The Academy of Medical Sciences

NHS National Institute for Health Research

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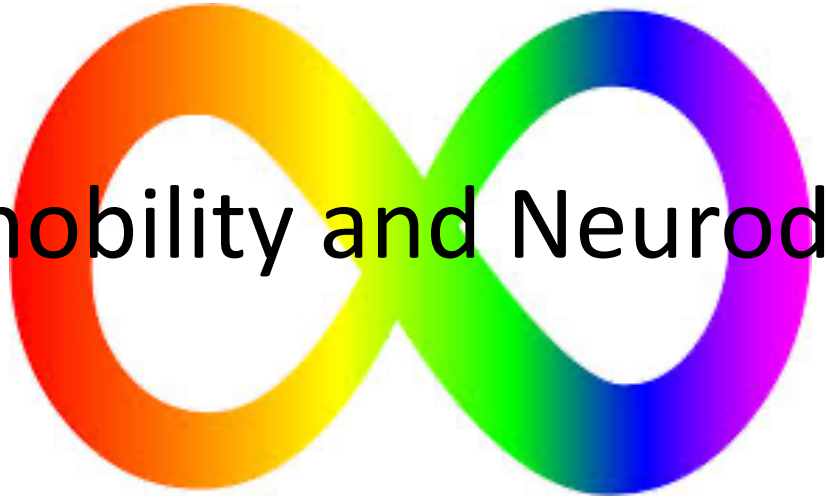
MQ Transforming mental health through research

VERSUS ARTHRITIS



Hypermobility and Neurodiversity

Dr Jessica Eccles @BendyBrain

Clinical Senior Lecturer, BSMS

Honorary Liaison Psychiatrist, SPFT
Neurodevelopmental Service

Brighton and Sussex University Hospitals NHS Trust

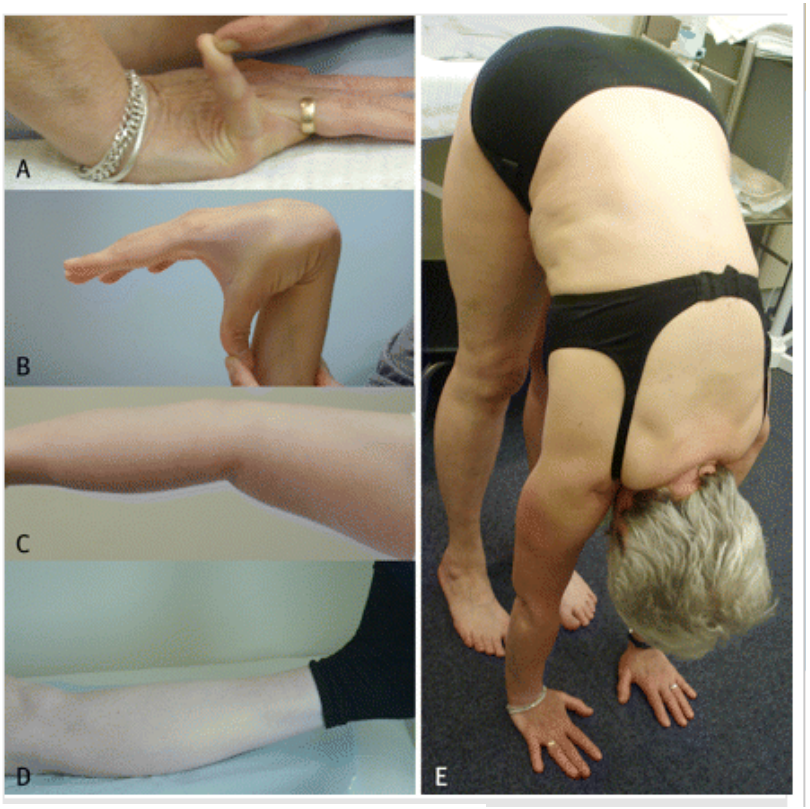
brighton and sussex medical school

Sussex Partnership NHS Foundation Trust

Outline

- Variant connective tissue: hypermobility (JH)
- Neurodevelopmental disorders/Neurodiversity (ND)
- Common links
- Research findings
- Conclusions and future directions

Hypermobility: Variant Connective Tissue



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ARTICLE

A Framework for the Classification of Joint Hypermobility and Related Conditions

MARCO CASTORI,* BRAD TINKLE, HOWARD LEVY, RODNEY GRAHAME, FRANSISKA MALFAIT, AND ALAN HAKIM

Clinical Spectrum of Hypermobility

Table 3
Clinical Spectrum of EDS-HT/JHS (Hamonet et al., 2014; Colombi et al., 2015).

Osteoarticular	i.e. mild scoliosis, flat foot, lumbar hyperlordosis, joint hypermobility
Muscular	i.e. hypotonia, fibromyalgia, recurrent myalgias and cramps, dystonia
Mucocutaneous	i.e. mildly hyperextensible skin, velvety/silky/soft skin texture, striae rubrae and/or distensae in young age, small or post-surgical atrophic scars, Keratosis pilaris, hernias, light blue sclerae, gingival inflammation/recessions, hypoplastic lingual frenulum, easy bruising, resistance to local anaesthetic drugs
Gastrointestinal	i.e. dysphagia, dysphonia, reflux gastroesophageal, gastritis, unexplained abdominal pain, food intolerances
Cardiovascular	i.e. varicose veins, low progressive aortic root dilatation, pseudo-Raynaud's phenomenon, mitral valve prolapse
Urogynaecological	i.e. dyspareunia, dysmenorrhea, urinary stress incontinence, meno/metrorrhagia.
Ocular	i.e. myopia, strabismus, palpebral ptosis.
Dental	i.e. dental neuralgia, gingivitis, temporo mandibular joint pain, dental pains to cold/warm.
Neuropsychiatric	i.e. dysautonomia, clumsiness, proprioceptive dysfunction, paresthesia, headache, fatigue, sleep disturbances, cognitive impairment, anxiety, hyperaesthesia, hyperosmia, hyperacousis.

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Research in Developmental Disabilities

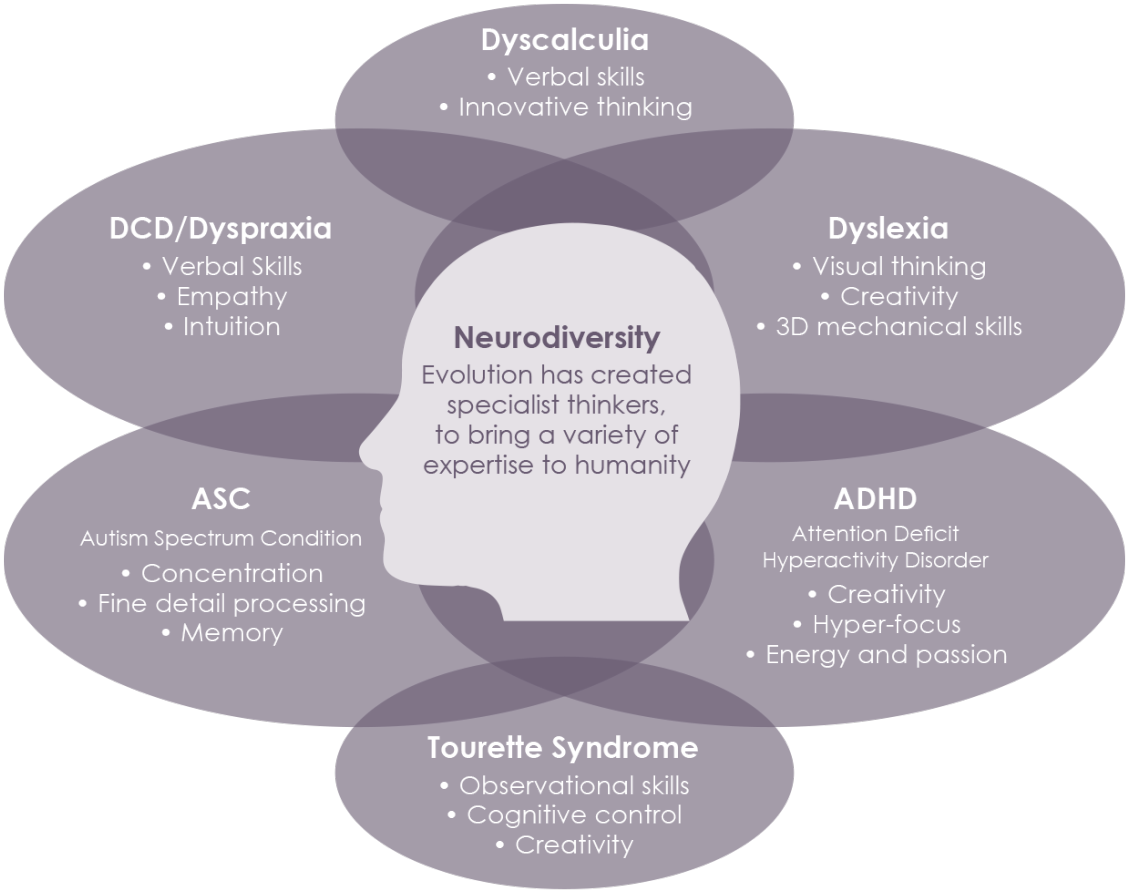
Review article

A connective tissue disorder may underlie ESSENCE problems in childhood

Carolina Baeza-Velasco[a,*], Rodney Grahame[b], Jaime F. Bravo[c,d]

[a] Department of Psychology, Laboratory of Psychopathology and Health Process, University Paris Descartes – Sorbonne Paris Cité, Boulogne-Billancourt, France
[b] Division of Medicine, University College London, London, UK
[c] Medical School, University of Chile, Santiago, Chile
[d] Rheumatology Unit, San Juan de Dios Hospital, Santiago, Chile

Neurodevelopmental conditions



Based on the highly original work of of Mary Colley, DANDA

Cederlöf et al. BMC Psychiatry (2016) 16:207
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BMC Psychiatry

RESEARCH ARTICLE Open Access

Nationwide population-based cohort study of psychiatric disorders in individuals with Ehlers–Danlos syndrome or hypermobility syndrome and their siblings

Martin Cederlöf[1*], Henrik Larsson[1], Paul Lichtenstein[1], Catarina Almqvist[1,2], Eva Serlachius[3] and Jonas F. Ludvigsson[1,4,5,6]

Abstract

Background: To assess the risk of psychiatric disorders in Ehlers-Danlos syndrome (EDS) and hypermobility syndrome.

Methods: Nationwide population-based matched cohort study. EDS, hypermobility syndrome and psychiatric disorders were identified through Swedish national registries. Individuals with EDS ($n = 1,771$) were matched with comparison individuals ($n = 17,710$). Further, siblings to individuals with EDS who did not have an EDS diagnosis themselves were compared with matched comparison siblings. Using conditional logistic regression, risk of autism spectrum disorder (ASD), bipolar disorder, attention deficit hyperactivity disorder (ADHD), depression, attempted suicide, suicide and schizophrenia were estimated. The same analyses were conducted in individuals with hypermobility syndrome ($n = 10,019$) and their siblings.

Results: EDS was associated with ASD: risk ratio (RR) 7.4, 95 % confidence interval (95 % CI) 5.2–10.7; bipolar disorder: RR 2.7, CI 1.5–4.7, ADHD: RR 5.6, CI 4.2–7.4; depression: RR 3.4, 95 % CI 2.9–4.1; and attempted suicide: RR 2.1, 95 % CI 1.7–2.7, but not with suicide or schizophrenia. EDS siblings were at increased risk of ADHD: RR 2.1, 95 % CI 1.4–3.3; depression: RR 1.5, 95 % CI 1.1–1.8; and suicide attempt: RR 1.8, 95 % CI 1.4–2.3. Similar results were observed for individuals with hypermobility syndrome and their siblings.

Conclusions: Individuals with EDS and hypermobility syndrome are at increased risks of being diagnosed with psychiatric disorders. These risk increases may have a genetic and/or early environmental background as suggested by evidence showing that siblings to patients have elevated risks of certain psychiatric disorders.

Keywords: Cohort study, Ehlers-Danlos syndrome, Hypermobility syndrome, Epidemiology, Psychiatric disorders

Common links between JH and ND

- Anxiety
  - Of those with neurodevelopmental conditions approx. 40% experience other psychiatric disorder (Tonge & Einfield, 2000)
  - Up to 70% JH in anxiety/panic (Bulbena et al., 1988, Martin-Santos et al., 1998)

- Dyspraxia
  - Very common in neurodevelopmental history
  - 50% of those with ADHD have DCD (Cairney et al. 2010)
  - JH is common in DCD (Celetti et al., 2015, Kirby and Davies, 2007)

- Dysautonomia
  - 80% of hEDS/HSD patients have orthostatic intolerance (Gazit et al., 2003)
  - JH in up to 70% of POTS patients (Mathias et al., 2012)
  - Poor orthostatic pulse pressure regulation in children increased risk for symptoms of ADHD (Casavant et al., 2012)
  - ? Shared abnormalities in NET gene (Fararone and Mick., 2010)
- Pain
  - High rates of ADHD in patients with Fibromyalgia (Dersken et al., 2015)
  - High rates of JHS (pain plus JH) in patients with ND (Eccles., in prep)

Potential Model

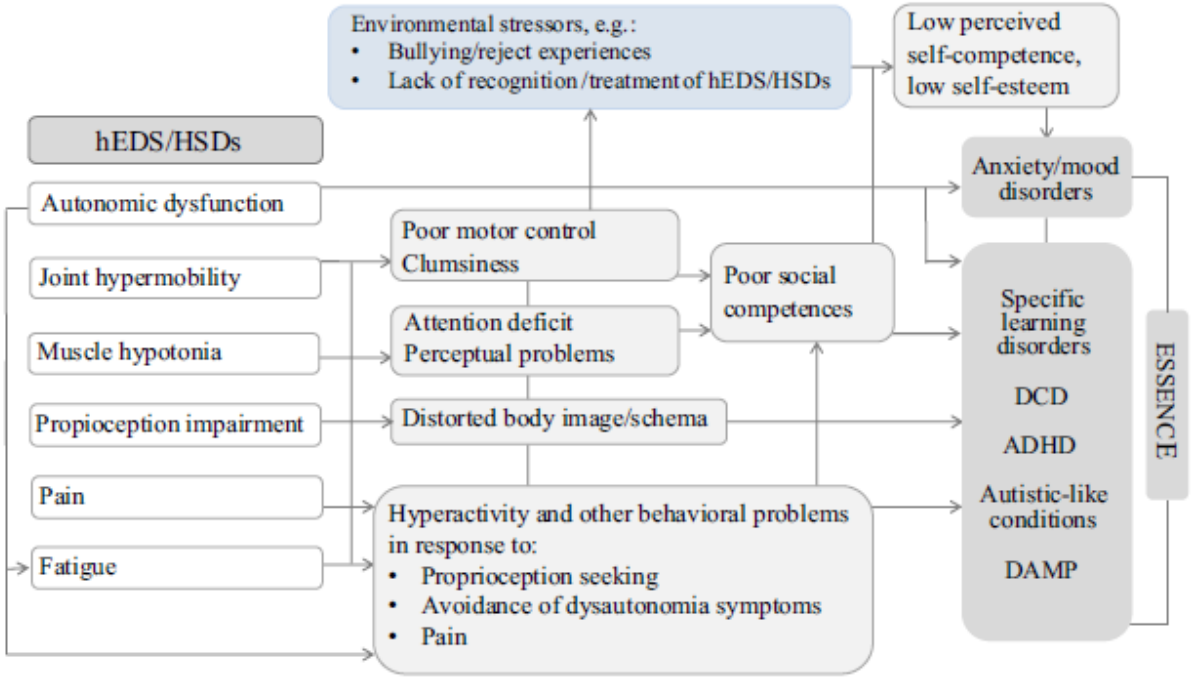

Fig. 2 Diagram illustrating possible relationships between some features of JHS/EDS-HT might contributing to neurodevelopmental disorders and psychopathology in the developmental age. JHS/EDS-HT: joint hypermobility syndrome/Ehlers–Danlos syndrome hypermobility type. *ADHD* attention-deficit/hyperactivity disorder, *DCD* developmental coordination disorder, *DAMP* deficits in attention, motor control, and perceptual abilities, *ESSENCE* early symptomatic syndromes eliciting neurodevelopmental clinical examinations

Attention-deficit/hyperactivity disorder, joint hypermobility-related disorders and pain: expanding body-mind connections to the developmental age

Carolina Baeza-Velasco[1,2,5] · Lorenzo Sinibaldi[3] · Marco Castori[4]

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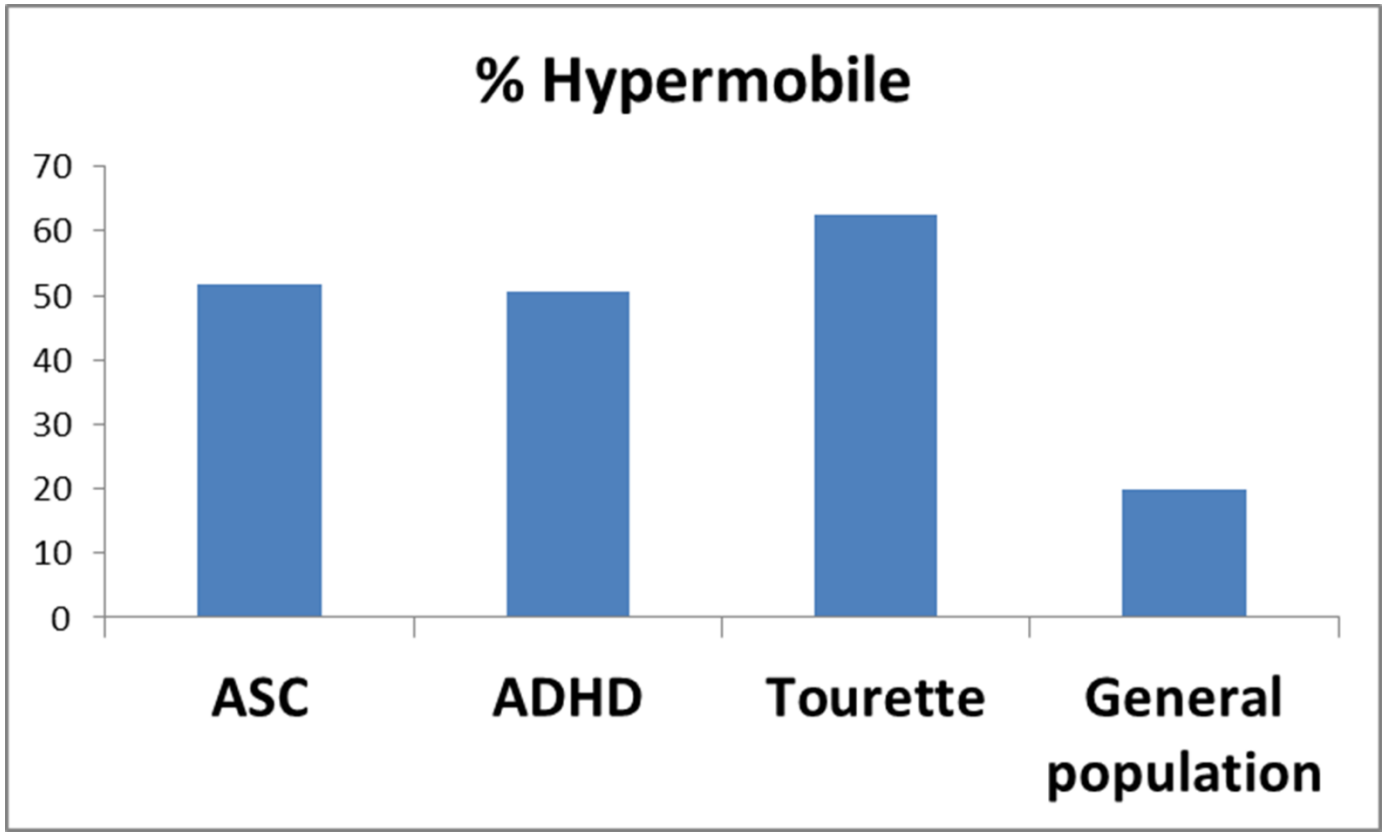
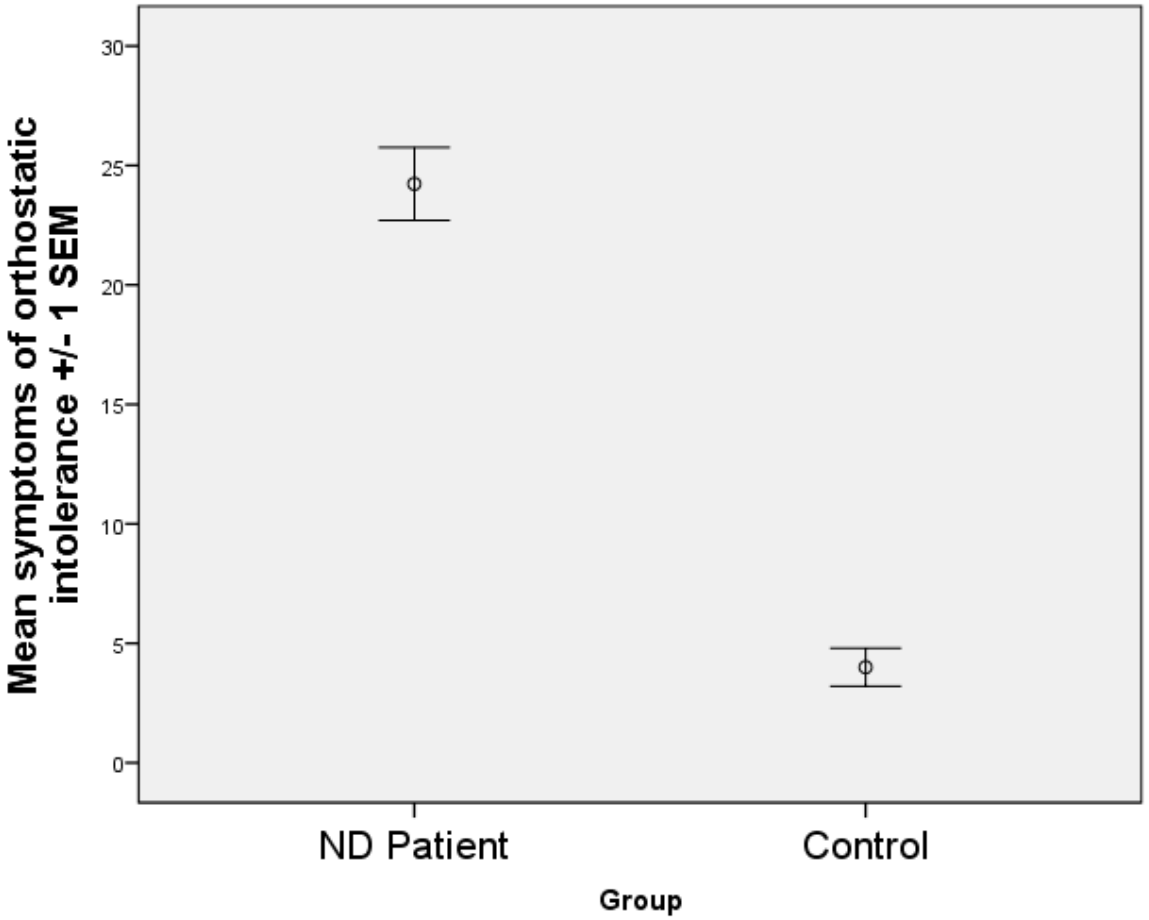
Research Findings – Prevalence JH



N=109, General population data from ALSPAC (Clinch et al., 2011)

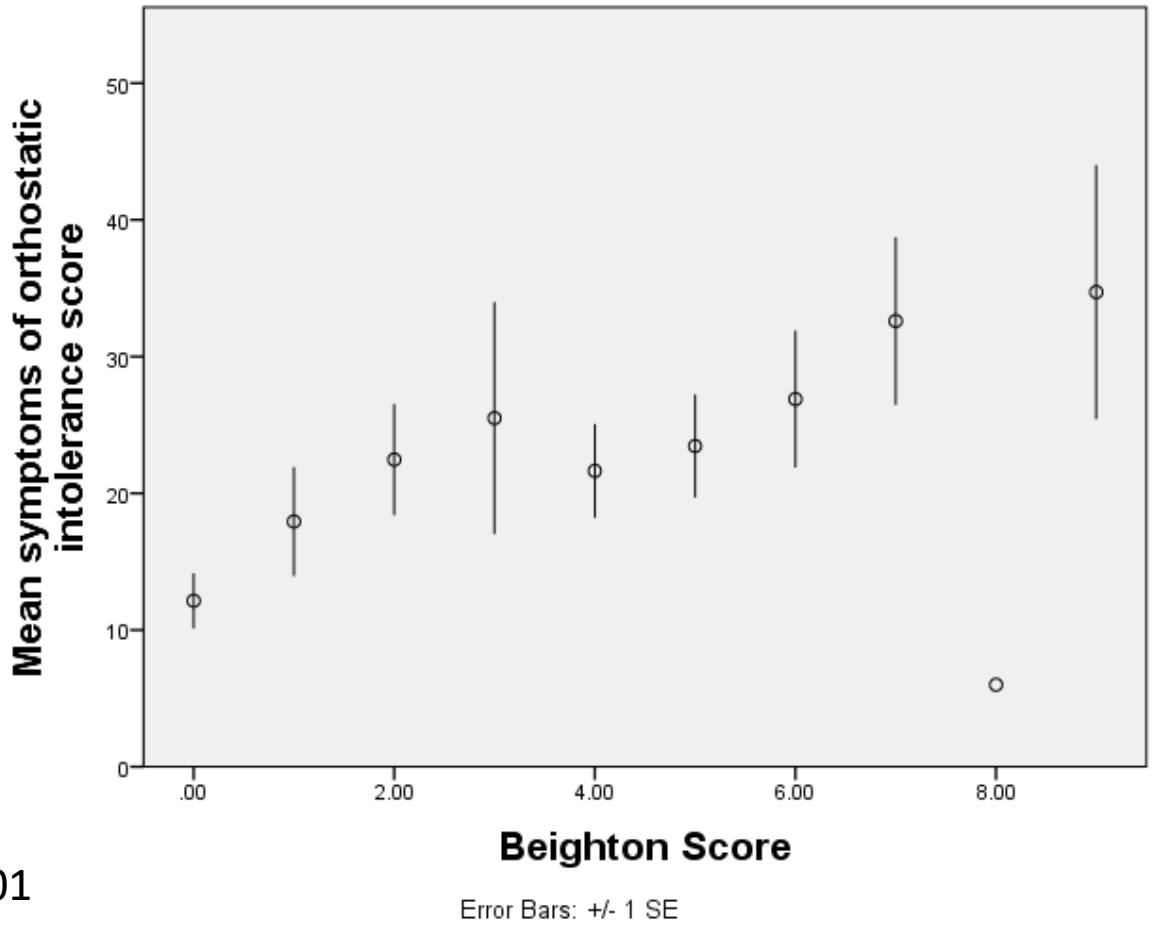
	ODDS RATIO (95% CI)
ASC	4.51 (2.17 - 9.37
ADHD	4.34 (2.67 - 7.03)
TS	7.016 (3.063-16.07)

Symptoms of Dysautonomia



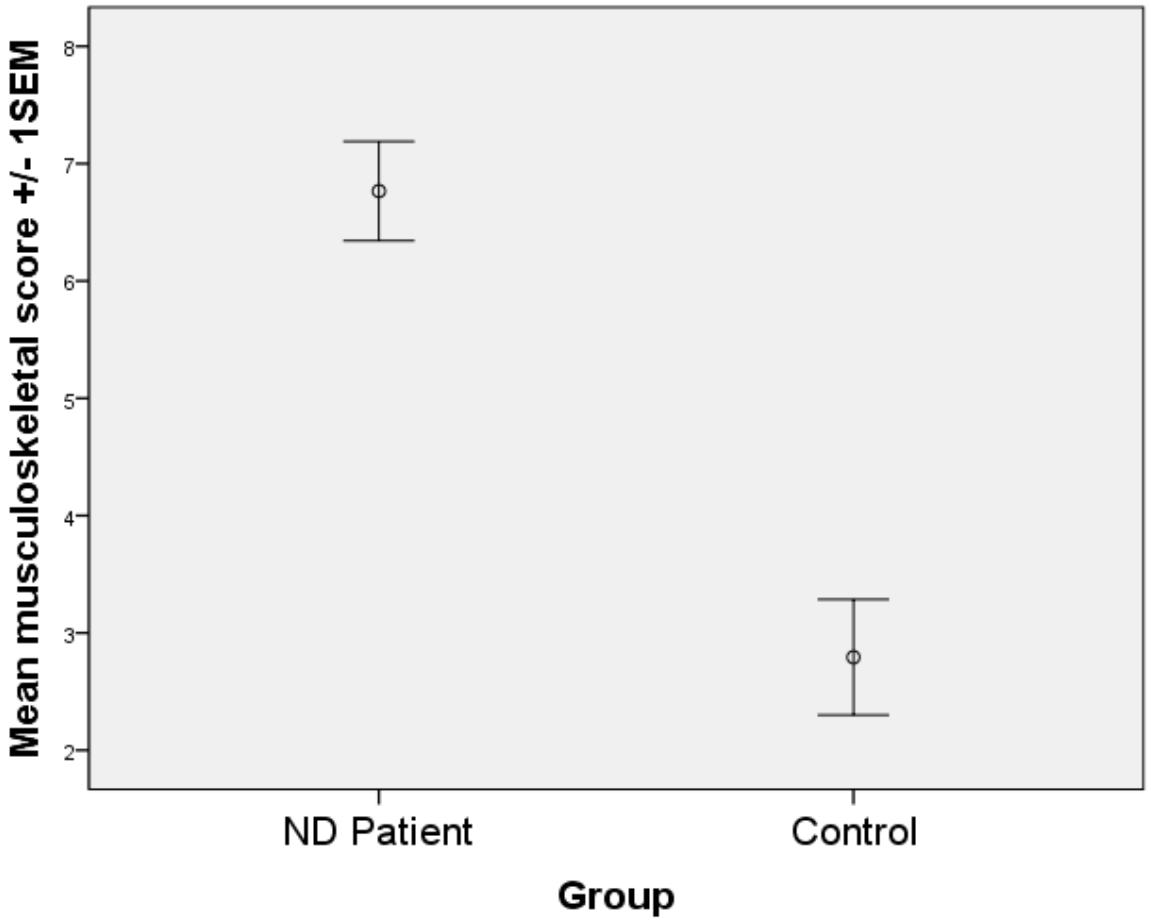
t=6.908, d.f 131, p=<0.001
Eccles et al., in prep

Correlation between hypermobility and symptoms of orthostatic intolerance



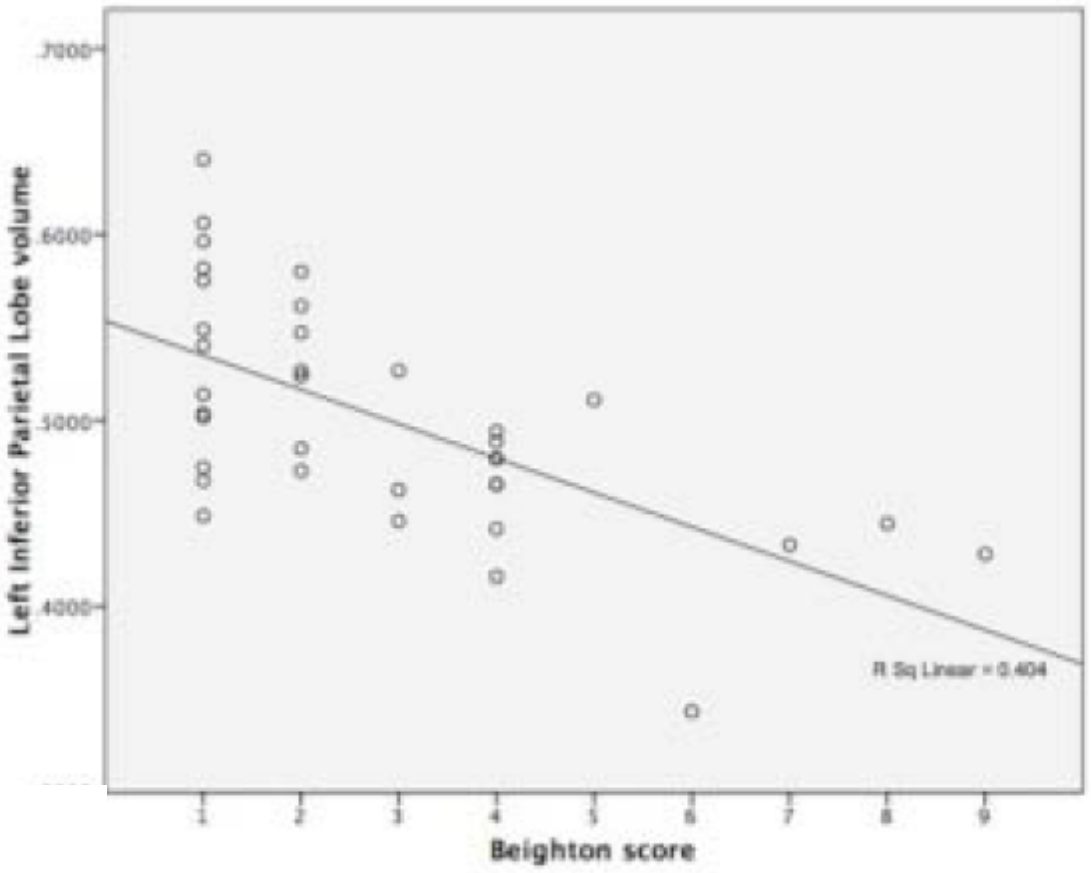
r=0.408, p=<0.001
Eccles et al., in prep

Musculoskeletal symptoms



t=5.272, df 104, p<0.001
Eccles et al., In prep

Link with dyspraxia
IPL volume negatively correlates HM



RC PSYCH
The British Journal of Psychiatry
BJPsych
Brain structure and joint hypermobility: relevance to the expression of psychiatric symptoms
Jessica A. Eccles, Felix D. C. Beacher, Marcus A. Gray, Catherine L. Jones, Ludovico Minati, Neil A. Harrison and Hugo D. Critchley
BJP 2012, 200:508-509.
Access the most recent version at DOI: 10.1192/bjp.bp.111.092460

Eating Disorder

- 33 patients
- 58% Generalized Joint Laxity
- 70% Hypermobility syndrome

ED: Relationship with thinking style

- 40% “Extreme Male Brain” (upper 2.5 centile, Goldenfield et al, 2005)
- 28% High Autism Quotient
- Significant relationship between high systematising and joint hypermobility syndrome

Eccles et al., in prep

Conclusions

- Importance of recognising JH in Autism/ADHD/Tourette Syndrome
- Importance of screening for neurodevelopmental disorder in JH
- Importance of screening for underlying autonomic dysfunction and pain
- Are ASC traits important in eating disorder in JH?

Thanks

- Prof Critchley
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