

The Links Between Fibromyalgia, Hypermobility and Neurodivergence

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Fibromyalgia and joint hypermobility are common coexisting conditions among younger females that are often accompanied with additional features of autonomic dysfunction. Mental health is frequently impacted with these conditions and an association with neurodivergence has been recently established. Neurodivergence is also prevalent among close relatives. Reasons for this association are poorly understood, although genetics, adverse early life experiences and autoimmunity all contribute. Pharmacological responses may differ in neurodivergence, while psychological support requires adaptation for individual sensitivities. Screening patients with fibromyalgia and hypermobility for neurodivergent traits and vice versa may facilitate diagnosis and management.

Keywords

Fibromyalgia, hypermobility, autism, neurodivergence, pain, dysautonomia, rheumatology, hypermobile Ehlers–Danlos syndrome (hEDS)

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Fibromyalgia (FM) is defined as widespread musculoskeletal pain and tenderness, in the absence of another explanation. Poor sleep, fatigue and pain are all associated with FM. Diagnostic criteria are well defined,¹ and the prevalence of FM appears to be steadily increasing, with patients presenting at progressively younger ages. Experience suggests that most patients are female, and FM accounts for a significant number of rheumatological referrals to secondary care.²

Hypermobility has been increasingly acknowledged as an important factor in the development of musculoskeletal symptoms. There is considerable overlap between established disorders of connective tissue (e.g. Marfan's syndrome, Ehlers–Danlos syndromes [EDS] and hypermobile EDS [hEDS]). Previously labelled benign familial joint hypermobility, hEDS lacks a genetic substrate unlike the other EDS subsets. Those who fail to meet strict criteria for Marfan's syndrome or EDS often meet less stringent definitions for hypermobility spectrum disorder (HSD). The prevalence of HSD among young adults is reported as 20% and is often linked to FM.³

The coexistence of FM and HSD/hEDS has been recognized for several decades, although the reason for this association remains unclear. Both FM and HSD patients have been reported to exhibit high levels of autonomic dysfunction, postural orthostatic tachycardia syndrome, migraine and irritable bowel syndrome, which are all commonly reported comorbid conditions.⁴

Many people with the combination of FM and HSD have a history of anxiety and/or depression,⁴ which often pre-dates the onset of their pain. Further common features include social isolation, self-harm, difficulty understanding and describing feelings, and extreme sensitivity to criticism. More recently, an association between FM and HSD with neurodivergent conditions (henceforth neurodivergence) such as autism and attention deficit hyperactivity disorder has been proposed.⁵ This is supported by the demonstration of close genetic clustering between patients with EDS/HSD and neurodivergence.⁶

Although the population prevalence of autism is reportedly much greater among males, most young patients with hEDS/HSD and neurodivergence are female.⁷ This gender reversal is as yet unexplained. One theory invokes subconscious masking among females with neurodivergence, resulting in post-traumatic stress disorder with clinical features overlapping both emotionally unstable and narcissistic personality disorder.⁸ There is considerable diagnostic uncertainty in this area and no clear consensus around the coexistence of personality disorders and autism has yet emerged. Magnetic resonance imaging studies demonstrate both functional and structural differences in cortical processing in high-functioning people with autism,⁹ and changes in the limbic system in people with autism and HSD may contribute to psychiatric features.¹⁰ Pain and fatigue may also be enhanced by coexisting autoimmune or endocrine disorders, which are common in women with autism and in patients with generalized joint hypermobility.¹¹

A recent pilot study from our group demonstrated a high prevalence of diagnosed neurodivergence (42%) among first- or second-degree relatives of index cases with FM and HSD. The prevalence of FM (30%) and HSD (18%) were also significantly raised among such relatives, with much individual overlap between these three diagnoses (unpublished data, James Cook University Hospital). This provides further evidence for linkage between these conditions, although causation cannot be inferred from this.

Inheritance is thought to play a significant role in each of these conditions and it appears that genetic and/or immunological factors may be important predictors of their coexistence.¹¹ However, Cambridge University's Spectrum 10K study, which proposed relating clinical comorbidity to genetic profiles in autism, was suspended after receiving much negative feedback from the autism community.¹² Nonetheless, prospects of an immunological explanation for FM have been enhanced by the discovery of peripheral immune aberrations,¹³ while evidence for an immune-mediated cause for FM is also supported by a recent report of the transference of fibromyalgic features following immunoglobulin G (IgG) autoantibody transfer from symptomatic to previously asymptomatic mice.¹⁴

Clinical experience in people with FM, HSD/hEDS and neurodivergence suggests that responses to analgesia, anti-inflammatory drugs and psychoactive therapy may differ to neurotypical people, and that opiates carry an increased risk of unwanted effects. By contrast, low-dose amitriptyline is often effective in producing restorative sleep by reducing nocturnal discomfort, and often improves daytime function. Pregabalin and duloxetine may benefit some patients. The influence of neurodivergence on drug responses is poorly understood and justifies further investigation.¹⁵ The role of clinical psychology in supporting patients with chronic pain is well established but there is concern that techniques such as cognitive behavioural therapy may be less effective for those with autism. Alternative models have been proposed, including

cognitive analytical therapy to adjust for individual hypersensitivity to external stimuli,¹⁶ but much work is needed to define optimal intervention. Recognition, support and validation are hugely important for people with autism with FM who often feel isolated, ignored or abandoned by both society and healthcare systems. This is likely to contribute to the high rates of self-harm and suicide experienced by such people.¹⁷

Clinician awareness and acceptance of FM and HSD is variable; many healthcare professionals tiptoe around the subject of neurodivergence, often lacking an in-depth understanding. We are very concerned that recent events within the National Health Service might further reduce access to and support for patients with these conditions, and that the opportunity to better understand and respond to the considerably complex requirements of such patients may be lost. It may be worth considering that the wide range of hypersensitivities often reported by people with autism may contribute to the development of chronic pain in those who are also hypermobile. This may be mediated by repetitive triggering of nociceptors in the capsules of hypermobile joints, leading to FM developing at a younger age among those with neurodivergence.

Increasing the awareness of links between FM, hypermobility and neurodivergence among healthcare professionals is a priority. Clinicians treating these conditions often work in silos with less understanding or awareness of the other comorbidities; this is a barrier to good therapeutic relationships and whole-person care. Adopting a screening tool for autism such as the Ritvo Autism Asperger Diagnostic Scale in those with FM and HSD, as well as screening tools for hypermobility and pain in those with neurodivergence could facilitate earlier referral of possible cases to appropriate services although, at present, we recognize that these services are struggling to cope with current workload. In parallel, we must understand the nature of the link between these conditions and the impact of neurodivergence to improve the natural history and therapeutic responsiveness of patients with FM and HSD/EDS. □

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