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[Commentary] Recognising and Responding to Physical and Mental Health Issues in Neurodivergent Females

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Abstract

People experience life and interact with others in many ways. The term ‘neurodivergence’ refers to variations from what is considered typical or normal. Research and education into neurodivergent conditions in females is essential in informing a reassessment of clinicians’ present approach to those who present with multiple unexplained symptoms. Neurodivergence may influence a person’s style of communication, learning, attitudes, and behaviour, and they may experience inequity and rejection. A formal diagnosis improves access to support services and helps them and their family better understand themselves and the challenges they face. Neurodivergent females are especially prone to many physical and psychological health issues, and it is essential that clinicians learn to recognise and respond to these. This commentary highlights the relative lack of research into clinical aspects of neurodivergent conditions in females, suggesting how clinicians might increase their awareness to mutual benefit.

Explaining neurodiversity and neurodivergence

The term ’neurodiversity’ acknowledges that there are many different ways in which people experience life and interact with others. It was first proposed by Judy Singer, an Australian sociologist, in her PhD thesis to promote equality for and inclusion of "neurological minorities" [1]. The term ‘neurodivergence’ refers to variations in mental or neurological function from what is considered typical or normal and usually incorporates autism, ADHD and Tourette’s syndrome, with increasing evidence of an overlap with dyslexia and dyspraxia [2]. Research and education into neurodivergent conditions is essential in shaping clinicians’ approaches to people who may present with a wide range of symptoms. Neurodivergence may influence a person’s style of communication, learning, attitudes, and behaviour, and they may experience social isolation and inequity. As Stenning and Rosqvist highlighted, the focus should be on problems that neurodivergent people have, rather than the problems that they are [3]. A formal diagnosis improves access to social and medical support and helps them and their family understand their challenges and differences. Neurodivergent people in general, and females in particular, are more prone to a wide variety of physical and psychological health issues, and it is important that clinicians learn to recognise and respond to various clinical cues and clues for these.

Increasing recognition of the high prevalence of neurodivergence in females

Traditionally neurodivergence has been diagnosed more commonly among males, but it has become increasingly recognised among females in the last decade [4]. The diagnosis is often made later in females because of their tendency to mask or 'camouflage' their differences to reduce the perceived risk of social exclusion [5]. Partially due to this, the pattern of symptoms that they may develop is often also different to that seen in males. Increased sensitivity to a wide variety of sensory and emotional stimuli underlies much of the widespread distress and discomfort perceived by neurodivergent women [6]. This may manifest from an early age as anxiety, hyperfocus and rigidity of thought[7], leading to the later development of distress expressed through both mental and physical signs and symptoms. Difficulty in making and maintaining friendships despite often developing special interests and abilities can lead to low self-image and self-harm [8]. Widespread discomfort and an imbalance in their autonomic regulation may associate with increasing fatigue, even among those with a tendency to hyperactivity [9]. Such presentations often occur in primary care but not infrequently lead to contact with neurology, rheumatology or pain services at a relatively young age, with circulatory, metabolic, and endocrine involvement over time. Adjustment disorders and secondary personality disorders are common features, while associations with eating disorders and gender incongruence are increasingly prevalent and relevant [10].

The healthcare needs of neurodivergent females

A recent review of the literature demonstrated that autistic people were more likely to suffer from many disorders than their neurotypical peers [11]. Adverse childhood experiences can adversely affect health[12] and appear to occur more frequently among autistic females [13]. This may help explain why autistic females access healthcare more than neurotypical females [14][15] and are more likely to require hospital treatment as both outpatients and inpatients[15][16]. A systematic review suggested that hypersensitivity, impaired executive function and communication issues all contributed to autistic females experiencing difficulties with access to medical care [17]. Lack of awareness of these issues by health care professionals accentuated the neglect of their health care needs, leading to poorer outcomes as a result [18].

Whilst virtually every organ system is represented in the list of disorders experienced by neurodivergent people, very little published literature relates specifically to females. However, there is consensus within the limited available data that autistic females are at higher risk than their neurotypical female peers for many disorders and have a higher prevalence of circulatory disorders, asthma, symptomatic hypotension, and diabetes than neurotypical females, despite controlling for risk factors [11]. Data on mortality confirm that autistic females are higher risk of early death than autistic males[19][20][21]. Risks are greater for autistic females than autistic males for most disorders and their health status is generally reduced in comparison [22][23][24][25]. These findings apply across the age spectrum applying to both young autistic individuals [14][16][22][23][24][26], as well as older ones [27]. While some of these observations may be explained by genetic predisposition, especially to circulatory disorders, cancer, and diabetes [28], a further factor may relate to hormonal dysregulation which appears increased among autistic females both prior to birth and in later life [29][30][31][32][33]. This may promote obesity and predispose towards diabetes and circulatory disease [34][35][36].

Physical health issues in neurodivergent females

These are summarised in Table 1 and discussed here. Neurodivergent people have an increased risk of certain neurological conditions, especially epilepsy and rhythmic movement disorders [37]. Around 20% of autistic children have epilepsy, with the prevalence increasing with age and associated with female gender and intellectual impairment [38]. They may also have an increased prevalence of neurological structural anomalies such as the Chiari malformation [39] which commonly presents with headaches and may cause syncope or collapse due to compression at the foramen magnum. Magnetic resonance imaging of the brain is diagnostic. Other causes of syncope in females may relate to dysfunction of the autonomic nervous system producing postural hypotension and tachycardia (POTS) [40] which is well recognised as being associated with hypermobile joints [41]. Indeed, a range of joint hypermobility syndromes including Ehlers-Danlos (EDS) are now known to be linked to the presence of neurodivergence [42]. Furthermore, most patients with fibromyalgia are female and many exhibit neurodivergent features [43] which may have a familial link [44]. Sleep disturbance and disorders are common and may contribute to fatigue [45]. Other chronic pain syndromes are also over-represented among neurodivergent females, and a disproportionate number of women attending chronic pain clinics carry a diagnosis of autism and / or ADHD [46]. Asztely et al reported chronic pain in 77% of females with a neurodivergent condition who had a mean age of just 27 years [46]. Migraine [47] and irritable bowel syndrome [48] are other common causes of chronic pain among neurodivergent females.

Table 1.

To show the common physical health issues experienced by neurodivergent females
NEUROLOGICAL
Movement disorders
Epilepsy
Headache
Sleep disorder
Cerebrovascular accident (older)
CIRCULATORY
Syncope due to POTS
Raynaud's phenomenon
Hypertension (older)
Hyperlipidaemia (older)
Ischaemic heart disease (older)
MUSCULOSKELETAL
Hypermobility syndromes
Fibromyalgia
Rheumatoid arthritis
Connective tissue disease
Osteoporosis

GASTROINTESTINAL
Inflammatory bowel disease
Gluten sensitive enteropathy
Irritable bowel syndrome
Nutritional deficiency
ENDOCRINE
Autoimmune thyroiditis
Hypercortisolaemia
Type 2 Diabetes (older)
GYNAECOLOGICAL
Polycystic ovary syndrome
Dysmenorrhoea / menorrhagia
Premature menopause
RESPIRATORY
Asthma
Chest infection
DERMATOLOGICAL
Eczema
Hives
OTHERS
Mast cell activation syndrome
Chronic pain syndromes

Intestinal dysbiosis, characterised by profound gut microbiota alterations, is frequent in neurodivergent individuals[49], and offers both potential explanations for the increased prevalence of gastrointestinal symptoms and the possibility of novel therapeutic intervention [50]. Gut symptoms may however have more specific causes, especially in neurodivergent females. There is an increase in the prevalence of inflammatory bowel disease [51], especially ulcerative colitis in autistic females [52]. Another systematic review showed an association with coeliac disease for both autism and ADHD with a female preponderance [53][54]. There is an increased risk of eating disorders, especially of the restrictive intake type, and this is most prevalent among neurodivergent females [55]. This can lead to nutritional deficiencies especially of iron and of vitamins B and D. Autistic children have reduced bone mineral density at all skeletal sites compared to controls [56]. Low bone density in has also been shown in young people with ADHD and may relate to medication [57]. Osteoporosis contributes to a greatly increased risk of fractures at the hip, spine and forearm in both autistic children and adults, again especially in females. The odds ratio for hip fractures in females rises from 8.1 in autistic girls to 24.8 in adult neurodivergent females [58]. Multiple potential contributing factors to this greatly increased fracture risk include vitamin D deficiency and restrictive eating disorders [59].

Endocrine disorders are also over-represented among younger neurodivergent females, where there appears to be an increase in auto-immune thyroid disorders [60]. Maternal hypothyroidism is believed to contribute to an increased risk of autism in their offspring [61]. Other auto-immune disorders are also over-represented in mothers of neurodivergent

females, especially connective tissue disorders such as rheumatoid arthritis (RA) [62] and systemic lupus erythematosus [63][64]. Raynaud's phenomenon can potentially be an early manifestation of a similar tendency in their female offspring, and may be exacerbated by stimulants prescribed for ADHD [65]. Neurodivergent females also report an increased tendency to develop allergies and skin rashes including eczema and hives [66]. They may have an increased prevalence of mast cell activation syndrome, a condition that is attracting greater interest through its links with hypermobility and autism [67]. Perhaps related to this observation is the finding that the prevalence of airways disease, and especially of asthma, is much increased among neurodivergent females [11][68]. A relationship between intestinal dysbiosis and the occurrence of asthma and eczema in children with ADHD has now also been established [69][70]. With increasing age, obesity and diabetes become increasingly evident among autistic females, and females with ADHD [11][71], while hypertension and hyperlipidaemia contribute to the higher levels of cerebrovascular and cardiovascular disease observed in older neurodivergent females [11][71]. The significant reduction in the lifespan of neurodivergent females is likely to be due to a combination of accelerated vascular disease in older autistic females, along with suicide and epilepsy in younger females with autism or ADHD [72].

The challenges of navigating a world where neurodivergent people are the exception rather than the norm poses particular problems for females, who often adopt camouflaging behaviour in an attempt to disguise their difficulties[73]. De Vaan et al. argue that neurodivergent people 'are more susceptible to stress', due to missing 'auditory and visual information [which makes] situations more unpredictable, uncertain, and stressful' [74]. This additional stress may precipitate an enhanced cortisol response in autistic females [75] which may contribute to some of the physical co-morbidities of neurodivergent females. Polycystic Ovarian Syndrome (PCOS) is associated with both autism and ADHD [76] and produces hirsutism, elevated adrenal androgens, hypercortisolaemia and insulin resistance, with resulting hyperglycaemia [77]. A clinical trial of pioglitazone and metformin is being undertaken to assess the potential for reversibility in this setting [78]. Cortisol is also associated with inflammatory responses, particularly in the musculoskeletal system, and chronic hypercortisolaemia is associated with increased inflammation [79]. This may help explain the increased rates of EDS and RA among neurodivergent females and might contribute towards the mood disorders and emotional dysregulation often observed in autism and ADHD [80].

Hormonal events are believed to have a large impact on autistic females throughout their lives[81][82][83]. Clinically young autistic females report experiencing higher levels of dysmenorrhoea, menorrhagia, and more intrusive effects of menstruation than their neurotypical peers [84]. The sensory implications of menstruation care can also impact on the mental health and presentation of autistic females [82][83]. Parents report witnessing increased anxiety and emotional difficulties during menstruation, impacting socially and educationally [84]. Research indicates that autistic females and females with ADHD may experience the physical symptoms of menopause over a longer period [81], while also experiencing greater impact from psychological and emotional symptoms such as poor sleep, increased anxiety, impaired recall and concentration [83]. The menopause is known to impact on the mental health of neurotypical females, with greater impact on neurodivergent females who have experienced anxiety and/or depression from a young age [81][83]. Autistic females may also experience more difficulties in reporting their experiences or accessing appropriate support [82]. The effect of hormones from menarche to menopause in neurodivergent females merits further research.

Mental health issues in neurodivergent females

These are summarised in Table 2 and discussed here. Neurodivergent conditions are highly inheritable[85] while brain structure and function appear significantly different in neurodivergent females [86], along with both the peripheral and autonomic nervous systems [87]. Therefore, it may not be surprising that mental health problems occur frequently in neurodivergent people and are a particularly common feature in younger females. Environmental factors, especially adverse childhood experiences, may interact with structural changes to produce a wide range of clinical manifestations of disordered mental health in females. Emotional impulsivity is especially common among girls with ADHD [88] and may be associated with a variety of undesirable outcomes [89], including self-harm and suicidality [90][91].

Table 2.

To show the common mental health issues experienced by neurodivergent females
Anxiety disorders
Panic attacks
Meltdowns
Depression
Self-harm and suicidality
Addiction and substance abuse
Eating disorders
Body dysmorphia
Gender incongruence
Cluster B and C personality disorders
Bipolar disease
Schizophrenia

Suicide represents a leading cause of early death among neurodivergent females with two-thirds reporting considering suicide at some stage [92], and over half of these planning or attempting it[19]. Although completed suicide is more common in men across society generally [93], autistic females without learning difficulty are at higher risk of suicide than autistic males [19], with suicidal ideation often occurring in the absence of clinical depression[94]. Neurodivergent females are more likely to succeed in their suicide bid [95], and over 40% of completed female suicides have had a diagnosis of autism or exhibited strong neurodivergent traits [96]. Another study reported that over half of females who committed suicide had scored above the diagnostic threshold on the ASQ test [97]. Multiple risk factors for completed suicide have been implicated for neurodivergent females, including adverse life events [98], social isolation, impulsivity [88][99], cognitive inflexibility, camouflaging [100] and delayed diagnosis [92].

Anxiety disorders are an almost invariable accompaniment of neurodivergence in females, and ADHD is thought to be more strongly associated with anxiety than is autism alone [101]. Both autism and ADHD may associate with meltdowns and panic attacks. Depression is also found in 38% of neurodivergent people, although it is as common in adolescent

males as in young females [102]. Dysfunctional coping mechanisms can trigger self-harm[90], substance abuse [103] or eating disorders [104]. Some females with neurodivergence experience body dysmorphia, while gender incongruence is well-recognised among young autistic females [105], both often being associated with higher levels of chronic pain[106]. Working memory is frequently impaired and when combined with alexithymia, this can cause inter-personal conflict and misrepresentation of other people's actions and intentions [89].

Alexithymia is the failure to understand and respond appropriately to emotions[107]. It is associated with neurodivergent conditions [108] and is often misinterpreted as demonstrating a lack of empathy on the part of the sufferer. As females with ADHD especially experience strong emotional impulses [109], alexithymia can be very disabling and may be a major factor in the challenges many neurodivergent females experience with establishing and maintaining social contact with allistics [110]. Ultimately, attempts to camouflage these difficulties in achieving emotional insight can be so exhausting that social isolation often results. Another factor contributing to the loss of inter-personal contact may be rejection sensitive dysphoria (RSD), which has been described as "immense emotional pain from real or perceived failure to meet others' expectations" [111]. This is common to many neurodivergent conditions and may manifest as internal strife, producing low self-esteem, or externally triggering anger or argument. Females with autism and / or ADHD suffer more bullying at school [112] and experience more rejection from a variety of sources[113]. Rejection and the fear of abandonment can become a dominant feature and may ultimately destroy social encounters and relationships [114].

Personality disorders may develop because of disordered resilience and are more common in neurodivergent females [115]. The prevalence of bipolar disorder[116] and schizophrenia [117] are also each significantly increased, although it is important to appreciate that what is sometimes initially thought to be psychotic behaviour may simply reflect the rich inner life of certain autistic women whose imagination can be extremely vivid, and whose state of social withdrawal represents their construction of a self-absorbed inner world of fantasy based on special interests. Other aspects of the mental health of neurodivergent females and their consequences are addressed elsewhere [118].

Challenges for the clinician

The medical profession has generally been slow to appreciate the wide range of differing symptoms that neurodivergent females can develop. This has been compounded by the trend towards increasing medical specialisation, meaning that such patients may have already been referred to multiple different departments. The difficulty many neurodivergent people experience with accurately communicating their feelings and bodily experiences can compound these challenges, as does the frequent lack of any objective signs on physical examination. Previously, this often led to autistic females being described as having psychosomatic illness or those with ADHD as being hard to help. Such terminology is insensitive and outdated.

There are often subtle clues in the way that neurodivergent people present. They are more likely to bring a spokesperson and to avoid eye contact at consultation. They may appear unduly agitated or sometimes disengaged with the process. The frequent overlap in presentations between different specialities emphasises the need for all trainees to have 'common

stem' experience in general medicine. Within a general practice setting, a wider appreciation of the range of common disorders experienced by neurodivergent females is important to acquire. The art of 'learning to listen' remains an essential tool in diagnosis. Neurodivergent people can feel uncomfortable if they are not given enough time to share their concerns, and an open unhurried dialog is more likely to facilitate a diagnosis. However, given the service pressures and time constraints clinicians face, this can be difficult to guarantee. However, if patients are encouraged to share their lived experience, it becomes easier for the clinician to 'join the dots', which may allow the diagnosis of a neurodivergent condition to surface from what may have previously appeared to be a random collection of unrelated symptoms.

However, neurodivergent females may exhibit anxiety or anger in medical consultations, especially if they feel that they are invalidated or not taken seriously. Avoiding conflict with patients who may have fixed ideas and expectations of what they are entitled to receive is as much an art as a science and requires experience and patience. Consistency within clinical contact to ensure continuity of care can help develop trust which neurodivergent people often take time to achieve. Once a diagnosis of a neurodevelopmental condition is made or suspected, it is important to offer access to appropriate multidisciplinary support whilst avoiding unnecessary multiple cross-referral. It is relevant to recognise that the increasing delays to accessing such services at present may trigger a meltdown, panic attack, dissociative episode, or the threat of self-harm.

Future priorities

If we can help society increase insight and understanding into neurodivergence by developing a concept of '*neuroconvergence'*, with the aid of non-judgemental language and acceptance of inter-personal differences, the mental and physical health burdens carried by many females with autism, ADHD or related conditions may be diminished. It is essential that all clinicians are aware of the broad range of conditions experienced by neurodivergent females and the wide range of symptoms described by their patients. If we are to become more effective at managing these conditions, breaking down barriers between services for physical and mental health would be a great help. Improving access to eating disorder services and gender identity clinics are important examples, as neurodivergent females are greatly over-represented among those seeking such support. Increasing the evidence base around treatment for people in these situations would facilitate this aim.

Neurodivergent females also account for a high percentage of patients presenting with chronic pain syndromes to pain clinics and rheumatologists. A more comprehensive understanding of what pain means to those with neurodivergence is essential, as this seems to differ from the experience of many neurotypical people. Broadening our concept of pain to include the role of the autonomic nervous system is important as dysautonomia is both common and under-recognised in neurodivergent females and accounts for a significant component of their lived experience of discomfort and dysfunction.

The multiple conditions experienced by many neurodivergent females are influenced by both genetic and environmental factors. A better understanding of the relationship between these influences is essential, although it is important that we appreciate the reasons behind the heightened suspicion and sensitivity expressed by many autistic people over the use of

gene studies in autism [119]. However, we suggest that the complexity of polygenic influences on the clinical expression of diseases in autistic females justifies such an approach [120]. Further exploration of the reasons behind the physical and psychological hypersensitivity that many neurodivergent females exhibit would be invaluable to improving our insight into this phenomenon. This may allow the relationship between the limbic, endocrine, and immune systems in neurodivergent individuals to be more fully understood. Ultimately, the sense of isolation and alienation experienced by so many neurodivergent females could, and should be addressed, as this plays a significant part in their health-seeking behaviour and support needs.

How patients and the public contributed to this article

Two authors of this paper have direct lived experience of female neurodivergent conditions, and two authors work directly in the provision of health care delivery to females with neurodivergent conditions.

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