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[Commentary] Recognising and Managing Medical Issues in Neurodiverse Females

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Abstract

The term 'neurodiversity' acknowledges that there are many different ways in which people experience life and interact with others. It incorporates autism, ADHD and Tourette's syndrome, and there is increasing evidence of an overlap with dyslexia and dyspraxia [1]. It was first proposed by Judy Singer, an Australian sociologist, in her PhD thesis to promote equality for and inclusion of "neurological minorities" [2]. Research and education into neurodiversity is essential in shaping clinicians' approaches to people who may present with a wide range of symptoms. Neurodiversity may influence a person's style of communication, learning, attitudes, and behaviour, and they may experience social isolation and inequity. Therefore, the focus should be on problems that neurodiverse 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. Neurodiverse people 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 neurodiversity in females

Traditionally neurodiversity has been perceived to be more common 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 neurodiverse 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 dysmorphia are increasingly prevalent and relevant ^[10].

The healthcare needs of neurodiverse 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]}. Autistic females are more likely to feel that their physical health care needs are neglected, reporting with poorer outcomes as a result ^[17]. A systematic review suggested that hypersensitivity, impaired executive function and communication issues all contributed to difficulties with access to medical care and that lack of awareness of these issues by health care professionals accentuated this ^[18].

Whilst virtually every organ system is represented in the list of disorders experienced by neurodiverse 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]. 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 neurodiverse females

Whilst a full description of each of the disorders associated with neurodiversity is outside the scope of this article, the range of conditions are briefly described below.

Neurodiverse people have an increased risk of certain neurological conditions, especially epilepsy and rhythmic movement disorders. They may also have an increased prevalence of neurological structural anomalies such as the Chiari malformation ^[37] 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 usually diagnostic. Other causes of syncope in females may relate to dysfunction of the autonomic nervous system producing postural hypotension and tachycardia (POTS) ^[38] which is well recognised as being associated with hypermobile joints ^[39]. Indeed, a range of joint

hypermobility syndromes including Ehlers-Danlos (EDS) are now known to be linked to the presence of neurodiversity [40]. Many patients with fibromyalgia exhibit neurodiverse features [41] and this may have a familial link [42]. Sleep disturbance and disorders are common and may contribute to fatigue [43]. Other chronic pain syndromes are also over-represented among neurodiverse females and many women attending chronic pain clinics carry a diagnosis of neurodiversity [44]. Migraine and irritable bowel syndrome are also common causes of chronic pain in younger neurodiverse females [45], although gastrointestinal symptoms may have more specific causes. There appears to be an increase in the prevalence of inflammatory bowel disease [46], probably coeliac disease [47], and possibly bile acid malabsorption in this population, along with an increased risk of eating disorders, especially of the restrictive intake type [48]. 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 [49]. Low bone density has also been shown in young people with ADHD and may relate to medication [50]. This 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 rose from 8.1 in autistic girls to 24.8 in autistic adults [51]. Multiple potential contributing factors include vitamin D deficiency and restrictive eating disorders [52].

Endocrine disorders are also over-represented among younger neurodiverse females, where there appears to be an increase in auto-immune thyroid disorders [53]. Maternal hypothyroidism is also believed to contribute to an increased risk of autism in the offspring. Other auto-immune disorders are also over-represented in mothers of neurodiverse females, especially connective tissue disorders such as rheumatoid arthritis [54][55] and systemic lupus erythematosus [55][56]. Raynaud's phenomenon may be an early manifestation of a similar tendency in their female offspring. Neurodiverse females report an increased tendency to develop allergies and skin rashes including eczema and hives [57]. 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 [58]. Perhaps related to this observation is the finding that the prevalence of airways disease, and especially of asthma, is much increased among females with neurodiversity [11][59]. With increasing age, obesity and diabetes become increasingly evident among neurodiverse females [11][60], and hypertension and hyperlipidaemia contribute to their high levels of cerebrovascular and cardiovascular disease [11][60].

Hormonal events are believed to have a greater impact on autistic females throughout their lives [61][62][63]. Clinically young autistic females report experiencing high levels of dysmenorrhoea, menorrhagia, and more intrusive effects of menstruation [62]. The sensory implications of menstruation care can also impact on the mental health and presentation of autistic females [63]. Parents report witnessing increased anxiety and emotional difficulties during menstruation, impacting socially and educationally [64]. Research indicates that autistic females may experience the physical symptoms of menopause over a longer period, while also experiencing greater impact from psychological and emotional symptoms such as poor sleep, increased anxiety, poor memory and concentration [61][63]. The menopause is known to impact on the mental health of neurotypical females, with most impact on autistic females who have experienced anxiety and/or depression from a young age. Autistic females may also experience more difficulties in reporting their experiences or accessing appropriate support [62]. The whole subject of the effect of hormonal factors from menarche to menopause in autistic females merits further research.

Mental health issues in neurodiverse females

Neurodiverse conditions are highly inheritable [65] while brain structure and function appear significantly different in neurodiverse females [66] along with both the peripheral and autonomic nervous systems [67]. Therefore, it may not be surprising that mental health problems occur frequently in neurodiverse people and are a particularly common feature in younger females. Emotional impulsivity is especially common among girls with ADHD [68] and may be associated with a variety of undesirable outcomes [69], including self-harm and suicidality [70]. Anxiety is an almost invariable accompaniment of neurodiversity among females [71] with ADHD thought to be more strongly associated than autism alone. Both may lead to meltdowns and panic attacks, while depression is also found in 38% of neurodiverse people, although it is as common in males as in females [72]. Dysfunctional coping can trigger self-harm [70], substance abuse [73] or eating disorders [74]. Some females with neurodiversity experience body dysmorphia, while gender dysphoria is well-recognised among young autistic females [75], both often being associated with higher levels of chronic pain [76]. Personality disorders may develop as a consequence of disordered resilience and are more common in females [77]. The prevalence of bipolar disorder [78] and schizophrenia [79] are also each significantly increased among neurodiverse females.

Challenges for the clinician

The medical profession has generally been slow to appreciate the wide range of differing symptoms that neurodiverse 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 neurodiverse 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 being hard to help. Such terminology is insensitive and outdated.

There are often subtle clues in the way that neurodiverse 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 neurodiverse females is important to acquire. The art of 'learning to listen' remains an essential tool in diagnosis. Neurodiverse 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 neurodiverse condition to surface from what may have previously appeared to be a random collection of unrelated symptoms.

However, neurodiverse 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 neurodiverse people often take time to achieve. Once a diagnosis of neurodiverse 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, or the threat of self-harm.

Future priorities

It is essential that all clinicians are aware of the broad range of conditions experienced by neurodivergent females and the diverse presentations and symptoms expressed 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 neurodiverse females are greatly over-represented in those seeking such support. Increasing the evidence base around treatment for people in these situations would facilitate this aim.

Neurodiverse 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 neurodiversity 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 neurodiverse females and accounts for a significant component of their lived experience of discomfort and dysfunction.

The multiple conditions experienced by many neurodiverse females are influenced by both genetic and environmental factors. A better understanding of the relationship between these influences is important, although it is important to appreciate the reasons behind heightened suspicion and sensitivity expressed by some neurodiverse people over the use of gene studies in autism [80]

Further exploration of the reasons behind the physical and psychological hypersensitivity that many neurodiverse females exhibit would be useful. This may allow the relationship between the limbic, endocrine and immune systems in neurodiverse individuals to be more fully understood. Ultimately, the sense of isolation and alienation experienced by so many neurodiverse females could, and should be addressed, as this plays a significant part in their health-seeking behaviour and support needs. If we can help society increase insight and understanding into neurodiversity by developing a concept of '*neuroconvergence*', rather than neurodivergence, with the aid of non-judgemental language and acceptance of inter-personal differences, the mental and physical health burdens carried by many neurodiverse females may be diminished.

How patients and the public contributed to this article

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

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