impairment in depression: a systematic review and meta-analysis. *Psychological Medicine*, *44*(10), 2029–2040. doi:10.1017/S0033291713002535

Roefs, A., Huijding, J., Smulders, F. T., MacLeod, C. M., de Jong, P. J., Wiers, R. W., & Jansen, A. (2011). Implicit measures of association in psychopathology research. *Psychological bulletin*, *137*(1), 149-193. https://psycnet.apa.org/doi/10.1037/a0021729

Roelofs, K., Putman, P., Schouten, S., Lange, W.-G., Volman, I., & Rinck, M. (2010). Gaze direction differentially affects avoidance tendencies to happy and angry faces in socially anxious individuals. *Behaviour research and therapy*, *48*(4), 290-294. https://doi.org/10.1016/j.brat.2009.11.008

Roelofs, K., van Peer, J., Berretty, E., de Jong, P., Spinhoven, P., & Elzinga, B. M. (2009). Hypothalamus–pituitary–adrenal axis hyperresponsiveness is associated with increased social avoidance behavior in social phobia. *Biological psychiatry*, *65*(4), 336-343. https://doi.org/10.1016/j.biopsych.2008.08.022

Russell, C., Wiese, J. L., Ruocco, A. C., Bozinoff, N., Gonzalez, R., Jennings, S., Leyton, M., Nikolova, Y. S., Orson, J., Potenza, M. N., Quilty, L. C., Shield, K. D., Verdejo-Garcia, A., Wells, S., & Lange, S. (2025). Experiences and barriers to alcohol use disorder treatment among adults with and without self-reported executive functioning challenges: A mixed-methods study. *Clinical & Evxperimental Research*, *49*(10), 2334-2348. https://doi.org/10.1111/acer.70154

Salemink, E., & Wiers, R. W. (2012). Adolescent threat-related interpretive bias and its modification: The moderating role of regulatory control. *Behaviour Research and Therapy*, *50*(1), 40-46. https://doi.org/10.1016/j.brat.2011.10.006

Sanchez-Moreno, J., Martínez-Arán, A., Tabarés-Seisdedos, R., Torrent, C., Vieta, E., & Ayuso-Mateos, J. L. (2009). Functioning and disability in bipolar disorder: An extensive review. *Psychotherapy and Psychosomatics*, *78*(5), 285–297. \https://doi.org/10.1159/000228249

Schacter, D. L., & Tulving, E. (1994). Memory systems 1994. *Memory Systems*, 341-380.

Schippers, G. M., Broekman, T. G., Buchholz, A., Koeter, M. W., & Van Den Brink, W. (2010). Measurements in the Addictions for Triage and Evaluation (MATE): An instrument based on the World Health Organization family of international classifications. *Addiction*, *105*(5), 862-871. https://doi.org/10.1111/j.1360-0443.2009.02889.x

Schoenmakers, T., Wiers, R. W., & Field, M. (2008). Effects of a low dose of alcohol on cognitive biases and craving in heavy drinkers. *Psychopharmacology*, *197*(1), 169-178. https://doi.org/10.1007/s00213-007-1023-5

Schuck, K., Keijsers, G., & Rinck, M. (2012). Implicit processes in pathological skin picking: Responses to skin irregularities predict symptom severity and treatment susceptibility. *Journal of Behavior Therapy and Experimental Psychiatry*, *43*(1), 685-691. https://doi.org/10.1016/j.jbtep.2011.09.004

Seidel, E.-M., Habel, U., Finkelmeyer, A., Schneider, F., Gur, R. C., & Derntl, B. (2010). Implicit and explicit behavioral tendencies in male and female depression. *Psychiatry research*, *177*(1-2), 124-130. https://doi.org/10.1016/j.psychres.2010.02.001

Sharbanee, J. M., Stritzke, W. G., Jamalludin, M. E., & Wiers, R. W. (2014). Approach-alcohol action tendencies can be inhibited by cognitive load. *Psychopharmacology*, *231*(5), 967-975. https://doi.org/10.1007/s00213-013-3318-z

Sharbanee, J. M., Stritzke, W. G., Wiers, R. W., Young, P., Rinck, M., & MacLeod, C. (2013). The interaction of approach-alcohol action tendencies, working memory capacity, and current task goals predicts the inability to regulate drinking behavior. *Psychology of addictive behaviors*, *27*(3), 649-661.

Sherman, B. J., Baker, N. L., Squeglia, L. M., & McRae-Clark, A. L. (2018). Approach bias modification for cannabis use disorder: A proof-of-principle study. *Journal of substance abuse treatment*, *87*, 16-22. https://doi.org/10.1016/j.jsat.2018.01.012

Shields, G. S., Sazma, M. A., & Yonelinas, A. P. (2016). The effects of acute stress on core executive functions: A meta-analysis and comparison with cortisol. *Neuroscience and Biobehavioral Reviews*, *68*, 651–668. https://doi.org/10.1016/j.neubiorev.2016.06.038

Sleuwaegen, E., Hulstijn, W., Claes, L., Houben, M., Gandhi, A., Berens, A., & Sabbe, B. (2018). Are emotional action tendencies and attentional bias related to temperament dimensions in patients with borderline personality disorder? *Psychiatry Research*, *266*, 247-252. https://doi.org/10.1016/j.psychres.2018.03.004

Smith, E. R., & Coster, J. M. (2000). *Dual-process models in social and cognitive psychology: Conceptual integration and links to underlying memory systems*. https://doi.org/10.1207/S15327957PSPR0402_01

Snelleman, M., Schoenmakers, T. M., & van de Mheen, D. (2015). Attentional bias and approach/avoidance tendencies do not predict relapse or time to relapse in alcohol dependency. *Alcoholism: Clinical and Experimental Research*, *39*(9), 1734-1739. https://doi.org/10.1111/acer.12817

Snyder, H. R., Miyake, A., & Hankin, B. L. (2015). Advancing understanding of executive function impairments and psychopathology: Bridging the gap between clinical and cognitive approaches. *Frontiers in psychology*, *6*, 328. https://doi.org/10.3389/fpsyg.2015.00328

Solarz, A. K. (1960). Latency of instrumental responses as a function of compatibility with the meaning of eliciting verbal signs. *Journal of Experimental Psychology*, *59*(4), 239-245. https://doi.org/10.1037/h0047274

Solé, B., Jiménez, E., Torrent, C., Reinares, M., Bonnin, C. D. M., Torres, I., Varo, C., Grande, I., Valls, E., Salagre, E., Sanchez-Moreno, J., Martínez-Arán, A., Carvalho, A. F., & Vieta, E. (2017). Cognitive impairment in bipolar disorder: Treatment and prevention strategies. *The International Journal of Neuropsychopharmacology*, *20*(8), 670–680. https://doi.org/10.1093/ijnp/pyx032

Solms, M., & Friston, K. (2018). How and why consciousness arises: Some considerations from physics and physiology. *Journal of Consciousness Studies*, *25*(5-6), 202-238. https://discovery.ucl.ac.uk/id/eprint/10057681

Sømhovd, M., Hagen, E., Bergly, T., & Arnevik, E. A. (2019). The Montreal Cognitive Assessment as a predictor of dropout from residential substance use disorder treatment. *Heliyon*, *5*(3). https://doi.org/10.1016/j.heliyon.2019.e01282

Sopena, S., Dewar, B. K., Greenfield, E., & Wilson, B. (2005). Implicit Memory Assessment and its Implication for Rehabilitation. Brain Impairment, 6(2), 143. https://search.informit.org/doi/10.3316/informit.977745940550291

Spear, L. P. (2018). Effects of adolescent alcohol consumption on the brain and behaviour. *Neuroscience*, *19*(4), 197-214. https://doi.org/10.1038/nrn.2018.10

Spruyt, A., De Houwer, J., Tibboel, H., Verschuere, B., Crombez, G., Verbanck, P., Hanak, C., Brevers, D., & Noël, X. (2013). On the predictive validity of automatically activated approach/avoidance tendencies in abstaining alcohol-dependent patients. *Drug and alcohol dependence*, *127*(1-3), 81-86. https://doi.org/10.1016/j.drugalcdep.2012.06.019

Spruyt, A., Laporte, W., Boffo, M., Herremans, S., Impe, P., Vercruysse, I., Verdée, T., Verhelst, M., Wiers, R. W., & De Raedt, R. (2025). On the Efficacy of Cognitive-Bias-Modification Training in Alcohol-Dependent Inpatients: A Double-Blind, Multisite Randomized Control Trial. *Clinical Psychological Science*, *0*(0). https://doi.org/10.1177/21677026251385934

Squire, L. R. (2004). Memory systems of the brain: A brief history and current perspective. *Neurobiology of Learning and Memory*, *82*(3), 171-177. https://doi.org/10.1016/j.nlm.2004.06.005

Staal, M. A. (2004). *Stress, cognition, and human performance: A literature review and conceptual framework*. National Aeronautics and Space Administration. https://ntrs.nasa.gov/citations/20060017835

Stacy, A. W., & Wiers, R. W. (2010a). Implicit cognition and addiction: A tool for explaining paradoxical behavior. *Annual review of clinical psychology*, *6*, 551-575. https://doi.org/10.1146/annurev.clinpsy.121208.131444

Stanojevíc, D., Krsti´c, M., Jaredi´c, B., & Dimitrijevi´c, B. (2014). Proactive coping as a mediator between resources and outcomes: A structural equations modeling analysis. *Applied Research in Quality of Life*, *9*(4), 871–885. https://doi.org/10.1007/s11482-013-9274-2

Stavro, K., Pelletier, J., & Potvin, S. (2013). Widespread and sustained cognitive deficits in alcoholism: A meta-analysis. *Addiction Biology*, *18*(2), 203-213. https://doi.org/10.1111/j.1369-1600.2011.00418.x

Strack, F., & Deutsch, R. (2004). Reflective and impulsive determinants of social behavior. *Personality and social psychology review*, *8*(3), 220-247. https://doi.org/10.1207/s15327957pspr08031

Struijs, S. Y., Lamers, F., Vroling, M. S., Roelofs, K., Spinhoven, P., & Penninx, B. W. (2017). Approach and avoidance tendencies in depression and anxiety disorders. *Psychiatry research*, *256*, 475-481. https://doi.org/10.1016/j.psychres.2017.07.010

Taylor, C. T., & Amir, N. (2012). Modifying automatic approach action tendencies in individuals with elevated social anxiety symptoms. *Behaviour research and therapy*, *50*(9), 529-536. https://doi.org/10.1016/j.brat.2012.05.004

Taylor, R., Cella, M., & Wykes, T. (2025). Cognitive Remediation Is an Evidence-Based Psychological Therapy: Isn't It Time It Was Treated Like One?. *Behavior Modification*, *49*(5-6), 502-526. https://doi.org/10.1177/01454455251343303

Thérond, A., Pezzoli, P., Abbas, M., Howard, A., Bowie, C. R., & Guimond, S. (2021). The Efficacy of Cognitive Remediation in Depression: A Systematic Literature Review and Meta-Analysis. *Journal of Affective Disorders*, *284*, 238-246. https://doi.org/10.1016/j.jad.2021.02.009

Thewissen, R., Havermans, R. C., Geschwind, N., van den Hout, M., & Jansen, A. (2007). Pavlovian conditioning of an approach bias in low-dependent smokers. *Psychopharmacology*, *194*(1), 33-39. https://doi.org/10.1007/s00213-007-0819-7

Thomas, K. R., Puig, O., & Twamley, E. W. (2017). Age as a moderator of change following compensatory cognitive training in individuals with severe mental illnesses. *Psychiatric Rehabilitation Journal, 40*(1), 70.

Thompson, J. M., Gallagher, P., Hughes, J. H., Watson, S., Gray, J. M., Ferrier, I. N., & Young, A. H. (2005). Neurocognitive impairment in euthymic patients with bipolar affective disorder. *The British Journal of Psychiatry, 186*(1), 32–40. https://doi.org/10.1192/bjp.186.1.32

Thoolen, B. J., de Ridder, D., Bensing, J., Gorter, K., & Rutten, G. (2009). Beyond good intentions: The role of proactive coping in achieving sustained behavioural change in the context of diabetes management. *Psychology & Health*, *24*(3), 237–254. https://doi.org/10.1080/08870440701864504

Thush, C., Wiers, R. W., Ames, S. L., Grenard, J. L., Sussman, S., & Stacy, A. W. (2008). Interactions between implicit and explicit cognition and working memory capacity in the prediction of alcohol use in at-risk adolescents. *Drug and alcohol dependence*, *94*(1-3), 116-124. https://doi.org/10.1016/j.drugalcdep.2007.10.019

Tielemans, N. S., Schepers, V. P., Visser-Meily, J. M., Post, M. W., & Van Heugten, C. M. (2015). Associations of proactive coping and self-efficacy with psychosocial outcomes in individuals after stroke. *Archives of Physical Medicine and Rehabilitation*, *96*(8), 1484–1491. https://doi.org/10.1016/j.apmr.2015.04.009

Tielemans, N. S., Visser-Meily, J. M., Schepers, V. P., Post, M. W., & van Heugten, C. M. (2014). Proactive coping poststroke: Psychometric properties of the Utrecht Proactive Coping Competence Scale. *Archives of Physical Medicine and Rehabilitation*, *95*(4), 670–675. https://doi.org/10.1016/j.apmr.2013.11.010

Torrent, C., Bonnin, C. D. M., Martínez-Arán, A., Valle, J., Amann, B. L., González-Pinto, A., Crespo, J. M., Ibáñez, Á., Garcia-Portilla, M. P., Tabarés-Seisdedos, R., Arango, C., Colom, F., Solé, B., Pacchiarotti, I., Rosa, A. R., Ayuso-Mateos, J. L., Anaya, C., Fernández, P., Landín-Romero, R., Vieta, E. (2013). Efficacy of functional remediation in bipolar disorder: A multicenter randomized controlled study. *The American Journal of Psychiatry, 170*(8), 852–859. https://doi.org/10.1176/appi.ajp.2012.12070971

Trapp, W., Heid, A., Röder, S., Wimmer, F., & Hajak, G. (2022). Cognitive remediation in psychiatric disorders: State of the evidence, future perspectives, and some bold ideas. *Brain sciences*, *12*(6), 683. https://doi.org/10.3390/brainsci12060683

Trew, J. L. (2011). Exploring the roles of approach and avoidance in depression: An integrative model. *Clinical Psychology Review, 31*(7), 1156-1168. https://doi.org/10.1016/j.cpr.2011.07.007

Twamley, E. W. (2016). Compensatory approaches to improving functioning. *Cognitive Remediation to Improve Functional Outcomes*, 176-194.

Twamley, E. W., Burton, C. Z., & Vella, L. (2011). Compensatory cognitive training for psychosis: who benefits? Who stays in treatment?. *Schizophrenia bulletin*, *37*(suppl_2), S55-S62. https://doi.org/10.1093/schbul/sbr059

Twamley, E. W., Thomas, K. R., Burton, C. Z., Vella, L., Jeste, D. V., Heaton, R. K., & McGurk, S. R. (2019). Compensatory Cognitive Training for People with Severe Mental Illnesses in Supported Employment: A Randomized Controlled Trial. *Schizophrenia Research*, *203*, 41-48. https://doi.org/10.1016/j.schres.2017.08.005

Valls-Serrano, C., Caracuel, A., & Verdejo-Garcia, A. (2016). Goal Management Training and Mindfulness Meditation improve executive functions and transfer to ecological tasks of daily life in polysubstance users enrolled in therapeutic community treatment. *Drug and Alcohol Dependence*, *165*, 9-14. https://doi.org/10.1016/j.drugalcdep.2016.04.040

van der Zee, C. H., Priesterbach, A. R., van der Dussen, L., Kap, A., Schepers, V. P. M., Visser-Meily, J. M. A., & Post, M. W. M. (2010). Reproducibility of three self-report participation measures: The ICF measure of participation and activities screener, the Participation Scale, and the Utrecht Scale for evaluation of rehabilitation-participation. *Journal of Rehabilitation Medicine*, *42*(8), 752–757. https://doi.org/10.2340/16501977-0589

Van Dessel, P., De Houwer, J., & Gast, A. (2016). Approach–Avoidance training effects are moderated by awareness of stimulus–action contingencies. *Personality and Social Psychology Bulletin*, *42*(1), 81-93. https://doi.org/10.1177/0146167215615335

Van Dessel, P., Hughes, S., & De Houwer, J. (2018). Consequence-based approach-avoidance training: A new and improved method for changing behavior. *Psychological Science*, *29*(12), 1899-1910.

Van Dessel, P., Hughes, S., & De Houwer, J. (2019). How Do Actions Influence Attitudes? An Inferential Account of the Impact of Action Performance on Stimulus Evaluation. *Personality and Social Psychology Review*, *23*(3), 267-284. https://doi.org/10.1177/1088868318795730

van Duijvenbode, N., Didden, R., Voogd, H., Korzilius, H. P., & Engels, R. C. (2012). Cognitive biases in individuals with mild to borderline intellectual disability and alcohol use-related problems. *Research in Developmental Disabilities*, *33*(6), 1928-1936. https://doi.org/10.1016/j.ridd.2012.05.026

Van Kessel, M., Fasotti, L., Berg, I., van Hout, M., & Wekking, E. (2010). *Training geheugenstrategieën* [Training memory strategies]. Boom Publishers.

Van Tilborg, I. A., Kessels, R. P., Kruijt, P., Wester, A. J., & Hulstijn, W. (2011). Spatial and nonspatial implicit motor learning in Korsakoff's amnesia: Evidence for selective deficits. *Experimental brain research*, *214*(3), 427-435. https://doi.org/10.1007/s00221-011-2841-6

Veenstra, E. M., & de Jong, P. J. (2011). Reduced automatic motivational orientation towards food in restricting anorexia nervosa. *Journal of Abnormal Psychology*, *120*(3), 708.

Velligan, D. I., Prihoda, T. J., Ritch, J. L., Maples, N., Bow-Thomas, C. C., & Dassori, A. (2002). A randomized single-blind pilot study of compensatory strategies in schizophrenia outpatients. *Schizophrenia Bulletin*, *28*(2), 283–292. https://doi.org/10.1093/oxfordjournals.schbul.a006938

Verdejo-Garcia, A. (2016). Cognitive training for substance use disorders: Neuroscientific mechanisms. *Neuroscience & Biobehavioral Reviews*, *68*, 270-281. https://doi.org/10.1016/j.neubiorev.2016.05.018

Verdejo-Garcia, A., & Albein-Urios, N. (2021). Impulsivity traits and neurocognitive mechanisms conferring vulnerability to substance use disorders. *Neuropharmacology*, *183*, 108402. https://doi.org/10.1016/j.neuropharm.2020.108402

Verdejo Garcia, A., Rezapour, T., Giddens, E., Khojasteh Zonoozi, A., Rafei, P., Berry, J., ... & Ekhtiari, H. (2023). Cognitive training and remediation interventions for substance use disorders: a Delphi consensus study. *Addiction*, *118*(5), 935-951. doi:10.1111/add.16109.

Vita, A., Barlati, S., Ceraso, A., Nibbio, G., Ariu, C., Deste, G., & Wykes, T. (2021). Effectiveness, Core Elements, and Moderators of Response of Cognitive Remediation for Schizophrenia: A Systematic Review and Meta-analysis of Randomized Clinical Trials. *JAMA Psychiatry*, *78*(8), 848-858. https://doi.org/10.1001/jamapsychiatry.2021.0620

von Borries, A. K. L., Volman, I., de Bruijn, E. R. A., Bulten, B. H., Verkes, R. J., & Roelofs, K. (2012). Psychopaths lack the automatic avoidance of social threat: Relation to instrumental aggression. *Psychiatry Research*, *200*(2-3), 761-766. https://doi.org/10.1016/j.psychres.2012.06.026

Voncken, M. J., Rinck, M., Deckers, A., & Lange, W.-G. (2012). Anticipation of social interaction changes implicit approach-avoidance behavior of socially anxious individuals. *Cognitive therapy and research*, *36*(6), 740-749. https://doi.org/10.1007/s10608-011-9408-5

Vrijsen, J. N., Fischer, V. S., Müller, B. W., Scherbaum, N., Becker, E. S., Rinck, M., & Tendolkar, I. (2018). Cognitive bias modification as an add-on treatment in clinical depression: Results from a placebo-controlled, single-blinded randomized control trial. *Journal of affective disorders*, *238*, 342-350. https://doi.org/10.1016/j.jad.2018.06.025

Vrijsen, J. N., Grafton, B., Koster, E. H. W., Lau, J., Wittekind, C. E., Bar-Haim, Y., Becker, E. S., Brotman, M. A., Joormann, J., Lazarov, A., MacLeod, C., Manning, V., Pettit, J. W., Rinck, M., Salemink, E., Woud, M. L., Hallion, L. S., & Wiers, R. W. (2024). Towards implementation of cognitive bias modification in mental health care: State of the science, best practices, and ways forward. *Behaviour Research and Therapy, 179*, 104557. https://doi.org/10.1016/j.brat.2024.104557

Vrijsen, J. N., van Oostrom, I., Speckens, A., Becker, E. S., & Rinck, M. (2013). Approach and avoidance of emotional faces in happy and sad mood. *Cognitive therapy and research, 37*(1), 1-6. https://doi.org/10.1007/s10608-012-9436-9

Wager, T. D., Davidson, M. L., Hughes, B. L., Lindquist, M. A., & Ochsner, K. N. (2008). Prefrontal-subcortical pathways mediating successful emotion regulation. *Neuron, 59*(6), 1037-1050.

Walsh, M. M., Krusmark, M. A., Jastrembski, T., Hansen, D. A., Honn, K. A., & Gunzelmann, G. (2023). Enhancing learning and retention through the distribution of practice repetitions across multiple sessions. *Memory & Cognition, 51*(2), 455-472. https://doi.org/10.3758/s13421-022-01361-8

Walvoort, S. J., van der Heijden, P. T., Kessels, R. P., & Egger, J. I. (2016). Measuring illness insight in patients with alcohol-related cognitive dysfunction using the Q8 questionnaire: A validation study. *Neuropsychiatric Disease and Treatment*, 1609-1615. https://doi.org/10.2147/NDT.S104442

Walvoort, S. J. W., Wester, A. J., & Egger, J. I. M. (2013). Neuropsychologische diagnostiek en cognitieve functies bij alcoholabstinentie [The neuropsychology of cognitive functions in alcohol abstinence]. *Tijdschrift Voor Psychiatrie, 55*(2), 101-111. https://hdl.handle.net/2066/121121

Watson, P., De Wit, S., Hommel, B., & Wiers, R. W. (2012). Motivational mechanisms and outcome expectancies underlying the approach bias toward addictive substances. *Frontiers in psychology, 3*, 440. https://doi.org/10.3389/fpsyg.2012.00440

Watson, P., O'Callaghan, C., Perkes, I., Bradfield, L., & Turner, K. (2022). Making habits measurable beyond what they are not: A focus on associative dual-process models. *Neuroscience & Biobehavioral Reviews, 142*, 104869. https://doi.org/10.1016/j.neubiorev.2022.104869

Webb, S. S., Jespersen, A., Chiu, E. G., Payne, F., Basting, R., Duta, M. D., & Demeyere, N. (2022). The Oxford digital multiple errands test (OxMET): Validation of a simplified computer tablet based multiple errands test. *Neuropsychological Rehabilitation, 32*(6), 1007–1032. https://doi.org/10.1080/09602011.2020.1862679

Wechsler, D. (2005). *WAIS-III Nederlandstalige bewerking: Technische handleiding (E. Klinkenberg & A. Kooij, Trans.)[Dutch WAIS-III: Manual]*. Harcourt Test Publishers, Amsterdam.

Wechsler, D. (2008). Wechsler Adult Intellligence Scale, (WAIS-IV), administration and scoring manual. *The Psychological Corporation*.

Wechsler, D. (2012). WAIS-IV-NL: Wechsler Adult Intelligence Scale—Fourth Edition, Nederlandstalige bewerking. Afname- en scoringshandleiding. Pearson Assessment and Information B.V.

Weidacker, K., Kärgel, C., Massau, C., Weiß, S., Kneer, J., Krueger, T. H. C., & Schiffer, B. (2018). Approach and avoidance tendencies toward picture stimuli of (pre-) pubescent children and adults: An investigation in pedophilic and nonpedophilic samples. *Sexual Abuse, 30*(7), 781-802. https://doi.org/10.1177/1079063217697134

Weil, Z. M., Corrigan, J. D., & Karelina, K. (2018). Alcohol use disorder and traumatic brain injury. *Alcohol research: current reviews, 39*(2), 171. https://doi.org/10.35946/arcr.v39.2.07

Weldam, S. W. M., Lammers, J.-W. J., Decates, R. L., & Schuurmans, M. J. (2013). Daily activities and health-related quality of life in patients with chronic obstructive pulmonary disease: Psychological determinants: A cross-sectional study. *Health and Quality of Life Outcomes, 11*(1), Article 190. https://doi.org/10.1186/1477-7525-11-190

Wester, A. J., Van Herten, J. C., Egger, J. I., & Kessels, R. P. (2013). Applicability of the Rivermead Behavioural Memory Test–Third Edition (RBMT-3) in Korsakoff's syndrome and chronic alcoholics. *Neuropsychiatric Disease and Treatment*, 875–881. https://doi.org/10.2147/NDT.S44973

Wiers, C. E., Gladwin, T. E., Ludwig, V. U., Gröpper, S., Stuke, H., Gawron, C. K., Wiers, R. W., Walter, H., & Bermpohl, F. (2017). Comparing three cognitive biases for alcohol cues in alcohol dependence. *Alcohol and Alcoholism, 52*(2), 242-248. https://doi.org/10.1093/alcalc/agw063

Wiers, C. E., Kühn, S., Javadi, A. H., Korucuoglu, O., Wiers, R. W., Walter, H., Gallinat, J., & Bermpohl, F. (2013). Automatic approach bias towards smoking cues is present in smokers but not in ex-smokers. *Psychopharmacology, 229*(1), 187-197. https://doi.org/10.1007/s00213-013-3098-5

Wiers, C. E., Ludwig, V. U., Gladwin, T. E., Park, S. Q., Heinz, A., Wiers, R. W., Rinck, M., Lindenmeyer, J., Walter, H., & Bermpohl, F. (2015). Effects of cognitive bias modification training on neural signatures of alcohol approach tendencies in male alcohol-dependent patients. *Addiction Biology*, *20*(5), 990-999. https://doi.org/10.1111/adb.12221

Wiers, C. E., Stelzel, C., Gladwin, T. E., Park, S. Q., Pawelczack, S., Gawron, C. K., Stuke, H., Heinz, A., Wiers, R. W., Rinck, M., Lindenmeyer, J., Walter, H., & Bermpohl, F. (2015). Effects of Cognitive Bias Modification Training on Neural Alcohol Cue Reactivity in Alcohol Dependence. *American Journal of Psychiatry*, *172*(4), 335-343. https://doi.org/10.1176/appi.ajp.2014.13111495

Wiers, C. E., Stelzel, C., Park, S. Q., Gawron, C. K., Ludwig, V. U., Gutwinski, S., Heinz, A., Lindenmeyer, J., Wiers, R. W., & Walter, H. (2014). Neural correlates of alcohol-approach bias in alcohol addiction: The spirit is willing but the flesh is weak for spirits. *Neuropsychopharmacology*, *39*(3), 688-697.
https://doi.org/10.1038/npp.2013.252

Wiers, C. E., & Wiers, R. W. (2017). Imaging the neural effects of cognitive bias modification training. *Neuroimage*, *151*, 81-91. https://doi.org/10.1016/j.neuroimage.2016.07.041

Wiers, R. W. (2017). *Cognitive bias modification does hold promise in the treatment of addiction: A commentary on Cristea et al 2016. PlosOne. 2016.* https://journals.plos.org/plosone/article/comment?id=10.1371/annotation/8cde1186-7802-4dd5-b686-d4a66c84fb84

Wiers, R. W., Boffo, M., & Field, M. (2018). 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*, *79*(3), 333-343. https://doi.org/10.15288/jsad.2018.79.333

Wiers, R. W., Eberl, C., Rinck, M., Becker, E. S., & Lindenmeyer, J. (2011). Retraining automatic action tendencies changes alcoholic patients' approach bias for alcohol and improves treatment outcome. *Psychological Science*, *22*(4), 490-497.
https://doi.org/10.1177/0956797611400615

Wiers, R. W., Gladwin, T. E., Hofmann, W., Salemink, E., & Ridderinkhof, K. R. (2013). Cognitive bias modification and cognitive control training in addiction and related psychopathology: Mechanisms, clinical perspectives, and ways forward. *Clinical psychological science*, *1*(2), 192-212. https://doi.org/10.1177/2167702612466547

Wiers, R. W., Houben, K., Fadardi, J. S., Van Beek, P., Rhemtulla, M., & Cox, W. M. (2015). Alcohol cognitive bias modification training for problem drinkers over the web. *Addictive behaviors*, *40*, 21-26. https://doi.org/10.1016/j.addbeh.2014.08.010

Wiers, R. W., Pan, T., van Dessel, P., Rinck, M., & Lindenmeyer, J. (2023). Approach-bias retraining and other training interventions as add-on in the treatment of AUD patients. *Current Topics in Behavioral Neurosciences*, *Advance online publication*. https://doi.org/10.1007/7854_2023_421

Wiers, R. W., Rinck, M., Dictus, M., & Van Den Wildenberg, E. (2009). Relatively strong automatic appetitive action-tendencies in male carriers of the OPRM1 G'allele. *Genes, Brain and Behavior*, *8*(1), 101-106. https://doi.org/10.1111/j.1601-183X.2008.00454.x

Wiers, R. W., Rinck, M., Kordts, R., Houben, K., & Strack, F. (2010). Retraining automatic action-tendencies to approach alcohol in hazardous drinkers. *Addiction*, *105*(2), 279-287. https://doi.org/10.1111/j.1360-0443.2009.02775.x

Wiers, R. W., & Stacy, A. W. (2006). Implicit Cognition and Addiction. *Current Directions in Psychological Science*, *15*(6), 292-296. https://doi.org/10.1111/j.1467-8721.2006.00455.x

Wiers, R. W., Teachman, B. A., & De Houwer, J. (2007). Implicit cognitive processes in psychopathology: An introduction. *Journal of Behavior Therapy and Experimental Psychiatry*, *38*(2), 95-104. https://doi.org/10.1016/j.jbtep.2006.10.002

Wiers, R. W., Van Dessel, P., & Köpetz, C. (2020). ABC Training: A New Theory-Based Form of Cognitive-Bias Modification to Foster Automatization of Alternative Choices in the Treatment of Addiction and Related Disorders. *Current Directions in Psychological Science*, *29*(5), 499-505. https://doi.org/10.1177/0963721420949500

Wiers, R. W., & Verschure, P. (2021). Curing the broken brain model of addiction: Neurorehabilitation from a systems perspective. *Addictive Behaviors*, *112*, 106602. https://doi.org/10.1016/j.addbeh.2020.106602

Wiers, R. W., Zerhouni, O., Den Uyl, T., & Boffo, M. (2020). Cognitive bias modification in the treatment of addiction. *Cognition and Addiction*, 231-241. https://doi.org/10.1016/B978-0-12-815298-0.00017-4

Winkens, I., & Fasotti, L. (2010). Protocol "*Mentale traagheid*" [Protocol: "Mental slowness"]. Boom Publishers.

Wittekind, C. E., Bierbrodt, J., Luedecke, D., Feist, A., Hand, I., & Moritz, S. (2019). Cognitive bias modification in problem and pathological gambling using a web-based approach-avoidance task: A pilot trial. *Psychiatry research*, *272*, 171-181.

Wittekind, C. E., Feist, A., Schneider, B. C., Moritz, S., & Fritzsche, A. (2015). The approach-avoidance task as an online intervention in cigarette smoking: A pilot study. *Journal of behavior therapy and experimental psychiatry*, *46*, 115-120. https://doi.org/10.1016/j.jbtep.2014.08.006

Wittekind, C. E., Luedecke, D., & Cludius, B. (2019). Web-based Approach Bias Modification in smokers: A randomized-controlled study. *Behaviour Research and Therapy*, *116*, 52-60. https://doi.org/10.1016/j.brat.2018.12.003

Wittekind, C. E., Reibert, E., Takano, K., Ehring, T., Pogarell, O., & Ruether, T. (2019). Approach-avoidance modification as an add-on in smoking cessation: A randomized-controlled study. *Behaviour Research and Therapy*, *114*, 35-43. https://doi.org/10.1016/j.brat.2018.12.004

Wolf, P. A., Salemink, E., & Wiers, R. W. (2016). Attentional retraining and cognitive biases in a regular cannabis smoking student population. *SUCHT*, *62*(6), 355-365. https://doi.org/10.1024/0939-5911/a000455

Wong, D., Pike, K., Stolwyk, R., Allott, K., Ponsford, J., McKay, A., Longley, W., Bosboom, P., Hodge, A., & Kinsella, G. (2024). Delivery of neuropsychological interventions for adult and older adult clinical populations: An Australian expert working group clinical guidance paper. *Neuropsychology Review*, *34*(4), 985-1047. https://doi.org/10.1007/s11065-023-09624-0

Wykes, T. (2025). Implementing Cognitive Remediation Therapy (CRT) in the routine treatment of schizophrenia. *European Psychiatry*, *68*(S1), S42–S43. doi:10.1192/j.eurpsy.2025.153

Wykes, T., Bowie, C. R., & Cella, M. (2024). Thinking about the future of cognitive remediation therapy revisited: What is left to solve before patients have access? *Schizophrenia bulletin*, *50*(5), 993-1005. https://doi.org/10.1093/schbul/sbae075

Wykes, T., Huddy, V., Cellard, C., McGurk, S. R., & Czobor, P. (2011). A meta-analysis of cognitive remediation for schizophrenia: Methodology and effect sizes. *The American Journal of Psychiatry*, *168*(5), 472-485. https://doi.org/10.1176/appi.ajp.2010.10060855

Yücel, M., Oldenhof, E., Ahmed, S. H., Belin, D., Billieux, J., Jones, H., & Garcia, A. (2019). A transdiagnostic dimensional approach towards a neuropsychological assessment for addiction: An international Delphi consensus study. *Addiction*, *114*(6), 1095-1109. https://doi.org/10.1111/add.14424

Zedlitz, A. M. E. E., & Fasotti, L. (2010). *Protocol "Omgaan met beperkte belastbaarheid: Behandelprotocol voor ambulante hersenletselpatiënten met (ernstige) vermoeidheid*" [Protocol: "Managing limited work capacity: Treatment protocol for outpatient brain injury patients with (severe) fatigue"]. Boom Publishers.

Zelazo, P. D. (2020). Executive function and psychopathology: A neurodevelopmental perspective. Annual Review of Clinical Psychology, 16(1), 431–454. https://doi.org/10.1146/annurev-clinpsy-072319-024242

Zerhouni, O., Houben, K., El Methni, J., Rutte, N., Werkman, E., & Wiers, R. W. (2019). I didn't feel like drinking, but I guess why: Evaluative conditioning changes on explicit attitudes toward alcohol and healthy foods depends on contingency awareness. *Learning and Motivation*, *66*, 1-12. https://doi.org/10.1016/j.lmot.2019.02.001

Zhou, Y., Li, X., Zhang, M., Zhang, F., Zhu, C., & Shen, M. (2012). Behavioural approach tendencies to heroin-related stimuli in abstinent heroin abusers. *Psychopharmacology*, *221*(1), 171-176. https://doi.org/10.1007/s00213-011-2557-0

Zlomuzica, A., Machulska, A., Roberts, S., von Glischinski, M., Rinck, M., Lester, K. J., Eley, T. C., & Margraf, J. (2018). The dopamine D2 receptor mediates approach-avoidance tendencies in smokers. *European Archives of Psychiatry and Clinical Neuroscience*, *268*(3), 261-268. https://doi.org/10.1007/s00406-017-0793-y

Zuckerman, H., Pan, Z., Park, C., Brietzke, E., Musial, N., Shariq, A. S., Iacobucci, M., Yim, S. J., Lui, L. M. W., Rong, C., & McIntyre, R. S. (2018). Recognition and treatment of cognitive dysfunction in major depressive disorder. *Frontiers in Psychiatry, 9*, Article 655. https://doi.org/10.3389/fpsyt.2018.00655

Nederlandse samenvatting (Dutch summary)

Inleiding en doel van het onderzoek

Impliciete, automatisch geactiveerde cognitieve processen spelen een belangrijke rol bij tal van psychische aandoeningen en stoornissen in middelengebruik. Vertekeningen in deze processen, oftewel cognitieve *biases*, dragen bij aan het ontstaan en het voortduren van deze problematiek en zijn bovendien geassocieerd met een verhoogd risico op terugval. Automatische actietendensen vormen één van deze processen; wanneer zij verstoord raken kunnen maladaptieve toenaderings- of vermijdingsgedragingen (*approach-avoidance bias*) ontstaan, zoals onder andere wordt gezien bij stoornissen in middelengebruik en angststoornissen. De rol van deze *approach-avoidance bias* en de klinische effecten van interventies gericht op de modificatie van deze *biases* bij psychische aandoeningen en stoornissen in middelengebruik, wordt uitgebreid besproken in een systematische literatuurreview (**hoofdstuk 2**).

Zowel impliciete cognitieve vertekeningen als neurocognitieve tekorten in de informatieverwerking komen frequent voor en zijn transdiagnostisch van aard. Deze cognitieve verstoringen belemmeren het herstelproces en gaan gepaard met een verhoogd risico op terugval of recidive (Abramovitch et al., 2021; East-Richard et al., 2020; Melugin et al., 2021). Desondanks worden dergelijke cognitieve verstoringen binnen de specialistische geestelijke gezondheidszorg (SGGz) nog beperkt en weinig systematisch geadresseerd. In **hoofdstuk 3** wordt daarom de haalbaarheid van een transdiagnostische toepassing van een cognitieve compensatietraining onderzocht, met als doel bij te dragen aan de klinische implementatie van cognitieve interventies binnen de SGGz.

Bij stoornissen in alcoholgebruik kan een automatische neiging ontstaan om alcoholgerelateerde informatie sneller te benaderen dan neutrale stimuli, aangeduid als de *alcohol approach bias*. Deze *alcohol approach bias* hangt samen met een verhoogd risico op alcoholgebruik (Wiers et al., 2010). Met behulp van een alcohol-*avoidance* training (AATr) kunnen deze automatische actietendensen, die stoornissen in alcoholgebruik mede in stand houden, worden beïnvloed. Tijdens deze training oefenen deelnemers met het herhaaldelijk wegduwen van alcoholgerelateerde afbeeldingen en het naar zich toe trekken van neutrale stimuli, via een indirecte instructie en met behulp van een joystick. Deze bewegingen gaan gepaard met een zoomeffect, waarbij beelden groter worden bij toenadering en kleiner bij wegduwen. Op deze wijze wordt de automatische toenaderingsneiging ten opzichte van alcoholgerelateerde stimuli systematisch hertraind (Rinck & Becker, 2007; Wiers et al., 2011).

Eerder onderzoek heeft herhaaldelijk aangetoond dat de AATr effectief kan bijdragen aan terugvalpreventie (Eberl et al., 2013; Manning et al., 2016; 2022;

Rinck et al., 2018; Wiers et al., 2011). Deze training is daarom in het bijzonder relevant voor patiënten met alcoholgerelateerde cognitieve stoornissen (ACS) en het syndroom van Korsakov (SvK). Deze patiëntengroep kan namelijk, vanwege stoornissen in onder andere het declaratieve geheugen, in mindere mate profiteren van reguliere behandelmethoden. Omdat de AATr gebruik maakt van impliciete leerprocessen, die doorgaans relatief goed behouden zijn binnen deze populatie (Rensen et al., 2018), vormt deze interventie een veelbelovende aanvulling in de behandeling van stoornissen in alcoholgebruik voor deze doelgroep. In **hoofdstuk 4** wordt de haalbaarheid van de toepassing van de AATr bij patiënten met ACS en SvK onderzocht. In een vervolgstudie (**hoofdstuk 5**) wordt de relatie tussen veranderingen in de *alcohol approach bias* en de kwaliteit van het declaratieve geheugen nader geëxploreerd.

De bevindingen van deze studies dragen bij aan zowel het verbeteren van behandelmogelijkheden voor patiënten met ernstige alcoholgerelateerde neurocognitieve stoornissen, als aan het theoretische inzicht in de werkingsmechanismen van AATr. Aan de hand van een klinisch neuropsychologisch perspectief worden zowel theoretische als klinische implicaties van de onderzoeksbevindingen besproken. Hierbij wordt onderscheid gemaakt tussen de aard van de cognitieve verstoring (het behandeldoel) en het veranderingsproces van verschillende type cognitieve interventies, conform het *framework* van Braunstein en collega's (2017). Dit theoretisch kader werd primair ontwikkeld voor emotieregulatie interventies, maar kan goed worden toegepast op de genoemde cognitieve interventies. Dit ten gunste van de verdere verbetering en geïntegreerde toepassing van cognitieve interventies in de SGGz.

Samenvatting van de studies en voornaamste bevindingen

Allereerst is er een systematische review naar verstoringen in *approach-avoidance* (AA) gedrag bij psychopathologie uitgevoerd **(hoofdstuk 2).** Dit resulteerde in 97 geïncludeerde studies die betrekking hadden op 17 DSM-IV-classificaties. De meeste studies zijn gedaan naar het vaststellen en modificeren van een AA *bias* bij stoornissen in het gebruik van middelen. In deze populaties werd gevonden dat een *approach bias* een risicofactor is voor middelengebruik en voorkomt in subklinische populaties. Een disfunctionele *approach bias* voor alcoholgerelateerde stimuli bleek een consistent te meten kenmerk van een stoornis in alcoholgebruik en herhaaldelijk werd gevonden dat modificatie van deze *bias* bij patiënten met een stoornis in alcoholgebruik leidt tot lagere terugvalpercentages. Daarom wordt bepleit dat de a*lcohol-avoidance training* (AATr) standaard onderdeel zou moeten zijn van de reguliere behandeling van alcoholverslaving. Voorts werden met betrekking tot andere vormen van psychopathologie alleen voor depressie klinische effecten van AA *bias* modificatie gevonden: succesvolle beïnvloeding van

de natuurlijke *approach bias* richting positieve stimuli leidde tot symptoomreductie. Bij angststoornissen werd een consistente automatische vermijdingstendens (*avoidance bias*) vastgesteld, maar modificatie hiervan leverde nog geen significante klinische effecten op. Over het geheel genomen lijkt modificatie van een *approach bias* (of het stimuleren van een 'natuurlijke' *approach bias* wanneer deze ontbreekt of relatief zwak is) beter mogelijk dan de modificatie van een *avoidance bias*.

In **hoofdstuk 3** wordt de studie naar cognitieve compensatietraining (CCTr) 'Master Mind' beschreven. Deze interventie werd toegepast bij 44 patiënten met diverse psychische aandoeningen. Proactieve coping en tevredenheid met het dagelijks leven werden gemeten op drie meetmomenten (vóór de training n= 42, na de training n= 34) en een follow-up meting vier maanden na training (n= 18). De beoordelingen van deelnemers na iedere sessie waren positief: de beoordelingen door deelnemers lieten een goede acceptatie zien ten aanzien van trainingsdoelen, methoden, sessieonderwerpen evenals de therapeutische alliantie met de therapeut. Een eerste verkennende analyse toonde een toename van proactieve coping gedurende de training en dit was gerelateerd aan een toename van tevredenheid met het dagelijks leven bij follow-up. Er werd geen verband gevonden tussen cognitieve capaciteiten (werkgeheugencapaciteit en snelheid van informatieverwerking) en proactieve coping. Deze bevinding suggereert dan ook dat mensen met cognitieve tekorten baat kunnen hebben bij deze CCTr interventie. Dit werd eerder ook aangetoond in andere studies, waarin patiënten met een minder sterk cognitief functioneren eveneens profiteerden van CCTr (Twamley et al., 2011). Deze resultaten illustreren een goede haalbaarheid en acceptatie van de CCTr Master Mind in een behandelgroep van deelnemers met diverse neuropsychiatrische diagnoses.

In een eerste haalbaarheidsstudie werd een AATr met zes sessies (ACS: n= 51; SvK: n= 54) toegepast (**hoofdstuk 4**). Er werd een significante reductie van de *alcohol-approach bias* gevonden en werd er een afname in *craving* bij participanten met het SvK vastgesteld. De toepassing van de AATr bij deze specifieke doelgroep bleek dus mogelijk. In **hoofdstuk 5** wordt een tweede AATr studie beschreven. Nu met 12 sessies en naast participanten met ACS en Svk werden nu ook participanten geïncludeerd met enkel een stoornis in alcoholgebruik, zonder cognitieve stoornissen (totale n= 64). In deze studie werd onderzocht of de afname van de *alcohol approach bias* binnen een trainingssessie samenhing met de kwaliteit van het declaratieve geheugen. Allereerst bevestigden de uitkomsten de resultaten van hoofdstuk 4, namelijk dat de *alcohol approach bias* ook bij patiënten met neurocognitieve stoornissen kan worden hertraind. Vervolgens werd gevonden dat in geval van een verminderde declaratieve geheugenfunctie meer dan zes sessies nodig waren voor voldoende biasmodificatie. Bij een relatief intacte geheugenfunctie was dit effect van tijd echter niet aanwezig. Dit suggereert dat bij

geheugenstoornissen (meer) herhaling nodig is en dat procedureel (impliciet) leren voornamelijk bepalend is voor het effect, terwijl bij een intact geheugen er sneller biasreductie kan plaatsvinden en inferentiële leerprocessen mogelijk een rol spelen.

Deze bevindingen onderstrepen het belang van het uitvoeren van individueel neurocognitief onderzoek in de klinische praktijk, na voldoende duur van abstinentie bij stoornissen in alcoholgebruik. Op basis van individuele cognitieve sterktes en zwaktes kan de behandeling worden gepersonaliseerd. Ook duiden deze bevindingen erop dat biasmodificatie middels de AATr mogelijk minder samenhangt met impliciete leerprocessen dan initieel gedacht, tenminste wanneer het declaratief geheugen (relatief) intact is.

Discussie

Het *framework* van Braunstein en collega's (2017) wordt hier toegepast op de beschreven cognitieve interventies, met als doel de eigenschappen van deze interventies te verduidelijken. Binnen dit theoretische kader wordt onderscheid gemaakt tussen de aard van het behandeldoel, dat meer of minder expliciet kan zijn (impliciet versus expliciet), en het veranderingsproces dat door de interventie wordt bewerkstelligd, dat meer of minder gecontroleerd van aard kan zijn (automatisch versus gecontroleerd). Op basis van deze tweedimensionale indeling worden vier kwadranten onderscheiden: impliciet-automatisch, expliciet-automatisch, impliciet-gecontroleerd en expliciet-gecontroleerd.

De *alcohol-avoidance training* (AATr) kan worden gepositioneerd binnen het impliciet-automatische kwadrant, terwijl de cognitieve compensatietraining (CCTr) overwegend valt binnen het kwadrant van expliciet-gecontroleerde interventies.

Wanneer we kijken naar de aard van maladaptief AA gedrag blijkt uit de uitgebreide literatuurstudie (**hoofdstuk 2**) dat de modificatie van een *approach bias* klinische effecten heeft opgeleverd. Dit is nog niet zo duidelijk gelukt voor de modificatie van de *avoidance bias*.

Het *Research Domain Criteria* (RDoC) onderscheid een aantal fundamentele systemen die ten grondslag liggen aan adaptief menselijk gedrag (Cuthbert & Insel, 2013). Twee van deze systemen zijn het zogenoemde positieve en negatieve valentiesysteem. Maladaptief automatisch toenaderingsgedrag (*approach bias*) zou kunnen worden gerelateerd aan het positieve valentiesysteem en maladaptief automatisch vermijdingsgedrag (*avoidance bias*) aan het negatieve valentiesysteem. Mogelijk zijn cognitieve processen en gedrag gerelateerd aan het positieve valentiesysteem meer ontvankelijk voor beïnvloeding middels cognitieve *bias*-modificatie. Dit kan aanknopingspunten geven voor de doorontwikkeling van deze interventies.

Wanneer gekeken wordt naar het proces van verandering van de *alcohol approach bias* door de AATr (de andere as van het model van Braunstein et al., 2017) wordt dit proces over het algemeen opgevat als een automatisch, *bottom-up* proces waarbij directe beïnvloeding van de cognitieve *bias* wordt beoogd. Er wordt aangenomen dat dit veranderingsproces op een impliciet niveau plaatsvindt en door de repetitieve aard van de training procedureel leren weerspiegelt. Bevindingen uit **hoofdstuk 5** suggereren echter dat AATr-leereffecten samenhangen met de kwaliteit van het declaratieve geheugen: bij een relatief intact declaratief geheugen droegen meerdere AATr-sessies niet duidelijk bij aan verdere vermindering van de *alcohol approach bias*. Dus als het declaratief geheugen intact is, zijn mogelijk inferentiële leerprocessen méér verklarend voor het proces leidend tot biasreductie door de AATr, terwijl er bij beperkte cognitieve vermogens met name sprake is van procedureel leren. Dit betekent dat daar waar de AATr eerder werd beschouwd als een bij uitstek 'impliciet- automatisch' interventietype, deze interventie mogelijk als impliciet-gecontroleerd kan worden geclassificeerd volgens de classificatie van Braunstein en collega's (2017). Daarbij zijn er verdere ontwikkelingen die erop duiden dat het expliciteren van het beoogde doel (vermijding van alcoholstimuli) kan bijdragen aan verbeterde uitkomsten. Daarmee zou de behandeling verder verschuiven naar het 'expliciet-gecontroleerde' kwadrant (Van Dessel et al., 2018; Wiers et al., 2020, 2023).

Klinische toepassing van cognitieve interventies

De acceptatie van een transdiagnostische toepassing van CCTr 'Master Mind' in patiëntgroepen met verschillende psychische aandoeningen werd onderzocht in **hoofdstuk 3**. Slechts enkele andere CCTr-studies zijn uitgevoerd in groepen met gemengde diagnoses (Thomas et al., 2017; Twamley et al., 2019). De goede acceptatie van de training en de bevinding dat verbetering in proactieve coping niet samenhing met de kwaliteit van het cognitieve functioneren, maakt dat noch de aard van de psychische aandoening als de ernst van de cognitieve stoornis exclusiecriteria hoeven te zijn. Deze eerste resultaten effenen het pad voor een transdiagnostische toepassing van CCTr, waardoor de toegang tot integratieve cognitieve behandeling in de SGGz kan worden verbeterd (Allott et al., 2025; Wong et al., 2024).

Met betrekking tot de modificatie van de alcohol *approach bias* is gebleken dat de toepassing van de AATr haalbaar is in een patiëntenpopulatie met ACS of SvK (**hoofdstukken 4 en 5**). Het wordt aanbevolen om meer dan zes (zes tot 12) AATr-sessies toe te passen wanneer er sprake is van tekorten in het declaratieve geheugen. Voor patiënten met het SvK bleek dat de training bijdroeg aan vermindering van *craving*, maar deze bevinding moet met voorzichtigheid worden geïnterpreteerd gezien het ontbreken van een controlegroep. Het feit dat ook de

AATr aanpassingen vraagt wanneer er sprake is van cognitieve stoornissen, die een hoge prevalentie kennen bij alcoholmisbruik, bevestigt het belang van het verrichten van neurocognitief onderzoek bij mensen met (ernstige) stoornissen in alcoholgebruik. Dit om de behandeling te personaliseren en overvraging te voorkomen. Tenslotte is het van belang om replicatiestudies naar het effect van de AATr op terugvalpreventie bij patiënten met ACS of SvK uit te voeren.

Beperkingen van huidig onderzoek

Het opnemen van follow-upmetingen voor het meten van terugval in alcoholgebruik bij de AATr studies of het includeren van controlegroepen viel buiten de reikwijdte van deze thesis. Dit beperkt de mogelijkheid om conclusies te trekken over de effecten van de interventiestudies. Hoewel de inclusieaantallen van de AATr studies redelijk goed zijn, bracht het uitvoeren van onderzoek in de klinische praktijk bij patiënten met neuropsychiatrische aandoeningen duidelijk uitdagingen met zich mee met betrekking tot consistente trainingsdeelname (Domínguez-Salas et al. 2016). Ondanks goede begeleiding, dagelijkse structuur en onderzoeksfaciliteiten binnen de klinische setting was er sprake van gemiste trainingssessies of uitval. Met name in de tweede AATr studie (**hoofdstuk vijf**) speelde dit een rol. Om zoveel mogelijk data te kunnen behouden werd in de analyse dan ook gekozen voor de toepassing van *linear mixed* modeling. Ook werd de factor *Tijd* op twee verschillende manieren geoperationaliseerd, zodat verschillen in het interval tussen opeenvolgende sessies als gevolg van gemiste afspraken konden worden meegewogen in de analyses.

Voor de Master Mind-studie (**Hoofdstuk 3**) geldt eveneens dat het ontbreken van een controle- groep en de beperkte respons bij de follow-up meting maken dat de gevonden effecten niet zonder meer aan deze training kunnen worden toegeschreven. De conclusies over langetermijneffecten dienen eveneens met voorzichtigheid te worden geïnterpreteerd. De uitkomsten bieden nochtans aanknopingspunten voor vervolgonderzoek naar proactieve coping als mediërende variabele van de effecten van cognitieve compensatietrainingen op (onder meer) algeheel welbevinden.

Ondanks de hierboven genoemde beperkingen hebben de onderzoeksbevindingen van de in deze thesis beschreven studies relevante klinische en theoretische implicaties. Juist de inclusie van studies met participanten met (sub) klinische symptomen in de literatuurstudie, evenals de participatie van patiënten met diverse neuropsychiatrische aandoeningen in de CCTr-studie en van patiënten met (ernstige) neurocognitieve stoornissen ten gevolge van alcoholmisbruik, vormen een sterk punt van de studies in deze thesis. Dit is een belangrijke meerwaarde, zowel op klinisch als op theoretisch vlak, temeer daar deze patiëntpopulaties vaak worden uitgesloten van wetenschappelijk onderzoek en behandelprogramma's binnen de SGGz.

Aanbevelingen voor toekomstig onderzoek en klinische praktijk

Het neuropsychologisch perspectief op *approach-avoidance* gedrag bij psychopathologie draagt bij aan het onderkennen van de relevantie van cognitieve verstoringen bij psychische aandoeningen en stoornissen in alcoholgebruik. De uitkomsten van de studies in deze thesis bieden tevens aanknopingspunten voor de doorontwikkeling van verschillende typen cognitieve interventies.

Gezien de hoge prevalentie van neurocognitieve tekorten bij psychopathologie en stoornissen in alcoholgebruik als ook de impact van deze tekorten op behandelsucces en terugvalpercentages, is het van belang dat neurocognitief onderzoek (inclusief prestatievaliditeitstaken) vaker wordt ingezet. Middels inzicht in de individuele cognitieve sterktes en zwaktes kan een gepersonaliseerde behandeling worden ingezet en overvraging worden voorkomen. Gepersonaliseerde evaluatiestrategieën, zoals *single-case designs* of idiografische evaluatiemethoden (Piccirillo & Rodebaugh, 2019), kunnen vervolgens worden toegepast om deze gepersonaliseerde doelen ook wetenschappelijk te evalueren.

Voor verder inzicht in AA gedrag bij psychopathologie kan het waardevol zijn om toekomstige hypothesen en bevindingen te plaatsen binnen het RDoC-framework. Het relateren van *approach-avoidance biases* aan kenmerken van het positieve en negatieve valentiesysteem kan de verdere ontwikkeling van cognitieve biasmodificatieprocedures ondersteunen. Zo kan het bijvoorbeeld relevant zijn om behandelstrategieën te onderzoeken die natuurlijk toenaderingsgedrag versterken, waar dit verminderd aanwezig is zoals bij stemmingsstoornissen en anorexia nervosa.

Een voortgezet klinisch neuropsychologisch perspectief kan bijdragen aan de verdere ontwikkeling van de AATr. Zowel vervolgonderzoek naar het aandeel van en de interactie tussen procedurele en inferentiële leerprocessen, als het systematisch bestuderen van de verschillende fasen van leren (inprenting, consolidatie en opdiepen) is hierbij van belang. Variabelen zoals trainingsfrequentie, tijdsintervallen tussen sessies, boostersessies, evenals contextuele factoren zoals *craving* en cognitieve depletie, dienen daarbij expliciet in aanmerking te worden genomen (Ghilardi et al., 2009; Gast, 2018; Musfeld et al., 2023; Walsh et al., 2023; Yücel et al., 2019).

Met betrekking tot de toepassing van cognitieve interventies in de klinische praktijk wordt aanbevolen om de AATr te implementeren in de behandeling van alcoholafhankelijkheid bij patiënten met ACS en SvK. Deze interventie vormt een zinvolle aanvulling op bestaande interventies gericht op cognitieve revalidatie en algeheel herstel van stoornissen in alcoholgebruik (Kwako et al., 2016; Maurage et al., 2024; Verdejo-Garcia et al., 2023; Wiers et al., 2023). Gezien het eerder aangetoonde positieve effect van AATr op terugvalpreventie bij patiënten zonder neurocognitieve stoornissen, is herhalingsonderzoek hiervan bij deze specifieke

doelgroep met (ernstige) neurocognitieve stoornissen een belangrijke volgende stap.

Wanneer er sprake is van tekorten in het declaratief geheugen, wordt aanbevolen om een AATr van zes tot 12 sessies aan te bieden. Bovendien is het onderzoeken van de mogelijkheid tot aanpassing van de AATr naar een foutloos lerenprotocol (waarin het kunnen maken van een andere beweging dan vermijding van alcohol niet mogelijk is in de trainingsfase). Mogelijk kan dit het procedurele leerproces verder versterken bij declaratieve geheugentekorten (Kessels & Haan, 2003; Rensen et al., 2019; Twamley, 2016).

Een relevante vraag voor vervolgonderzoek naar het veranderingsproces van de cognitieve compensatietraining (CCTr) betreft de mate waarin effecten op tevredenheid met het dagelijks functioneren worden gemedieerd door proactieve coping. Tot slot liet het onderzoek naar Master Mind zien dat een transdiagnostische benadering in de SGGz haalbaar en acceptabel is. Deze benadering biedt een schaalbare strategie voor implementatie binnen de gespecialiseerde geestelijke gezondheidszorg.

Conclusie

Gezamenlijk bieden deze studies, uitgevoerd binnen de hoogspecialistische patiëntenzorg, waardevolle inzichten in de relevantie en behandelbaarheid van cognitieve verstoringen bij psychopathologie, in het bijzonder voor patiënten met alcoholgerelateerde cognitieve stoornissen of het syndroom van Korsakov.

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Judith, wat was het fijn en inspirerend om met je samen te werken in de staf-convent-jaren. En zo goed dat jij nu ook van start gaat als promovenda, we houden contact!

Mijn zo fijne KNP12 intervisie groep, daar waar het hele project begon. Climmy (ja daar gaan we!), Niki, Ineke, Nina, Rhody, Kim, Lydia, Thelma en Susan, bedankt voor de support, gezellige congressen en alle leerzame contacten samen!

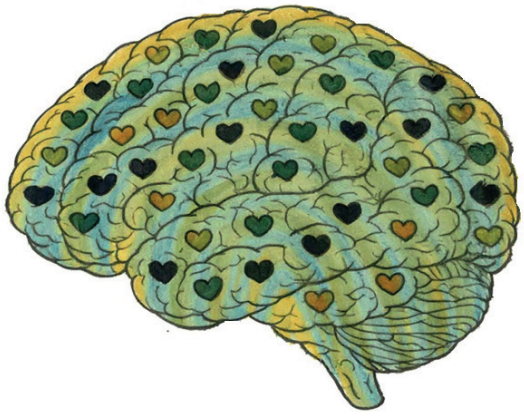
Dan het thuisfront. De Rythovius dames, Mieke, Dorieke, Lenka, Carla, Ilse, Marijke, Annemarie en Anneke. Jemig wat gaan we al lang terug samen, zo waardevol, laten we de ruimte voor elkaar blijven vinden! Mieke, dankjewel voor al je tips en steun! Jij hebt deze klus al succesvol geklaard en ik hoop dat ik iets van je rust over kan nemen. Anneke, Kardesh, dat er nog veel moois voor ons in verschiet mag liggen. De Meissies uit Nijmegen, lieve Karin, Annemie, Sarah en Eva. Altijd garant voor *instant* goede gesprekken én de slappe lach, wat wil je nou nog meer. Ik ben

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Curriculum Vitae

Anke Loijen werd op 15 april 1983 geboren te Eindhoven en groeide op in Eersel. Nadat zij in 2001 haar gymnasiumdiploma behaalde aan het Rythovius college te Eersel, startte ze met haar studie psychologie aan de Radboud Universiteit Nijmegen. Vanuit haar bijzondere interesse in de relatie tussen hersenen en gedrag koos zij binnen deze opleiding voor de afstudeerrichting Neuro- en Revalidatiepsychologie. Haar stage en afstudeerscriptie volbracht ze binnen revalidatiecentrum Groot Klimmendaal te Arnhem. Na afronding van haar opleiding in 2005 werkte ze als psycholoog in de revalidatie waarna ze in 2006 de overstap maakte naar de psychiatrie, bij Julianaoord te Laren (nu GGz Centraal). Hier deed zij ervaring op in de multidisciplinaire zorg voor mensen met neurocognitieve stoornissen ten gevolge van ernstig psychisch lijden en/ of alcoholgebruik, waaronder het syndroom van Korsakov. In 2009 startte zij met de GZ-opleiding, eveneens bij Julianaoord en de afdeling Stemming en Angststoornissen, Rembrandthof (GGz Centraal). Eenmaal gezondheidszorgpsycholoog (2011) oriënteerde zij zich direct op de praktijkopleidingsplaatsen tot klinisch neuropsycholoog en zo kwam ze uit bij het Topklinisch Centrum voor Neuropsychiatrie, Vincent van Gogh instituut te Venray. In 2012 startte ze met de opleiding tot specialist klinische neuropsychologie aldaar en bij het Topklinisch Centrum voor Korsakov. Na afronding van haar opleiding tot klinisch neuropsycholoog (2016) vervolgde zij haar klinische werkzaamheden binnen beide centra en zette zij haar wetenschappelijk onderzoek voort bij het Centrum voor Korsakov en als buitenpromovenda bij het Donders Institute for Brain, Cognition and Behaviour, Radboud Universiteit Nijmegen. Vanaf 2018 werkt zij volledig binnen de kliniek en poliklinieken van het Centrum voor Neuropsychiatrie. Aldaar zet zij zich in voor de (hoogspecialistische en bovenregionale) zorg voor mensen met zeldzame (genetische) aandoeningen en complexe, persisterende (neuro)psychiatrische problematiek in alle levensfasen. Ook binnen beleid en management is zij actief. Van 2018 tot 2023 was Anke voorzitter van de vakgroep psychologen binnen Vincent van Gogh en was zij betrokken bij de oprichting van het Stafconvent. Van 2020 tot 2022 vervulde zij de rol van (vice)voorzitter van dit advies- en inspraakorgaan.

Sinds 2026 maakt zij onderdeel uit van het praktijkopleidersteam klinische neuropsychologie binnen het opleidingsconsortium te Venray en verzorgt zij onderwijs binnen de specialistische opleidingen tot psychologisch specialist. Na afronding van haar proefschrift zal ze haar wetenschappelijk onderzoek naar behandelmogelijkheden bij cognitieve verstoringen gerelateerd aan psychopathologie verder voortzetten.

Anke woont in 's-Hertogenbosch met haar man en hun twee dochters.

Anke Loijen was born on April 15, 1983, in Eindhoven and grew up in Eersel. After completing the Gymnasium in 2001 at the Rythovius College in Eersel, she began her studies in psychology at Radboud University Nijmegen. Driven by her particular interest in the relationship between the brain and behavior, she chose to specialize in Neuro- and Rehabilitation Psychology. She completed her internship and thesis at the Groot Klimmendaal Rehabilitation Centre in Arnhem. After graduating in 2005, she worked as a psychologist in rehabilitation before transitioning to psychiatry in 2006 at Julianaoord in Laren (now GGz Centraal). There, she gained experience in multidisciplinary care for people with neurocognitive disorders resulting from severe mental disorders and/or alcohol use, including Korsakoff's syndrome. In 2009, she started the mental health psychology training program, also at Julianaoord and the 'Mood and Anxiety Disorders' department at Rembrandthof (GGz Centraal). Once she became a healthcare psychologist (2011), she immediately began exploring placements for clinical training to become a clinical neuropsychologist, which led her to the Centre of Excellence for Neuropsychiatry, Vincent van Gogh Institute in Venray. In 2012. Here she began her training as a specialist in clinical neuropsychology as well as at the Centre of Excellence for Korsakoff and Alcohol-Related Cognitive Disorders. After completing her training as a clinical neuropsychologist (2016), she continued her clinical work at both centres and pursued her scientific research at the Korsakov Centre and as an external Ph.D. candidate at the Donders Institute for Brain, Cognition, and Behavior at Radboud University Nijmegen. Since 2018, she has been working fully in the inpatient and outpatient clinics of the Centre for Neuropsychiatry. There, she is dedicated to providing (highly specialized and national) care for people with rare (genetic) disorders and complex, persistent (neuro)psychiatric conditions at all stages of life. She is also active in policy and management. From 2018 to 2023, Anke served as chair of the psychologists' professional group at Vincent van Gogh and was involved in the establishment of the Staff Council. From 2020 to 2022, she served as (vice)chair of this advisory board.

Since 2026, she is one of the educational supervisors of clinical neuropsychology within the psychological postgraduate consortium in Venray and has been involved in teaching within training programs for psychological specialists. After completing her dissertation, she will continue her scientific research, focusing on treatment options for cognitive impairments associated with psychopathology.

Anke lives in 's-Hertogenbosch with her husband and her they have two daughters.

Research Data Management

This thesis was conducted as an external PhD research project at the Centre of Excellence for Korsakoff and Alcohol-Related Cognitive Disorders at the Vincent van Gogh Institute for Psychiatry in Venray, the Netherlands, in collaboration with the Donders Institute for Brain, Cognition and Behaviour.

The research was conducted in accordance with the relevant legal and ethical guidelines, and the data management adhered to the FAIR principles (Findable, Accessible, Interoperable, Reusable; doi.org/10.1038/sdata.2016.18). The sections below detail how these principles were implemented.

Ethics

This thesis is based on research involving human subjects conducted in accordance with the Declaration of Helsinki. The institutional protocols of the Vincent van Gogh Institute for Psychiatry were strictly adhered to, and the studies in Chapters 3, 4 and 5 were performed within the context of standard clinical care at the Centre of Excellence for Neuropsychiatry (Chapter 3) and the Centre of Excellence for Korsakoff (Chapters 4 and 5). These studies were approved by the Vincent van Gogh Institutional Review Board (CWOP Nr. 2018.00.18 & Nr. U12.054).

Funding

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Findable and accessible

Anonymised data from all empirical chapters is stored locally on the internal research database of the Vincent van Gogh Institute for Psychiatry (on the project/network drive of the local server). The data were accessible only to the contributing authors and will be preserved for at least 10 years. Paper-based informed consent for the anonymous use of data was obtained in accordance with institutional procedures, and the signed forms are archived at the Centres of Excellence for Korsakoff and Neuropsychiatry. All neuropsychological assessment forms are likewise securely stored at the centres in accordance with institutional protocols.

The data cannot be shared in a public repository due to specific personal information. Furthermore, participants were not asked to consent to the anonymous publication of their data at the time of providing informed consent. The data can be primarily accessed by, and requested at, the first author.

Interoperable and Reusable

Raw data are retained in long-term, accessible formats (.sav, .csv) to ensure future usability. Detailed descriptions of the experimental procedures can be found in the associated publications.

Privacy

The privacy of the participants was guaranteed by the use of personal identification codes. Only the principal investigator had access to the document linking these codes with identification numbers, in accordance with internal privacy protocols. All materials are archived at the Centres of Excellence for Korsakoff and Neuropsychiatry at the Vincent van Gogh Institute for Psychiatry, Venray the Netherlands.

Donders Graduate School

For a successful research Institute, it is vital to train the next generation of scientists. To achieve this goal, the Donders Institute for Brain, Cognition and Behaviour established the Donders Graduate School in 2009. The mission of the Donders Graduate School is to guide our graduates to become skilled academics who are equipped for a wide range of professions. To achieve this, we do our utmost to ensure that our PhD candidates receive support and supervision of the highest quality.

Since 2009, the Donders Graduate School has grown into a vibrant community of highly talented national and international PhD candidates, with over 500 PhD candidates enrolled. Their backgrounds cover a wide range of disciplines, from physics to psychology, medicine to psycholinguistics, and biology to artificial intelligence. Similarly, their interdisciplinary research covers genetic, molecular, and cellular processes at one end and computational, system-level neuroscience with cognitive and behavioural analysis at the other end. We ask all PhD candidates within the Donders Graduate School to publish their PhD thesis in de Donders Thesis Series. This series currently includes over 600 PhD theses from our PhD graduates and thereby provides a comprehensive overview of the diverse types of research performed at the Donders Institute. A complete overview of the Donders Thesis Series can be found on our website: https://www.ru.nl/donders/donders-series

The Donders Graduate School tracks the careers of our PhD graduates carefully. In general, the PhD graduates end up at high-quality positions in different sectors, for a complete overview see https://www.ru.nl/donders/destination-our-former-phd. A large proportion of our PhD alumni continue in academia (>50%). Most of them first work as a postdoc before growing into more senior research positions. They work at top institutes worldwide, such as University of Oxford, University of Cambridge, Stanford University, Princeton University, UCL London, MPI Leipzig, Karolinska Institute, UC Berkeley, EPFL Lausanne, and many others. In addition, a large group of PhD graduates continue in clinical positions, sometimes combining it with academic research. Clinical positions can be divided into medical doctors, for instance, in genetics, geriatrics, psychiatry, or neurology, and in psychologists, for instance as healthcare psychologist, clinical neuropsychologist, or clinical psychologist. Furthermore, there are PhD graduates who continue to work as researchers outside academia, for instance at non-profit or government organizations, or in pharmaceutical companies. There are also PhD graduates who work in education, such as teachers in high school, or as lecturers in higher education. Others continue in a wide range of positions, such as policy advisors, project managers, consultants, data scientists, web- or software developers, business owners, regulatory affairs specialists, engineers, managers,

or IT architects. As such, the career paths of Donders PhD graduates span a broad range of sectors and professions, but the common factor is that they almost all have become successful professionals.

For more information on the Donders Graduate School, as well as past and upcoming defences please visit: **http://www.ru.nl/donders/graduate-school/phd/**


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