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Review

Biased approach-avoidance tendencies in psychopathology: A systematic review of their assessment and modification

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HIGHLIGHTS

- Biased approach-avoidance tendencies are a relevant feature of mental disorders.
- Approach bias for substance-related stimuli is present and trainable in addiction.
- In depression there is loss of positivity bias which can be regained with training.
- Avoidance bias characterizes anxiety, with little evidence for successful training.
- Future research should increase statistical power and comparability of designs.

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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.

1. 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

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(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; Marteau, Hollands, & Fletcher, 2012; Mathews & MacLeod, 2005).

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 15 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; Watson, De Wit, Hommel, & Wiers, 2012; Wiers, Gladwin, et al., 2013), 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 et al., 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.

2. Methods

2.1. 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, 2000) 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 et al. (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.

2.2. 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, and the PRISMA Group, 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.

2.3. 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.

2.4. 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 recategorizing 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.

3. Results

3.1. 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 Fig. 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.

3.2. Substance-related disorders

3.2.1. 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, Field, Healy, & Mogg, 2008). However, the ApB may be stronger in low-dependency smokers than in moderate dependency (Mogg, Field, & Bradley, 2005; Watson et al., 2012; but see Elfeddali, de Vries, Bolman, Pronk, & Wiers, 2016, for contrasting results). The relation between dependence and bias strength is possibly mediated by genetic vulnerability for a decreased natural reward

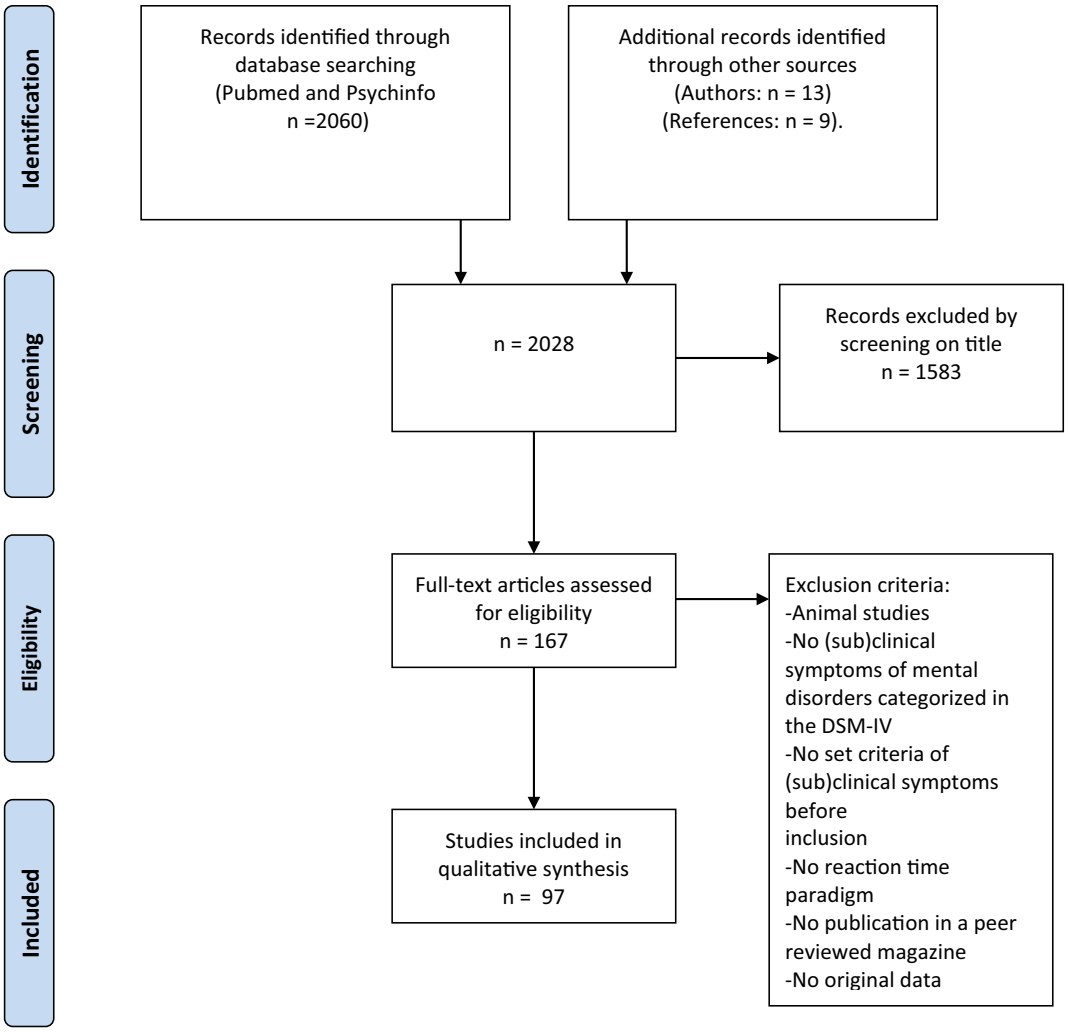

Fig. 1. Flowchart.

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]	Task and materials[f]	Clinical measures/outcomes
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	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.
	Substance-related Disorders							
2	Nicotine use disorder							
2.1	Mogg, Bradley, Field, and De Houwer (2003)	1	18 smokers 21non-smokers	FTND 4.5 (0)	B	B	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.
2.2	Bradley, Field, Mogg, and De Houwer (2004)	1	20 smokers 18 non-smokers	FTND 3.5 (1.6)	C	A	1, 3 (smoking-related/ matched control stimuli)	ApB for smokers. No bias present in non-smokers. Corr. with clinical measures N/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	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.
2.4	Bradley et al. (2008)	1	22 smokers 23 non-smokers	FTND 3.1 (1.4)	B	C	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.
2.5	Wiers, Kühn, et al. (2013)	1	24 smokers 20ex-smokers 20 non smokers	FTND 5.08 (1.18), (4(1.41))	A	B	2, 4, 5 (smoking/neutral stimuli)	ApB smokers > non-smokers/ex-smokers for smoking-related stimuli. Corr. of ApB with urge, not with FTND.
2.6	Machulska et al. (2015)	1	90 smokers 49 non-smokers	FTND 3.38(2.3)	D	A	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
2.7	Elfeddali et al. (2016)	1	434 smokers	FTND 4.30 (2.33	X	X	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.
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	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.
2.9	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	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.
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, 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.
2.11	Kong et al. (2015)	3 (4/5 sessions)	Non-treatment seeking adolescents 21 Training +TAU 20 Sham + TAU	mFTQ0 .2.86 (1.35)	G	D	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.

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Table 1 (*continued*)

	Authors (year)	Study type[a]	N[b]	Symptom severity[c]	Control group[d]	Duration of abstinence[e]	Task and materials[f]	Clinical measures/outcomes
2.12	Wittekind et al. (2015)	3 (AAT pretest, unknown number of sessions; online training/control condition/waitlist, AAT post-test after 4 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 (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.
2.13	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, 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.
2.14	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, 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.
2.15	Wittekind, Lüdecke, and Cludius (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)	A	N/A	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
2.16	Wittekind, Reibert, et al. (2019)	3	105 smokers: 54 active training+TAU 51 sham training+TAU	FTND 5.4 (2.1) 5.7 (1.8)	A	N/A	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.
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	1, 3 (cannabis/matched neutral stimuli)	ApB for cannabis in cannabis users for cannabis-related stimuli, no comparison with control stimuli.
3.2	Cousijn, Goudriaan, and Wiers (2011)	1	32 heavy cannabis users 39 non-users	MINICUDIT 12.4(5.8)	A	C	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.
3.3	Cousijn et al. (2012)	1	33 heavy cannabis users 36 low frequent users	CUDIT 12.4 (5.7) (0.0)	A	C	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 6 months. ApB activations in various fronto-limbic areas were more pronounced with increased lifetime cannabis use.
3.4	Cousijn et al. (2015)	1	57 treatment seeking adolescents	CUDIT 21.8 (8.3; 5–39)	N/A	N/A	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 6 month follow-up.
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	1,3; 2, 4 (cannabis/ neutral stimuli)	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.
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	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.

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Table 1 (*continued*)

	Authors (year)	Study type[a]	N[b]	Symptom severity[c]	Control group[d]	Duration of abstinence[e]	Task and materials[f]	Clinical measures/outcomes
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	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.
3.8	Sherman et al. (2018)	3 (pre- post training plus 2 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	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.
4	Alcohol Use Disorder (AUD)							
4.1	Wiers 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	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.
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	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.
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	2, 4, 5 (alcohol/non-alcohol drinks)	No interaction effect. Neither IQ level or AUD severity was related with AA tendencies.
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	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.
4.5	Spruyt et al. (2013)	1	40 AUD 40 HC	DSM-IV criteria AUD (after clinical detox)	A	D	1, 3 (alcohol/matched neutral stimuli)	AvB in AUD group, ApB in control group. AvB was related to relapse measures
4.6	Wiers et al. (2014)	1	20 AUD 17 HC	AUD (inpatients) AUDIT 27.05 (7.82) 2.82 (1.67)	A	D	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.
4.7	Ernst et al. (2014)	1	21 AUD 21 HC	DSM-IV criteria, AUD (inpatients)	A, HC AUDIT 3.86(2.29):	D	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.
4.8	Snelleman et al. (2015)	1	50	DSM-IV criteria AUD (Outpatients receiving treatment)	A	D	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.
4.9	Wiers et al. (2017)**	1	30 AUD 15 HC	Inpatients DSM-IV criteria AUD	A	A-E	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.

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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	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.
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	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.
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	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.
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	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.
4.14	Beraha et al. (2018)	2 Mood induction at t1 and t2. Between t1 and t2 4 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	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.
4.15	Wiers 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	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.
4.16	Wiers et al. (2011)	3 (four sessions)	102 active training 98 sham training	DSM-IV criteria AUD (inpatients) AUDIT 24.(17.7)	G	E	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.
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	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.
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	2, 4, 5 (alcohol/soft drink stimuli)	Less relapse at 1-year FU after active training compared to both control groups.
4.19	Wiers, Stelzel, et al. (2015)	3 (six session)	15 active training 17 sham training	Inpatients DSM-IV criteria AUD	G (active/ sham)	D/E	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.
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 (experi-mental/ control)	N/A	2, 4, 5 (alcohol/water stimuli)	No sign. Interaction; no bias at pretest.

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Table 1 (*continued*)

	Authors (year)	Study type[a]	N[b]	Symptom severity[c]	Control group[d]	Duration of abstinence[e]	Task and materials[f]	Clinical measures/outcomes
4.21	Wiers, Houben, 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	Mouse-AAT, 3, 5/4,5 (alcohol/soft drinks stimuli)	No sign. Interaction for any condition. Decrease in drinking quantity, but no difference between active and sham training group.
4.22	Wiers, Ludwig, et al. (2015)***	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	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 behavioral alcohol ApB in the active training group.
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	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.
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	2, 4, 5 (alcohol/soft drinks stimuli)	Main effect of time, no tDCS enhancement of training effects.
4.25	Di Lemma and Field (2017)	3 (AA pretest, one training session, AA posttest,	120, randomization over two intervention types, sham per intervention N per group N/A	heavy drinkers >24 or 21 units per week.	G (experi-mental/control training)	N/A	2, 4, 5 (alcohol/matched control stimuli)	Active training reduced ApB no more than sham training, but reduced alcohol intake after active training.
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.	2 (56 cm long lever), 3, 30 min break (heroin-related/vehicles stimuli)	ApB for heroin in heroin user group.
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	2, 3 (happiness, sadness, anger, fear, disgust, neutral expression)	No interaction, generally slower RTs in patient group.
6.2	de la Asuncion, Docx, Sabbe, Morrens, and de Bruijn (2015)	1	37 patients with schizophrenia 29 HC	DSM-IV criteria schizophrenia	A	X	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.
6.3	Reddy et al. (2016)	1	92 patients with schizophrenia 68 HC	Ouptatients DSM-IV criteria schizophrenia	C	X	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.
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	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.

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7.2	Derntl et al. (2011)	11	15 depression 15 HC	Inpatients DSM IV criteria major depression BDI 25.6 (6.05)	A	X	2, 4 compatible for fMRI (happy, neutral, angry expressions)	No interactions.
7.3	Radke et al. (2014)	11	30 depression 20 HC	Patients DSM-IV criteria depression BDI 27.0 (11.5),	A	X	2, 3, 5 (angry, happy, neutral expressions with indirect/direct gaze)	HCs approached happy faces more quickly than angry faces, depressed patients not.
7.4	Bartoszek and 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	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.
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	2, 4, 5 (angry, happy, neutral, disgusted expressions, checkerboards)	No sign. Group differences.
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	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.
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	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.
7.8	Vrijsen et al. (2018)	3 (four sessions, active/control condition)	121	DSM-IV criteria depression	G (active/ control)	X	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.
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	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 mediations.

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	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	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.
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	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.
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)	2, 4 (skin irregularities/ healthy skin/control stimuli)	ApB in SPD, no bias in HCs.
8.4	Cludius et al. (2017)	1	63 OCD 30 HC	DSM-IV criteria OCD Y-BOCS 22.25 (6.32)	A	X	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
8.5	Maas et al. (2018a)	1	54 hair pulling disorder (HPD) (pretest)	Outpatients DSM-IV criteria HPD	X	(Before AAT invitation to touch their hair.)	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.
8.6	Maas et al. (2018b)	3 (six sessions, active condition, sham condition)	HPD: 25 active condition 27 sham condition	Outpatients DSM-IV criteria HPD	G	(Before AAT invitation to touch their hair.)	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.
9	Posttraumatic Stress Disorder (PTSD)							
9.1	Fleurkens et al. (2014)	1	15 PTSD (sexual trauma) 23 HC	DSM-V criteria PTSD	A	X	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.
10	Specific Phobia (Spider Phobia, SP)							
10.1	Rinck and Becker (2007) (Study 1)	1	25 SP 22 HC	DSM-IV criteria A t/m D	A	X	2, 3, 5 (spiders/neutral stimuli)	AvB for spiders in SPs, no bias in HCs.
10.2	Rinck and Becker (2007) (Study 3)	1	21 SP 24 HC	DSM-IV criteria A t/m D	A	X	2, 4, 5 (spiders/neutral pictures)	Compared to HCs, SFs showed AvB for spiders
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	2, 4, 5 (spiders/butterflies stimuli)	AvB for spiders decreased after CBT, this reduction was positively correlated with reduction in subjective spider fear.
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	2, 3 (angry/happy/ neutral expressions/ puzzles)	HSA showed AvB for angry and smiling faces. HCs did not show any bias.
11.2	Lange et al., 2008	1	25 HSA 30 HC	LSAS 35,6 (7.1), ((9.0(2.6))	A	X	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.

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11.3	Roelofs et al., 2010	1	20 HSA 19 LSA	LSAS 56.1 (11.5) (15.1 (7.5))	A	X	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.
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	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.
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	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.
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	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.
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	2, 4, 5 (happy, angry, and neutral facial expressions)	Significant interaction; significant increase of approach tendencies towards angry faces after testosterone administration in SAD participants.
11.8	Taylor and 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	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.
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	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.
12	Seksual Disorder Paraphilias							
	Weidacker et al. (2018)	1	38 pedophiles 27 controls	ICD-10 criteria for pedophilia	A	X	2, 5 (women, men, (pre-)pubescent boys, (pre-)pubescent girls)	ApB for sexual preferences
13	Eating Disorders							
13.1	Veenstra and de Jong (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 eating as a covariate	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.

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13.2	Khan and Petróczi (2015)	1 (2)	54 ED 41 'at-risk' 23 HC	Diagnosed of Eating disorder EDE-Q > 4	B unbalanced ethnic distribution	X	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.
13.3	Paslakis et al. (2016)	1	41 AN 42 HC	Inpatients DSM 5 criteria AN	A	X (≤ 4 h meal before experi-ment)	Mouse-AAT, 4, 5 (high/ low calorie food stimuli)	HCs showed an ApB for food in general, this effect was not present in AN.
13.4	Paslakis et al. (2017)	1	24 obesity + BED 32 obesity 25 HC	In- and outpattients DSM-5 criteria of BED	B	X	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.
13.5	Leins et al. (2018)	1	55 disordered eating behaviour 45 without disordered eating behaviour	>2.3 on EDE-Q	A	X	2, 4, 5 (thin/normal weight stimuli)	Faster pushing than pulling independent of group or picture content.
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	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.
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	X	X	2, 4, 5 (food/marched non-food stimuli)	ApB at baseline, AvB after training. Reduced craving, improved eating habits. No control group.
13.8	Brockmeyer et al. (2019)	3	56 BN/BED 28 active training 28 sham training	EDE-Q 2.5 (1.17) DSM IV criteria (SCID)	A	B	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.
	Impulse Control Disorders							
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 10.0 (3.3)	C	N/A	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.
14.2	Wittekind, Bierbrodt, et al. (2019)	3	141 gamblers 66 active condition 65 sham condition	10.3 (3.3)	A	N/A	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.
	Somatoform Disorders							
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	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.
	Personality Disorders							
16	Psychopathy							
16.1	von Borries et al. (2012)	1	17 Psychopathy 15 HC	Inpatients PCL-r ≥26	N/A	X	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.
17	Borderline personality disorder							
17.1	Kobeleva et al. (2014)	1	25 BPD 25 HC	Inpatients DSM criteria BPD	B	X	2, 4 (sad/anger/fear/ neutral expressions)	No sign. Interaction.

(*continued on next page*)

Table 1 (*continued*)

	Authors (year)	Study type[a]	N[b]	Symptom severity[c]	Control group[d]	Duration of abstinence[e]	Task and materials[f]	Clinical measures/outcomes
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	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.

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);

* 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, Ludwig, et al., 2015, Wiers, Stelzel, et al., 2015).

*** Pre-training neuroimaging data of the first 20 patients were reported previously in Wiers et al. (2014) and effects of CBM on a passive alcohol cue reactivity task were reported in Wiers, Stelzel, et al. (2015).

[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.

[d] 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.

[e] Abstinence: A ≤1 h before the experiment abstinent, B = 1–5 h, C = 5–24 h/day of testing, D = ≤ 1 month, E = 1 month to 1 year, F = ≤ 10 years, G = ≥ 10 years, X = not relevant.

[f] Task and Materials: 1 = SRC, 2 = AAT, 3 = Relevant feature, 4 = Irrelevant feature, 5 = Zoom function, (Stimulus categories).

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, Zlomuzica, Adolph, Rinck, and Margraf (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 (Wiers, Kühn, 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, Havermans, Geschwind, van den Hout, & Jansen, 2007; Watson et al., 2012). These priming effects are clinically relevant because an increased approach bias may lower the threshold for smoking.

Finally, six Type 3 modification studies were found for nicotine use disorder. In a training study including adolescents (Kong et al., 2015), no difference between the active training group and the sham training group was present, both groups showed a decreased approach bias after training. Wittekind, Feist, Schneider, Moritz, and Fritzsche (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 4 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, and Cludius, 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, Zlomuzica, Rinck, Assion, and Margraf (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 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.

3.2.2. 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, van Benthem, van der Schee, & Spijkerman, 2015). Wolf, Salemink, and Wiers (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, Eastwood, Bradley, and Mogg (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 6 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, Snoek, and Wiers (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, Baker, Squeglia, & McRae-Clark, 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.

3.2.3. 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, Rinck, Dictus, & van den Wildenberg, 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, Dickson, Roper, & Field, 2012), whereas severity of AUD itself was not found to be related (van Duijvenbode, Didden, Voogd, Korzilius, & Engels, 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, Schoenmakers, and van de Mheen (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, Salemink, Krediet, & Wiers, 2018; Mitchell, Arcuni, Weinstein, & Woolley, 2016; Schoenmakers, Wiers, & Field, 2008). Neither did Houben, Havermans, Nederkoorn, and Jansen (2012) find an effect of a Go/NoGo training on AA tendencies. Finally, Cousijn, Luijten, and Wiers (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, Wiers, Becker, & Lindenmeyer, 2018; Wiers, Eberl, Rinck, Becker, & Lindenmeyer, 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 (6–12) will yield better results. The fMRI studies by C. Wiers et al. (2014; Wiers, Ludwig, et al., 2015, Wiers, Stelzel, et al., 2015) 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, Houben, et al., 2015) might not be as effective, and neuromodulation does not seem to strengthen the training effect (den Uyl, Gladwin, Rinck, Lindenmeyer, & Wiers, 2017).

3.2.4. 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.

3.3. 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, Güths, André, Müller, & de Bruijn, 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).

3.4. Anxiety-related disorders

3.4.1. 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, Kuckertz, & Amir, 2010). A sample with clinical symptom levels of the checking-related OCD symptomatology was faster at pulling than pushing checking-related stimuli (Cludius, Külz, Landmann, Moritz, & Wittekind, 2017), indicative of an ApB in this subtype. Amir, Kuckertz, and Najmi (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, Keijsers, & Rinck, 2012). 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, Keijsers, Rinck, & Becker, 2018a). 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, Keijsers, Rinck, & Becker, 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.

3.4.2. Posttraumatic stress disorder (PTSD)

Only one Type 1 study (Fleurkens, Rinck, & van Minnen, 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.

3.4.3. Specific phobias

All 3 included studies focused on spider phobia (Rinck & Becker, 2007, Studies 1 and 3; Reinecke, Soltau, Hoyer, Becker, & Rinck, 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.

3.4.4. 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, Keijsers, Becker, & Rinck, 2008). Another study (Voncken, Rinck, Deckers, & Lange, 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, Rinck, and Becker (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, Spinhoven, & Roelofs, 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 et al. (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.

3.5. 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, Kuhn, Grunert, & Erim, 2017) and for two samples with "disordered eating behavior" (Khan and Petróczi, 2015; Leins, Waldorf, Kollei, Rinck, & Steins-Loeber, 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, de Jong, & Roefs, 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, Hahn, Reetz, Schmidt, and Friederich (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.

3.6. Sexual Disorders

3.6.1. 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.

3.7. Impulse control disorders

3.7.1. 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 6-months follow-up. Wittekind 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.

3.8. 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, Pfersmann, and Derntl (2015) found no specific pathology-related AA tendencies, however, they did not use relative bias scores. Finally, Reddy, Green, Wynn, Rinck, and Horan (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.

3.9. Somatoform disorders

3.9.1. Non-epileptic seizures

In patients diagnosed with non-epileptic seizures, an AvB for angry

faces was found in a relevant-feature task (Bakvis, Spinhoven, Zitman, & Roelofs, 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.

3.10. Personality disorders

3.10.1. 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.

3.10.2. 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.

3.11. Delirium, dementia, amnestic, and other cognitive disorders

3.11.1. 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.

4. 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.

4.1. 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).

4.2. 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.

4.3. 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.

4.4. 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.

4.5. 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 6 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.

4.6. 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 (Kersbergen, Woud, & Field, 2015; Krieglmeyer & Deutsch, 2010; 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.

4.7. 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.

4.8. 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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Contributors

All authors designed the study and protocol. Authors AL and JV conducted literature searches, AL was responsible for the first draft and results table which was checked by JV and MR. JV and MR commented on the first drafts and EB and JE commented on all subsequent versions. All authors contributed to and have approved the final manuscript.

Declaration of competing interest

There are no conflicts of interest.

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