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Avoidance in Anorexia Nervosa: Towards a research agenda

Hanna Melles [a,1], Michelle Spix [a,1], Anita Jansen [a,*]

[a] Clinical Psychological Science, Maastricht University, the Netherlands

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ABSTRACT

Anorexia Nervosa is a severe and disabling mental disorder and a huge challenge to treat. Intense fears of e.g., food, eating, weight gain and social evaluation are core features of anorexia nervosa and obstacles during treatment. The perceived threats trigger avoidance and safety behaviors like highly restrictive eating, strict eating rules, vomiting and body checking, to minimize feared outcomes. The role of avoidance in anorexia nervosa is however hardly studied experimentally. In the present article, the focus is on a new transdiagnostic research agenda featuring both basic and clinical experimental research into avoidance as a most important mechanism maintaining the eating disorder. Avoidance learning and the generalization of learned avoidance behaviors are discussed, as well as safety behaviors and the need for inhibitory learning as a treatment target during exposure therapy.

1. Introduction

Anorexia nervosa is a severe and disabling eating disorder that carries a high disease burden for affected individuals, their relatives and the society [100]. The seriousness of the disorder is reflected in long illness duration (over 20 years for more than half of the patients; [32]) and high mortality rates [3, 31]. Meanwhile, only about one third of the people suffering from anorexia nervosa do seek professional help [50]. Treatment of the patients who do seek help is a huge challenge; dropout rates usually are high (~20–40%; [24]) and treatment outcomes are only modest, most patients do not recover (>50%). In the long run, specialized treatments are not more effective than treatments as usual [81, 123]. Developing effective treatments for anorexia nervosa thus is a necessary and challenging endeavor.

The disappointing treatment outcomes are perhaps not that surprising considering our scant knowledge about key processes that are crucial to clinical improvement [52]. We also do know little to nothing about the mechanisms that keep the disorder going: what mechanisms drive anorexia nervosa patients to defend low to extremely low body weights, their eagerness to persistently lose weight and their striving for an ever-thinner body? This lack of understanding the maintaining mechanisms and the mechanisms of change, hampers the development of interventions that could be fine-tuned to target these mechanisms and, therefore, the development of more effective treatments for anorexia nervosa [38, 52].

A promising development in the science of eating disorders is the emergence of fear models and the identification of fear as a possible treatment target (e.g., [16, 48, 111], 2011, 2012, 2014). Fear was recognized as a core symptom of anorexia nervosa decades ago (e.g., [22, 42, 43]) and more recent findings show that eating disorders and anxiety disorders frequently co-occur: studies show about 65% of eating disorder patients meeting the criteria of a comorbid anxiety disorder, with social anxiety disorder being diagnosed most often [55, 67, 85, 113, 114]. Generally, fears of food (e.g., feeling uncomfortable or tense in the presence of high caloric food items or fears of foods of unknown composition), eating (e.g., being afraid of eating with others), unpleasant physical sensations like feeling satiated, loss of control, and fears of body shape and weight are omnipresent in anorexia nervosa (see [66], and [70], for detailed discussions of eating disorder related fears). Anorectic fears might additionally involve issues related to perfectionism, drive for thinness and social evaluation [48, 56, 62, 65, 69, 107]. These fears are supposed to be involved in both the maintenance and persistence of the disorder, for example, fear of negative social evaluation as well as fear of food predict drive for thinness [65, 67].

It is assumed that fears seriously impact the course of anorexia nervosa [13, 62, 95, 116] and predict treatment outcomes [14, 134]. The more anxious a patient is, the more severe the eating disorder and the worse the disorder prognosis [65, 81, 113]. Studies show that higher levels of pre-meal anxiety are associated with reduced calorie intake [110]. So, fear makes the anorexia nervosa worse and fear maintains the

* Corresponding author.
E-mail address: a.jansen@maastrichtuniversity.nl (A. Jansen).
[1] These authors contributed equally to this article and share the first authorship

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illness. Yet, despite increasing knowledge about the dynamics of fears in anorexia nervosa and its worsening effects, treatments have not yet progressed beyond a few promising preliminary studies to tackle fears (e.g., [16, 39, 68, 107, 108]) and surprisingly little basic research has been done into anorexia nervosa's fear dynamics. To really improve treatments and reduce relapse, we need to acquire better knowledge about the maintenance of core fears in anorexia nervosa.

Recent transdiagnostic theoretical accounts of anorexia nervosa point to a crucial role of fear-related learning processes in the origin and maintenance of the eating disorder (e.g., [16, 48, 49, 65, 80, 82, 99, 111], 2010, 2011; [112]). These models view food avoidance as the behavioral response to a classically conditioned association between food or eating cues and an aversive outcome (e.g., immediate weight gain, unpleasant physical sensations, feelings of guilt and shame; [49]). Fear-induced food avoidance (i.e., not eating) is maintained by negative reinforcement as the avoidance prevents feared aversive outcomes from occurring. Avoidance behaviors are defined as all kinds of behaviors that aim to downregulate unpleasant experiences through avoidance, suppression, distraction or control [20, 40, 57]. Clinical analogues are often called safety behaviors or safety aids: actions that one undertakes within a specific context to prevent or minimize a feared outcome, or to escape from it [40, 126].

In sum, maladaptive anorectic avoidance or safety behaviors are supposed to be critical contributors to the maintenance of the eating disorder psychopathology. Anorectic avoidance is a mechanism to mitigate anorectic fears. The avoidance behaviors do not only reduce fears, they may also help to achieve one's goals and therefore trigger rewards, like losing weight, feeling in control and a successful drive for thinness (see [104, 130]). In this article, we will focus on the role of fear for avoidance learning in anorexia nervosa. After a short theoretical introduction into avoidance learning, we will discuss how hypotheses about avoidance learning in anorexia nervosa can be studied in mechanistic laboratory experiments. The avoidance model offers new starting points for interventions to reduce avoidance or safety behaviors, and therefore fears. The conceptualization of core anorectic symptoms in terms of avoidance or safety behaviors enables to study whether and how we can tackle these illness maintaining mechanisms. This translation from laboratory models to clinical research and treatment will be made in the second part of this article.

2. Avoidance learning

The most striking and destructive avoidance behavior of patients with anorexia nervosa involves the avoidance of eating enough calories, i.e., the excessively restrictive eating. Restrictive eating reduces fears in anorexia nervosa [73, 82], but this fear reduction usually is short-term. Central anorectic fears relate to actual weight gain, unpleasant physical sensations after eating, and others judging them for gaining weight. Relatedly, patients with anorexia nervosa often hold the disordered beliefs that relatively small weight gains will culminate in uncontrollable and endless weight gain: *"If I gain 1 pound, I will become obese"* [65, 80]. While the avoidance of threatening stimuli or situations is adaptive when objectively dangerous stimuli or situations are involved, avoidance in the absence of real threats is dysfunctional [59, 60]. Anxious individuals disproportionately use avoidance strategies (for a more detailed discussion see [89]) but the continuous avoidance of harmless stimuli prevents them from experiencing that the original stimulus or situation is safe, or at least not as dangerous or harmful as expected. The limited opportunities to encounter evidence contradicting the dysfunctional threat beliefs maintain the anxiety [18, 76, 79, 129]. The continuous avoidance of eating enough calories prevents anorexia nervosa patients from the recognition that adequate eating does not by definition result in the expected uncontrollable and infinite weight gain, thereby preserving high anxiety levels.

In addition, avoided situations are gradually evaluated as increasingly dangerous because people use their own behavior as information; 'If I avoid, there must be danger' [37, 127, 133]. Likewise, inferences such as 'If I avoid eating these foods, then they must be bad for me' will increase threat perception and eventually result in greater anxiety and therefore food restriction.

Also, avoidance behavior itself can turn into signals of threat over time and may, therefore, increase one's fear in the long-term [129]. Learning that an aversive event occurs if the avoidance behavior is not performed, leads to the avoidance behaviors concurrently being associated with both safety and threat [60, 129]. Consequently, avoidance behaviors support the maintenance of mental disorders, including anorexia nervosa, and they negatively affect the outcome of treatment interventions [18, 76, 79, 129].

It has long been known that maladaptive avoidance behaviors are key characteristics of several mental disorders, like anxiety disorders and obsessive-compulsive disorders. Therefore, avoidance learning was predominantly studied in the context of these disorders in the past decades. It has been suggested that both Pavlovian (or classical) and instrumental learning processes play a role in the development and maintenance of avoidance behaviors [60, 64, 75, 90]. During the initial Pavlovian learning, a neutral stimulus (conditional stimulus or CS) becomes associated with an aversive event (unconditional stimulus or US) and thereby, turns into a predictor of threat. Eventually, merely the presence of the CS, or its representation, triggers aversive responding, like heightened bodily arousal, feelings of fear, and avoidance tendencies. Whether these avoidance tendencies are then expressed as overt behavior and persist over time, depends on instrumental learning processes.

Avoidance and fear do not perfectly align and can also occur independently [2, 75, 88, 90, 92]. During instrumental learning, individuals acquire knowledge about the consequences of their behavior: the avoidance of the aversive event (US) is negatively reinforced by fear reduction, thereby increasing the possibility that the avoidance behavior is performed again in the future. Fear reduction due to the omission of the US, an escape from the CS, or the presence of stimuli that signal safety might all reinforce the execution of avoidance behaviors [60, 64].

For anorexia nervosa, eating high-calorie foods involves, for example, the terrifying risk of uncontrollable weight gain, whereas avoiding the eating of aversive calories reduces both the chances of uncontrollable weight gain, as well as fear caused by the anticipation of weight gain. So, the anorectic avoidance of aversive calories is negatively reinforced by, amongst others, fear reduction. Besides the negative reinforcement (removing aversive consequences), anorectic avoidance behaviors might also be maintained by positive reinforcement (adding rewarding consequences). Food avoidance is (at least initially) followed by a range of rewarding consequences such as weight loss, compliments from significant others, an elevated sense of control and increased self-esteem (e.g., [17, 104, 130]). Moreover, food avoidance helps patients with anorexia nervosa to achieve their goals (a low body weight) and can provide them with a sense of self-determination [104]. In line with this, patients with anorexia nervosa show strong reward responses when viewing illness-compatible information, such as pictures of emaciated bodies or cues related to exercise (O'Hara, Campbell & Schmidt, 2015). Eventually, performing avoidance behaviors can become rewarding in itself [84, 130]. Thus, both positive and negative reinforcement play an important role in the acquisition and maintenance of food avoidance in AN.

3. Laboratory studies

Laboratory experiments with healthy participants can increase our understanding of involved mechanisms in the maintenance and change of a mental disorder [52]. A frequently used laboratory model for the acquisition and expression of avoidance behaviors consists of a Pavlovian and an instrumental learning task. In the Pavlovian conditioning task, a neutral stimulus (CS+, e.g., a geometrical shape) is repeatedly paired with an aversive outcome (US, e.g., a loud scream or

shock). Eventually, the presentation of the CS+ elicits conditioned responses (CR), like an increase in skin conductance, a potentiated startle response and/or increased subjective fearfulness ratings. Usually a second neutral stimulus, which is not paired with the US, is included in the task. Overtime, this stimulus becomes a conditioned safety signal (CS-). Accordingly, the CS- signals the absence of threat and elicits less arousal and fearfulness than the CS+. Therefore, the CS- is often used as a control condition to rule out non-associative explanations for behavior change (e.g., habituation and sensitization; see [23], p. 37 - 49).

In the following instrumental learning task participants can avoid the aversive US. For this, they need to perform an experimenter-defined response during CS presentation (e.g., a button press). Depending on the goal of the study, participants are informed about the nature of the required behavior (e.g., [33]) or they need to find this out themselves (e.g., [105]).

Additionally, an extinction phase, in which the CS+ is repeatedly presented without the US, can be included in the avoidance learning paradigm. This allows the researcher to investigate the influence of avoidance behaviors on the extinction process. While extinction normally leads to the formation of a new CS – noUS association and a reduced expression of acquired conditioned responses [74], this process can be hampered because of avoidance behaviors [18, 76, 79]. The experimental set-up works as a laboratory analogue for exposure therapy and might help to understand the detrimental impact that avoidance or safety behaviors can have on treatment outcome (e.g., [60, 126]).

Such an experimental paradigm may also serve to be useful in the study of food avoidance behaviors. However, an obvious difference between food avoidance and the avoidance of aversive stimuli, such as painful electrical shocks, is that healthy individuals usually perceive tasty high-caloric foods as rewarding [106]. In line with this, the prospect of eating tasty foods typically triggers approach behaviors in healthy participants [87], as well as a range of appetitive responses, such as increased salivation, appetite and cravings (e.g., [119–121, 131]). These differences in appreciation of high-calorie foods between anorexia nervosa patients and healthy controls will in all probability lead anorexia nervosa patients to avoid the food stimuli faster and more often than matched healthy controls, but what does this mean? Such a finding could indeed reflect a process that only applies to disorder-relevant stimuli such as tasty high-calorie foods, but it could as well be the result of a generally aberrant processing of appetitive and/or aversive stimuli. In line with this idea, patients with AN report a heightened sensitivity for punishment [35], elevated levels of anhedonia [8] and reduced sensation-seeking, which falls under the larger category of reward sensitivity [5]. Furthermore, patients with anorexia nervosa endorse more negative attitudes and beliefs towards intense emotional states (negative and positive) and therefore, might engage in more experiential avoidance or suppression [63, 96]. Moreover, ANs show blunted emotional responses not only to food cues but also food-unrelated positive stimuli [28, 36]. Consequently, thoughtfully selected control conditions are necessary, such as the inclusion of generally rewarding (e.g., money) and generally aversive stimuli (e.g., a loud scream or shock). The inclusion of such control conditions will indicate whether aberrant avoidance behaviors of anorexia nervosa patients are specific for food and eating or generalize to a broader range of appetitive and aversive stimuli.

Future studies include both anorexia nervosa subtypes and the other eating disorders bulimia nervosa and binge eating disorder as well, to allow for even more fine-grained conclusions. In addition to the study of avoidance processes in anorexia nervosa patients and other eating disorders, it could be helpful for the field to design a laboratory model for the learning and maintenance of food avoidance in healthy individuals (see e.g., [86]). Based on the previously outlined avoidance learning theory, we suggest that a combination of reward and punishment supposedly triggers food avoidance in a healthy student sample. Specifically, the avoidance of food intake should be rewarded (e.g., with a small monetary gain), while food consumption should be punished (e.g., by hearing an aversive sound). Once validated, this experimental model of anorexia nervosa could help researchers to find out how, why and when the avoidance of (initially) rewarding stimuli can arise in healthy people and how positive and negative reinforcement might shape anorectic-like avoidance behaviors.

4. Generalization of avoidance behaviors

Maladaptive avoidance might not only be determined by the initial acquisition of avoidance behaviors, but also the extent to which behaviors spread towards new cues and contexts. While avoidance can be useful and protective in situations of danger, the same behavior can become disabling when displayed under conditions of safety [98]. Excessive fear and avoidance generalization appear to be a key feature of anxiety disorders [26, 89] and might be equally important in the development of anorexia nervosa. Initially, patients with anorexia nervosa might eliminate certain high-caloric snacks, such as chocolate or crisps, from their diet. Over time, more and more food items e.g., bread or pasta, become forbidden foods. Eventually, only a narrow range of foods is consumed leading to underweight and malnutrition. Thus, excessive generalization of avoidance behaviors could explain the rigid and inflexible responding of patients with anorexia nervosa across various eating-related situations [45].

To assess generalization under controlled conditions, a laboratory analogue has been developed (e.g., [26, 98, 125]; for a detailed discussion of fear generalizations see [25]). For this, an additional generalization phase is added to the previously described Pavlovian and Instrumental learning task. In the generalization phase, participants are shown new stimuli that resemble the CS+ or CS- (generalization stimuli, GSs) and that are never followed by the US. Thus, avoidance behaviors during the GSs presentation are not adaptive as these stimuli do not predict threat. Often GSs are used that are graded in their resemblance to the CS+ and CS-. For example, a small and a large circle can be used as CSs with intermediately sized circles as GSs (e.g., [122]). By comparing avoidance responses for the GSs that strongly, medium-strongly and slightly match the CS+ and CS- the extent of generalization can be measured. Thereby, this laboratory task offers a way to quantify maladaptive avoidance generalization. Using this paradigm, it was shown that avoidance generalization can occur towards cues that perceptually [98, 125] or symbolically/conceptually [12, 27] resemble the originally feared and avoided stimulus. Laboratory studies demonstrate that healthy individuals show stronger conditioned responses and more avoidance behaviors towards GSs that are perceptually more similar to the CS+ than the CS- (i.e., generalization gradient; [98, 122, 125]). Correspondingly, in a conditioning task, using words as CSs, participants displayed more avoidance behaviors in response to GSs (e.g., soup and help) that are semantically related to the CS+ (e.g., broth) but not for GSs that fall into similar categories as the CS- (e.g., assist) [12]. Thus, a patient with anorexia nervosa, who initially restricts her intake of chocolate might generalize this avoidance to other foods that are bar-shaped or fall into the category of high-calorie sweets.

The spread of aversive conditioned responses towards new stimuli appears to play a crucial role in the generalization of avoidance behaviors [90]. When comparing Pavlovian and instrumental generalization, van Meurs and colleagues (2014) found that the generalization of self-reported threat expectancies, startle responses, and avoidance behaviors follow a similar pattern. Moreover, the generalization gradients for aversive conditioned responses and avoidance behaviors are positively correlated. Interestingly, heightened threat expectancies and startle responses generalized more strongly across the GSs than the avoidance behavior (see also [98]). Thus, the generalization of conditioned responses, such as fear and physiological arousal, might be a mechanism underlying the generalization of avoidance. Once avoidance behaviors are in place, they prevent the disconfirmation of incorrect threat beliefs. Individuals cannot learn anymore that cues that resemble their initially feared stimuli are not indicative of danger or precede an

aversive outcome [133]. The anorectic fear of (catastrophic) weight gain after eating certain high-caloric foods will easily spread to food items that perceptually or symbolically/conceptually resemble the initially feared foods. Once food intake is further restricted, patients do not realize anymore whether their fears and avoidance are actually warranted and disabling eating patterns stay in place. Therefore, the generalization of avoidance behaviors should also be studied when trying to understand and explain the excessive food restriction displayed by patients with anorexia nervosa.

In sum, learning theory offers an intriguing theoretical framework and useful laboratory paradigms to understand more exactly how dysfunctional avoidance and safety behaviors displayed by anorexia nervosa patients are associated with the maintenance of eating disorder psychopathology. Especially, research into the excessive generalization of avoidance behaviors could help us to explain the rigid food restriction displayed by patients with anorexia nervosa. The possibility to include additional learning phases, such as extinction and generalization phases, into basic laboratory tasks proves the paradigm sufficiently flexible to investigate a wide range of avoidance related phenomena. Carefully designed laboratory studies can eventually inform the refinement of present and future clinical exposure interventions.

5. Exposure interventions

Exposure-based interventions for anorexia nervosa are not yet systematically applied in clinical eating disorder practice and research, but interest in the use of exposure therapy for eating disorders seems to have increased significantly recently (e.g., [15, 16, 29, 39, 53, 54, 58, 97, 99, 101–103, 109]). The main focus of exposure interventions for restrictive eating disorders is on the reduction of fear. Given that fear of weight gain is central to anorexia nervosa, all treatments striving for weight restoration in anorexia nervosa – most of them do – induce high levels of fear in anorexia nervosa patients. Not targeting these fears explicitly may lead to worse treatment outcomes since it has been documented more than once that persisting fears may worsen prognosis and predict relapse [82, 117].

Initially, exposure interventions for anxiety disorders consisted of repeatedly confronting patients with fear-inducing stimuli in the absence of the adverse outcomes, according to a gradual hierarchy [6, 21]. Simplified, these exposure interventions activate fear and initiate habituation which was thought to be critical to extinguish the fears [34, 93]. The few early studies investigating the effectiveness of habituation-based exposure therapies in anorexia nervosa were also focused on habituation and the reduction of food- and intake-related fears ([9, 111], 2010, 2012, 2014). Although these habituation-based exposures worked well, fear reduction during exposure seems not to be predictive of treatment success. Therefore, reduction of fear during the exposure is not a good indicator of a change in conditioned associations: habituation being the working mechanism of exposure therapy is questioned [20, 91]. Learning theory experts introduced inhibitory learning and the disconfirmation of expectancies as potential decisive candidates for the working mechanisms of exposure interventions [10, 20]. The inhibitory learning model states that the original association between CS and US is not erased during exposure. The CS → US association remains intact, but an additional non-threat association is taught as well, namely, that the CS no longer predicts the US (CS → noUS). During conditioning the CS → US association is learned while during extinction or its clinical analogue exposure the CS → noUS association is learned. This means that, after extinction/exposure, the meaning of the CS has become ambiguous: it might predict both the US and noUS. The original association and behavior are still in the memory system, though inhibited, and they can return easily under certain conditions [11]. New inhibitory pathways are tenuous in the beginning of an exposure intervention, indicating the need for frequent exposures to strengthen the newly learned CS → noUS association. For example, the patient might learn that the eating of a cheese sandwich does not predict a five pounds increase in weight or infinite weight gain. During the exposure, the expectancy of gaining five pounds or a never-ending weight gain, could be tested and violated. The violation of expectancies is supposed to be critical and needs to be optimized [20, 21, 128]; A patient needs to learn that the stimulus does not yield the expected feared outcome or, say, that she is capable of tolerating aversive feelings in the context of weight gain [16, 132]. The bigger the mismatch between expectation and experience, the stronger the inhibitory learning.

Of course, treatment of anorexia nervosa should always lead to weight gain, it is a primary treatment aim. One could therefore argue that, for anorexia nervosa patients, the eating and weight gain fears are real and, at least partly, rational. It is, however, quite irrational to be afraid of gaining weight when one is (severely) underweight. For the exposure intervention this means that it is important to catch the right USs: What does the patient expect to happen when she gains, for example, two pounds? What does she expect to happen when she eats a sandwich every day at lunch time, for a whole week? The patient may believe that eating a sandwich a day will lead to a weight gain of two pounds every future day. Or that gaining two pounds means that she loses control ending up in binge eating. Or that gaining weight will lead to negative social evaluations, e.g., to criticisms about her fat body and her unattractiveness. Or that gaining weight is a sign of weakness. The power of the inhibitory exposure treatment is that these beliefs can be reformulated in testable hypotheses. So, it is important to find out what the fears of the patient exactly are, to reformulate the fear in a clear and testable hypothesis, and to design an exposure exercise to test the belief about an assumed catastrophic effect of controlled weight gain. This procedure should be repeated frequently, to test many of the patient's fears. The patient may learn that she is in control of her weight gain, and that the feared social evaluations will not happen. Even in the unlikely scenario of negative evaluations happening during her weight gain, it is important to identify a new US: what is the problem of a negative social evaluation, why does it bother you so much? The excessive avoidance may possibly be pinned down to a feeling of being worthless after gaining weight ('becoming fat'), which may again be challenged. And so on.

Up until now, as far as we know, only one single study investigated the effects of exposure therapy based on the inhibitory learning model in anorexia nervosa [16]. Eight sessions of inhibitory based exposure therapy reduced anorectic fears and food restriction, and increased BMI. No participant dropped out early and the therapy was highly accepted by the patients. Though the study was underpowered (small sample) and uncontrolled, its results are impressive and promising.

6. Safety behaviors

Avoidance behaviors are defined as behaviors aiming to down-regulate unpleasant experiences and safety behaviors are the clinical analogue of avoidance behaviors; they refer to overt or covert actions to prevent, escape, or minimize a feared catastrophe and/or associated distress in a specific context ([7], p2; [40, 115]). Safety behaviors need to be differentiated from adaptive coping applied in the presence of actual threat [118]. Safety behaviors are in line with one's fearful beliefs, e.g., when someone believes that eating a small piece of chocolate will lead to a weight gain of five pounds, not eating the chocolate or self-induced vomiting to prevent weight gain are logical behaviors to remain 'safe'. Although safety behaviors are in line with one's own fearful beliefs, they are often performed in the absence of real danger and therefore unnecessary. The temporary effect of a safety behavior is relief, but the fear soon returns because the safety behavior prevents the person to be exposed to experiences that would disprove their fear belief. In this way, fears will not extinguish and be maintained [7, 47, 77]. In anorexia nervosa, safety behaviors are common, like restrained eating, strict eating rules, eating rituals, the counting of calories (and/or fat, carbohydrates), spitting out the food, self-induced vomiting, excessive exercising, and body checking.

Based on their ascribed anxiety maintaining effects, the elimination of safety behaviors used to be an undisputed element of exposure treatments [1], but recent research has initiated a debate on the actual impact of safety behaviors on exposure [40, 126]. Findings so far are inconclusive and show that safety behaviors can be beneficial, but they could also interfere with treatment [7, 77]. This inconsistency in findings may be based on ambiguous definitions and categorizations of safety behaviors. Safety behaviors form a category entailing various behavioral patterns that differ in terms of timing, their relation to the threat, their operationalization and the way there are measured [40]. Safety behaviors in their entirety should not be understood as a concept that is either beneficial or detrimental to exposure treatment. Rather, the category of safety behaviors may entail a range of patterns that can be harmful, neutral or even beneficial, depending on their characteristics.

One assumed factor on which adaptative and maladaptive safety behaviors can be differentiated is their impact on belief restoration vs prevention [7, 40]. Restorative safety behaviors are supposed to be less harmful because they do not interfere with full fear confrontation, thereby enabling a successful violation of the threat beliefs and expectancies [40, 51]. For example, Blakey & Abramowitz [7] describe a spider phobic person who fears a spider jumping on her head to lay eggs in her hair. This patient only wants to engage threat confrontation when allowed to wear gloves. Given that wearing gloves is unrelated to the actual fear belief, the patient would be able to fully test her expectancies while wearing gloves. These so-called restorative safety behaviors enable inhibitory learning. The anorexia nervosa patient fearing a weight gain of five pounds after eating a slice of pizza, might want to know the exact number of calories of the slice and she wants to eat very slowly. These safety behaviors are unrelated to the threat of gaining five pounds after eating a slice of pizza, so they do not interfere with the expectancy violation. The anorexia nervosa patient fearing loss of control after eating a piece of chocolate might want to replace the chocolate for the eating of a salad. This may be a so-called preventive safety behavior that precludes or reduces the occurrence of the threat (Hoffmann & Hay, 2018). In the context of inhibitory learning, preventive safety behaviors diminish the mismatch, which may reduce or prevent the inhibitory learning and negatively affect treatment outcomes [7]. Accordingly, the general recommendation seems to reduce preventive safety behaviors during exposure treatments while restorative safety behaviors are assumed to be harmless.

However, data seem to not fully support this claim. First, differentiating (harmless) restorative vs. (harmful) preventive safety behaviors is not as simple as it seems. Milosevic and Radomsky [78] encouraged preventive safety behaviors which facilitated the confrontation with threat. Van Uijen et al. [126] manipulated full avoidance vs. 'subtle' preventive safety behaviors, meaning that the expected threat was not precluded but reduced in intensity (reduction of the volume of a loud noise). So, preventive safety behaviors do not have to fully block threat expectancies. Second, preventive safety behaviors were found to promote learning instead of attenuating it [78], and subtle safety behaviors were associated with reduced threat expectancies and extinction learning in about half of the sample [126]. These findings show that preventive safety behaviors that reduce but not fully preclude threat, can nevertheless lead to the extinction of conditioned fears. In addition, it is argued that the seemingly harmless restorative safety behaviors might undermine inhibitory learning, especially regarding the long-term consequences of exposure [40].

In sum, it is not yet clear whether or when safety behaviors counteract or just enhance the outcomes of exposure treatments. Diverse researchers and clinicians argue that the use of 'subtle' safety behaviors during the early stages of treatment can be helpful [94]. Safety behaviors could be conceptualized as a tool to foster therapy progress, especially when working with extremely hesitant patients who would not approach threat confrontation at all without the usage of safety behaviors [124]. Indeed, the use of safety behaviors was found to increase the acceptability of exposure treatments [71].

In the early stages of treatment, safety behaviors could thus generate inhibitory learning opportunities for patients they would have missed otherwise. Still, it must be considered that even though safety behaviors may stimulate engagement in threat confrontation, they diminish the mismatch between expectation and outcome and thereby hamper inhibitory learning [21]. Applying safety behaviors withholds the opportunity to test fearful beliefs to a full extent. This holds for safety behaviors that are directly related to the threat stimuli. Safety behaviors that are unrelated to the threat might indeed be beneficial when they enable threat confrontation without affecting the inhibitory learning [7]. This is not only helpful when patients are hesitant to threat confrontation but also when contexts change and generalization could be promoted with safety behaviors [94]. Patients who fear immediate weight gain after little food intake still engage in threat confrontation when they apply unrelated safety behaviors such as counting the number of calories or eating slowly.

The literature reviewed above depicts that still a lot of research needs to be done on safety behaviors, especially in the field of eating disorders, to resolve inconsistencies around their definition, impact on therapy and the precise circumstances under which they need to be eliminated or not. Our preliminary conclusion is that safety behaviors that fully block threat confrontation are harmful to the effects of exposure. Some safety behaviors, e.g., subtle safety aids, appear to be helpful because they can enhance treatment acceptability, approach behavior or self-efficacy [7]. The general preliminary conclusion is however that, throughout the course of treatment, it should be achieved that exposures can be completed without any sort of safety behaviors in order to maximize inhibitory learning [21].

7. Future research

We discussed the role of transdiagnostic avoidance or safety behaviors in the maintenance of the eating disorder anorexia nervosa. Fear is one of the core symptoms of anorexia nervosa and only recently identified as a treatment target; fear not only impacts the course of anorexia nervosa but also treatment outcomes. We still know very little about the mechanisms that maintain the fears in anorexia nervosa. We first discussed the need for experimental studies into the mechanisms associated with food avoidance; these basic mechanistic studies can lead to a greater understanding of the development and maintenance of anorectic fears. A crucial first step in this direction is the development of paradigms to successfully investigate food avoidance in anorexia nervosa patients, as well as healthy samples. To identify differences in avoidance behaviors between individuals, the laboratory tasks should preferably constitute a 'weak situation'. By featuring ambiguous stimuli or less motivationally salient outcomes, 'weak situations' facilitate the manifestation of interindividual differences [72]. This means that individuals who avoid more excessively in real-life, also avoid more in the laboratory task. The inclusion of generalization and extinction phases, as well as the introduction of costs and rewards for avoidance behaviors are possibilities to create 'weak situations' and to collect clinically relevant information [61].

Currently, we do not know to what extent and under what conditions patients with anorexia nervosa show maladaptive avoidance patterns. Therefore, avoidance responses during laboratory conditioning tasks should be studied in clinical and subclinical samples, and control groups. In a similar vein, future studies should disentangle whether patients with anorexia nervosa show dysfunctional avoidance to disorder-specific stimuli only, such as food and weight gain, or whether they show broader avoidance responses, that is, to generally appetitive and generally aversive stimuli, like money and pain. Moreover, the role of excessive avoidance generalization for restrictive eating should be elucidated, as well as the mechanisms and moderators of dysfunctional avoidance behaviors in anorexia nervosa. Especially, aberrant conditioned responses (e.g., heightened fear or reduced appetite), as well as

abnormal avoidance and approach tendencies may be of interest [4, 83, 87]. Besides, the perceived (un)controllability of aversive events and feelings of control in general, might affect avoidance behaviors [44], especially in AN [46] and is, therefore, an interesting research target. In addition, studies into the role of reward-oriented avoidance behaviors, like drive for thinness, are highly relevant. Overall, future laboratory studies should elucidate the characteristics, boundary conditions and mechanisms of avoidance behaviors, in order to understand the disorder better and to eventually improve anorexia nervosa treatments.

To counter or combat the avoidance behaviors, inhibitory learning during exposure therapy seems most appropriate. Notwithstanding several advocacies for the use of inhibitory learning exposures in anorexia nervosa treatment (e.g., [16, 80, 82, 99]), empirical studies on the effectiveness of inhibitory-based exposures are still largely missing. Now is the time to find out if exposures based on inhibitory learning indeed are effective interventions for this severely ill group of patients. The exposure interventions require the identification of the individual's core fears, expectancies and safety behaviors. A core fear and its related threat expectancy should be framed within a testable hypothesis. During the exposure session, the hypothesis is tested, to disconfirm the expectancy. The exposure experiences will give rise for new fears and new expectancies that require testing. The patient should be actively involved in the set-up of the exposure experiments and it seems wise to repeatedly rate how strongly the patient believes in the expected dreaded outcome, and how anxious she is. As we discussed above, safety behaviors should be identified and removed throughout the treatment when they could reduce the level of mismatch. When safety behaviors do not prevent the mismatch learning, or even are the only way to get the patient doing the exposure exercises, they can be used. But, in order to maximize inhibitory learning, the use of safety behaviors could better be reduced and eventually stopped during treatment. To promote consolidation of what was learned in the exposure session, a discussion of what was learned at the end of the session is recommended [19].

During exposure therapy, hypotheses about threat expectancies should be tested repeatedly in a variety of ways. When fears, such as gaining a substantial amount of weight or being negatively criticized after gaining weight, are difficult to challenge in real life, the use of virtual reality could be promising. Virtual reality enables to test fears that fall off the scope of in-vivo exposure. Within virtual reality, stimulus and context variations can be introduced while patients stay in a safe environment, which may reduce the number of dropouts [30, 41].

To conclude, anorexia nervosa is a very serious mental disorder and a challenge to treat. The new developments in avoidance learning that were discussed here, and the clinical implications of individualized inhibitory learning-based exposure interventions, are exciting and promising; at least they deserve it to be tested.

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