



Mini Review

Anorexia nervosa and autism spectrum disorder: A different perspective

Shamon Gumbs*

Marbourne Ave, Baltimore, Maryland, USA

*Corresponding author's E-mail: shamon27@hotmail.com

ABSTRACT

This article is aimed to facilitate further discussion on the topic and hopefully lead to the development of more effective treatment options for Anorexia Nervosa. There has been increased interest in the associations between Anorexia Nervosa (AN) and Autism Spectrum Disorder (ASD) due to overlapping symptoms. On the surface, AN and ASD have always seemed as completely unrelated disorders. The oversensitive, underweight individual who is intensely worried and preoccupied with the number of calories consumed in order to attain the 'ideal body figure'. The individual with unusually focused interests, repetitive movements, and difficulty with social interactions. Individuals must be able to look pass already established definitions and misconceptions to observe the number of similarities associated with both disorders and explore different treatment strategies. After all, medical practice is constantly changing and evolving in response to new information and new technologies.

Keywords: Anorexia Nervosa, Eating disorder, Autism Spectrum Disorder, Female ASD

MINI REVIEW

On the surface, Anorexia Nervosa (AN) and Autism Spectrum Disorder (ASD) have always seemed as completely unrelated disorders. The oversensitive, underweight individual who is intensely worried and preoccupied with the number of calories consumed in order to attain the 'ideal body figure'. The individual with unusually focused interests, repetitive movements, and difficulty with social interactions. We must be able to overlook the already established definitions and misconceptions in order to observe the similarities associated with both disorders and explore different treatment strategies. After all, the medical practice is constantly changing and evolving in response to new information and new technologies. AN is listed as an Eating disorder. However, recently many patients are being classified as having the residual category of 'eating disorder not otherwise specified' in DSM-IV.

AN is an eating disorder that is a potentially life-threatening illness associated with high levels of functional and social impairment (Tchanturia et al., 2013). It is characterized by an excessive restriction on food intake and irrational fear of gaining weight, often

accompanied by a distorted body self-perception. It typically involves excessive weight loss and is usually found to occur more in females than in males (Hockenbury, 2008). AN is an illness with many etiologies attributed to risk factors such as developmental, family history, psychiatric comorbidity, substance abuse and biologic factors (Haller, 1992; Strober, 1990; Rastam, 1992; Halmi et al., 1991 and Stern et al., 1992). AN tends to manifest during adolescence and has the highest mortality rate of any psychiatric disorder, with no gold standard treatment, high treatment dropout and relapse rates (Micali, 2013 and British Psychological Society, 2004).

On the other hand, there is the Autism Spectrum Disorder (ASD). ASD is a range of neurodevelopmental disorders that includes autism and other related conditions. ASD can present with predominantly two types of symptoms, that is, problems in social communication and social interaction, and restricted, repetitive patterns of behaviour, interests or activities. These symptoms are typically recognized between one and two years of age (American psychiatric association, 2013). The cause of ASD is uncertain. It is usually present in the early developmental periods, but

sometimes it may not manifest until later on in life. The notion of the spectrum relates to ASD symptom severity, with its expression ranging from mild to severe, and to some extent with intra-individual variability over time and across contexts. The prevalence of ASD in the United States (US) has climbed steadily to 2.76% of the general population in 2016, possibly due to changes in the way prevalence is measured, increased awareness, and shifts in the criteria for diagnosing autism (Xu, 2018).

In the 1980s, A professor by the name of Christopher Gillberg observed that individuals with AN and those with ASD presented with a number of overlapping features. AN patient's present with an inflexible, preoccupation with food restriction, at the expense of their health. It has been suggested that AN may be a female presentation of ASD (Treasure, 2013). ASD has been reported with an approximately 4:1 male-female ratio as compared to AN with an approximately 1:10 male-female ratio (Surveillance Summaries, 2008). These disorders present with opposite gender ratios.

There are several reasons for considering that AN and ASD traits may be linked. AN involves rigid attitudes and behaviour, which can be seen as resembling the unusually narrow interests, rigid and repetitive behaviour in ASD, though in AN their focus is mainly on food or weight. AN individuals are generally self-preoccupied and display social anhedonia, presenting as a failure to empathize with others also resembling the social difficulties in autism (Tchanturia, 2012; Chevallier, 2012 and Cohen, 2013). Both autism and anorexia show atypical structure and function in 'social brain' regions, including in the superior temporal sulcus, fusiform face area, amygdala, and orbitofrontal cortex (Zucker, 2007). For these reasons, it is possible that autism and anorexia share common underlying cognitive and neural phenotypes (Zucker, 2007 and Treasure, 2007).

The hypothesis concerning the associations between AN and ASD have sparked interest leading to research in certain areas, such as the shared genetic vulnerability interacting with environmental factors leading to AN in females during adolescence and ASD in males during infancy (Gillberg, 1983).

A study decided to investigate the presence of autistic traits in AN, which included the use of the Autism Spectrum Quotient for Adults (AQ-10) questionnaire. Individuals with AN scored significantly higher on the AQ-10 than typical control participants. This study along with previous research showed that there may be several factors accounting for the autistic traits in AN individual's. Starvation has been shown to reduce the quality of interpersonal relationships, interest in other people, and libido (Tchanturia et al., 2013). Another study at the Autism Research Centre at Cambridge

University tested how 66 adolescent girls (aged 12-18) with anorexia but without autism scored on tests to measure traits related to autism. They compared them to over 1,600 typical teenagers in the same age range and measured their autistic traits using the AQ, their 'systemizing' using the Systemising Quotient (SQ), and their empathy using the Empathy Quotient (EQ).

They found that on the AQ, five times more girls with anorexia scored in the range that people with autism scored in, as compared to the typical girls. In addition, on the AQ, over half of the girls with anorexia showed the 'broader autism phenotype', compared to just 15% of typical girls. On the tests of empathy and systemizing (how strong an interest the person has in repeating patterns and predictable rule-based systems), girls with anorexia had a higher SQ, and a reduced EQ, a profile that parallels that seen in autism (Baron, 2013). Missed or delayed diagnosis of ASD in females during childhood could leave those individuals vulnerable to the development of secondary mental health problems (Yau, 2008) including AN, which may obscure the identification of ASD when manifested as extreme rigidity or obsessive interest in calories or exercise (Lai, 2015). Management of AN can be difficult and with the presence of ASD symptoms it can lead to poorer outcomes and treatment efficacy.

Recent research has linked AN to specific alterations in social cognition that is typically associated with ASD, such as impaired understanding of other people's mental states, or theory of mind (ToM) (Gillberg, 2010; Jewell, 2016; Russell, 2009; Sampaio et al., 2013 and Sampaio, 2013). Studies that specifically target ToM processes have identified reduced activity in brain circuits associated with social cognition including the superior temporal cortex and temporoparietal junction (TPJ). A study recruited patients diagnosed with AN according to DSM-IV from an in-and outpatient Anorexia-Bulimia unit at the Queen Silvia Children's University Hospital in Gothenburg, Sweden (McAdams, 2011). They aimed to determine whether elevated autistic traits in women (Schulte, 2012 and Gallagher, 2003) with AN may be reflected in morphometric brain alterations specifically in the cortical grey matter volume (Bjornsdotter et al., 2017). The study had a small sample size but showed that women with AN (n=25) had higher AQ scores and lower bilateral superior temporal sulcus (STS) grey matter volumes than the control group (n=25). The AQ scores correlated negatively with average left STS grey matter volume in women with AN. However, the study had limitations because they did not control for cognitive ability and examined only women with ongoing AN. The results did support the notion that patients with AN may benefit from treatment that acknowledges ASD-like difficulties (Gordon, 2013). Treatment approaches such as highly structured and concrete pedagogic

methods or experimental pharmacological procedures such as oxytocin administration, (Insel, 1999) may accelerate recovery in patients with AN who exhibit high levels of autistic traits (Insel, 2001).

The potential link between oxytocin functions and core deficits in ASD has led to oxytocin receiving increased attention as a potential therapeutic target for these disorders (Romano, 2016). Human studies have demonstrated that oxytocin promotes the retention of social information and reduces repetitive behaviours in individuals with ASD (Hollander, 2003 and Hollander, 2007). Moreover, studies performed on children and adolescents with ASD who were subjected to intranasal oxytocin administration over a period of 2-6 months suggest that oxytocin improves social communication in these individuals (Kosaka, 2012 and Tachibana et al. 2013).

Intravenous (IV) administration of oxytocin in adults with ASD lead to reduced repetitive behaviors as compared to placebo (Hollander, 2003). In a second experiment, adults diagnosed with ASD were treated with IV oxytocin and were required to identify the mood of a person. All subjects that were treated with oxytocin had improved comprehension of affective speech and this was interpreted as oxytocin increasing the retention of social cognition (Hollander, 2007).

Certain types of autism may be caused by an imbalance between excitation and inhibition at various neuronal systems. It has been reported that both autistic human and animal subjects display dysfunction in GABA signalling (Rubenstein, 2003; Gogolla, 2009 and Blatt, 2011). Interestingly, GABA in adults has an inhibitory role, but during early development it plays an excitatory role (Ben, 2007). The shift from excitatory to inhibitory occurs at birth and research has shown that oxytocin plays a key role in this process, causing a reduction in the intracellular concentration of Cl⁻ (Tyzio, 2006).

Demitrack et al. (Demitrack, 1990) reported that women affected by the restricting-type AN showed oxytocin CSF levels significantly lower than in the control subjects. Results from another study revealed that oxytocin significantly reduced selective attention toward anxiety-laden eating stimuli (Maguire, 2013).

The associations between AN & ASD is a fairly new topic, and diagnosing ASD in individuals with AN is a complex process. Individuals with AN tend to exhibit behaviours that are also typically present in individuals with ASD. There are various diagnostic tools and criteria used to establish a relationship between ASD and AN; and with the presence of other comorbidities, it may be difficult to establish clear neurological or genetical associations. Standard diagnostic tools such as the ADOS-2 and Autism Diagnostic Interview-Revised, ADI-R; (1994) and DSM-5 diagnostic criteria

(American psychiatric association, 2013) have not reflected on these gender differences. Most diagnostic tools are validated with males, therefore females are less likely to present with symptoms detected with such tools, leading to an underestimation of ASD in females (Beggiato, 2016). There is also a lack of consistency among the studies, which may be due to the heterogeneous nature of ASD (Westwood, 2017).

Research should be focused on the development of gender-specific diagnostic algorithms and screening tools, further elucidating the relationship between AN & ASD, and determining whether specific treatment adaptations may be beneficial.

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