SYMmetry of Foot Alignment and Ankle Flexibility in Children with Charcot-Marie-Tooth Disease

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SUMMARY
Charcot-Marie-Tooth disease (CMT) typically presents with pes cavus deformity and ankle equinus during childhood. Symmetry of lower limb involvement across the clinical population is unknown, despite early reports depicting gross asymmetry. We measured left and right foot alignment and ankle flexibility using accurate and reliable standardised paediatric measures. While a large range of differences existed between left and right feet for a small proportion of children, there was no significant difference between limbs.

INTRODUCTION
Charcot-Marie-Tooth disease (CMT) is the most common genetic nerve disorder. CMT usually presents with lower limb muscle imbalance and ankle contracture associated with a painful cavus (medial high-arched) foot deformity which becomes increasingly severe and rigid as the disease progresses [1]. Involvement of the foot and ankle is 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) [2]. Understanding the frequency and extent of foot and ankle involvement between lower limbs of children with CMT will ensure appropriate data collection methods for research, and targeted therapy in clinic.

METHODS
As part of the Inherited Neuropathies Consortium (NIH Rare Diseases Clinical Research Network), children with a variety of CMT types were recruited in Sydney (Australia), Detroit, Philadelphia and Rochester (USA), London (England) and Milan (Italy). Using the CMT Pediatric Scale [3] left and right measures of foot alignment were collected using the Foot Posture Index (FPI) [4], and left and right measures of ankle dorsiflexion range of motion were assessed using the weight bearing ankle lunge test [5]. Cross-validation using baseline data from the Australian Ascorbic Acid Trial of children with the most common type of CMT (1A) [6], was also conducted.

RESULTS AND DISCUSSION
From the Inherited Neuropathies Consortium, 82 children (38 girls and 44 boys) aged 2-21 years (mean 11.0, SD 4.6 years) with a variety of CMT types (39 cases of CMT type 1A, 7 Type 1B-F, 1 Type 2A-L, 33 Unidentified gene) were evaluated.

Foot pain was reported in 34 (41%) children, leg cramps in 28 (34%), ankle instability during walking in 40 (49%) and daily trips/falls in 40 (49%) cases. Sixty-six (80%) children had difficulty heel-walking, 32 (39%) had difficulty toe-walking and 44 (54%) had foot drop.
The mean Foot Posture Index (FPI) of the left foot was 1.8 (SD 4.9, range -10 to 12) and the mean FPI of the right foot was 1.5 (SD 4.7, range -10 to 11). Despite a large range of differences between left and right feet for foot alignment (-8 to 11) (Figure 2), there was no significant difference between limbs (mean difference 0.3, SD 2.6, \( t =1.161, p=0.249 \)).

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

The mean lunge angle of the left ankle was 21.5° (SD 9.9, range -11.8 to 36.6) and the mean lunge of the right ankle was 21.6° (SD 9.5, range 0 to 38.9). Despite a large range of differences between left and right ankles for dorsiflexion range of motion (-31.4 to 10.0°) (Figure 3), there was no significant difference between limbs (mean difference 0.4°, SD 6.2, \( t =-0.530, p=0.598 \)).

Figure 3: Symmetry of ankle flexibility in childhood CMT.

Age, gender, CMT type or the presence of foot pain, leg cramps, ankle instability during walking or daily trips/falls were not associated with the magnitude of difference between left and right limbs for foot alignment or ankle dorsiflexion range of motion \( (p>0.05) \).

Cross-validation with the Australian Ascorbic Acid Trial of 81 children (47 boys, 34 girls) aged 2-16 years, showed that the mean FPI of the left foot was 2.0 (SD 5.2, range -12 to 11) and the mean FPI of the right foot was 1.7 (SD 4.9, range -12 to 11). Again, there was no significant FPI difference between limbs (mean difference 0.4, SD 2.7, range -7 to 11, \( t =0.1224, p=0.224 \)).

CONCLUSIONS
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 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 treatment is required.

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REFERENCES