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Autistic Traits Correlate with Chronic Musculoskeletal Pain: A Self-Selected Population Based Survey

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Abstract

Chronic musculoskeletal pain is an increasingly frequent feature in young people. Many exhibit a range of additional physical and psychological features and fulfil criteria for fibromyalgia. Hypermobility, irritable bowel syndrome and migraine are frequent comorbid conditions. These are all in part mediated by dysfunction of the autonomic nervous system and commonly include fatigue, poor sleep and brain fog. Anxiety, social withdrawal and a range of autistic traits are frequently described by those with chronic musculoskeletal pain, and autistic people are over-represented among patients attending pain clinics. This study was designed to explore the correlation between the degree of pain and autistic traits described within a self-selected community-based population. The study used a nonexperimental, correlational design with data collected from a volunteer sample of 448 adults (aged 18-60) who completed online self-report questionnaires assessing each of autistic traits (RAADS-R score), fibromyalgia symptoms (ACR criteria) and hypermobility (Beighton's test). Correlation analysis and linear regressions were used to test the relationships between each disorder. Data was analysed using parametric and non-parametric techniques to assess prevalence, strength and significance of relationships,

causes of variance within populations and mediations. Our self-selected community population had a mean age of 24 years and was 77% female. The prevalence of significant autistic traits, fibromyalgia and hypermobility were all much greater than expected at 63.4%, 40.6% and 43.7% respectively. Those identifying as non-binary or trans had the highest rates. Fibromyalgia was significantly associated with autistic traits, with dysautonomia a stronger predictor than chronic pain. Regression analyses revealed hypermobility partially mediated the relationship between autistic traits and fibromyalgia. This is the first community study to provide evidence for a direct association between fibromyalgia and autistic traits. Although self-selected, the findings in our predominantly young female population confirm that these conditions are common and that those with autistic traits are at significantly increased risk of developing fibromyalgia, especially if they are hypermobile.

Keywords
Fibromyalgia; autism; neurodivergent; hypermobile

1. Introduction

Chronic widespread musculoskeletal (MSK) pain lasting over 3 months is the hallmark of fibromyalgia [1]. It has a prevalence of approximately 2-5% in the UK population [2] and is most common in young and middle-aged women [3-5]. Affected individuals often report other symptoms, including both emotional and physical fatigue, and subjective cognitive dysfunction (brain-fog) [6]. It is also associated with sleep disturbance, autonomic dysfunction and a variety of psychological complaints [7-9].

The main biological explanation for fibromyalgia is abnormal central pain processing. People with fibromyalgia experience a heightened pain response to sensory stimuli due to increased pain transmission in the central nervous system. Increased sensitisation of a-beta and c-fibres play a causal role in fibromyalgia [10-12], related to higher levels of neurotransmitters such as glutamate and substance P [13]. Fibromyalgia is commonly found in people with joint hypermobility, with prevalence estimates in such people ranging from 24% to 86% [5, 14-16].

Joint hypermobility refers to the capacity for a joint to move beyond its normal range due to ligamentous laxity [17]. This increased joint motion is caused by an alteration of collagen synthesis in the body [14]. Hypermobility is characterised by fragility of soft connective tissue, resulting in joint hyperextension and hyperlaxity, often accompanied by chronic pain [18, 19]. Although some people with hypermobility will meet the criteria for hypermobile Ehlers Danlos Syndrome (hEDS), the majority will be more accurately classified as having hypermobility spectrum disorder (HSD).

The prevalence of HSD is between 11-30% [6, 20] and this varies according to age, gender, and race. A higher prevalence is reported in those assigned female at birth [21], children and young adults [22, 23]. Hypermobility does exist as an asymptomatic feature, explaining the high prevalence rates found in large, unselected populations [24]. However, it is often symptomatic and is associated with a wide range of MSK symptoms, predominantly chronic pain [25].

Hypermobility was first noted to be associated with anxiety in 1988 [26], and a decade later with attention deficit hyperactivity disorder (ADHD) [27]. Kalisch et al [28] confirmed the strong

correlation between hEDS and MSK pain and reported that 52% of hEDS patients also exhibited anxiety, emphasising the link between physical and psychological factors. Motor impairment, hyperextensible skin, joint dislocation, gastrointestinal and proprioceptive dysfunction have all been noted in autistic children [29, 30]. More recently, studies have confirmed and quantified the increased prevalence of hypermobility in this population [31, 32].

Neurodivergent conditions include Autistic spectrum disorder (ASD), attention deficit hyperactivity disorder (ADHD) and Tourette's syndrome. ASD is a neurodevelopmental disorder characterised by the presence of specific interests, repeated patterns of behaviour and deficits in social interactions [33]. ASD is prevalent in approximately 2.2% of western adults [34]. In one study, 49% of a neurodivergent cohort had confirmed hypermobility [35], while Cederlof et al [36] reported a heightened risk ratio of 7.4 for ASD and 6.0 for ADHD in a large population-based case control study of people with 8hEDS/HSD. Recent studies confirm markedly increased rates of hypermobility among neurodivergent populations [32, 37, 38, 39]. Csecs et al. [39] reported a risk ratio for having generalised joint hypermobility of 4.5 in individuals with ASD, showed that MSK symptoms were the predominant form of chronic pain among neurodivergent people and suggested that joint hypermobility mediated much of the relationship between neurodivergence and pain in this population, with a marked genetic component.

Asztély et al. [40] reported that 77% of neurodivergent females suffered chronic pain, with fibromyalgia described in almost a quarter of those with ASD. ADHD co-occurs in up to 83% of the autistic population. Young neurodivergent females are often diagnosed with anxiety, low mood, panic or obsessive-compulsive disorder long before receiving an autism or ADHD diagnosis. This delay can worsen physical and psychological outcomes for such individuals. Mixed-gender studies have consistently shown a higher prevalence of hypermobility and pain in autistic females compared to autistic males [41]. Although this gender difference is not entirely understood, it suggests that it is important to routinely assess pain and hypermobility in autistic females.

Hypermobile individuals have greater exteroception (sensitivity to the environment), nociception (sensitivity to pain) and somatosensory amplification whilst also experiencing decreased proprioception (perception of position of own body) [42]. These features are often also reported by people with ASD and ADHD and relate to altered sensitivity of the autonomic nervous system. Furthermore, many studies have shown a high prevalence of gastrointestinal disorders in both those with hypermobility and ASD [16, 43], and this often also relates to dysautonomia. Fibromyalgia [6], hEDS [44, 45] and ASD [46, 47] are all associated with autonomic nervous dysfunction. Recognising that dysautonomia may be a common factor in the relationship between the three conditions, Csecs [39] suggested that HSD may be a mediating factor for dysautonomia in neurodivergent people.

In a case-control study, Kelly et al. [48] reported a prevalence of 42% of confirmed neurodivergent conditions among relatives of index patients with HSD and fibromyalgia. In addition, hypermobility was reported in 31%, and fibromyalgia in 18% of first- and second-degree relatives. Dysautonomia was also more commonly reported by relatives than by controls. This demonstrates a significant familial overlap of these disorders, with the prevalence of hypermobility and fibromyalgia in relatives with neurodivergence being 50% and 30% respectively. Such findings support anecdotal evidence from early case studies of a link between ASD, MSK pain and hypermobility and further suggests a significant hereditary component [39].

Most of the published work on the link between chronic pain and neurodivergence is limited to clinical populations. Glans et al confirmed that ASD was associated with generalised joint hypermobility and that the association was strongest among those with comorbid ADHD [49] in a large Swedish study. Our present study explores the prevalence of, and relationship between, each of fibromyalgia, hypermobility and autistic traits within a large young, self-selected community-based adult population from the English-speaking world.

2. Methods

2.1 Participants

Inclusion criteria were (a) being aged between 18-60 and (b) being fluent in English. Participants were recruited online or through the School of Psychology's Research Participation Scheme (RPS) at Newcastle University. Participants were excluded if they did not complete full scales/questionnaires and all who completed the study were invited to partake in a lottery draw as an incentive. Ten randomly selected participants were each awarded £10. In addition, those recruited via the RPS were granted 1 research credit upon study completion. All participants gave informed consent and were provided with a unique code to withdraw from the research at any time. Ethical approval was obtained via Newcastle University's FMS Research Ethics Committee (Ref: 15052/2021).

2.2 Procedure

Participants completed an online survey hosted by Qualtrics Survey Software. The survey was advertised to participants through various online and social media platforms, including Facebook, Instagram, Twitter, Reddit, Survey Circle and LinkedIn. Researchers also displayed posters around the university campus and contacted university departments across the UK to share the study nationally. For undergraduate psychology students at Newcastle University, the survey was made available via the Sona System that is part of the RPS.

Participants were directed to a welcome video where a brief explanation of the purpose and procedure of the study explained, as well as its potential real-world implications. Next participants read through the digital consent form explaining the purpose of the study, the estimated duration and that participation was voluntary. They were also informed that they could withdraw any time and that the data would all be anonymised. If consent was given, participants were asked to complete a comprehensive demographic questionnaire, created by the researchers which contained questions pertaining to age, sex, gender, ethnicity, religion, and employment status. Participants were required to answer every question before proceeding to the next questionnaire.

2.3 Design

The study was a non-experimental, correlational design. The predictor variable was autistic traits, the outcome variable was fibromyalgia symptoms (pain/dysautonomia), and the mediator variable was hypermobility.

2.4 Materials/Measures

2.4.1 Autistic Traits

The Ritvo Autism Asperger Diagnostic Scale-Revised (RAADS-R) [50] is a modified version of the RAADS that was developed as a clinical adjunct diagnostic tool for ASD. It is an 80-item scale which screens for the presence of autistic traits in adults (18+) based on the revised DSM-IV scale (APA, 2000). Items are comprised of four sub-scales that are lifespan focused: social relatedness (39 items), circumscribed interest (14 items), language (4 items) and sensory-motor symptoms (20 items). Participants rate the degree to which they relate to each statement on a 4-point Likert scale ranging from, 0 = "never true", 1 = "true only when I was young", 2 = "only true now" and 3 = "true now and when I was young" (see Appendix A). Cronbach alpha coefficients for the subscales in the ranged from 0.79 to 0.92, showing high internal consistency [51]. A score of over 65 is consistent with a diagnosis of ASD but is not in itself diagnostic.

2.4.2 Fibromyalgia

The Fibromyalgia Survey Questionnaire (FSQ) is the primary diagnostic criteria for fibromyalgia, developed and adapted by the American College of Rheumatology [1]. It is comprised of two scales: the Widespread Pain Index (WPI) and the Symptom Severity scale (SSS). The WPI consists of a diagram listing 19 non-articular body regions (i.e., shoulder, hip, back, abdomen) that participants score as either 0 = no pain or 1 = pain over the past week, giving a score between 0-19.

The SSS is composed of two parts. Part 2a assesses symptom severity scores for: fatigue; waking unrefreshed and cognitive symptoms (brain fog and difficulty remembering), scored on a scale of zero-to-three (0 = none; 1 = slight or mild problems; 2 = moderate or considerable problems; 3 = severe or pervasive/continuous problems). The second part measures the severity of somatic symptoms reported by participants using a similar scale. When combined, a total score of between 0-12 is obtained.

A diagnosis of fibromyalgia must fulfil one of two conditions: WPI ≥ 7 and SSS ≥ 5, or WPI = 3-6 and SSS ≥ 9. The total FSQ score (WPI + SSS) ranges between 0-31, with a score of ≥12 meeting criteria for the diagnosis of fibromyalgia. The FSQ has been validated across cultures and shows acceptable levels of sensitivity (64-96%), specificity (60-100%) and validity (Cronbach's α = 0.60-0.87) [52].

2.4.3 Hypermobility

The Beighton Score (BS) [53] comprises a set of manoeuvres used as the standard measure for assessing hypermobility. The items record the ability to touch the forearm with the ipsilateral thumb, hyperextension at both fifth metacarpo-phalangeal joints, hyperextension at both elbows and at both knee joints and hyperflexion at the lumbosacral spine. The maximum score is 9 and a score of at least 5 suggests hypermobility in adults aged 18-49, according to the 2017 diagnostic criteria for hypermobility [54]. The cut-off scores do vary with age, with a score of 4/9 for adults over 50 and 6/9 for children and adolescents under 18 equating to hypermobility. We chose this method over the self-reporting 5-point questionnaire (5-PG) because the BS was reported to correlate better with autistic features than the 5-PQ [49].

Our questionnaire presented the scales in the following order: RAADS-R, BS, WPI and SSS. After completion, a debrief form was presented to participants, reiterating the research aims, with the

researchers' contact information provided. Participants were then invited to enter a £10 lottery draw, and were granted 1 participation credit, if part of the RPS. As the survey included material that could have raised concern for participating individuals, contact information for mental health services and support helplines were provided for further guidance.

Diagrams and a further two visual aids were provided to ensure participants understood how the assessment worked. A meta-analysis of 24 studies assessed the inter-rater reliability of the Beighton measure to be substantial to excellent, for users of all backgrounds and experience levels with Cronbach's α scores all above 0.7 [55].

2.5 Data Analysis

To prepare the data for hypothesis testing, preliminary analyses were conducted on the raw data prior to the main analysis using the software package SPSS v27. Data from 320 participants were removed due to incomplete responses. 17 items on the RAADS-R were reverse-coded and total scores for the scales were obtained. Cronbach's alpha was calculated for the RAADS-R and the SSS. The BS and the WPI items were scored as dichotomous (yes/no) variables, which omitted analysis of internal consistency.

To visually assess normality, scatterplots, histograms, outliers, skewness, and kurtosis were examined for each scale using unstandardised residuals. The BS and SSS met the normality assumptions, but data for the RAADS-R, WPI and FSQ appeared skewed. Thus, a log transformation and square root transformation were applied to the skewed scales to assess the best normality fit. A log10 transformation was confirmed for the RAADS-R, a log-natural transformation was confirmed for the WPI, and a square root transformation was confirmed for the FSQ. Therefore, transformed data for the RAADS-R, WPI and FSQ and the raw data for the BS and SSS was used for the analyses.

The percentage of participants who fulfilled criteria for the diagnosis of each of ASD, FM and hypermobility was calculated for the overall group and for age and gender bands, with Chi-square analyses to assess the relationships between each condition and both variables. Directional Pearson correlations were conducted to assess the strength of the relationships between each disorder. Bivariate correlations were first conducted to determine the relationships between the scales. An alpha value of 0.05 was used for all statistical analyses. Hayes method [56] was used to determine the degree to which correlations between ASD and fibromyalgia were mediated by hypermobility.

3. Results

3.1 Demographics

There were 448 participants whose data was complete and therefore suitable for analysis. Their median age was 24 (range 18-60) years. Of these, 343 identified their gender as female (76.6%), 71 as male (15.8%), 22 as non-binary (4.8%), 6 as trans-male (1.3%), 2 as trans-female (0.4%) and 4 as 'prefer not to say' (0.9%). These demographic data are shown in more detail in Table 1.

Table 1 To show demographics of cohort by gender and condition prevalence, along with gender correlations with those conditions.

	Prevalence of Conditions					
	RAADS-R		Beighton		FSQ	
Gender	ASD	Non-ASD	JH	Non-JH	FM	Non-FM
Female	209	134	156	187	140	203
Male	46	25	23	48	21	50
Non-Binary	21	1	8	14	13	9
Trans Female	2	0	2	0	2	0
Trans Male	6	0	6	0	6	0
Prefer not to say	0	4	1	3	0	4

$\chi^2(7) = 19.797$, $p = 0.006$ (Gender and RAADS-R)

$\chi^2(7) = 17.752$, $p = 0.013$ (Gender and Hypermobility)

$\chi^2(7) = 20.462$, $p = 0.005$ (Gender and Fibromyalgia)

3.2 Prevalence

The number of participants meeting the diagnostic threshold for each of the major rating scales was as follows: autistic traits 284 (63.4%), fibromyalgia 182 (40.6%) and Beighton's test for hypermobility 196 (43.7%). The mean (SD) scores achieved by the 448 participants on each of the major rating scales were as follows: autistic traits 83.81 (34.31); fibromyalgia 11.53 (6.81) and Beighton's test for hypermobility 3.87 (2.77). For this study, the Cronbach's alpha for the subscales ranged from 0.72 to 0.88, while the overall Cronbach's alpha for the RAADS-R was 0.94.

3.3 Effect of Age

Two-tailed Chi-square analysis showed a significant positive relationship between age and fibromyalgia (16.642, $p = 0.002$). However, no significant relationship between age and autistic traits was evident (13.390, $p = 0.063$).

3.4 Effect of Gender

Chi-square analysis also showed a significant relationship between female gender and fibromyalgia (20.462, $p = 0.005$). Relationships between female gender and hypermobility (17.752, $p = 0.013$) and female gender and autistic traits (19.797, $p = 0.006$) also proved to be significant. Although females had higher rates than males for each scale, non-binary people had higher rates of both fibromyalgia and autistic traits. However, the highest rates for all three variables were seen among trans-males and trans-females, with the details of each group shown in Table 1.

3.5 Subgroup Differences for Fibromyalgia Scores by Gender

Within the 182 participants who met criteria for fibromyalgia, both females and males were more likely to meet the threshold for dysautonomia, as assessed by the SSS, than the threshold for chronic pain, as assessed by the WPI: females 69% vs 30%, and males (51% vs 18%).

3.6 Subgroup Differences for Those with Fibromyalgia and Autistic Traits by Gender and Age

Within the 182 participants with fibromyalgia, high percentages in each gender group exhibited autistic traits. Among hypermobile females under 25 years of age, 89.1% scored >65 on the RAADS-R scale, while this fell in those aged 25-30 to 86.7%, and among those females aged over 30 to 67.7%.

Among hypermobile males (n = 21), 19 (90.5%) scored over 65 on the RAADS-R scale, as did 96% of non-binary people (n = 22) and 100% of both trans males (n = 6) and trans females (n = 2).

3.7 Subgroup Differences for Beighton Scores by Gender

There were significant gender influences on the rates of those meeting criteria for hypermobility on the Beighton score. While 45.5% of females and 32.4% of males were hypermobile, rates were 36.4% for non-binary and 100% for both trans males and trans females.

3.8 Effect of Hypermobility on Autistic Traits and Fibromyalgia

Individuals that met the Beighton criteria (>5) for hypermobility scored on average higher above the threshold (>65) on the RAADS-R for autistic traits (mean 91.6, SD: 36.3), compared to those that did not meet the Beighton criteria for hypermobility (mean 77.6, SD: 30.8) P = 0.02 as shown in Figure 1.

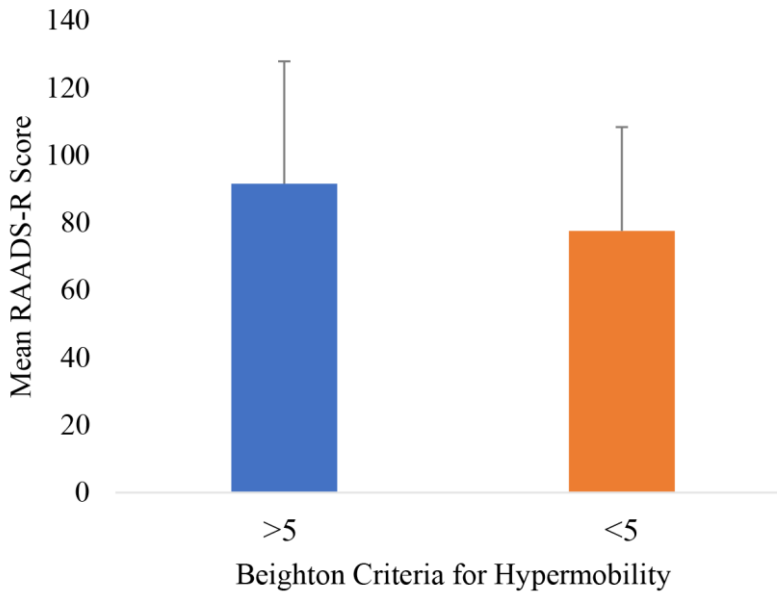

Figure 1 Descriptive Statistics of RAADS-R Scores Including Mean and Standard Deviation for Individuals that Scored Above (>5) and Below (<5) the Beighton Criteria for Hypermobility.

Individuals that met the Beighton criteria for hypermobility scored on average higher on the combined fibromyalgia score (mean 13.4, SD: 7.3) when compared to those that did not meet the Beighton criteria for hypermobility (mean 10.0, SD: 6.0). For the WPI assessing pain, higher average scores were found in those that met the Beighton criteria (mean 6.6, SD: 5.1) than those that did not (mean 4.6, SD: 4.1). For the SSS assessing dysautonomia, higher average scores were seen in individuals that met the Beighton criteria (mean 6.8, SD: 2.8) compared to those that did not (mean 5.5, SD: 2.5). These comparisons are presented in Figure 2.

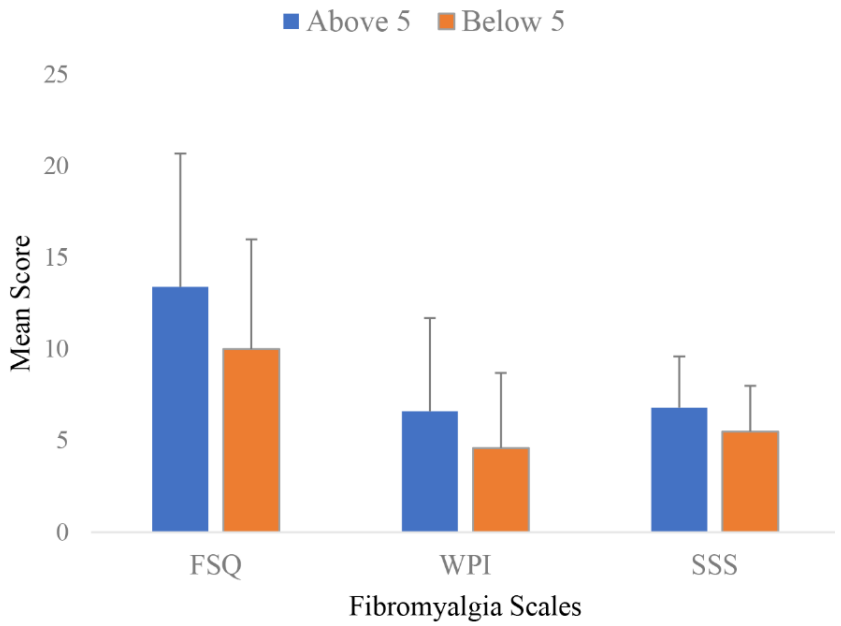

Figure 2 Descriptive Statistics of FSQ, WPI and SSS Scores Including Mean and Standard Deviation for Individuals That Scored Above (>5) and Below (<5) the Beighton Criteria for Hypermobility.

3.9 Correlation between Autistic Traits, Hypermobility and Chronic Pain

The overall Pearson correlation coefficient between the RAADS-R score and the combined fibromyalgia score was 0.354 (p = 0.001). The correlation between the RAADS-R and the WPI was 0.243 (p = 0.01), while the correlation between RAADS-R and the SSS was 0.452 (p = 0.0001). Equivalent correlations between the Beighton score and the combined FM score, WPI and SSS were 0.224, 0.250 and 0.237 respectively, all again significant with a p value of >0.01.

For the 284 participants who scored at least 65 on the RAADS-R scale, the overall Pearson correlation coefficient between the RAADS-R score and the combined fibromyalgia score was 0.186 (p = 0.01). The correlation between RAADS-R and the WPI was 0.530 (p = 0.00001) and the correlation between RAADS-R and the SSS was 0.308 (p = 0.0001). Within this group, equivalent correlations between the Beighton score and the combined FM score, WPI and SSS were 0.252, 0.255 and 0.292 respectively, all again significant with p values of >0.01.

For the 182 participants who scored 12 or above on the combined fibromyalgia scales, the overall Pearson correlation coefficient between the RAADS-R score and the combined fibromyalgia score was significant at 0.237 (P = 0.01). The correlation between RAADS-R and the SSS was greater at 0.421 (p = 0.001), while the correlation between RAADS-R and the WPI was not

significant at 0.006. Hence, the symptom severity score accounted for almost all the observed correlation between autistic traits and fibromyalgia among those who met the criteria for this condition. The correlation between the Beighton score and the combined fibromyalgia score was also significant at 0.256 (p = 0.01).

For the 196 participants who scored above 5 on the Beighton scale, the overall Pearson correlation coefficient between the RAADS-R score and the combined fibromyalgia score was 0.365 (p = 0.0001). The correlation between RAADS-R and the WPI was 0.235 (p = 0.01) and the correlation between RAADS-R and the SSS was 0.472 (p = 0.0001). Equivalent correlations between the Beighton score and the combined FM score, WPI and SSS were 0.201, 0.184 and 0.177 respectively, all again significant with p values of >0.01.

3.10 Regressions and Variance

Simple linear regressions were conducted to test whether the scales used significantly predicted one another and to establish the proportion of variance they explained. Overall, Beighton scores significantly predicted total fibromyalgia scores, B = 0.093, t = 5.463, p = 0.0001, explaining a significant proportion of the variance in total fibromyalgia scores R2 = 0.063, F(29.846) = 447, hence accounting for 6.3% of their variance. Beighton scores also significantly predicted SSS scores, B = 0.238, t = 5.160, p = 0.0001, explaining a significant proportion of their variance R2 = 0.056, F(26.626) = 447, indicating that 5.6% of the variance in SSS scores could be explained by Beighton scores. Beighton scores significantly predicted WPI scores, B = 0.084, t = 4.856, p = 0.0001 and also explained a significant proportion of the variance in WPI scores, R2 = 0.050, F(23.583) = 447. Thus, Beighton scores explained 5% of the variance in WPI scores.

Overall, RAADS-R scores significantly predicted total fibromyalgia scores, B = 2.071 t = 7.994, p = 0.0001, explaining a significant proportion of their variance R2 = 0.125, F(63.898) = 447, thus accounting for 12.5% of their variance. A significant partial mediation between ASD and total fibromyalgia was found through hypermobility (t = 3.606, p = 0.0001). RAADS-R scores significantly predicted SSS scores, B = 7.143, t = 10.697, p = 0.0001, in addition to, explaining a significant proportion of their variance, R2 = 0.204, F(114.421) = 447, indicating that RAADS-R scores accounted for 20.4% of the variance in SSS scores. Hence, significant partial mediation between autistic traits and SSS was found through hypermobility (t = 3.514, p = 0.0001). RAADS-R scores also significantly predicted WPI scores, B = 1.435, t = 5.279, p = 0.0001. RAADS-R scores therefore also explained a significant proportion of variance in WPI scores R2 = 0.059, F(27.871) = 447. However, this again only explained 5.9% of the variance in WPI scores. A significant partial mediation between autistic traits and WPI was confirmed through hypermobility (t = 3.414, p = 0.0001). These results are summarised in Figure 3 and Figure 4.

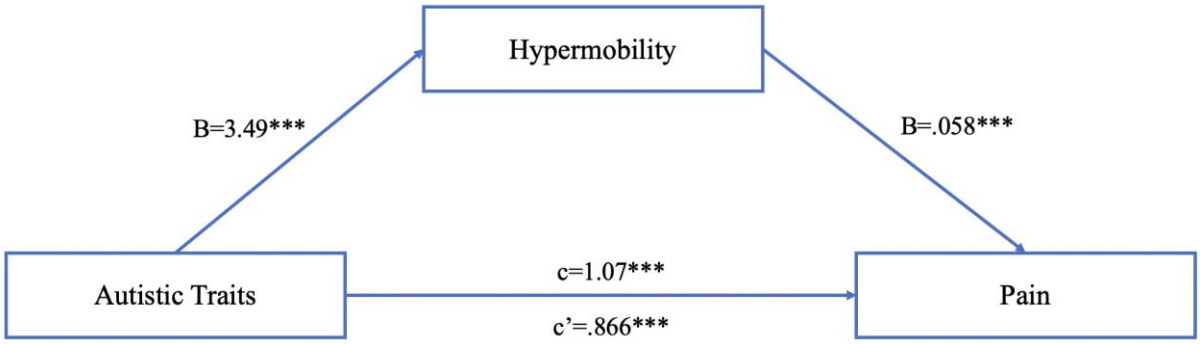

Figure 3 Mediation Effects of Autistic Traits on Fibromyalgia Symptoms Through Hypermobility. Note. *p < 0.05, **p < 0.01, ***p < 0.001.

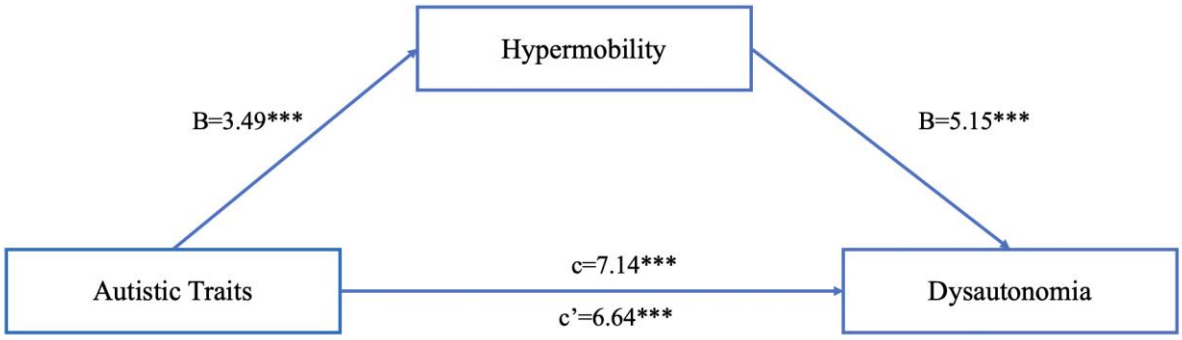

Figure 4 Mediation Effects of Autistic Traits on Dysautonomia Symptoms Through Hypermobility. Note. *p < 0.05, **p < 0.01, ***p < 0.001.

4. Discussion

Recent work has confirmed that patients with fibromyalgia and other forms of chronic pain are more likely to have a neurodivergent condition [36, 37] and that autistic people are more likely to have chronic musculoskeletal pain [38, 39] and to demonstrate hypermobility [49]. The presence of hypermobility has been previously proposed to mediate the relationship between pain and neurodivergence among symptomatic individuals [35, 39]. The aims of our study were to explore the relationships between fibromyalgia, autistic traits and hypermobility in a large, self-selected community-based population. We calculated the prevalence of these conditions in our study population to establish how representative our sample was of the general population. We examined the effects of age and gender on the relationships between each of the three conditions. In addition, we calculated the correlations and linear regressions between each variable, in addition to assessing the mediation effect of hypermobility on the association of fibromyalgia with autistic traits.

Our population was predominantly young, and female, so was not an accurate representation of the population at large. Nonetheless, this is the demographic group that now present most often with chronic musculoskeletal pain and associated hypermobility. They are also the group with a rapid recent increase in the prevalence of diagnosed neurodivergence, so they are representative of those people who present to medical services for help with such symptoms. In addition, those who chose to participate in the study were entirely self-selected. Given that the social media link and associated video emphasised the rationale for this study, it is hardly

surprising that so many of those who responded fitted this age and gender profile. However, it should be noted that 30 people (6.6% of responders) self-identified as either non-binary or trans male/female. This is an important group of people, and their results offer an important insight into the issues experienced by this subgroup.

The prevalence of each of the three variables we studied were much higher than reported in a random population and this was most marked among females and in those who self-identified as non-binary or as trans-males/females. Indeed, all eight of the latter group met criteria for each of fibromyalgia, autistic traits and hypermobility. This suggests that such individuals are likely to be over-represented among those who present to medical services with features of these conditions.

Criteria for fibromyalgia were met by around 40% of participants, proving most prevalent in females aged over 40. Such results are supported by others [9, 39, 57] who demonstrated women to have significantly more tender points than men. Furthermore, Wolfe [16] reported higher prevalence of fibromyalgia in women (3.4%) compared to men (0.5%). In general, participants reported significantly more features of dysautonomia than of widespread pain which suggested that fatigue, poor sleep and brain fog dominated chronic pain among younger respondents, and this observation applied equally to males as to females.

Criteria for hypermobility were fulfilled by approximately 44% of participants, and again this was more prevalent in females as expected. Higher rates of hypermobility are reported in females [22] but estimates of prevalence in an unselected population are between 11-30%, emphasising the self-selected nature of our study respondents. Those who met hypermobility criteria were also more likely to have fibromyalgia and higher levels of autistic traits.

Most striking in our study was the fact that about 65% of participants scored above the threshold of 65 points on the RAADS-R scale, demonstrating significant autistic traits in the majority. This was also most common among younger females as expected. Those scoring above 65 points on the RAADS-R test had the highest correlations with chronic widespread pain and dysautonomia.

As expected, fibromyalgia significantly correlated with both RAADS-R and Beighton scores. Hypermobility however, whilst still a significant element in mediating the relationship between autistic traits and fibromyalgia, was less of a factor in our community setting than that reported among patient populations where hypermobility and autism are significantly associated [32, 36, 39] and most people with fibromyalgia or chronic fatigue are also hypermobile [5, 24, 35, 39].

Casanova [38] that found three-quarters of autistic females with hypermobility experienced chronic pain. Similarly, in a longitudinal follow-up study of females that had received a diagnosis of ASD and/or ADHD in childhood, Asztély [40] found that three-quarters had chronic pain by adulthood, after first receiving a diagnosis of ASD/ADHD. Together, these findings not only highlight pain as a progressive outcome in autistic female adults, but the prevalence pattern seen across the studies indicate that chronic pain in autistic females is evidently not due to chance. Such findings are important given the large gender bias observed in autism and pain sensitivities. Most research to date has suggested that females have lower pain thresholds than males, particularly those with musculoskeletal disorders [1, 58]. Hence, oversensitivity to pain has been linked to later diagnosis of ASD. Late diagnosis of ASD can result in inappropriate treatment, distress, and further disability [59] which may explain why hypermobility and fibromyalgia are highly co-morbid with neurodivergence in young and middle-aged female adults, as we found.

Among individuals displaying both autistic traits and hypermobility, a stronger association was found with the symptom severity scale than with widespread pain. These features correlate strongly with autonomic dysfunction (dysautonomia) [60]. Indeed, in females, dysautonomia symptoms were twice as prevalent as widespread pain. This is consistent with previous work showing greater predisposition to chronic pain and neural dysfunction among females [61]. Among the participants who met criteria for fibromyalgia, the correlation with autistic traits was particularly high. This was accounted for by the very high prevalence of fatigue, sleep disturbance and autonomic dysfunction, rather than the presence of widespread musculoskeletal tenderness or pain. This is an important observation that should encourage reappraisal of the definition of 'pain' in neurodivergent people.

Many autistic individuals do not specifically localise pain to a definitive area, as a neurotypical person might. Instead, they often use terms such as 'discomfort' and 'anxiety' to express pain to their doctors, so perhaps clinicians' understanding of how pain is perceived in autism should include a broader definition of pain language. Autistic people may express their pain very differently because their internal symptoms are even more debilitating than widespread tenderness.

Together, these findings indicate that the internal features of pain may be more prevalent in autistic individuals than external features, particularly for females. Indeed, enhanced internal bodily awareness, related to impaired interoception (i.e., perceptual changes in internal bodily states), is linked to autism, hypermobility, and chronic pain [62]. Thus, it is very plausible that impaired interoception could indicate dysfunction of the autonomic nervous system explaining the high levels of dysautonomia observed in each of autistic people, hypermobile and fibromyalgia populations.

Hypersensitisation of pain mechanisms has even been suggested as a cause of fibromyalgia [13, 63]. Di Stefano [25] suggested hypermobility may also arise due to central sensitization, while Riquelme [29] demonstrated hypersensitivity to pain and touch in autistic children. The concept of generalised hypersensitivity is worth exploring in a wider context for autistic adults as it can apply to each of sensory stimuli, food intolerance and emotional factors producing rejection sensitive dysphoria.

Additionally, it is important to note that with more access to individual and personal experiences (via social media), the importance of enforcing intersectionality in healthcare grows. Women and minority ethnic groups have experience of dismissal by doctors [64] and as this study demonstrates a significantly higher prevalence of all conditions in females, gender identity must be considered in the assessment and implications of these conditions. Recent research on autism in women highlights striking differences with their male counterparts both in the community and in prison [65-67]. The presence of autistic traits and pain was reported by all trans and most non-binary participants, so further research into the high prevalence rates in these populations are also warranted.

The prevalent view is that autistic people tend to have limited understanding of the social 'rules' of neurotypicals and are inclined to view situations in fixed terms, not necessarily using contextual cues. Masking is a strategy used by autistic women [68], to help cope with day-to-day life in a neurotypically designed world [69]. This can increase the risk of delayed or misdiagnosis and is significantly correlated with suicidal tendencies [70]. Furthermore, anxieties about not meeting expectation of others due to fundamental differences in emotional processing can cause pain,

anxiety and depression in autistic individuals [71] exacerbated by features of dysautonomia leading to fibromyalgia.

The very high prevalence of autistic traits, chronic pain and hypermobility seen among those with self-reported gender dysphoria are striking. This is the first time such an association has been proven within a community setting and has many implications for them. It may explain some of the serious physical and psychological challenges they experience and highlights their increased requirements for access to both mental and physical health support services. An integrated holistic approach to the provision of medical care may be preferred over the present multiple speciality approach.

4.1 Limitations

Unlike previous studies which have investigated hypermobility in smaller clinical populations [36-39], with established neurodivergent conditions or hypermobility, the present study observed a larger sample in the general population, where pre-existing diagnoses of neurodivergence/hypermobility/fibromyalgia were not necessarily established. These methodological differences make it difficult to conclude that hypermobility fully mediates the relationship between neurodivergent conditions and pain solely in clinical populations. Future work controlling for pre-existing diagnoses in the general population as a comparison group is warranted to observe whether a difference in the mediating role of hypermobility is found. Alternative mediators for this association within a population could be investigated and we suggest these might include autonomic dysfunction and food intolerance.

The prevalence of all three conditions was much higher than the literature predicted for a random population, confirming that our study group represented a highly self-selected sample. As such, our results cannot be extrapolated to represent the population as a whole. In addition, Jones [51] demonstrated no association between RAADS results and clinical diagnoses, noting that the RAADS-R lacks predictive value for a diagnosis of autism prior to adulthood. This suggests that the use of the RAADS-R scale could potentially exaggerate the prevalence of autistic traits among younger people, or even that these traits are a consequence of fibromyalgia rather than contributory. However, this seems unlikely given the age distribution of our population.

A further limitation is the high withdrawal rate experienced. A lot of participants refused to participate or left during the RAADS-R questionnaire, which suggests the RAADS-R may have been too long, so a shorter validated assessment tool should be considered for future research.

Despite additional effort made to avoid advertising the study onto certain platforms (eg. online autism forums) and restraining the use of hashtags that may attract specific groups, it is difficult to confirm the lack of bias without having screened for existing diagnoses. Further limitations reside in the measures used. All measures were self-reported questionnaires which decreases the internal validity as participants may exaggerate or underreport symptoms. For example, clinicians usually assess hypermobility, and the accuracy of participant's self-diagnosis cannot be guaranteed. Alternative measures validated for use in large population studies could be used in future studies.

4.2 Future Research/Implications

Chronic pain is a frequent comorbidity for those with autistic traits and hypermobility. Hence, longitudinal studies are advised to map the development of pain in autism and hypermobility to understand the precipitating, perpetuating and preventative factors that impact upon the complex symptom severity observed in these populations. The prevalence of, and associations between, autistic traits, hypermobility and fibromyalgia within the general population underline the need for health specialists to reconsider the relationship between physical and mental health. Understanding the association between neurodivergence and pain is paramount if clinicians are to adopt an effective multidisciplinary approach to the diagnosis and treatment of these common conditions.

Potential overlap exists between the pathophysiology of autism and fibromyalgia. The gut microbiome is thought to be an essential element in both the pathophysiology of autism [72] and fibromyalgia [73]. Upregulation of short-chain fatty acids, such as butyrate (an important epigenetic regulator of mitochondrial function), and the melatonergic pathway [74] are related to serotonin production. Suppression of melatonin might reduce mitochondrial function [75] and may contribute to prolonged or excessive inflammatory processes within the central nervous system [76]. Pain may be a consequence of these processes, while augmentation of both butyrate and melatonin might reduce some of the features seen in each of autism and fibromyalgia [77].

5. Conclusions

In conclusion, this study demonstrated a highly significant association between autistic traits and fibromyalgia in a self-selected community population and demonstrated that symptoms of autonomic dysfunction were more strongly associated with autistic traits than was chronic pain. Hypermobility only partially mediated the relationship between autistic traits and fibromyalgia, suggesting that additional mediators should be considered in future studies. Screening for autonomic dysfunction in autism, hypermobility and fibromyalgia may aid insight into the underlying processes contributing to the association. Increasing clinician awareness of these conditions and their inter-relatedness is an essential aspect in the development of an evidence-based therapeutic approach.

Author Contributions

CK designed and supervised the study, while LR, HB, ET and EP designed the questionnaire, performed and analysed the study. All authors contributed to preparing the paper in final written form.

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Competing Interests

None of the authors have any conflicts of interest to declare.

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