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Extinction theory & anorexia nervosa: Deepening therapeutic mechanisms

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ABSTRACT

By virtue of adopting the core symptomatic fear (i.e., a fear of weight gain) as a primary treatment target, the treatment of AN centrally involves exposure-driven processes. However, exposure trials targeting the fear of weight gain in AN have been sparse, yielding mixed results to date. In translating extinction theory to the treatment of AN, it is likely that the absence of a clear distinction between what constitutes the core feared cue and the core feared outcome has stymied the application of exposure treatments in AN. This review considers several configurations of the core fear association in AN, noting distinct therapeutic strategies which may allow for more precise efforts in violating fear-based expectancies. Specific guidance is offered in the clinical decision making process as to which strategies might best promote inhibitory learning, and a clinical case is discussed, in which treatment was adjusted to specifically violate the core underlying fear association.

Anorexia nervosa (AN) is a disorder of complex etiology, characterized by self-imposed starvation, an overvaluation of shape and weight, an intense fear of weight gain, and a distorted body image, and involves strict restriction of dietary intake, with or without binge eating and/or purging (American Psychiatric Association, 2013). Alongside these core symptomatic features, AN is inclusive of profound medical morbidities, demonstrating elevated rates of medical complexity (Mitchell & Crow, 2006), mortality (Arcelus, Mitchell, Wales, & Nielson, 2011; Steinhausen, 2002), suicidality (Arcelus et al., 2011; Pompili, Mancinellia, Girardi, Ruberto, & Tatarelli, 2004), and impaired quality of life (Jenkins, Hoste, Meyer, & Blissett, 2011).

Despite the marked dangers associated with AN, treatment outcomes continue to cause concern (Fairburn, 2005; Watson & Bulik, 2012). For instance, approximately 20–40% of those with AN are likely to drop out of treatment prior to completion (DeJong, Broadbent, & Schmidt, 2012). Those who do complete treatment demonstrate a roughly equal chance of experiencing some symptom remission, versus developing a long-term chronic and relapsing illness course (Hay, Touyz, & Sud, 2012; Kass, Kolko, & Wilfley, 2013). Adolescent populations generally report more favourable outcomes, with family-based treatment (FBT) evidencing the most promising treatment outcomes to date, with approximately 50% of patients reporting full weight restoration by the end of FBT (Lock, 2015), which appears relatively well-maintained at 4 year follow-up (Le Grange et al., 2014). However, only 40% of those undergoing FBT demonstrate cognitive symptom remission by the end of treatment (Lock et al., 2010), leaving a substantial portion of those with AN with some aspect of continued suffering.

In light of these concerns, a growing consensus has implored the development of more effective treatment approaches that target the unique illness-specific pathology of AN (cf., Strober & Johnson, 2012). This mirrors broader efforts in psychiatry towards the development of 'precision medicine', in which illness-specific treatments are based on the distinct genetic, neurobiological, cognitive and behavioural hallmarks of individual illness pathways (Cuthbert & Insel, 2013; Insel, 2014). For AN, this may involve the development of novel treatment approaches borne out of

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developing data illustrating AN-specific pathophysiology (Kaye et al., 2015; Knatz, Wierenga, Murray, Hill, & Kaye, 2015), or may involve the modification of existing treatments in line with emerging data relating to the unique clinical features of AN (Koskina, Campbell, & Schmidt, 2013; Steinglass et al., 2011). One existing treatment approach that has received renewed empirical interest in the treatment of AN is exposure therapy (Hildebrandt, Bacow, Greif, & Flores, 2014; Koskina et al., 2013; Steinglass et al., 2011, 2012, 2014).

1. Why is exposure relevant in the treatment of anorexia nervosa?

AN is uniquely placed amongst psychiatric illnesses, in that the most feared outcome (i.e., weight gain) is adopted as a core treatment goal, which inevitably results in the treatment of AN centrally featuring exposure-driven processes. Indeed, two longstanding central tenets of treatment for AN posit that (i) full weight restoration must be swiftly undertaken to offset the potential medical dangers and state-related neurocognitive impairments associated with starvation, and (ii) restrictive dietary practices should be abated throughout the course of treatment (Dally & Sargant, 1966). More fundamentally, one cannot recover from AN while (i) failing to maintain a developmentally normative bodyweight, and (ii) actively restricting food types or volumes based on the assumption that weight or shape will be catastrophically impacted by their consumption.

In conjunction with this core symptomatic fear around weight gain in AN, food intake often precipitates marked anxiety (Steinglass, Eisen, Attia, Mayer, & Walsh, 2007). The consumption of even marginal caloric volumes yields expectations of a catastrophic and immediate impact upon shape and body weight (Steinglass, Eisen et al., 2007; Sternheim et al., 2012), triggering sustained anxiety around food consumption and subsequent avoidance-driven behaviors (Waller et al., 2007). The severity of this anxiety in AN is comparable to that reported in clinical anxiety disorders (Sternheim, Startup, & Schmidt, 2015), and directly impacts eating behaviors, with, for instance, pre-meal anxiety being directly linked to reduced food consumption during meals (Steinglass et al., 2010). Ecological momentary assessment further demonstrates the functional impact of anxiety in AN, noting that temporally distributed 'spikes' in AN symptomatic behavior vary according to peaks in self-reported anxiety (Lavendar et al., 2013). Cumulatively, these data suggest a central role of anxiety in the symptom profile of AN, with the avoidance of dietary energy intake and calorie-dense foods serving to mitigate the anxiety surrounding potential weight gain.

Alongside its functional role in AN symptomatology, the presence of comorbid anxiety disorders serves as a specific vulnerability factor in the development of AN (Buckner, Silgado, & Lewinsohn, 2010). Unlike other common comorbidities, such as depression, clinically significant anxiety typically predates the onset of AN (Swinbourne et al., 2012), and persists after recovery (Hughes, 2012), with up to two thirds of those with AN reporting a lifetime history of an anxiety disorder (Kaye et al., 2004). Further evidence independently suggests that (i) those with more severe premorbid anxiety experience greater AN symptom severity (Brand-Gothelf, Leor, Apter, & Fennig, 2014), (ii) anxiety symptoms may distinguish between patients who remit and those who do not remit from treatment (Yackobovitch-Gavan et al., 2009), and (iii) anxiety is an important prognostic indicator of treatment outcome in AN (Buckner et al., 2010). Thus, anxiety may serve both distal and proximal roles in the development and maintenance of AN.

2. The theoretical mechanisms underpinning exposure-based treatments

The most empirically supported treatment for anxiety-based symptomatology is exposure treatment (Hofmann & Smits, 2008; Tolin, 2010), which is based on the well-established principles of fear extinction. During exposure-based treatment, the patient repeatedly and systematically confronts anxiety-provoking cues (conditional stimuli or CS) that are anticipated to lead to an aversive outcome (unconditional stimulus or US), while refraining from engaging in escape, avoidance, checking or other anxiety-neutralizing responses. With repeated practice, cues that were originally anxiety-provoking will no longer elicit such reactivity because patients learn that the likelihood of an aversive event happening due to encountering such stimuli is minimal (or non-existent), even in the absence of cognitive or behavioural rituals and compulsions originally designed to avoid distress or avert "negative" consequences.

Exposure-based treatment, and the process of anxiety reduction during extinction, are thought to operate most centrally through *inhibitory* processes (Bouton, Mineka, & Barlow, 2001; Craske, Liao, Brown, & Verliet, 2012, 2014, 2008; Herman, Craske, Mineka, & Lovibond, 2006), rather than habituation processes, as was initially assumed (Baker et al., 2010). Inhibitory learning rests on the notion that acquired fear associations are not completely eradicated during extinction, but posits that new learning about the feared stimulus may take place (i.e., a non-threat association, CS does not lead to US), which mitigates anxious responses (Bouton, 1993; Bouton & King, 1983). More specifically, while the original fear-evoking content of the association is retained throughout extinction, the generation and retrieval of competing, non-threat associations around the feared stimulus serve to inhibit the activation of the original fear association (Vervliet, Craske, & Hermans, 2013). As such, the aim of inhibitory learning is for the excitatory fear-based association to be superseded by the retrieval of inhibitory, non-threat-based associations relating to the feared stimulus.

The deepened understanding of the mechanisms of extinction learning has significantly impacted the clinical delivery of exposure-based treatments in the anxiety disorders field. Such interventions now seek to actively violate anxiety-based expectations and promote the acquisition of new non-threat associations, rather than promoting mere exposure to feared stimuli alone (Deacon et al., 2013). For instance, in enhancing inhibitory learning throughout exposure training, (i) the discrepancy between the feared outcome and the actual (non-threat) outcome ought to be highlighted through the use of Socratic questioning and behavioural experiments, (ii) multiple feared cues may be presented concurrently to magnify the discrepancy between feared outcomes and the actual outcome, and (iii) use of a varied approach to exposure instead of following the traditional fear hierarchy from least feared to most feared is typically advised (Craske et al., 2008; Craske, Treanor, Conway, & Zbozinek, 2014). Similarly, in enhancing the retrieval of inhibitory learning, exposures are typically conducted across diverse contexts to offset context renewal effects, and patients are instructed to mentally "reinstate" the inhibitory learning from exposure therapy prior to re-encountering the feared stimulus/situation outside of the therapy context (Craske et al., 2008, 2014).

3. The application of exposure-based treatments to anorexia nervosa

Pathogenic and over-generalized fear conditioning has been implicated, at a theoretical level, in the etiology of AN (Strober, 2001), in a manner similar to that empirically documented in the

etiology of anxiety disorders (Lissek et al., 2005, 2010). However, while little empirical evidence has examined fear acquisition and fear extinction pathways in AN, an interest in exposure-based treatments for AN has recently emerged, demonstrating mixed results to date. For instance, one recent food-based exposure and response prevention study demonstrated statistically significant, but clinically modest, outcomes in impacting food intake among weight-restored AN patients, noting a marginal increase of 49 kcal (Steinglass et al., 2014). A separate case series recently modified a family-based form of exposure and response prevention for adolescent AN, aiming to empower parents with the responsibility of administering feared foods and preventing compensatory (avoidant) responses (Hildebrandt et al., 2014). Preliminary data demonstrates improvements in body mass index by the end of treatment, although only moderate improvements in the cognitive components of AN psychopathology, with little impact on shape and weight concerns (Hildebrandt et al., 2014).

Further trials have also attempted to investigate the impact of D-Cycloserine in the exposure-based treatment of AN (Levinson et al., 2015; Steinglass, Sysko, Schebendach, Broft, Strober, 2007), following data reporting its augmentative effect in the exposure-based treatment of anxiety disorders (Norberg, Krystal, & Tolin, 2008). D-Cycloserine is an *N*-methyl-D-aspartate (NMDA) receptor agonist known to facilitate extinction learning by augmenting glutamatergic function of NMDA receptor sites, and when administered in conjunction with exposure treatment, typically ameliorates the behavioural correlates of anxiety (i.e., avoidance behaviours) (Davis, Ressler, Rothbaum, & Rishardson, 2006; Norberg et al., 2008). When applied to the treatment of AN, D-Cycloserine alongside exposure resulted in greater caloric intake (Steinglass, Sysko, et al., 2007), and greater weight gain with reduced anxiety over the course of treatment (Levinson et al., 2015).

Cumulatively, these data suggest that exposure treatment may hold some efficacy in the treatment of AN, although these findings are limited by small sample sizes, modest positive findings, an over-reliance on behavioural as opposed to cognitive indicators of outcome, and important theoretical confounds (Koskina et al., 2013). As such, a recent systematic review concluded that "if the theoretical rationale associated with exposure treatment in the eating disorders was improved, the field would advance" (Koskina et al., 2013), imploring a reassessment of how exposure treatments may be developed and applied in the context of AN.

4. Applying extinction and associative learning principles to anorexia nervosa: deepening therapeutic mechanisms

Conceptualizing AN treatments through the lens of extinction theory may yield new avenues for treatment delivery, depending on how the core fear (i.e., CS-US association) in AN is conceptualized (Murray, Loeb & Le Grange, in press). To this end, little empirical data exists beyond the current DSM-5 criteria for AN noting a core 'fear of weight gain' (American Psychiatric Association, 2013). At present however, it remains unclear whether this core fear places weight gain as (i) a feared stimuli (i.e., CS), in which case the anticipated fearful consequences of weight gain (i.e., US) are not well explicated, (ii) a feared outcome (i.e., US), in which case the fearful stimuli (i.e., CS) preceding the feared outcome are not well explicated, or (iii) both (see Fig. 1). The imprecise definition of this core fear is problematic, as to precisely optimize exposure-based treatments, one must accurately discern the most feared outcomes, and the conditions under which they are deemed most likely, in order to tailor treatments towards violating these expectations and promote inhibitory learning. Failure to identify the feared outcome (e.g., US) may result in conditions that inadvertently contain stimuli that predict the non-occurrence of the US (e.g., safety signals or conditioned inhibitors) and therefore reduce extinction learning. For example, if a patient with AN is concerned that eating certain foods will result in negative social evaluations by others, then completing such an exposure alone, without testing the outcome, would not lead to any violation of expectancy.

Recent accounts have contested that the core 'broken cognition' in AN centers around a dysfunctional 'food-weight gain' connection, i.e., *any* food consumption is deemed liable to cause immediate weight gain (Waller & Mountford, 2015; Waller et al., 2007). This core assumption is thought to drive the characteristic behavioural attempts to avoid or limit food intake, and is particularly accentuated in relation to the 'fear foods' deemed most likely to result in the weight gain (Waller & Mountford, 2015; Waller et al., 2007). This assertion lends itself to the notion that food consumption is the primary fearful stimuli (i.e., CS), and weight gain the primary feared outcome (i.e., US) (see Fig. 1). However, alternate accounts posit that weight gain itself represents the feared stimulus (i.e., CS), portending an array of aversive outcomes, including social judgements and rejection, intolerable affective states, loss of the thin ideal and controlled behavior as important determinants of self-concept, and behavioural loss of control (i.e., US) (see Fig. 1). Further still, accounts also report the notion of weight gain being both the feared stimulus and the feared consequence, with any degree of weight gain (i.e., CS) serving as a notification of impending uncontrollable weight gain (i.e., US) (see Fig. 1).

When applied to clinical practice, the precise configuration of these feared stimuli and predicted outcomes likely warrant different treatment approaches (see Fig. 1). For instance, in regard to the reported 'broken' cognition linking food consumption (stimulus) to immediate weight gain (predicted outcome), the timing of inhibitory learning warrants consideration. That is, upon starting treatment, when immediate weight gain *is* necessary, and eliminated foods *are* reintroduced, it is theoretically unlikely that the fear of weight gain becomes inhibited throughout an extended period of rapid weight gain as a result of introducing previously avoided food types or volumes. To the contrary, it is plausible that the weight gain necessitated during weight restoration provides *confirmatory* evidence that previously avoided food types or volumes do indeed result in weight gain, further potentiating one's fear-based associations to these particular food cues. In this instance, it may be theoretically impossible to introduce inhibitory learning around this fear until weight has been restored, and these feared foods can be consumed in the context of stable weight maintenance (e.g., learning that food consumption, or the consumption of 'feared foods', will not lead to uncontrollable weight gain). An ongoing focus on feared food consumption beyond weight restoration is critical, and an avoidance of feared foods once weight has been restored may serve to reinforce the notion that those particular foods do result in uncontrollable weight gain, and therefore remain dangerous. Thus, even in the context of weight restoration, it is possible that one's cognitive fear of foods, and in particular the fear of foods that assisted in bringing about weight gain, may remain. This 'broken' cognition may warrant abundant exposure to feared food cues en route to weight restoration in ensuring maximal exposure. However, it is important to adjust clinician expectations around improved cognitive symptomatology on weight restoration, as this fear association may be *most* primed at the point of weight restoration.

Alternately, when considering the notion that weight gain is the primary feared stimulus, which subjectively signals impending arrival of a self-concept-violating or socially aversive outcome (i.e., social rejection and criticism), a slightly different clinical approach

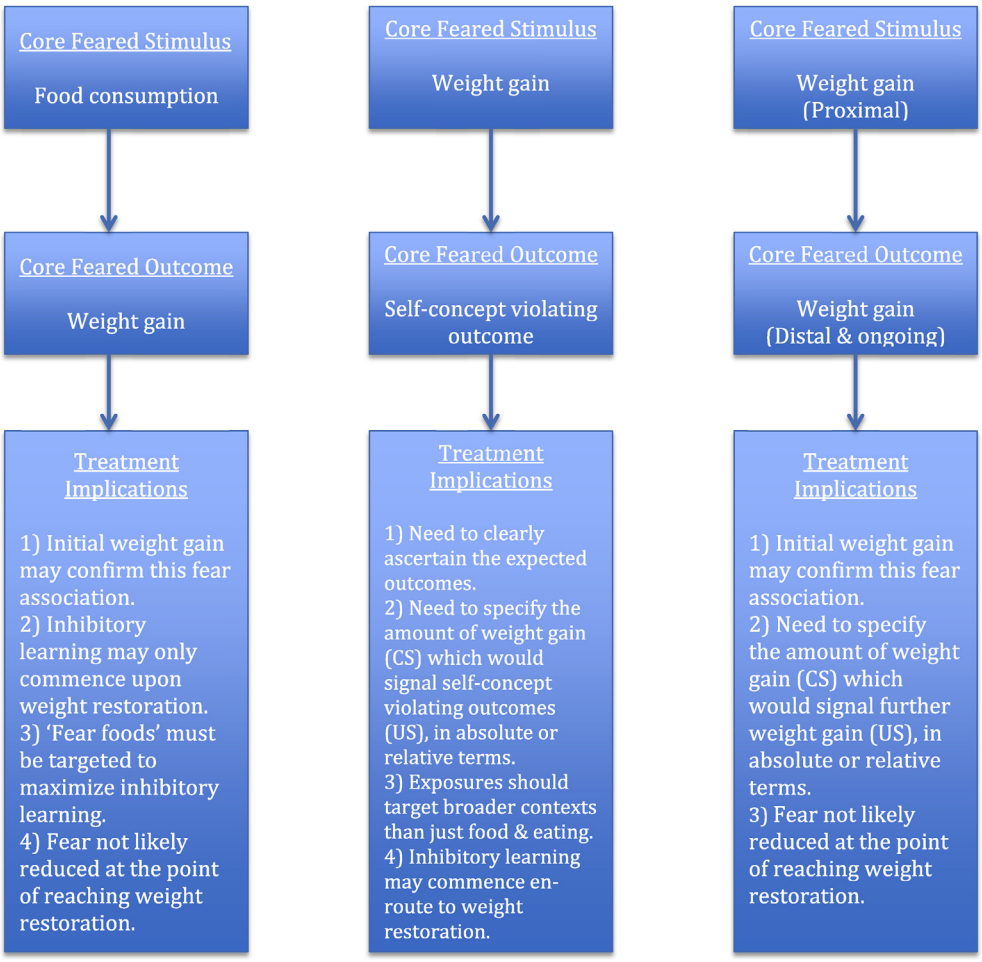

Fig. 1. Potential cue-outcome fear associations in anorexia nervosa.

may be warranted in maximizing inhibitory learning. In this instance, relatively less emphasis may be oriented towards optimizing the exposure to an array of foods that bring about weight restoration, as inhibitory learning endeavours must focus on violating the predicted social/self-concept-related consequences of weight gain. As such, a clear set of expectations surrounding the consequences of weight gain are required in devising exposures in which these expectations can be violated, although these exposures may be introduced en route to weight restoration. For example, actual weight gain may serve as a useful exposure to violate the expectancy that individuals will comment negatively on the patient's appearance or weight gain, provided that patients are exposed to settings where one predicts the aversive outcomes are most likely to occur, and are asked to carefully attend to cues relating to the confirmation or disconfirmation of their predicted outcomes. An early start to these exposures (i.e., during weight restoration) may help generate opportunities to violate the predicted impact of incremental weight gain throughout the refeeding process, such that upon reaching weight restoration one may have already generated ample inhibitory learning in mitigating the anxiety previously associated with weight gain. Thus, this fear association may be reduced upon weight restoration, although it is important that treatment during weight restoration broadens the scope of clinical focus beyond weight restorative and food-based processes (see Fig. 1).

The determination of the precise conditional and unconditional stimuli that comprise the fearful association in AN is essential in order to successfully target extinction learning. For example, many traditional exposure treatments include interoceptive exposure, or exposure to anxious sensations. It is clear that individuals with AN demonstrate physiological reactivity to feared cues such as certain foods. However, from a learning theory perspective, one would only expose an individual to conditional stimuli (stimuli that predict the US) as this is necessary to generate prediction error and extinction learning. Unless the interoceptive sensations in AN are predictive of an aversive outcome (e.g., in panic disorder they may predict physical catastrophes), they represent portions of the conditional response and not the CS. Exposure to the conditional response will not result in extinction learning, while exposure to the CS in the absence of the US will result in expectancy violation and a gradual decrease in the conditional response (e.g., anxiety). This is another key difference between exposure from learning theory perspective and traditional habituation-based models, as the latter would advocate exposure to any anxiety related stimuli.

As discussed previously, it is also essential to determine what the US is for a given client. Although uncontrollable weight gain may represent the US for many individuals with AN, it is also possible that weight gain portends an additional aversive outcome such as social rejection. In the latter case, exposure to food cues alone would be insufficient, as these represent *second-order conditional stimuli*. In second order conditioning, one CS predicts a second CS, which then predicts the US (e.g., food → weight gain → social rejection). Unfortunately, conducting extinction with a second order stimulus (e.g., food) does not impact fear to the first

order CS (e.g., weight gain; Debiec, Doyere, Nader, & LeDoux, 2006). This highlights the importance of idiographic assessments when designing exposures. For example, standard cognitive-behavioural techniques such as the "downward arrow" can be used to try and determine the US for an individual. In addition, further empirical research is needed in order to explore the variety of fearful associations in AN.

In more precisely applying extinction theory to the treatment of AN, it is clear that treatment foci ought to be driven by the core fear which serves to maintain psychopathology. To date, little evidence has explicated what precedes or proceeds the fear of weight gain, and whether these predicted outcomes are held in absolute (i.e., any weight gain at all) or relative (i.e., weight gain beyond an arbitrary value) terms, or whether proximal or distal. Without determining these key criteria, treatment approaches may be too non-specific, or even contraindicated (Murray et al., in press).

5. Habituation as a potential mechanism

In modern learning theory, habituation refers to a decrease in responding when an individual repeatedly confronts an *unlearned* stimulus (e.g., a US). With repeated presentations, the US is devalued and unconditional responding decreases (Rankin et al., 2009). Unlike extinction learning, which results in the formation of a new association which can be modulated by context, habituation results in modification to the original association and therefore generalizes more easily across contexts. Unfortunately, habituation is relatively restricted in its application as it can only be employed when confronting an unlearned stimulus or a stimulus without additional associations. That is, if a stimulus is predictive of something (e.g., weight gain leads to social rejection) then, by definition, habituation cannot take place. In addition, it is often unethical to expose an individual repeatedly to a US (e.g., a heart attack in panic disorder). However, for a select few individuals with AN, who fear even a minor amount of weight gain, it may be possible to expose them to the US (e.g., minor weight gain).

Indeed, this may be one mechanism underlying improvement during the early stages of treatment when weight restoration is the goal. As the individual gains weight, he or she is continually exposed to the US. However, in clinical reality it is likely that individuals with AN have multiple associations. In instances where a stimulus is predictive of a given outcome (food consumption will lead to uncontrollable weight gain, weight gain will lead to social rejection, etc.) extinction learning, and not habituation, is the goal. However, in limited circumstances where the individual fears even normal weight gain, and weight gain is not predictive of an additional outcome, the clinician can target habituation.

6. Evaluative conditioning and counter-conditioning

Evaluative conditioning refers to the valence (positive or negative) that is conditioned alongside a given CS. For example, an individual with social phobia may not only expect that social interactions (CS) may lead to rejection (US), they may also feel negatively towards the CS. Unfortunately, unlike excitatory CS associations, evaluative conditioning is more resistant to extinction (Vansteenwegen, Francken, Vervliet, De Clercq, & Eelen, 2006). In terms of AN, this may mean that despite successful extinction in which the individual no longer fears that certain food cues will lead to uncontrollable weight gain, or that weight gain may lead to social rejection, she/he may still feel negatively towards certain foods and weight gain.

Evaluative processes are targeted through *counter-conditioning* (e.g., Van Gucht, Baeyens, Hermans, & Beckers, 2013). As opposed to extinction, in which the CS is repeatedly presented without the US, counter-conditioning entails repeatedly presenting the CS with a US of different valence. For example, in AN consuming food may be paired with positive family interactions or the therapist may work with the client to draw her/his attention to the rewarding aspects of consuming a certain food. As a result of counter-conditioning the negatively valence previously associated with certain stimuli may be reduced. In the treatment of AN, counter-conditioning procedures may be employed in the later phases of treatment following successful exposure and extinction. However, like extinction, counter-conditioning may also be context dependent (Bouton, 1993).

7. Maximizing inhibitory learning in the context of anorexia nervosa

Given the abundance of exposure to both feared foods and feared volumes of food as a necessary component of treatment for AN, a deeper synthesis of extinction theory may allow for food exposures to be delivered in a manner which optimizes their potency in targeting the core symptomatic fear. In the context of an array of anxiety disorders, efforts to enhance inhibitory learning throughout exposure-based treatments have been earmarked as an important endeavour in augmenting treatment outcomes (Craske et al., 2008, 2014). However, given the scope for idiosyncrasies in the precise configuration of core feared stimuli and outcomes in AN, several strategies to optimize inhibitory learning are likely to be of assistance during treatment (see Fig. 2.).

7.1. Expectancy violation

Expectancy violation refers to the notion that exposure-based treatments, and inhibitory learning, are underpinned by the mismatch between expectancies and actual outcomes relating to the feared stimuli (Rescorla & Wagner, 1972). As such, exposure trials should aim to maximally violate anticipatory expectations regarding feared stimuli, and exposure trials should continue not until fear declines, but until one's fear expectation has been maximally violated (Craske et al., 2014).

In the context of AN, if one assumes that the primary fear is a fear of weight gain, and that the most central precursor to this fear is the consumption of food, in the absence of compensatory behaviors (Waller & Mountford, 2015), then inhibitory learning cannot theoretically begin until beyond the point of weight restoration, when the expectation of food consumption resulting in uncontrollable weight gain can be violated. This notion has important clinical implications, as the greatest violation of AN beliefs may come from eating 'fear foods' (in normative volumes) without experiencing catastrophic weight gain. For instance, in family-based treatment, extending the period of parental control over food-based decision-making may be warranted, since the avoidance of feared foods in weight-restored adolescents may be equally as detrimental to inhibitory learning than similar avoidance in underweight adolescents. Procedurally, this may involve an extended phase 1 of FBT in two sequential components, focusing on (i) weight restoration and (ii) inhibitory learning respectively. Interestingly, while structured weight measurement may be necessary to violate the expectancy of uncontrollable weight gain, this may gradually develop into a safety behavior (e.g., confirming that consuming feared foods did not result in weight gain). The clinical application of extinction learning requires continued assessment regarding the function a particular behavior is serving (e.g., is it enhancing violation of expectancy or functioning as a safety behavior), and modifying exposure procedures accordingly. This challenge also highlights the importance of a detailed idiographic assessment in order to determine the feared stimuli (CS)

Fig. 2. Potential pathways for augmenting extinction learning in anorexia nervosa.

and feared outcome (US). For example, if the feared US is negative social evaluation resulting from consumption of "feared foods" or weight gain, then exposures should include interaction with others following a week of consuming feared foods.

7.2. Deepened extinction

Deepened extinction facilitates inhibitory learning by augmenting the discrepancy between what is predicted and what actually happens (Rescorla, 2000, 2006). Procedurally, two different stimuli, which are believed to predict the same aversive outcome, are first extinguished separately, but are then combined together for further fear extinction. In theory, when two feared stimuli are presented together, the expectation of the feared outcome (US) increases, which in turn magnifies the degree of discrepancy between what was predicted and what actually occurs, enhancing extinction learning. In the context of AN, this may involve exposing patients to two fear foods concurrently in the same meal if the

patient believes that weight gain is more likely with the combination of the two feared foods. Alternately, when weight gain is conceptualized as the feared stimuli (CS), and negative evaluation by others on the basis of shape and/or weight is the feared outcome (US), extinction may be deepened by the combination of a feared social context (i.e., a party) whilst wearing feared items of clothing.

Although further research is needed, it may be important for both stimuli to predict the same US. If each CS predicts a different US, then expectation of a given US is not heightened by the presence of both cues. For example, both exposure to high caloric foods and mirror exposure may be important treatment interventions in eating disorders. High caloric foods (CS) may be predictive of uncontrollable weight gain (US), while staring at oneself in the mirror (CS) may be related to fear of intolerable distress (US). However, if one were to pair exposure to high caloric foods with mirror exposure this may not increase the expectation of either US, and extinction might proceed normally for each CS-US association rather than deepening the extinction to either.

7.3. Removal of safety signals/behaviors

Safety signals/behaviors constitute objects or actions, which are perceived to reduce the likelihood that the US (feared outcome will occur), and thereby reduce extinction learning. For example, for some patients, mentally counting calories, body checking, or reassurance seeking from family members during the food exposure would be blocked if engaging in such behaviors would lead to a reduced expectation of the aversive event. In this instance, rather than learning that they didn't gain weight because non-restrictive food consumption doesn't continue to result in weight gain, the patient is more likely to learn that they didn't gain weight because they calculated and counted their calories, meaning that not doing so would still be dangerous. In addition, if the feared outcome is social judgement as a result of weight gain, then wearing loose-fighting or oversized clothing may function as a safety behavior. Because safety behaviors/signals could come in various forms and subtleties, engaging a family member to help identify and block safety behaviors during and/or after food exposures may continue to be critical beyond the point of weight restoration.

7.4. Variability

Robust evidence from empirical cognitive science literature posits that stimulus variability enhances the storage capacity of newly learned information (Bjork & Bjork, 1992, 2006), and thus facilitates extinction learning. Traditional exposure proceeds steadily from one hierarchy item to the next, with each item repeated a number of times until anxiety decreases. Instead, in variable exposure, exposure is conducted to items from the hierarchy in random order, with less regard to fear levels or fear reduction. As such, patients may be encouraged to conduct exposures of fearful foods eliciting various levels of fear in a random order instead from least fearful to most fearful. Incorporating "mystery" food exposures to foods of unknown caloric composition may also capitalize on the benefits of stimulus variability in optimizing extinction learning. Further, "surprise foods" that are not specifically listed on the hierarchy may also assist, and ought to be continued beyond the point of weight restoration.

7.5. Multiple contexts

Because inhibitory learning is context dependent (Bouton, 1993), to maximize extinction learning, exposures should ideally be conducted in *every* context where the inhibitory, non-fear association may need to be retrieved. Indeed, due to the fragility (or context-specificity) of extinction learning, involving family members initially in all relevant food exposure contexts (e.g., therapy room, home, restaurant, social events with friends, etc.) is critical to long-term recovery (Hildebrandt, Bacow, Markella, & Loeb, 2012). This is particularly salient in the treatment of AN, where patients often commence re-feeding in hospital or partial-hospital settings, before transitioning to home-based living and outpatient treatment sessions (Friedman et al., in press).

Of note, the presence of family members and therapists during food exposures also constitutes a context change compared to patients having to complete meals by themselves. It is therefore equally important to incorporate exposures where patients eat by themselves in later stages of treatment, beyond weight restoration. Similarly, for individuals who fear negative social evaluation as a result of any incremental weight gain then it is necessary to include a variety of social contexts (e.g., school, social gatherings) in exposures.

8. Targeting habituation in the context of anorexia nervosa

When the fear is of normal weight gain itself, and weight gain is not thought to portend further aversive consequences such as uncontrollable weight gain, negative social evaluation, or intolerable distress, then it may be helpful to repeatedly expose the individual to the US (minor weight gain) in order to facilitate habituation.

Habituation relies on repeated exposure to the US (e.g., minor weight gain). In the treatment of AN, this may entail repeated measurement of weight throughout the day and week to draw an individuals attention to the US. In addition, unlike extinction learning, habituation is potentiated with repeated presentations of the same stimulus and reduced variability. The presence of novel stimuli can lead to dishabituation or the return of conditional responding (Rankin et al., 2009). In terms of AN, this may entail repeated weight measurement by the same individual, in the same context, during the same time of day. Finally, habituation proceeds most rapidly with weaker or less aversive stimuli (Grissom & Bhatnagar, 2009). Thus, it is ideal for minor increases in weight.

9. Case study[1]

Jenny is a 14-year-old girl who presented to treatment with an 8-month history of restricting type AN. While medically stable, Jenny's weight trajectory over the last year had dropped from the 57th percentile to the 14th percentile, and she described a marked fear of weight gain. During the previous 8 months, Jenny reportedly eliminated all 'danger foods', such as pasta, bread, dairy, and potato chips, and restricted her food intake to small portions of foods carefully screened for low caloric value, such as salad (with no dressing), dry crackers, rice crackers, and steamed vegetables. In discussing her dietary changes, Jenny stated that the only way to avoid weight gain (her primary fear) was to avoid her expansive list of 'fear foods', which she deemed likely to result in rapid weight gain.

Given Jenny's age and medical stability, a course of FBT (Lock & Le Grange, 2013) was introduced. Jenny's parents were empowered with the task of assuming parental authority over all food-based decisions to ensure weight restoration, and interrupting all disordered eating behaviors. Throughout Phase 1 of FBT, Jenny gained weight steadily, and her parents swiftly reintroduced all previously eliminated foods, blocking the avoidance of her 'feared foods'. However, upon reaching weight restoration and aiming to gradually transition some ownership over food-based decisions to Jenny,

[1] Jenny's name and identifying details have been altered to protect her identity.

she demonstrated an ongoing avoidance of her 'fear foods', noting that "I don't need to gain weight any more, so I don't need to eat those foods". As such, Jenny's weight-based recovery did not lead to cognitive symptom recovery, and her parents were unable to transition ownership of food-based decisions to Jenny. In further exploring Jenny's ongoing fear and avoidance of these foods, she stated "I know first hand now that these foods cause big weight gain, just look at what happened to me when my parents made me eat them … and now that I'm a normal weight, there's no way I'm eating these foods." In this instance, Jenny described a deepened fear of her feared foods, which stymied her cognitive recovery and her ability to manage her own food intake.

9.1. Moving beyond this quandary

In response to this quandary, Jenny's parents temporarily abandoned the notion of transitioning control over food-based decisions to Jenny, and instead expanded their parental support in order to extend new learning around the consequences of eating her 'fear' foods. Specifically, they opted to provide continued servings of 'fear foods' in normative quantities, which they deemed unlikely to result in weight gain, aiming to underscore the notion that these foods do not necessarily result in rapid weight gain. During weekly treatment sessions, Jenny was first asked to predict her weight, based on what she had consumed over the preceding week, and then read off her recorded weight on the scales. Further, in maximally violating Jenny's expectations around these foods, her parents meticulously charted her predictions around weekly weight gain, alongside the graphed line of her actual weight status, which remained stable within a healthy range, and discussed this prediction error with Jenny. Parental questioning was intended to (i) maximally violate her prediction error by emphasizing the discrepancy between predicted versus actual weight status, (ii) link her moment-to-moment anxiety to her predicted rather than actual weight gain, and (iii) encourage a recalibration of moment-to-moment anxiety levels which was based on actual weight data instead of predicted weight data. This extended Phase 1 of parental support also included sporadic and randomized clusters of several 'feared foods' in the same meal (deepened extinction) in an array of social settings (multiple contexts). Over time, Jenny parent's noted that she gradually began to hold less conviction in her predicted weight gain, and then started to predict smaller increments of weight gain, which corresponded to discernable reductions in anxiety around food intake. The transition towards Jenny's control over food-based decision making was only started when the two lines on the graph (expected weight and actual weight) had consistently converged, indicating accurate expectations around the consumption of previously eliminated foods not resulting in weight gain. Following these additional parental efforts, Jenny was able to successfully manage her food intake without restricting previously avoided food types, and had not relapsed by 18-month follow-up.

10. Summary

Given the unique nature of AN, in which the core symptomatic fear (i.e., weight gain) is adopted as a primary treatment target, exposure-based processes are intertwined with treatment pathways. However, the application of exposure-based treatments in the context of AN has been sparse, and has been met with mixed results (Koskina et al., 2013; Steinglass et al., 2014). Perhaps the most salient barrier to exposure-based treatment in the context of AN is that little consensus exists in determining what constitutes the core feared cue/stimulus, and what constitutes the core feared outcome in AN (Murray et al., in press). The absence of this necessary distinction stymies the application of exposure-based treatments and the targeted violation of feared expectancies, as effective exposure-based interventions ought to be tailored to specifically target the core fear associations that underpin illness psychopathology. Thus, the application of exposure-based treatments in AN warrants careful consideration, and conceptualizing AN treatment through the lens of extinction theory offers several distinct pathways for treatment delivery. Clearly, a greater distillation of the core fear association in AN is required in determining optimal pathways for translating extinction learning theory to the exposure-based treatment of AN (Murray et al., in press).

However, an important point to consider in aiming to optimize exposure treatments for AN relates to the potential temporal effects of neurological and hormonal changes throughout the trajectory of weight restoration, during recovery from a starvation state. For instance, robust evidence has illustrated a diminished capacity for cognitive flexibility and set shifting among those with AN (Tchanturia et al., 2004), which when considering the marked starvation-related neurocognitive changes, including reduced grey matter volume in the frontal lobes (Mainz, Schulte-Rüther, Fink, Herpetz-Dahlmann, & Konrad, 2012), suggests that inhibitory learning and the generation of new non-fear associations may be most stymied during an underweight state. Furthermore, both human and animal research has illustrated the augmentative effect of estrogen during fear extinction (Milad & Quirk, 2012), such that the characteristic reduction in estrogen during states of low bodyweight may impair extinction learning during states of low bodyweight. While speculative, these data may suggest neurological and hormonal modulation of the impact of exposure treatment for AN, depending on illness severity and the degree of starvation.

More broadly, the precise distillation of cue-outcome fear associations may be of assistance in optimizing psychosocial treatments for bulimia nervosa, and other variants of disordered eating. Indeed, with the emerging emphasis on illustrating and engaging key mechanisms underlying psychiatric presentations, across diagnostic categories (Cuthbert & Insel, 2013), the investigation of fear extinction may be an important endeavor in augmenting treatment approaches for eating disorders, agnostic of diagnostic category.

Conflict of interest

Dr. Murray, Dr. Treanor, Dr. Liao, and Dr. Griffiths have no conflict of interest to disclose.

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