A Review of Anorexia Nervosa, Its Relationship to Autism and Borderline Personality Disorder, and Implications for Patient Related Outcomes

Clive Kelly*, Matthew Davies

University of Newcastle upon Tyne, Tyne and Wear, UK

*Corresponding Author: Dr. Clive Kelly, University of Newcastle upon Tyne, Tyne and Wear, UK, E-mail: cliveryton@gmail.com

Received: 06 August 2019; Accepted: 19 August 2019; Published: 27 August 2019

Abstract
Anorexia Nervosa (AN) is a serious psychiatric disorder associated with reduced intake of food, increased energy expenditure and psychological features, in which a low body weight is deliberately maintained and the patient experiences an associated body-image distortion. AN has recently been shown to share expression with additional mental health disorders including both Autistic Spectrum Disorder (ASD) and Borderline Personality Disorder (BPD). These associations may have implications for outcomes and therapeutic intervention. Phenotypes of ASD and BPD merge in the psyche of some women with AN. In essence, women with early onset AN in whom the diagnosis of ASD is made a decade or more later, are most likely to demonstrate a mix of personality features. The abnormal Neuropsychology underpinning the links between these three conditions is complex. The limbic system which controls emotions, via the hippocampus, amygdala and prefrontal cortex, is known to be both structurally and functionally different in patients with AN, ASD and BPD, as evidenced by neuroimaging studies. AN is associated with multiple effects on the endocrine system. Growth hormone, sex hormones and cortisol levels all rise, producing an unpredictable mix of outcomes. Bone density is reduced in 90% of cases, with an additional acceleration in bone loss. Fractures of the spine and pelvis occur in women as young as thirty. Women who develop early onset AN often demonstrate above average competitive drive and intelligence but may be stunted in terms of skeletal growth, social integration and emotional maturity. As the limbic system is linked to the endocrine system via the HPA axis, the exaggerated physiological responses associated with endocrine hyperactivity described above may directly or indirectly relate to the transference of heightened emotional states into harm of self or others. This combination of clinical features produces a range of challenges for those who suffer with, or care for, those with AN and associated ASD or BPD. It is essential to address both long and short term physical complications associated with the disease, and this requires close cooperation between Psychiatrists, Physicians and a multidisciplinary team.
Keywords: Anorexia nervosa; Eating disorders; Autism spectrum disorder; Borderline personality syndrome

1. Anorexia Nervosa

Anorexia Nervosa (AN) is a serious psychiatric disorder associated with reduced intake of food, increased energy expenditure and psychological features, in which a low body weight is deliberately maintained and the patient experiences an associated body-image distortion. Sufferers experience a dread of fatness as an intrusive, overvalued idea [1] and this condition may affect up to 4.2% of women during their lifetime [2]. The condition is associated with a significantly elevated mortality, and in fact carries the highest mortality rates of any mental health disorder [3] with 17% of patients succumbing to the disease or its effects [4]. A recent meta-analysis of 36 studies found a standardised mortality ratio of 5.86 (95% CI, 4.17-8.26) over an average follow-up period of 14.2 years [4]. Up to 40% of deaths are due to suicide [5, 6] which is increased by a factor of 56 over control subjects [7]. Factors associated with a poor outcome in AN include recurrent disease, alcohol abuse and other psychiatric comorbidities [7-9]. Eating disorders such as AN are associated with feelings of despair and hopelessness for many, and under 50% of patients make a full recovery [10] with many of the remainder suffering from chronic eating issues.

AN has recently been shown to share expression with additional mental health disorders including both Autistic Spectrum Disorder (ASD) and Borderline Personality Disorder (BPD). These associations may have implications for outcomes and therapeutic intervention. This review explores the comorbidity between these three conditions, and highlights areas for further research.

2. Autism Spectrum Disorder

ASD characterised by impairment in social interaction, and restricted and repetitive set of behaviours and interests. In the high functioning form there is no general delay or retardation in language acquisition or cognition [1]. Specific issues associated with high functioning ASD include difficulty with recognition and regulation of emotions. Interpersonal function is also often a challenge, with difficulty in learning how to understand and connect with others [11-14]. ASD is increasingly well recognised in females but is often diagnosed later than in males because of more effective masking of symptoms [15-17]. It has been suggested that ‘masking’ or ‘camouflaging’ of difficulties with social interaction can be exhausting and may produce profound fatigue or episodes of melt down. Anxiety and depression [18] may be precipitated by changes in routine such leaving home or starting a new job. ASD also has a significantly negative impact on life expectancy, with a Swedish study reporting a mean age of death of 54 in ASD patients compared to 70 years in a matched control group [19]. Sadly, suicide again contributes to this reduction in life expectancy [19].

3. Overlap between AN and ASD

A link between eating disorders and ASD is increasingly recognised [20]. Baron-Cohen et al found elevated autistic traits in girls with AN compared to a control population, with over half of the girls with anorexia displaying a ‘broader autism phenotype’ compared to just 15% of controls. The conditions overlap in several areas with a tendency towards rigidity of thought and behaviour, and an increased focus on self. Self-image is less likely to relate to the concept of body dysmorphism, than to the need to take and maintain tight control over all aspects of their...
lives. Whilst the presence of increased autistic traits in AN patients is increasingly well characterised, it remains to be seen whether a diagnosis of ASD is predictive of the development of a subsequent eating disorder. Nevertheless, there is a well-established link between ASD and unusual food behaviours such as the consumption of a restricted range of foods [21]. Those in whom the diagnosis of AN is made before the age of 14, and in whom autism is not recognised until after 20 do least well [22], because some behavioural traits associated with ASD can become irreversibly engrained in the psyche and self-justification makes it very difficult to reverse the resultant food restriction which the individual will often aggressively defend on the grounds of their ethical and moral beliefs.

The Minnesota starvation study demonstrated that normal men develop behavioural abnormalities when subjected to starvation, and their behaviour exhibited features of paranoia and psychosis, which actually accentuated when they began refeeding, prior to full recovery [23]. Starvation usually aggravates and may precipitate mental health problems. Social and family dynamics play a large part in the generation of AN [24], in addition to psychological factors, such as obsession and perfectionism [25]. Excess serotonin is present in most patients with AN [26] and may help potentiate the process [27]. Neuroimaging has demonstrated abnormalities that may contribute to the cognitive deficits described in association with this condition [28, 29]. Those with obsessive compulsive personality disorder have a worse prognosis [30] and there is a strong link with BPD [31] and other personality disorders [32]. The presence of anxiety and depression are common, are often associated with alexithymia, and are also linked with worse outcomes [33].

4. Borderline Personality Disorder

BPD is a biopsychosocial disorder secondary to a combination of highly emotionally sensitive temperament and an early invalidating environment. Evidence suggests that rates of BPD are significantly elevated in first-degree relatives of individuals with the condition, suggesting that the condition is often transmitted generationally [34,35]. An early study showed that over half of patients presenting with eating disorders also had a personality disorder [36], although numbers were small. More recently, von Lojewski and Abraham [37] investigated personality factors amongst inpatient eating disorder patients. They found five significant factors: ‘interpersonal anxiety’, ‘instability’, ‘self-uncertainty’, ‘obsessiality’ and ‘perfectionism’. Herzog et al [38] demonstrated that over a quarter of 210 women with eating disorders had evidence of at least one personality disorder, with the commonest type being BPD. This was associated with a longer history of anorexia [38]. People with BPD have been denied the opportunity to develop appropriate internal insight, so they have difficulty in identifying their own feelings and deciphering differences between what they want and what they need. As a result, establishing healthy relationships becomes a challenge.

5. Overlap between AN and BPD

The evidence linking eating disorders to BPD was reinforced by Skodol et al [39] who assessed 200 women with AN with similar conclusions, showing that chronicity of and adverse outcome from AN were associated with having BPD. In a much quoted study, Zanirini [38] showed that 54% of people with BPD had eating disorders, more than twice the rate seen in those with other personality disorders. In this study of 290 patients, improvement in AN was the rule rather than the exception, but in many patients the condition migrated from AN to another form of eating disorders.
disorder, frequently orthorexia or rigidity around eating, often associated with an obsessive-compulsive tendency to exert control through eating the same food in the same place at the same time – and often alone. This was often also associated with autistic features [38].

A review of the 28 relevant papers published in the last fifteen years of the twentieth century concluded that 58% of women with eating disorders had features of a personality disorder [40]. The latest data suggest that a quarter of all people with AN fulfil diagnostic criteria for BPD, and that a similar percentage of those with BPD have AN [31, 32]. The link now seems both significant and undisputed. However, whilst women with the condition are more likely to have AN, men are at greater risk of addiction or substance abuse. Those of either sex who demonstrate a combination of these features are in the worst prognostic group. This most often features the coexistence of AN and alcohol binge drinking, which not only carries a high risk of early death, but long term adverse physical and psychological outcomes [7, 41].

6. Implications of Overlap between AN, ASD and BPD: Clinical Expression and Mechanisms

The findings described linking both ASD and BPD to AN may at first sight appear contradictory as the classic image of someone with BPD (outgoing, capricious, unreliable) appears the opposite persona to the typical image of the person with ASD (solitary, predictable, honest). However, it appears that the two phenotypes merge in the psyche of some women with anorexia [42], with those carrying the worst prognosis most likely to demonstrate the overlap [39-41]. In essence, women with early onset or resistant AN and in whom the diagnosis of ASD is made a decade or more later, are most likely to demonstrate a mix of personality features. While they are often very determined to the point of being stubborn, they may show disproportionate anger in the face of disagreement [43] and a complex range of emotions [44]. Often highly intelligent, they may nonetheless lack logic and demonstrate inflexible thinking but find debate difficult, as they often perceive it as criticism which they find hard to accept [45]. Anxiety is almost invariable and the episodes of panic that sometimes develop show overlapping features with autistic meltdowns when sensory overload is too hard to handle, a scenario in which therapeutic intervention can be challenging [46].

The abnormal neuropsychology underpinning the links between these three conditions is fascinating. The limbic system which controls emotions, via the hippocampus, amygdala and prefrontal cortex, is known to be both structurally and functionally different in patients with AN, ASD and BPD, as evidenced by neuroimaging studies [47-50]. In patients with AN, neuroimaging studies in early-onset anorexia nervosa provide evidence of limbic system dysfunction, with a significant association between unilateral reduction of blood flow in the temporal region and impaired visuospatial ability, impaired visual memory, and enhanced speed of information processing [47] This correlates with neuropsychological investigations suggesting poor performance in AN sufferers on frontal lobe tests, with a significant reduction in regional cerebral blood flow. It is suggested that these deficits could be interpreted in terms of limbic system dysfunction. In those with ASD, connections to the limbic system are altered, and extensive abnormalities in connectivity within frontal, temporal and cerebellar regions have been recognised [48]. Underactivity in the frontal and amygdala has been recognised during empathy or 'mentalising' tasks, as part of the defect in the 'social brain', a network including the prefrontal cortex which does not function normally in ASD [51].
Among patients with BPD the increased activity of the amygdala is thought to modify the perceptual cortex [52]. Although the amygdala itself may be smaller in volume than normal in such patients, they exhibit excessive activation of the amygdala to negative emotions [53]. Links between the amygdala and frontal lobe are altered in BPD, both in the resting state [54] and on emotional distraction [55]. The structure and function of the cingulate cortex is altered in BPD [54,55], and reduced frontal lobe regulation of emotional responses mediated via the amygdala results [53,55]. In addition, hypoactivity in other areas of the brain related to cognitive empathy has also been reported in patients with BPD [56]. Taken together, these studies suggest that BPD is associated with dysregulation of emotional control and empathy as a result of functional changes in the connectivity of the amygdala with the areas of the brain specifically charged with regulating responses to such stimuli [49,50,52-56].

Recent data showing reduced mentalizing in patients with eating disorders has emerged. The study by Sacchetti et al (57) showed significant reductions in the capacity of such individuals to understand the mental states of themselves and others and showed links to features of BPD in the same patients. Interestingly, they excluded people with ASD which, given the theory of mind issues experienced by such patients, might have provided further evidence for these links. This not only offers evidence to demonstrate eating disorders are associated with reduced insight, but that this may be explained by the coexistence of BPD as well as ASD.

The reasons for the overlap in autistic and personality influences in AN may have its origin in early life. Both ASD and BPD have significant genetic components, but each may also be influenced by early life experiences. Stress, caused by maternal rejection or conflict, may play a part in the expression of both autistic features and BPD [58], while abuse of a physical or emotional nature, is thought to be a highly relevant factor in the later development of personality disorders [42,59]. Both are associated with an excess of cortisol production which shapes the behaviour and development of the limbic system via hypothalamic - pituitary - adrenal (HPA) axis [60]. The endocrine system therefore can be programmed to over respond to later stresses, and this may be highly significant if the person then develops calorific restriction.

7. Implications of Overlap between AN, ASD and BPD: Impact on Patient Related Outcomes

AN is associated with multiple effects on the endocrine system [61]. Cortisol levels are elevated during calorie restriction [62] and may remain high in a subset of sufferers [63,64]. Although menses will usually return in those who regain weight, anxiety and depression are common in those with persistent hypercortisolaemia and the redistribution of fat and fluid around the face and trunk can cause a further reduction in self-image and contribute to social isolation [65]. The presence of salivary gland, especially parotid enlargement may contribute significantly to this process [66]. Growth hormone, sex hormones and cortisol levels all rise, producing a heady and often unpredictable mix of outcomes. Growth hormone resistance may result in short stature, while anorexia of early onset may also delay the onset of puberty and prevent the development of optimal skeletal maturity [67]. Bone density is reduced in 90% of cases, with an additional acceleration in bone loss. Increased circulating cortisol levels contribute towards this reduction in bone mineral density [65, 68]. Excessive stress and overactivity may add to weight loss and further reduce bone density leading to a sevenfold increase in the fracture rate [69]. Indeed, fractures seen usually in older women occur in those with an early onset of AN. Fractures of the spine and pelvis are reported in
women as young as thirty, whose bone density is often 2 or 3 standard deviations below normal despite weight bearing exercise [70]. Even the subsequent return of menses does not restore bone density to normal values [71]. The role of excessive exercise by undertaking excessive swimming or cycling without weight bearing may also be an important factor in accelerated bone loss in some women with AN [72].

The adrenal medulla can produce excess adrenaline with an overdrive of activity explaining the association with attention deficit hyperactivity disorder (ADHD). This can, given the competitive nature of these folk, lead to an excessive adherence to exercise programs producing an almost obsessive-compulsive element to their behaviour. Resultant fatigue is common in those with AN and ASD, especially if the sleep pattern is disturbed [73]. Sexual disinhibition is well recognised as a feature of BPD [74] but is often offset by the loss of libido frequently associated with AN [75], or the social isolation seen in some people with ASD [74], so that almost half of all affected women avoid sexual intercourse [76]. So those girls who develop early onset AN often demonstrate above average competitive drive and intelligence but may be stunted in terms of skeletal growth, social integration and emotional maturity.

With increasing evidence of the overlap in clinical features, emotional responses and social functioning in those with BPD and people with ASD [77-80], the relevance of these findings for patients with eating disorders has become more apparent. Self-harm is well described both in those with ASD and BPD. Although the rationale is arguably different in each condition, with the need to exert control often quoted as the major factor in the former, while emotional dysregulation is cited as a reason in those with BPD, where the damage may be a feature of self-loathing. In those with eating disorders the mechanisms may coexist, and this would explain the high rate of serious self-harm and threatened suicide in this group of individuals [7]. Patients response to stress, particularly criticism or adverse comments, can intensify to the point of inducing anger or rage. If this is externalised, then social destruction results. If it is internalised, then self-destruction can occur [81]. As the limbic system is linked to the endocrine system via the HPA axis, the exaggerated physiological responses associated with endocrine hyperactivity described above may directly or indirectly relate to the transference of heightened emotional states into harm of self or others. This combination of clinical features produces a range of challenges for those who suffer with, or care for, those with AN and associated ASD or BPD. It remains interesting to speculate whether those AN sufferers who also have ASD may be less likely to make a complete recovery.

8. Implications of Overlap between AN, ASD and BPD for Therapeutic Intervention

It is important that both clinicians and the public are aware of the frequency with which AN occurs in Western societies, the links that exist with ASD, and with personality disorders. Evidence exists that these disorders are becoming more common among young people, with reduced connectivity and increasing dependency on the mixed messages shared by social media a potential contributory factor.

This combination is dangerous for the sufferer, with high rates of suicide and self-harm, and may also be difficult to treat as the therapist and / or carer may become a target of suspicion or criticism. Expert input from Clinical Psychologists in an Eating Disorder Unit specialising in this area is required, and a course of treatment may take
many months with a risk of relapse an ever-present concern. Psychotherapy using Cognitive Behavioural Therapy (CBT) is the treatment of choice in the first instance for most, but family therapy is often useful. Patients may resist therapy, and adverse prognosis may be associated with alcohol or substance abuse, severe comorbidity with anxiety or depression, and the presence of an associated personality disorder where the sufferer is unable to accept responsibility for their own actions, instead transferring this to the therapist. It is also essential to address both short and long term physical complications associated with the disease, and this means working with a Physician competent in diagnosing and managing metabolic and endocrine aspects of the condition.

Acknowledgement
Our thanks go to Naomi Clark for her thoughtful and informed critique of our paper

References


