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Symmetry of foot alignment and ankle flexibility in paediatric Charcot-Marie-Tooth disease

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Abstract

Background—Charcot-Marie-Tooth disease is the most common inherited nerve disorder and typically presents with pes cavus foot deformity and ankle equinus during childhood. Level in the variation of symmetry of musculoskeletal lower limb involvement across the clinical population is unknown, despite early reports describing gross asymmetry.

Methods—We measured foot alignment and ankle flexibility of the left and right limbs using accurate and reliable standardised paediatric outcome measures in 172 patients aged 3–20 years

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with a variety of disease subtypes recruited from the United States, United Kingdom, Italy and Australia.

Findings—While a large range of differences existed between left and right feet for a small proportion of children, there was no overall significant difference between limbs.

Interpretation—There are two important implications of these findings. Children with Charcot-Marie-Tooth disease generally exhibit symmetrical foot alignment and ankle flexibility between limbs. As such, analysing one limb only for biomechanical-related research is appropriate and satisfies the independence requirements for statistical analysis. However, because there are large differences between feet for a small proportion of children, an individualised limb-focused approach to clinical care is required.

Keywords

Foot; ankle; Charcot-Marie-Tooth disease; Foot Posture Index; children; pes cavus

1. Introduction

Charcot-Marie-Tooth disease (CMT), a group of genetically-based nerve disorders, affects ~1 in 2500 people and is among the most common inherited neurological disorders (Skre, 1974). It is characterised by demyelination and/or axonal loss of the peripheral nerves. As a result there is progressive weakness of the distal, and to a lesser extent proximal, limb musculature, hand, foot and ankle deformities, impairment of motor function, and sensory loss.

During childhood, CMT usually presents with lower limb muscle imbalance and ankle contracture associated with a painful cavus (high-arched) foot deformity which becomes increasingly severe and rigid as the disease progresses (Burns et al., 2005). Foot alignment and ankle flexibility are thought to be generally symmetrical; however cases of asymmetry are reported and are considered more severe. Indeed the original description by *Charcot* and *Marie* in 1886 shows gross foot and ankle asymmetry (Figure 1) (Charcot and Marie, 1886). Retrospective chart reviews have previously identified a small proportion of children (4 of 52) with one cavovarus and one planovalgus foot (Wines et al., 2005), and a small proportion of adults (5 of 61) with pes cavus and ankle contracture asymmetry (Bienfait et al., 2006). However, these studies are limited by their retrospective design and unclear methods of foot and ankle assessment.

The aim of this study was to prospectively evaluate the frequency and extent of symmetrical foot and ankle involvement between limbs of children with CMT using reliable and validated outcome measures.

2. Methods

This study was conducted as part of the Inherited Neuropathies Consortium and included leading paediatric tertiary healthcare institutions of Detroit, London, Milan, Philadelphia, Rochester and Sydney. Ethics approval from all institutions for all studies, and written informed assent/consent from all children and their families was obtained.

Objective measurements of left and right foot alignment and ankle flexibility were obtained from all children using highly reliable and validated age-appropriate items from the Charcot-Marie-Tooth disease Pediatric Scale (CMTPedS) (Burns et al., 2012). Specifically, foot alignment was measured using the Foot Posture Index (FPI) (Cain et al., 2007, Menz and Munteanu, 2005, Redmond et al., 2006), and ankle dorsiflexion range of motion assessed with the lunge test (Burns and Crosbie, 2005, Khan et al., 1997).

Data were analysed in SPSS version 18.0 (Chicago, IL, USA). Normality of data distribution was assessed using the Kolmogorov-Smirnov test, and the appropriate parametric or non-parametric tests subsequently employed. To account for the ordinal nature of FPI data, left and right total FPI scores were transformed to their equivalent logit values as per the Rasch model for parametric statistical analysis (Keenan et al., 2007) and back transformed to raw FPI values for descriptive purposes. Cross-checking for external validation using baseline data from the Australian Ascorbic Acid Trial of 81 children with the most common type of CMT, Type 1A, was also conducted (Burns et al., 2009).

3. Results

During a 14-month prospective period, 172 patients aged 3–20 years were recruited. Patient profile was: 90 female (52%); mean age 10.8yrs (SD 4.2); mean height 1.44m (SD 0.22); mean weight 42.5kg (SD 18.9). The sample comprised a broad range of CMT subtypes. Lower limb symptoms reported by the children included: foot pain in 66 (38%); leg cramps in 68 (40%); ankle instability during walking in 84 (49%); daily trips/falls in 82 (48%); sensory symptoms in 54 (31%). Foot drop was evident in 104 (60%) cases, difficulty heel walking in 146 (85%) and difficulty toe-walking was evident in 65 (38%) children. Sixteen (9%) children required Ankle-Foot-Orthoses to walk.

The raw mean FPI of the left foot was 1.2 (SD 4.6, range −12 to 12) and raw mean FPI of the right foot was 1.2 (SD 4.4, range −11 to 11). The mean FPI logit of the left foot was 0.7 (SD 3.1, range −10.5 to 8.7) and mean FPI logit of the right foot was 0.6 (SD 2.9, range −8.0 to 7.8). According to FPI criteria (Redmond et al., 2008), 55 (32%) children had pes cavus (FPI logit < -0.21) which became more prevalent with advancing age ($r=0.317$, $p<0.0001$, point-biserial correlation coefficient). Based on absolute values of left-right differences there was a large range between individual left and right FPI logit scores (0 to 8) (Figure 2a), but there were no significant group differences between limbs (mean difference 0.02, SD 1.7, $t=1.44$, $p=0.89$). Correlation between feet was very high ($r=0.84$, $p<0.001$). Nine (5%) children had a large clinically significant difference (>2SD) between limbs (FPI logit >3.4) and 138 (80%) children had a negligible difference (<1SD) between limbs (FPI logit <1.7). Asymmetrical cases were generally more disabled according to the CMTPedS (24 vs 20 points on the 0–44 point scale) (Burns et al., 2012).

The mean lunge angle of the left ankle was 22.1^0 (SD 8.9, range −12 to 38^0). Mean lunge angle of the right ankle was 22.6^0 (SD 8.6, range 0 to 39^0). Again based on absolute values of left-right differences there was a large range between individual left and right ankles for the lunge test (0 to 31^0) (Figure 2b), but there were no significant group differences between limbs (mean difference 0.7^0, SD 6.1, $t=1.34$, $p=0.18$). Correlation between ankles was high ($r=0.76$, $p<0.001$). Five (3%) children had a large clinically significant difference (>2SD) between limbs (Lunge >12.2^0) and 123 (72%) children had a negligible difference (<1SD) between limbs (Lunge <6.1^0). Asymmetrical cases were generally more disabled according to the CMTPedS (26 vs 19 points on the 0–44 point scale) (Burns et al., 2012).

Cross-checking with the Australian Ascorbic Acid Trial of 81 children (47 boys, 34 girls) aged 2–16 years, showed that the mean FPI logit of the left foot was 1.3 (SD 3.6, range -10.5 to 7.8) and the mean FPI logit of the right foot was 1.0 (SD 3.4, range −10.5 to 7.8). Again, there was no significant FPI difference between limbs (mean difference 0.3, SD 1.9, t=0.1.38, $p=0.17$).

4. Discussion

There are two important implications of these findings. Children with CMT generally exhibit symmetrical foot alignment and ankle flexibility between limbs. As such, analysing one limb only for biomechanical-related research (e.g. dominant foot, worst foot, or randomly selected foot) is appropriate and satisfies the independence requirements for statistical analysis (Menz, 2005). However, because there are large differences between feet for a small proportion of children, an individualised limb-focused approach to clinical care is required.

While asymmetry in this large cohort was rare, it was related to overall disability of the disease, as measured by the CMTPedS. The CMTPedS score has been shown to be highly sensitive to CMT type, worsens with age, and clearly reflects the severity of the disease (Burns et al., 2012). As such asymmetry of foot alignment and ankle flexibility is more likely to be observed in children more affected by the disease.

Interestingly, it has been reported that in pairs of male homozygotic twins with CMT1A the symmetry of neurophysiologic deficit contrasted markedly with the variable and asymmetric clinical presentations, including unilateral foot drop (Garcia et al., 1995). Variability of clinical expression in these patients with identical mutations, and in our sample, suggests the action of endogenous factors, environmental modulation or gene modifiers of disease asymmetry.

5. Conclusion

Despite early classical reports showing gross foot and ankle asymmetry (Figure 1), most children with CMT typically have symmetrical foot alignment and ankle flexibility, as shown in Figure 3.

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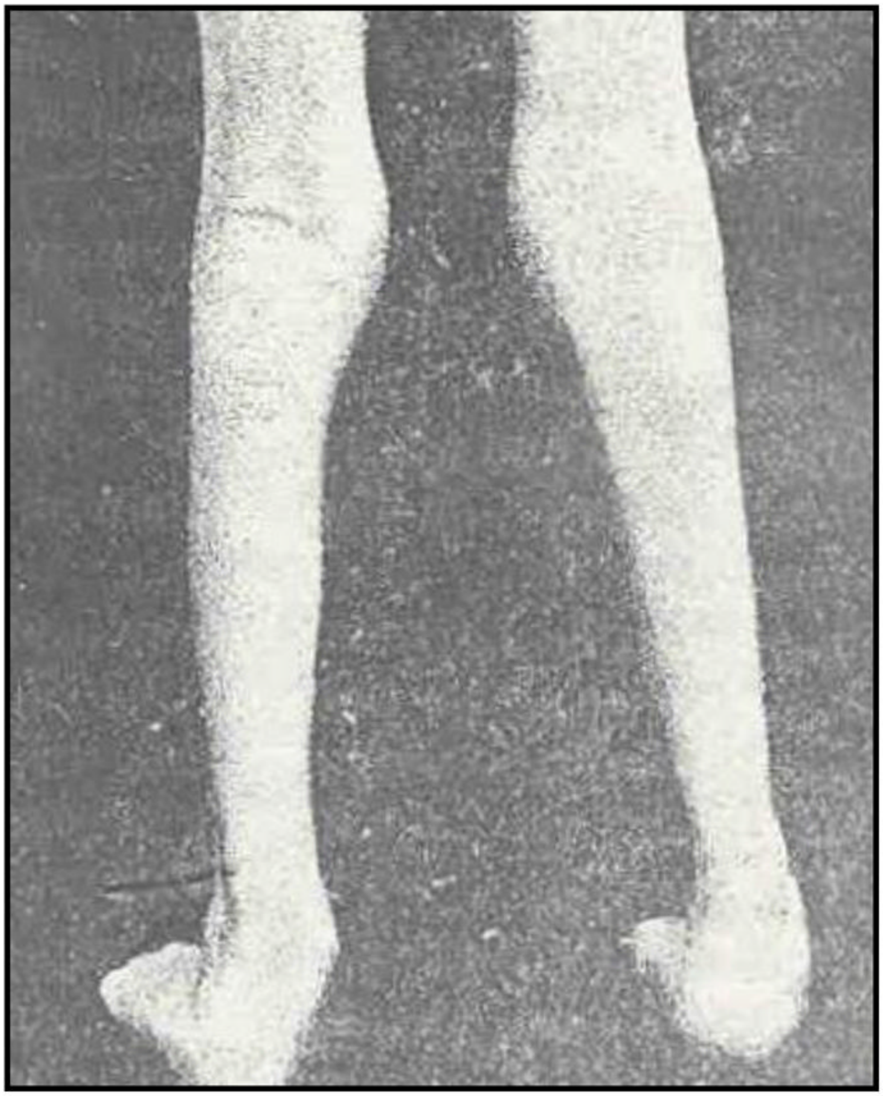
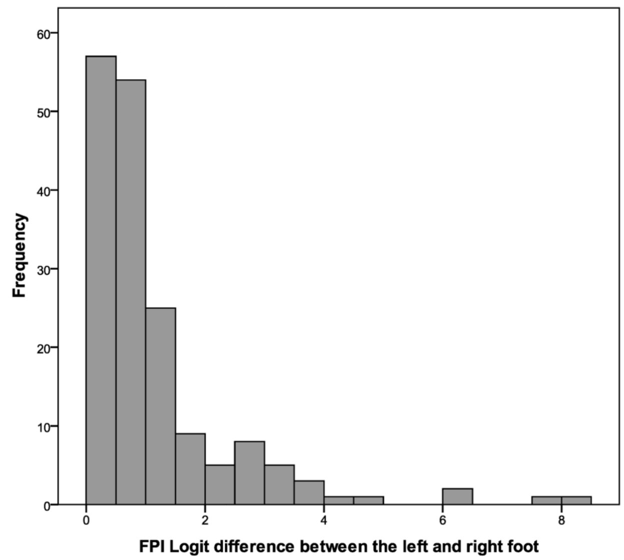


Figure 1.
Marked foot and ankle asymmetry as shown in the original description of CMT (Charcot and Marie, 1886).

Figure 2a:



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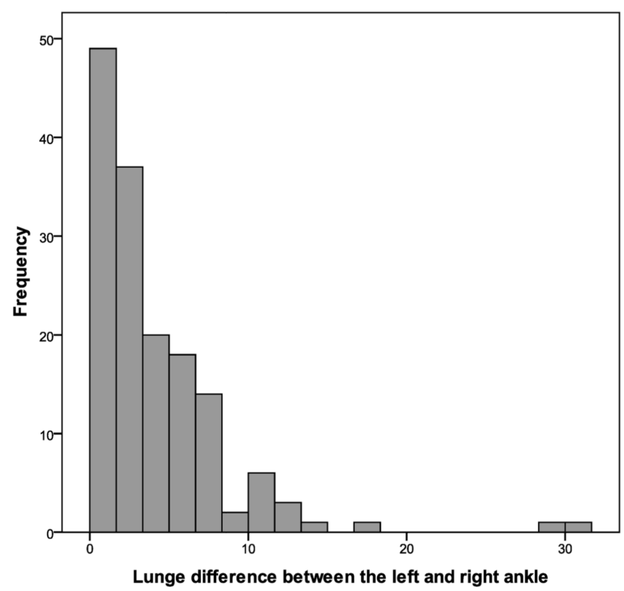

Figure 2.

Figure 2a: Symmetry of foot alignment in children with CMT.

Figure 2b: Symmetry of ankle flexibility in childhood CMT.

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Figure 3.
Foot and ankle pes cavus foot deformity shown in a typical symmetrical case of CMT.