3 Perpetuating Factors in Severe and Enduring Anorexia Nervosa

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One approach frequently utilized in the study of psychiatric illness is the exploration of central underlying mechanisms that predispose, precipitate and perpetuate symptom manifestations. Predisposing factors are considered inherent characteristics that motivate behavior and influence the type and amount of resources an individual can elicit to cope with stress (O'Toole, 2013). An individual's genetics, gender, age, values and attitudes, personality, culture and environment affect the way they behave. Understanding these predisposing factors can help identify those stimuli that render an individual susceptible to a psychiatric illness. Precipitating factors are elements associated with or contribute to the onset of the illness. These factors can be biological, psychological, social or environmental and are considered the catalyst or trigger for the symptom or illness. Perpetuating factors are conditions that maintain the disabling symptoms of the illness. Examining maintenance phenomena can assist in predicting symptom persistence among afflicted individuals and inform the development of more effective treatment interventions (Treasure et al., 2007).

This chapter will focus on perpetuating factors in severe and enduring anorexia nervosa (SE-AN). One caveat should be mentioned. Eating disorder (ED) diagnoses are fluid and exist on a continuum. For example, up to 50% of AN patients will develop bulimic symptoms during the course of their illness (Fairburn, 1995). This chapter will discuss hypothesized perpetuating factors found in both AN-restrictor subtype (AN-R) and AN-binge purge subtype (AN-BP). The chapter begins with a review of the neurobiological factors, genetic factors, psychological factors, cultural factors, social factors and environmental factors that can maintain ED symptoms and closes with a brief case example that highlights the impact of unresolved perpetuating factors in the treatment of severe AN.

Neurobiological Factors

CNS Endogenous Opioids

One potential perpetuating factor in SE-AN is a dysregulation in the opioid system during active illness. This hypothesis was derived from theories

based on self-starvation in animals. Early animal researchers discovered that rats with restricted access to food run much more than rats that have open access to food (Bolles & de Lorge, 1962; Hall & Hanford, 1954; Spear & Hill, 1962). Routtenberg and Kuznesof (1967) furthered this research into self-starvation in rats and discovered that weight loss was accompanied by more intense running, to the point that many rats, with unrestricted access to running, died. This phenomenon was later termed "activity-based anorexia" (ABA) and used to describe running-based weight loss (Epling, Pierce & Stefan, 1983). These discoveries laid the foundation for researchers interested in self-starvation in AN. Since the mid 1980s, ED researchers have been interested in the "auto-addiction" opioid model of chronic AN (Luby, Marrazzi & Sperti, 1987; Marrazzi & Luby, 1986; Marrazzi et al., 1990; Szmukler & Tantam, 1984). They hypothesized that "endogenous opioids functionally support adaption to starvation by conserving absorbed resources and by the concomitant decrease of the metabolic rate" (Fladung et al., 2010, p. 206) and termed this process "starvation dependence" (Luby, Marrazzi & Sperti, 1987). This model suggests that relentless dieting, the compulsive pursuit of weight loss, continued weight loss even when medically compromised, the ego-syntonic nature of the disorder, and patient reports of starvation-related euphoria may indicate an "auto-addictive" process that is mediated by the endogenous opioid system. They propose that endogenous opiates are released during the initial period of dieting or prolonged food deprivation, which creates a psychological "high" and, in turn, initiates and reinforces a state of starvation dependence. This theory also suggests that individuals with AN may have a malfunction of the neurotransmitter systems that modulate feeding. Early animal studies reported that the opioid peptide dynorphin appears to enhance feeding behavior in rats (Morley et al., 1984) while other opioid systems (such as the stimulation of the mu receptor system) appear to inhibit food intake.

Several studies have been conducted to explore this model. For example, Kaye and colleagues (1982) reported increased endogenous opioid activity in the CSF of severely underweight patients with AN, but not in weight restored or normal controls. Kaye and colleagues (1987) later reported decreased CSF levels of beta-endorphin as well as its three sister peptides, beta-lipotropin, adrenocorticotropic hormone (ACTH), and pro-opiomelanocortin (POMC), in underweight AN patients, suggesting that underweight anorexics have state-associated abnormalities that are part of the neurobiological syndrome of AN and may contribute to alterations in behavior and neuroendocrine function. Brambilla and associates (1995) reported that patients with AN (both AN-R and AN-BP) had significantly higher lymphocyte concentrations of beta-endorphin than in controls. This was especially true for patients with AN-BP. Marrazzi et al., (1997) reported elevated levels of endogenous plasma alkaloids in patients with AN and BN in comparison to controls. Lesem et al., (1991) did not find

significant differences in CSF levels of dynorphin in patients with AN or BN in comparison to controls. Although there have been no new studies in this century, taken together, the data clearly indicate that the opioid system is dysregulated in AN during the low-weight state and are compatible with the auto-addiction model of AN. Studies using the opiate antagonist naltrexone in the treatment of AN have been mixed, (Marrazzi et al., 1995a; Marrazzi et al., 1995b), but future studies using larger sample sizes are needed.

Results from a more recent fMRI study were interpreted to be in support of the starvation dependence model (Fladung et al., 2010). Patients with AN and healthy controls underwent a functional MRI during evaluation of visual stimuli. Subjects were shown different images consisting of underweight, normal weight, and overweight whole body images and asked to process each image in a self-referring way. Healthy controls had a pleasurable reaction to the normal weight body image (compared with the other two images), while AN patients had a much more pleasurable reaction to the thin body image (compared with the other two images). Given that activation in the ventral striatal reward system was higher during processing of underweight stimuli in the AN patients, the authors concluded that this differential activation toward disease-related stimuli was consistent with theories of starvation dependence. In a sense, the rewarding aspects of being underweight become "hard-wired" and the longer this condition persists, the more adverse weight restoration may become.

CNS Neurotransmitter Changes

The monoamine neurotransmitters, including serotonin (5-HT), dopamine (DA), and norepinephrine (NE), have been investigated during all phases of illness and recovery from AN (active illness, short-term weight recovery, and long-term weight recovery) using a variety of research methodologies. During the low weight state all central monoamine neurotransmitters and/or their metabolites (5-hydroyindole acetic acid [5-HIAA], homovanillic acid [HVA], and methylhydroxyphenylglycol [MHPG], respectively), have been reported to be significantly decreased when compared to normal weight healthy controls. Such alterations lead to altered neurotransmitter receptor subtype sensitivity (either upregulation or downregulation) in various brain circuits affecting a variety of psychobiological parameters or functions that are known to be disturbed in AN, for example, hunger, satiety, mood, anxiety, activity, impulsivity, and perception. These results have been considered in detail elsewhere (see Brewerton, 1995; 2002; Brewerton and Steiger, 2004; Brewerton, Frampton & Lask, 2009; Kaye, 2008), but will be reviewed brieflyhere.

Serotonin

Several avenues of research demonstrate disturbances of serotonin (5-hydroxytryptamine, 5-HT) function in patients with AN. 5-HT is

known to play a major role in the regulation of a number of physiological parameters and behavior that is intimately linked to ED, such as starvation, feeding, satiety, mood, anxiety, harm avoidance, obsessionality, impulsivity, aggression, social behavior, body image, and regulation of hormones and other neurotransmitters. In comparison to healthy controls, underweight patients with AN have been reported to have significantly reduced CSF concentrations of the 5-HT amino acid precursor, L-tryptophan (l-TRP), and the 5-HT metabolite, 5-hydroxyindoleacetic acid (5-HIAA). Normalization of these concentrations occurs with short-term weight recovery (goal-weight maintenance > 3 weeks). In direct contrast to the ill state, patients with AN who have achieved weight recovery for more than 1 year have significantly higher CSF 5-HIAA concentrations than controls (Kaye et al., 1991). These and other data led to the proposal that AN may involve a primary state of excessive serotonergic tone that is consequently counteracted by starvation-induced declines in 5-HT function during the active phase of the disorder and that this purported hyperserotonergic trait may correspond to the personality traits of obsessionality, perfectionism, and behavioral inhibition (Kaye, 2008). Corroborating the notion of hyperserotonergic status in AN, Bailer and colleagues (2007) used positron emission topography (PET) imaging of 5-HT-receptor-specific radioligands and found higher activity of 5-HT_{1A} receptor activity in low-weight patients with AN compared with healthy controls. These investigators also observed that 5-HT_{2A} receptor binding capacity was directly correlated with harm avoidance scores.

Other experiments using serotonergic drug challenges demonstrated impaired serotonergic neuronal function in AN (Brewerton & Jimerson, 1996; Monteleone et al., 1998). Significantly reduced prolactin (PRL) responses following pharmacologic challenges to the serotonin system, using agents such as meta-chlorophenylpiperazine (m-CPP), l-tryptophan (l-TRP) and fenfluramine (FEN), have been described in low-weight patients with AN, further verifying severe changes in serotonin metabolism accompanying this disorder. Following at least one full year of weight recovery, neurohormonal responses following m-CPP normalize in patients with AN. This complete normalization of PRL responsivity to serotonergic agents following weight restoration parallels the stabilization of hypothalamic-pituitary-gonadal function and the cessation of clinically evident ED behavior. Taken together, clinical research findings consistently indicate significantly reduced serotonin synthesis, uptake, and turnover, as well as altered post-synaptic serotonin receptor sensitivity during the active phase of AN. Moreover these changes are likely to be at least partially responsible for the perpetuation of the malignant signs and symptoms characteristic of patients with severe and enduring AN, including severe mood dysregulation, heightened anxiety, relentless obsessionality and compulsivity, marked impulsivity and self-aggression, persistent cognitive distortions, and impediments in learning healthy coping strategies.

There is considerable evidence for an impaired serotonergic responsiveness during the active phase of AN (Brewerton, 1995; Brewerton & Jimerson, 1996; Monteleone et al., 1998). Studies have shown an inverse relationship between symptom severity and measures of serotonergic responsiveness (Jimerson et al., 1992; Monteleone et al., 2000a). There is also evidence for an association between self-destructiveness, a history of sexual abuse, impulsivity and reduced serotonin function (Steiger et al., 2001b; Steiger et al., 2001a; Steiger et al., 2001c).

In addition to affecting eating behavior directly, alterations in CNS serotonin function may contribute to other psychological symptoms associated with AN. The diminished CNS serotonin could play a role in the high prevalence of depressive disorders in patients with AN. An impulsive-aggressive behavioral style, which is frequently seen in the binge-purge subtype of AN, may also be associated with diminished CNS serotonin function (Brewerton & Steiger, 2004).

Dopamine

Dopamine (DA) is known to be intimately involved in the hedonic reward responses to eating, feeding and other pleasurable behavior, which has made it an area of great relevance in AN. Moreover, DA is implicated in the regulation of mood, activity, social behavior, perception, as well as hormone and peptide release (Jimerson et al., 1992). Low-weight patients with AN have been described as having decreased measures of both central and peripheral DA activity, including reduced CSF and plasma concentrations of homovanillic acid (HVA). Although concentrations of CSF HVA have been reported to normalize after long-term recovery, during the active phase of the illness these purported neurotransmitter abnormalities may drive the expression and continuation of symptoms.

Anecdotal reports of the successful use of dopaminergic antagonists (atypical antipsychotic agents), particularly olanzapine, in the treatment of AN patients have been followed by encouraging controlled trials showing olanzapine's efficacy over either placebo or other antipsychotics (Brewerton, 2012).

Norepinephrine

Norepinephrine's (NE's) role in the regulation of eating, mood, anxiety, sympathetic tone, metabolic rate, temperature, and neuroendocrine control has made it a likely focus of study in AN. Low-weight AN patients demonstrate urinary, plasma, and CSF levels of the major metabolite of NE, 3-methoxy-4-hydroxyphenylethyleneglycol (MHPG). Although these levels completely normalize upon full weight restoration, low-weight patients with AN tend to have higher plasma NE levels than healthy controls. However, CSF NE levels are reported to be no

different in low-weight AN patients compared with controls and after short-term weight gain. Paradoxically, NE levels become significantly lower after weight recovery of at least six months. The extent to which the adrenergic alterations seen in AN play a role in the perpetuation of symptomatology are unknown. It may be that the profound depletion seen in all monoamine neurotransmitters works in concert to produce impairment and to perpetuate symptomatology.

Neuropeptide and Hormonal Alterations

Patients with AN characteristically have significantly higher plasma cortisol levels in comparison to controls, as well as altered cortisol responses to challenges with ACTH (Brewerton, 1995). Furthermore, plasma cortisol levels have been reported to be inversely correlated to serotonin receptor sensitivity. The stresses of weight loss and chronic starvation, as well as bingeing and purging, may lead to further compromises in serotonergic tone and thereby perpetuate eating and related symptomatology.

Connan and colleagues (2003) have proposed a neurodevelopmental model in which genetic factors and early life experience interact to create vulnerability to a chronic but passive stress response as well as marked hypothalamic–pituitary–adrenal (HPA) axis dysregulation. Psychosocial and biological alterations accompanying puberty intensify vulnerability in such a way that when stress arises, both maladaptive coping and aberrant HPA axis responses are triggered. In particular, the HPA axis does not adjust to the chronicity of the stress, and there is chronically raised corticotrophin releasing hormone (CRH) activity. Chronic elevation of CRH concentrations leads to a long-lasting dysregulation in nutritional homeostasis as well as a host of other effects on brain and body that may contribute to chronicity.

A number of other neuropeptide and hormonal parameters are reported to be significantly different from controls in low-weight AN patients, which may contribute to the perpetuation of the disorder. We have already reviewed evidence regarding alterations in opiates that may reinforce the starvation state and produce a "starvation dependence".

Altered leptin concentrations have been reported in low-weight AN patients in comparison to matched controls (Baranowska et al., 2001; Brewerton et al., 2000; Jimerson et al., 2000; Monteleone et al., 2000b). Leptin levels appear to remain decreased even after sustained recovery in comparison to controls with matched percent BMI.

There have been consistent reports that plasma ghrelin concentrations are significantly increased in low-weight patients with AN when compared with healthy controls. This increase is more pronounced in patients with AN-BP as compared to patients with AN-R in some, but not all studies (Otto, Cuntz & Fruehauf, 2001; Otto, Tschop & Cuntz, 2004; Soriano-Guillen et al., 2004; Tanaka et al., 2003b; Tanaka et al., 2003a; Troisi

et al., 2005; Monteleone et al., 2008). The higher concentrations of ghrelin in underweight AN patients becomes normal with weight recovery, which supports the contention that increased ghrelin release is a state-dependent phenomenon (Janas-Kozik et al., 2007; Otto, Cuntz & Fruehauf, 2001; Otto et al., 2005; Soriano-Guillen et al. 2004; Tanaka et al., 2004).

Genetic Factors

Endophenotype is a term used in psychiatric genetics to describe observable behavioral characteristics that underlie and contribute to certain disease vulnerabilities but are not part of the disorder itself. These characteristics are thought to be heritable, co-segregate with a psychiatric illness, yet exist in the individual regardless of whether or not the illness is active (state-independent). These traits are also found in non-affected family members at rates higher than found in the general population.

Current research has identified several endophenotypes that may contribute to the development and maintenance of AN that are present prior to the onset of the illness and persist after recovery (Bulik et al., 2007). These impairments appear to have a negative influence on ED treatment outcome (Hamsher, Halmi & Benton, 1981; Holliday et al., 2005; Roberts et al., 2007; Szmukler et al., 1992). They include impairments in executive functioning with weak central coherence ("inability to see the forest for the trees", i.e., imbalance between global and detail processing), and cognitive rigidity with impaired set shifting (inability to shift effortlessly from task to task or to a new life routine, i.e., difficulty adapting to change) (Lopez et al., 2008; Roberts et al. 2007; Tenconi et al., 2010). Perfectionism has also been identified as a potential endophenotype for AN in particular and ED in general (Bachner-Melman et al., 2007). Bulik and colleagues (2007) found that certain aspects of perfectionism (concerns over mistakes and doubts about actions) appear to be significantly associated with both AN and BN but were not associated with any other psychiatric disorder. Tendencies toward excessive motor activity and exercise have been suggested as potential endophenotypes in AN and BN. Studies suggest that physical activity and weight regulation may represent endophenotypes for eating pathology that contribute to etiology (Favaro et al., 2000; Shroff et al., 2006).

Comorbid Psychiatric Disorders

There are several comorbid psychiatric disorders that can maintain the disabling symptoms of SE-AN. In addition to the previously mentioned endophenotypes (i.e., impairment in executive functioning, cognitive rigidity, perfectionism and excessive motor activity), more than 55% of adult and adolescent patients with AN will have at least one other comorbid psychiatric disorder (Hudson et al., 2007; Swanson et al.,

Table 3.1 Lifetime Prevalence of Psychiatric Disorders in Anorexia Nervosa

Anorexia Nervosa	*Adults 18–44 (%)*[1]	*Adolescents 13–18 (%)*[2]
Mood disorders	42.1	10.9
Anxiety disorders	47.9	23.9
Substance use disorders	27.0	13.0
Impulse control disorders	30.8	31.7

Notes: [1]Adapted from Hudson et al., 2007 (n=2,980); [2]Adapted from Swanson et al., 2011 (n=10,123).

2011). In addition, approximately a fifth will have a personality disorder (Sansone, Levitt & Sansone, 2006) (see Table 3.1).

Comorbid mood disorders are common in adults with AN (42%) but less common in adolescents (11%), with major depressive disorder (MDD) being the most prevalent in both populations (adult 39%; adolescent 9%) (Hudson et al., 2007; Swanson et al., 2011). One of the major symptoms of MDD is recurrent suicidal ideation, with or without attempts or a specific plan to commit suicide. Rates of suicidal ideation in adolescents with AN are 31%, with 8% reporting at least one suicide attempt (Swanson et al., 2011). Although rates of suicide attempts are higher in patients with BN, the rates of completed suicide are greater in AN (Franko & Keel, 2006), which may be due to the use of more lethal methods (Bulik et al., 2008). Whether mood disorders are present prior to the onset of AN, concurrent with the AN, or the result of engaging in ED behavior (i.e., dietary restraint, weight loss, chronic exercise, purging or other compensatory behavior), they can complicate the treatment and recovery process and can persist even after the amelioration of AN symptoms.

Anxiety disorders (for example, specific phobia, social phobia, obsessive-compulsive disorder (OCD), post-traumatic stress disorder (PTSD), and generalized anxiety disorder) are the most prevalent comorbid psychiatric disorders in AN (adult 48%; adolescent 24%) (Hudson et al., 2007; Swanson et al., 2011). In approximately 75% of cases, anxiety disorders precede the onset of AN (Godart et al., 2000) and often persist after recovery. Anxiety disorders in adolescence, particularly premorbid OCD, increases vulnerability to AN (Buckner, Silgado & Lewinsohn, 2010). Unfortunately, anxiety disorders (particularly social anxiety and panic disorder) tend to be chronic illnesses associated with greater psychiatric and medical comobidty, higher rates of suicidal ideation and attempts, and substance use disorders (SUD) (Buckner et al., 2008; Weiller et al., 1996).

Impulse-control disorders (attention-deficit/hyperactive disorder (ADHD), oppositional defiant disorder (ODD), conduct disorder, and intermittent explosive disorder) are present in approximately 30% of adolescents and 31% of adults with AN (Hudson et al., 2007; Swanson et al., 2011). Problems with self-control of emotions and behavioral

regulation appear to be more common in AN-BP than in AN-R (Ptacek et al., 2010; Yates et al., 2009).

Substance use disorders are prevalent in adults (27%) and adolesents (13%) with AN (Hudson et al., 2007; Swanson et al., 2011). Rates of abuse/dependence vary greatly across AN subtypes, with the AN-BP group reporting a significantly higher incidence of alcohol use disorder (35%) and drug abuse (32%) than the AN-R group (14% and 6% respectively) (Root et al., 2010). Substance use disorders can develop before, during or after the onset of AN, and in some instances, after recovery from AN (Bulik et al., 1997; Strober et al., 1996).

Eating disorders are also comorbid with dissociative disorders (DDs), the presence of which may adversely influence recovery from AN. Dissociative symptoms are commonly encountered in association with PTSD, especially in instances involving severe, early and chronic childhood maltreatment (Carlier et al., 1996; Chu & Dill, 1990; Chu et al., 1999; Cloitre, Scarvalone, & Difede, 1997; Dancu et al., 1996; Farrington et al., 2002; Nijenhuis et al., 1998; Putnam et al., 1986; Putnam, 1997), but they also occur in the absence of any ostensible PTSD symptoms, which can be masked by the presence of an ED. Higher than expected rates of DDs and symptoms have been reported in individuals with eating disorders or ED symptoms (Abraham & Beaumont, 1984; Demitrack et al., 1990; Gleaves & Eberenz, 1995; Goodwin & Attias, 1993; Everill, Waller & Macdonald, 1995; Levin et al., 1993; Nagata et al., 1999; Meyer & Waller, 1998; Santonastaso et al., 1997; Tobin, Molteni & Elin, 1995; Valdiserri & Kihlstrom, 1995; Vanderlinden et al., 1995; Vanderlinden et al., 1993; Zerbe, 1993). Likewise, higher than expected frequencies of eating disorders and ED behavior has been noted in patients with DDs, especially dissociative identity disorder (DID) (previously called multiple personality disorder) and dissociative amnesia (previously called psychogenic amnesia) (Brewerton et al., 1999; Putnam et al., 1986; Torem, 1986; 1990; 1993). DD symptomatology typically may include depersonalization, derealization, memory alterations (primarily amnesia), identity and time alterations, marked cognitive distortions, somatic sensations, and experiential avoidance.

By definition, AN inherently involves somatic symptoms, for example, altered perception of body size and shape. Links between EDs and somatoform disorders (SDs), now called "somatic symptom and related disorders" in DSM-5 (American Psychiatric Association, 2013), have been reported by a number of investigators (Bienvenu et al., 2000; Grant, Kim & Eckert, 2002; Nijenhuis et al., 1999; Ruffolo et al., 2006). One family study revealed the grouping of OCD with EDs and SDs, particularly body dysmorphic disorder (BDD), which is now classified under "obsessive-compulsive and related disorders" in DSM-5 (American Psychiatric Association, 2013). BDD and EDs are similarly characterized by obsessive and compulsive phenomenology negatively focused on the body. Other researchers have observed an association between BDD and EDs.

Prior maltreatment or trauma, including childhood sexual abuse (CSA), is a recognized risk factor for SDs (Farley & Patsalides, 2001; Imbierowicz & Egle, 2003; Lieb et al., 2002; Roelofs et al., 2002; Sansone, Gaither & Sansone, 2001) and BDD (Didie et al., 2006). Among women, child maltreatment contributes not only to general somatic preoccupation but to specific somatic symptoms in the throat and chest areas (Sansone et al., 2001), bodily regions typically involved in eating and vomiting. SDs are closely linked to DDs with other psychiatric comorbidity. Measures of somatization and dissociation are significantly and positively correlated with each other (Badura et al., 1997). Somatoform dissociation is a distinct phenomenon commonly seen in individuals with DDs and SDs, and is an important subdivision of ED patients that may contribute to chronicity (Nijenhuis et al., 1999).

The presence of a personality disorder may also contribute to the persistence of AN. The two most common personality disorders found in AN are obsessive-compulsive personality disorder (OCPD) and borderline personality disorder (BPD). Personality disorders, by nature, are enduring ways of viewing and experiencing one's world that deviate markedly from the expectations of the individual's culture. These patterns are pervasive and inflexible, ego-syntonic and lead to significant distress and impairment. If personality disorders are not directly addressed in treatment, these symptoms often persist after the elimination of the ED and increase the likelihood of relapse.

Obsessive-compulsive personality disorder is the most prevalent personality disorder in AN-R (approximately 22%) with a somewhat lower prevalence rate in AN-BP (12%) (Sansone et al., 2006). However, Halmi and colleagues (2005) reported no significant differences across ED subtypes in the prevalence of OCPD and OCD, nor with the association between OCD and OCPD. Specifically, they found OCPD alone in 15% of the AN-R group and 12% of the AN-BP group, and the combination of OCD and OCPD was seen in 16% of the AN-R group and 20% of the AN-BP group. In contrast to OCD, individuals with OCPD have a pervasive preoccupation with orderliness, rules, details, and perfectionism, are devoted to work and productivity, and have a desire for mental and interpersonal control. Halmi and colleagues (2005) also demonstrated that perfectionism scores were highest in those with OCPD, whether alone or in combination with OCD, and concluded that perfectionism seems to be more strongly associated with OCPD symptoms rather than OCD. The pairing of perfectionism with OCPD may be a relevant core behavioral feature underlying vulnerability to ED. Furthermore, Tchanturia et al., (2004) showed that poor performance on set shifting tasks was associated with early childhood OCPD traits, including childhood rigidity and inflexibility. In addition, individuals with anxiety disorders have an increased likelihood of having a personality disturbance that meets the criteria for OCPD (American Psychiatric Association, 2013).

In a systematic review of 11 prospective longitudinal studies and 12 RCT's, researchers concluded that there is tentative support to suggest that OCPD traits mediate treatment outcome in AN and that AN patients with this personality disorder have a poorer prognosis (Bruce & Steiger, 2005; Crane, Roberts & Treasure, 2007). In a recent 18-year follow up study of adolescent onset AN, Wentz et al., (2009) found that a poor outcome was forecast by premorbid OCPD, early age at onset, and the presence of autistic spectrum traits. Similarly, in Steinhausen's review (2009) he concluded that features of obsessive-compulsive personality disorder contribute to chronicity and hence SE-AN.

Borderline personality disorder (BPD) is the most prevalent personality disorder in AN-BP (approximately 25%) with prevalence rates of 11% in AN-R (Sansone et al., 2006). Individuals with this personality style experience global dysregulation and have problems in several key areas of functioning, including affect regulation, impulse control, and interpersonal relationships. In addition to EDs, individuals with BPD have high rates of psychiatric comorbidity, including mood disorders, anxiety disorders, substance use disorders, impulse control disorders and PTSD.

An early study (Johnson, Tobin & Enright, 1989) compared ED patients with and without BPD and found relatively few differences between groups in symptom severity, eating behavior and attitudes. The only difference found in eating-related behavior at intake was laxative abuse. Eating disordered individuals with BPD endorsed the use and abuse of laxatives as a purging strategy at a clinically-significant higher rate than the non-borderline group. There were, however, striking differences between these two patient populations. The borderline group demonstrated significantly more general psychiatric symptoms, poorer psychosocial adaptation, higher levels of family conflict, and reported significantly higher rates of suicide attempts and engagement in self-injurious behavior. Additionally, the borderline group reported four times as many stressful events associated with the onset of their eating disorder, as did the non-borderline group.

Research suggests that individuals with ED and comorbid BPD have a protracted course of treatment, have a poorer response to treatment, and have higher rates of premature termination from treatment (Bruce & Steiger, 2005). Most researchers suggest that effective treatment with this complex patient group requires an integrated and comprehensive approach that focuses not only on the ED symptoms but also on deficits in the areas of interpersonal skills, affect regulation, and impulse control (Sansone, Fine & Sansone, 1994; Zeeck et al., 2007).

In a major review of outcome studies by Steinhausen (2009), it was concluded that comorbid psychiatric disorders, for example, anxiety disorder, major depression, or substance abuse, have a significantly negative effect on outcome and contribute to the development of SE-AN. Likewise, Steinhausen (2009) noted that borderline personality disorder symptoms "clearly stand out among the unfavorable factors because of

a replicated status in various studies". However, these findings on the prognostic function of comorbid disorders and personality features need further replication (Dennis & Sansone, 2015). Nevertheless, available data and clinical experience suggest that comorbid psychopathology predicts poorer outcome among patients with ED (Davies, Bekker & Roosen, 2011; Keel & Brown, 2010).

Sociocultural and Environmental Factors

Interpersonal Problems

An interrelated issue that can be associated with the maintenance of anorexic symptoms or non-responsiveness to treatment is the failure to resolve or fully process problematic interpersonal issues. Such issues may often intersect or overlap with the negative effects and cognitive distortions discussed elsewhere. Patients with AN are reported to have histories of more problematic social experiences, including histories of family dysfunction and interpersonal stressors that often lead to feelings of low self-esteem, social isolation, lack of perceived support, and poor coping and problem solving skills (Gual et al., 2002; Tiller et al., 1997; Troop et al., 1994). A recent literature review concluded that interpersonal difficulties in patients with AN are related to interpersonal distrust and negative interaction and conflict with others (Arcelus et al., 2013). Schmidt and Treasure (2006) have proposed a cognitive-interpersonal maintenance model of AN and have discussed its implications for research and practice. They emphasized four important and interwoven factors that contribute to chronicity: perfectionism/cognitive rigidity, experiential avoidance, pro-anorectic beliefs, and response of close others. Several researchers have suggested that certain family factors, such as high expressed emotion, misattributions about the illness or unhelpful methods of engaging with the ED symptoms, can affect adherence to treatment or outcome in AN (Eisler et al., 2000; van Furth et al., 1996). These factors are in addition to the various central and peripheral starvation-related maintenance factors of AN that have been discussed previously.

Trauma, Neglect and PTSD

As previously discussed, individuals with AN are particularly sensitive to stress and adversity. Anorexia nervosa sufferers have significantly higher rates of traumatic experiences and subsequent PTSD or partial PTSD (Mitchell et al., 2012; Reyes-Rodríguez et al., 2011). The literature consistently indicates higher rates of severe trauma and resulting PTSD in those with bulimic symptoms, i.e., bingeing and/or purging (Brewerton, 2014b; in press). Furthermore, the presence of lifetime PTSD or partial PTSD predicts a greater number and severity of comorbid psychiatric disorders, which as

noted elsewhere, likely contribute to SE-AN. Trauma-related disorders, such as BN, AN-BP, major depression, and PTSD, may share common underlying mechanisms that account for such interrelationships, including dysregulation in neuropsychobiological mechanisms that are activated by gene expression and subsequent underlying affective dysregulation, in addition to shared cognitive schemas involving issues of self-esteem, control, guilt and shame (Brewerton, 2004; 2014). This perspective is supported by several studies of mediating variables between previous abuse and later development of an ED. They demonstrate that impulsivity and fundamental beliefs involving self-esteem, shame, and perceived control are important considerations in understanding etiological mechanisms as well as treatment approaches (Brady et al., 2000; Murray & Waller, 2002; Waller, 1998; Waller et al., 2001; Wonderlich et al., 2001a; Wonderlich et al., 2001b). Rodriguez, Perez and Garcia (2005) reported that the highest likelihood of poor outcome was found in patients with sexual abuse and histories of other violent acts. In addition, this group of patients was at greatest risk for dropout and relapse following treatment. Similarly, Carter et al. (2006) found that patients with AN-BP and a history of CSA were more likely to terminate inpatient treatment prematurely compared to those without CSA. In their study, those with CSA had significantly worse measures of anxiety, depression, obsessive-compulsive symptoms, lower self-esteem, interpersonal problems, as well as eating disorder psychopathology. In a 5-year follow-up study, Vrabel et al., (2010) found that child sexual abuse and avoidant personality disorder interacted together in predicting ED chronicity. Taken together, available studies strongly suggest that severe childhood maltreatment contributes to treatment dropout, chronicity and the development of SE-AN (Brewerton 2004, 2007; Carter et al., 2006; Rodriguez, Perez & Garcia, 2005; Vrabel et al., 2010).

Schmidt et al. (1993) compared the defensive styles of AN and BN patients and healthy female controls in an attempt to establish a link between early childhood adversity and later adult defensive style. Excessive parental control during childhood was a negative predictor of mature defenses and physical abuse a positive predictor of immature defense style. The authors concluded that childhood adversity may constitute a vulnerability factor for the later development of bulimic eating disorders, which is mediated by personality development. In a later study, Schmidt et al. (1997) reported that critical life stresses frequently preceded the onset of AN and BN, and in particular, problems with sexuality appeared specific in triggering the onset of AN.

Cultural Effects

Western culture is a problematic environment for the individual recovering from AN. Pressures to be thin, young and physically attractive are ubiquitous in modern culture, while a simultaneous exposure to highly

palatable and immediately available foods in large quantities makes achieving healthy weight restoration, abstinence from dieting, bingeing and purging and subsequent recovery from AN very difficult. In addition, the existence of overt reinforcements for so-called "thinspiration" and maintenance of weight loss, such as pro-anorexia websites, can be important perpetuating factors to consider (Bardone-Cone & Cass, 2007).

However, Keel & Klump (2003) have argued that AN, unlike BN, is not a Western culture-bound syndrome. They point out that there are several accounts of AN from non-Western cultures, as well as documented examples from medieval times. Investigators have noted that the common denominator in these historical and non-Western cases is that their reasons for weight loss and psychopathology are not based on a thin body ideal or fears about body size or shape. Instead, their food restriction is better explained in terms of religious or ascetic ideals (Schmidt & Treasure, 2006). Furthermore, in an investigation of risk factors for AN, Fairburn et al. (1999) reported that weight- or shape-related criticism by family members had no independent effect on the development of AN. As a result, the cognitive-interpersonal model (Schmidt & Treasure, 2006) does not put emphasis on body size and shape concerns.

Social Reinforcement

Observations from clinical practice indicate that positive reinforcement for weight loss from others may play a powerful reinforcement role in rewarding drive for thinness and weight loss behavior. Patients often irrationally fear weight gain following cessation of bingeing and purging.

Family Dysfunction

In an important study by Dancyger et al. (2005), the mothers of ED patients were found to rate family functioning as significantly healthier and less chaotic than their daughters. Although there were fewer significant differences between maternal and paternal views of family functioning, there were no significant differences between fathers' and daughters' family perceptions. In addition, increased levels of depressive symptoms as reported by the daughters were linked to the perception of high family dysfunction. Differences in viewpoints between parents and daughters regarding family environment may negatively impact on the course of treatment and contribute to the continuation of dysfunctional family patterns.

Adaptive Function

Exploring the adaptive function of a patient's eating disorder symptoms and behavior can be a very helpful clinical tool. Recognizing the physical, psychological, social, or interpersonal problems that the ED solves or

governs and pinpointing the secondary gains that ensue from engaging in this behavior can inform the clinician about the predisposing, precipitating, and perpetuating factors that affect the disorder. ED behavior may fulfill an essential function or purpose. They answer a question, solve a problem (apparently), fulfill an unmet need, or modify the environment in a rewarding way (despite negative consequences). In many cases, the patient does not realize how this behavior is linked to underlying issues. Because these symptoms serve a purpose, they become difficult to relinquish. However, identifying and understanding adaptive function can direct the patient toward acquiring healthier coping strategies and more effective problem-solving methods. In the next section we review, in detail, the adaptive functions that are often found in patients with AN. Exploring the adaptive function can also guide case formulation, treatment team composition, the determination of appropriate level of care, therapeutic modalities, goals of treatment and treatment approach (Dennis & Helfman, 2010; Dennis, Pryor & Brewerton, 2014).

Common Adaptive Functions Found in Anorexia Nervosa

ED and associated behavior and symptoms are usually much more complicated than simply serving as ways to lose weight or improve one's body image. A variety of psychological problems can be displaced onto food, weight, and shape. Managing food intake and/or expulsion, and hence weight, body size and shape often generates a subjective sense of mastery over a world that is seen as "out-of-control". Hilda Bruch (1973) wrote that patients with AN have a "profound sense of ineffectiveness", "lack of awareness of their sensations", and "feel out of control". Severe dietary restraint and weight loss is thought to produce a desired outcome, such as offsetting or preventing some life event (for example, parental divorce or college attendance), or decreasing negative affect (for example, anxiety or depression), or enhancing self-esteem, boosting athletic abilities, attracting or avoiding a paramour, reducing sexual desire, or retarding the biological, social, sexual and psychological challenges of puberty (Arkell & Robinson, 2008; Brewerton, 2004; Costin, 2007; Dennis & Helfman, 2010; Dennis & Sansone, 1989; 1991; 1997; Johnson, Sansone & Chewning, 1992). Other clinical investigators (Persons, 2005; Persons & Tompkins, 2007; Zayfert & Becker, 2007) have also underscored the importance of recognizing the functional links and causative factors between symptoms when developing case formulations and applying evidenced-based therapies for patients with chronic and complex courses.

Managing Maturity Fears

AN most often develops during adolescence, especially as puberty emerges. One of the chief developmental tasks during the teen years is

to separate and individuate from one's parents or primary custodians. If the adolescent is developmentally not ready to move toward autonomy from the family, or is afraid of trusting their ability to negotiate the world on their own, they may employ "practice" behavior that is intended to promote independence and self-sufficiency, but may not actually result in true mastery. Taking charge of one's body through dieting or restricting food intake is one method of attempting to attain mastery and control while concurrently avoiding maturation or "growing up". Pushing their weight down by rigidly reducing food intake, engaging in vigorous exercise, and effectively eliminating one's menses or sex drive virtually guarantees not having to individuate from the family (see Crisp, 1967; 1980). Parents are much less inclined to allow their critically ill adolescent to go off to college on their own if they are unable or unwilling to manage the basic task of feeding themself. Therefore, the adaptive function of the ED effectively allows the individual to handle their maturity fears by remaining attached to adults, in an apparently safer and more predictable situation, until they feel sufficiently prepared to engage in the world independently. However, a subset of patients remain stuck indefinitely in this dependent, anxious and avoidant state which may lead to SE-AN.

Once established, SE-AN continues to interfere with physical and psychological maturation and leads to a psychobiological regression and loss of function. Due to the crippling nature of SE-AN, opportunities to individuate are curtailed and movement toward adult development is halted. Frequent medical crises or hospitalizations leave caregivers highly anxious, protective, hypervigilant and sometimes angry and rejecting. As the individual with SE-AN attempts to negotiate these challenges, they often become more dependent on family or caregivers, thus making separation and maturation more difficult to achieve.

Managing Sexual Conflicts

Both physical and sexual maturation begin during and continue through adolescence. Increases in the quality and intensity of drive activity, changes in appearance and reproductive capacity, and the sexualization of peer relationships can be tremendous challenges for developing adolescents. Self-induced starvation impedes normal growth and development and sharply reduces gonadal hormone profiles, thereby abolishing libido as well as the secondary sexual characteristics of a mature adult. As previously noted, by seizing control of the body, the adolescent can induce a return to the pre-pubertal psychobiological state where the threat of external sexual attention by peers or internal libidinous drives is reduced or eliminated (Crisp, 1967; 1980; Fornari & Dancyger, 2003; Leon et al., 1985). This particular adaptive function may be manifested in various configurations by patients of all ages with all types of ED. It is especially common for individuals who have suffered childhood sexual abuse or those that have

wrestled with sexual orientation or gender identity conflicts to engage in self-starvation, binge eating and/or purging to cope with sexual issues (Castellini et al., 2013; Ewan, Middleman & Feldmann, 2014).

Providing Structure, Predictability, and Control

The modern world is constantly changing, which requires a high level of adaptation. It can be challenging even for the most adept. It is well known that patients with AN have been reported to manifest cognitive rigidity, anxiety, high harm avoidance, resistance to change, and intolerance of uncertainty (Brewerton, Hand & Bishop, 1993; Holliday et al., 2005). These traits and tendencies are present even after long-term weight restoration, but are much worse during the low-weight, ill state. AN can appear to provide structure and predictability. Dieting and the pursuit of weight loss is a common activity in Westernized cultures that many people participate in, but few are successful. Having a healthy outcome from this endeavor demands commitment, self-sacrifice, and persistence. To attain a sense of control, individuals with AN seize command of their bodies and organize their lives around limiting calories, compulsive rigorous energy expenditure, rejecting previously desired foods, dodging activities that may interfere with their rituals and routines, and formulating a commitment to a long-range, often unrealistic goal. Self-discipline ensures that they do not become selfish or greedy; comfort is found in knowing they will never overindulge (Arkell & Robinson, 2008). For example: "If I exercise for 4 hours every day, eat no more than 500 calories a day, shun any foods that contain fat, and expel anything that is 'forbidden' or 'taboo,' then I can quickly and effectively achieve my weight loss goals." This behavior may yield noticeable results, which only reinforces the conviction that "I am strong, in control, and can accomplish something that most individuals can't." In a world that seems uncertain, unstable and "out of control," engaging in anorexic behavior thereby provides a strong sense of safety, mastery, and control.

Consolidating Self-Identity

Another essential but challenging developmental task during adolescence is to solidify a system of personal values, consolidate positive self-esteem, and acquire a stable and integrated self-identity. Adolescents endeavor to be unique individuals even within their own peer groups. AN is a relatively uncommon disorder, girls and women with AN are unique in that they are conspicuous to other people. Their sheer presence among a group of people frequently attracts either attention and concern or admiration. Patients with AN may feel a sense of pride in achieving their weight loss goals, even if the anorexic behavior compromises physical and emotional health (see Tan, Hope & Stewart, 2003). The glorification of thinness and the glamorization of ED among high-profile celebrities,

musicians, and athletes have contributed to the belief that having an ED is "not so bad". Unfortunately, they are consolidating a self-identity around a serious and enduring psychiatric illness.

Escaping, Avoiding, and Numbing

Patients often engage in ED behavior to modify their current emotional state (Engel et al., 2013; Goldschmidt et al., 2014). Unresolved interpersonal difficulties, problems at school or work, familial discord, teasing or bullying, domestic violence, emotional/sexual/physical abuse, post-traumatic stress disorder or symptoms, all can lead to the use of ED behavior to help individuals anesthetize themselves from negative mood states or to escape unbearable traumatic memories or thoughts or life circumstances. For some individuals, dieting, calorie-counting, exercising, procuring and eliminating food, and maintaining secrecy, becomes highly reinforced chronic behavior that has been conceptualized as addictive in nature (Brewerton, 2014) and which promotes the emergence of refractoriness and the development of SE-AN. They reduce their world to managing hunger and thirst; physical discomfort is often far more acceptable than emotional pain. As noted previously, Vrabel and colleagues (2010) found that avoidant personality disorder and childhood sexual abuse interacted to predict long-term chronicity and therefore SE-AN.

Punishing the Negative Self

Eating disorder behavior can be used as a way of inducing self-punishment or dealing with excessive guilt (Berghold & Lock, 2002). This adaptive function is most commonly seen in patients with markedly low self-esteem or histories of childhood maltreatment, as well as those with borderline personality disorder features. This behavior can be employed to reaffirm the patient's well-established belief that they are not good enough or unlovable, which reinforces their low self-esteem and negative self-concept (for example, "It is my fault what happened to me", "Bad things only happen to bad people, and they need to be punished"). ED behavior such as severe food restriction ("I am not worthy to eat"), self-induced vomiting ("I need to get all the bad out of me"), chronic use of laxatives ("I deserve to feel pain"), and excessive exercise ("Bad people should suffer") are often employed and serve as self-punishment. This subgroup of patients frequently exhibits significant dysregulation in numerous areas of their lives (for example, affect, sexual and aggressive impulses, cognitions, interpersonal relationships, and eating and sleep patterns). They may regularly engage in various forms of self-destructive behavior, including polysubstance abuse, or parasuicidal behavior (i.e., cutting, burning, and self-mutilation), other forms of violence, gambling, driving under the influence, sexual promiscuity, shoplifting, and compulsive buying.

This adaptive function is frequently seen in a subgroup of patients that was first identified and described as Multi-Impulsive Bulimia (MIB) by Lacey (1993). This includes a subset of patients that endorses a history of at least three of six impulsive forms of behavior (i.e., severe alcohol abuse, drug abuse, self-harm, suicide attempts, stealing or sexual promiscuity), has greater overall psychopathology, are likely to have experienced childhood abuse or trauma, and have poorer outcome than bulimic individuals without high levels of impulsivity (Fichter, Quadflieg & Rief, 1994). As authors, we contend that this clinical profile is also seen in patients with AN, particularly the AN-BP group. MIB has been linked to chronicity (Fichter et al., 1994; Wonderlich et al., 1994).

Managing Mood Disorders

There are significantly higher prevalence rates of comorbid mood disorders, such as major depressive disorder, bipolar disorder, and dysthymia in ED patients. Depressive symptoms or mood disorders can either precede (primary mood disorder) or follow (secondary mood disorder) the onset of AN. Wildman, Lilenfeld and Marcus (2004) reported that major depressive disorder preceded the onset of an ED in 33% of their female participants, however, a more recent study found that only 6% of female adolescents with first-onset AN had a premorbid mood disorder (Buhren et al., 2013). Furthermore, AN behavior (i.e., chronic dieting, excessive exercising) can lead to depression, as supported by the classic human semi-starvation study led by Ancel Keys (Keys et al., 1950). In this study, striking changes in emotional states, such as elevated levels of depression and anxiety were observed in previously mentally healthy men as dietary limitations and weight loss progressed. As noted elsewhere, major depression is among the comorbid psychiatric disorders that contribute to chronicity. Depression is therefore often a major perpetuating factor in AN and consequently a contributor to SE-AN.

Reducing Stress and Managing Anxiety

It has been well established that anxiety disorders, including separation anxiety disorder, social anxiety disorder, post-traumatic stress disorder, obsessive-compulsive disorder, panic disorder, and simple phobias are common comorbid conditions in individuals with AN (Hudson et al., 2007). In the majority of cases, anxiety disorders manifest before the onset of the ED (Deep et al., 1995; Godart et al., Flament, Lecrubier & Jeammet, 2000; Kaye et al., 2004). As noted previously, patients with AN may be especially susceptible to stress and its many dire effects. The preexistent presence of anxiety often results in an enhanced sensitivity toward perceived threats, stresses, traumas or adverse circumstances. This vulnerability has been demonstrated in many ways experimentally. Strober

(2004) maintained that patients with ED have a proclivity to intense fear conditioning, and higher than usual resistance to extinction. McFillin and colleagues (2012) reported that those with ED are more likely to sense aggressive intent in people's faces in comparison to controls. ED patients also make significantly more facial emotion recognition (FER) mistakes compared to controls. They frequently over interpret fear as anger (Ridout et al., 2012). Other investigators have noted that individuals with AN: (1) typically display high degrees of anxiety sensitivity exemplified by fear of loss of control (Fulton et al., 2012); (2) are usually over concerned with consequences and show exaggerated inhibition (Kaye, 2008); (3) demonstrate exaggerated anticipatory anxiety (Oberndorfer et al., 2011), and; (4) manifest high punishment sensitivity (Harrison et al., 2010; 2011; Jappe et al., 2011). Other studies reveal AN patients to have impaired flexibility, decreased set-shifting (Roberts et al., 2007; 2010), increased sensitivity to uncertainty (Frank et al., 2012), and weak central coherence (Lopez et al., 2008; 2009). As a consequence, patients often unable to understand what is important because they give too much attention to the details and are easily overwhelmed by adverse life events and stress.

Case Example

Diane was the oldest of three siblings whose parents divorced when she was 7 years old. She was raised by her mother and maternal grandparents in a rural community. From a young age, she was repeatedly sexually abused by her grandfather and forced to watch her younger siblings being sexually abused by him. To insure her silence, her grandfather would give her candy and refrain from abusing her if she did not tell. Her mother worked the afternoon/evening shift and her grandparents were the primary care givers after school and in the evenings for the children. The grandmother was present but "unseeing".

Commentary

- *Early loss age 7, parents' divorce.*
- *Repeated childhood sexual abuse and witnessing violence carries a negative prognosis.*
- *"Unseeing" responsible adult (emotional neglect).*

Diane was exceptionally bright and got a job after school taking care of the horses in order to avoid being home with her grandfather. However, at age 12, she was raped by the stable caretaker. At age 14 she finally revealed the abuse she and her siblings were experiencing but her mother refused to believe her and did not intervene.

Commentary

- *Being a 12-year-old rape victim by an adult male.*
- *Problematic disclosure of childhood sexual abuse to a disbelieving mother is a positive predictor of PTSD/dissociation.*

Throughout adolescence she was repeatedly treated at a local hospital for electrolyte imbalances and episodes of fainting due to low weight. She did not achieve a weight that could sustain a menstrual cycle. She never revealed that she was also bingeing on candy and vomiting after all meals. At age 16, she was admitted to the psychiatric unit of her local hospital for AN. She was re-fed to approximately 92% of expected weight and discharged three weeks later. Within two months, she had relapsed but refused further psychological treatment.

Commentary

- *Bulimic symptoms in AN carry a negative prognosis.*
- *Chronic low weight during puberty and adolescence can lead to primary/secondary amenorrhea, osteopenia and osteoporosis.*

At age 18, she attended college but remained significantly under expected weight and engaged in daily binge eating and purging. Her first realization of amnesia or "lost time" happened when she was in college, and periodically reoccurred for the next several years. For example, she realized that she had bought new clothes, found scored exams in her college papers, and had boyfriends (including one of her professors) that she did not remember. She described her college and graduate study years as a time of confidence, productivity and hypersexuality.

Commentary

- *Severe trauma, including rape and childhood sexual abuse, can cause tremendous emotional and mental disruption and can cause post-traumatic stress disorder.*
- *The trauma may be so overwhelming that the individual may slip into a dissociative state in order to escape and cope.*
- *Hypersexuality is a common response to sexual abuse, especially during childhood.*

Despite her continued eating disorder, she was able to complete an undergraduate degree and a PhD, get married, and start a very successful business in a town away from her family. However, by age 27, she became seriously ill and was admitted to a research hospital for several months for medical stabilization and treatment. Upon completion of her stay, she attended a two-month intensive treatment program, and for the first time revealed her history of rape and repeated childhood sexual abuse to her treatment providers. Her mother and one sibling attended family sessions during her stay, but refused to corroborate her recollections. Upon completion of the intensive program, she was referred for aftercare to an outpatient treatment program in her local community to continue weight restoration and trauma treatment.

Commentary

- *Repeated disclosure of sexual abuse to disbelieving authorities is a positive predictor of PTSD/dissociative symptoms.*
- *Repeated intensive treatments that discharge before full weight restoration and the achievement of biological normality increase the likelihood of ED relapse.*

For the next nine years she faithfully attended biweekly and weekly therapy sessions, worked on normalizing her eating patterns (with the assistance of a dietitian) and eliminating compensatory behavior, regularly saw her primary care physician to ensure medical stability, and was prescribed an antidepressant to reduce anxiety and depression. Treatment consisted of eating disorder and trauma based CBT and exposure with response prevention. However, treatment was hampered by dissociative episodes, which were brought on by severe anxiety and panic attacks, relaxation and mindfulness exercises, and when confronting traumatic memories. She was unable to reach her target weight range or give up her daily purging.

Her husband actively participated in treatment. He was her business partner, and was devoted to her and her treatment. She was open and candid with him about her abuse and attempted to incorporate him into the treatment process but often sabotaged any of his efforts to assist her in recovery. Additionally, Diane's mother attended numerous sessions with her but refused to accept her daughter was a victim of childhood sexual abuse.

The toll of AN-BP behavior was significant, including the loss of many of her teeth, bloody vomitus, severe fatigue, hyperacuity to light and sounds, severe osteoporosis, physical weakness, lanugo, significant constipation, severe depression and chronic anxiety.

Commentary

- *SE-AN leads to a break down in every organ system in the body.*
- *Forced into secrecy, ignored by mother and grandmother, and betrayed by a sister who was also abused, can create a double-bind and an extreme sense of abandonment.*
- *SE-AN results in chronically depleted neurotransmitter function, elevated stress hormone levels and damage to various neuronal circuits involved in attention and memory, emotional regulation and impulse control.*

Likewise, her marriage suffered as she was unable to be intimate and often stated that she avoided having sex or a menses because she did not want to have children. Her ability to manage stress and the physical challenges of her work were also compromised by her low weight and "forced absences" due to frequent inpatient hospital stays to stabilize her medical condition. She agreed to "medical stabilization" in a hospital setting but repeatedly refused specialized eating disorder treatment at a higher level of care (i.e., inpatient, residential, PHP).

Commentary

- *Childhood sexual abuse often leads to avoidance of intimacy in sexual relationships.*
- *Multiple failed treatment experiences where loved ones deny the reality of the patient, can lead to self-doubt, distrust of the therapeutic process and a sense of helplessness and hopelessness.*
- *Premature termination from inpatient treatment is a negative prognostic factor.*

In her late 30s, her weight plunged to a BMI of 12.9 and her family and outpatient team "insisted" on specialized inpatient care. Escalating dysphoria, increased dissociative episodes, suicidal ideations, and marital and work related problems precipitated this decline. During her inpatient stay, she was extremely uncooperative (vomiting daily, repeatedly pulling out her peripherally inserted central catheter (PICC line) and coded twice on the unit and was transported to the emergency room). As her weight declined and her opportunities to purge were curtailed, her dissociative episodes increased. After four months of treatment she was transferred

to an eating disorder inpatient program that also specialized in the treatment of DID. During her final inpatient stay, treatment focused on bringing all of her "alters" together at the table, in order to get her to eat. Against medical advice, she left inpatient treatment but continued outpatient treatment with a DID specialist in her local community. She died of complications of AN-BP at the age of 42.

Diane had a 28-year history of AN-BP brought on by severe childhood sexual abuse, witnessing the abuse of her siblings and rape as an adolescent. Although she was exposed to cutting-edge interventions at respected treatment facilities, her ability to recover was compromised by authority figures who refused to accept her reality. Her self-sabotaging behavior was indicative of deep-seated internal conflicts and ambivalence about recovery. Her chronic low-weight status interfered with the processing of traumatic memories and her need to avoid this material interfered with her ability to achieve weight recovery. This tragic and fatal case underscores the importance of integrated treatment by a therapist (and treatment team) skilled in both the treatment of severe AN and trauma.

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