Update on Rehabilitation Research in Charcot Marie Tooth Disease

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Charcot Marie Tooth disease

Hereditary Neuropathy

Over 100 causative genes

Length dependent sensorimotor neuropathy

Onset depends on type

Slow progression
Impairments, activities and participation for people with peripheral neuropathy

**Impairments**
- Primary weakness
- Secondary/disuse weakness
- Sensory impairment
- Musculoskeletal deformity
- Fatigue
- CV de-conditioning
- Pain
- Impaired balance

**Activities and Participation**
- Reduced efficiency of walking
- Difficulty climbing stairs
- ADL and occupational activities
- Increased risk of falls
- Community mobility
- Maintaining work and family roles
- Socialisation
- Leisure, sports performance
IMPAIRMENTS
Weakness

- Primary muscle weakness
- Atrophy
- Secondary muscle weakness
Joint deformity
Pes cavus in CMT
Primary weakness & foot deformity

Gallardo et al 2006 *Brain* 129: 426-437
Evidence for disuse atrophy

(Morrow et al 2012)
Evidence for disuse atrophy

(Morrow et al 2016)
Deconditioning

- Evidence of reduced aerobic capacity
- Reduced physical activity

(Ramdharry et al. 2017)
Fatigue

70% of people with CMT report severe fatigue (Kalkman et al 2005)

“...it’s like packing up, it’s like my body’s letting me down and it’s telling me to stop now or you’re not gonna carry on...”

“It really hurts when you hear other parents and other kids ...not only will they go and have a game of football they might have spent the morning doing the housework, ...then come home, do the tea, do the washing and sort out ... and there's no way you could even think about that”

(Ramdharry et al. 2012)
Fatigue

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“...it’s like packing up, it’s like my body’s letting me down and it’s telling me to stop now or you’re not...” (Ramdharry et al. 2012)

Possible impact of obstructive sleep apnoea and restless legs (Boentert et al. 2014)

“It really hurts when you hear other parents and other kids ... not only will they go and have a game of football they might have spent the morning doing the housework, ... then come home, do the tea, do the washing and sort out ... and there's no way you could even think about that” (Ramdharry et al. 2012)
Pain in CMT

N=49 people with CMT1a

- 88% complained of pain
- Localized to the feet in 61%
- 18% of patients had neuropathic pain
- Cold (53%) and warm (12%) detection thresholds elevated

- Mainly musculoskeletal pain
- Neuropathic pain may be due to thinly myelinated Aδ fibres
- CMT2 and CMTX have greater small fibre dysfunction so greater prevalence of neuropathic pain

Cramps

Children


- 81 children with CMT
- 32% reported calf cramps
- Toe, quadriceps, arm cramps

Adults

(Johnson et al. Muscle Nerve. 2015 Apr;51(4):485-8)

- Survey of 110 pwCMT
- Reported 9.3 (±12.3) cramps per week
- 23% had daily cramps
- 22% reported impact on QOL
ACTIVITY LIMITATIONS
Gait
Impact of pes cavus on gait biomechanics

No heel rocker with foot drop
Centre of pressure stays lateral
Windlass mechanism: foot remains rigid throughout stance
Reduced propulsion at toe off

(Ramdharry 2008)
Impact of pes cavus on gait biomechanics

Proximal consequences:

Correlation between foot supination and range of pelvic rotation

$r = -0.69$, $p = 0.007$

(Ramdharry 2008)
Changes in temporal spatial gait parameters over one year: n=27; mean age 12.2 ±3.7

<table>
<thead>
<tr>
<th>Parameter</th>
<th>Baseline Mean (SD) 95% CI</th>
<th>12 month Mean (SD) 95% CI</th>
<th>Mean difference</th>
<th>p value</th>
<th>Effect size (Cohen’s d)</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Speed (m/s)</strong></td>
<td>1.18 (0.16) (1.12–1.24)</td>
<td>1.15 (0.14) (1.09–1.20)</td>
<td>−0.03</td>
<td>p = 0.22</td>
<td>d = 0.25</td>
</tr>
<tr>
<td><strong>Nspeed</strong></td>
<td>0.43 (0.07) (0.40–0.46)</td>
<td>0.41 (0.05) (0.39–0.43)</td>
<td>−0.02</td>
<td>p = 0.036</td>
<td>d = 0.40</td>
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<td><strong>Cadence (steps/min)</strong></td>
<td>123.5 (13.6) (118.1–128.9)</td>
<td>118.9 (10.6) (114.7–123.1)</td>
<td>−4.60</td>
<td>p = 0.016</td>
<td>d = 0.38</td>
</tr>
<tr>
<td><strong>Ncadence</strong></td>
<td>0.56 (0.04) (0.55–0.58)</td>
<td>0.57 (0.04) (0.55–0.58)</td>
<td>−0.01</td>
<td>p = 0.307</td>
<td>d = 0.23</td>
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<tr>
<td><strong>Stride length (m)</strong></td>
<td>1.16 (0.13) (1.10–1.21)</td>
<td>1.16 (0.15) (1.10–1.23)</td>
<td>0</td>
<td>p = 0.6</td>
<td>d = 0.06</td>
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<tr>
<td><strong>Nstride length</strong></td>
<td>1.49 (0.18) (1.42–1.56)</td>
<td>1.43 (0.13) (1.38–1.48)</td>
<td>−0.06</td>
<td>p = 0.010</td>
<td>d = 0.36</td>
</tr>
<tr>
<td><em><em>Step width</em> (m)</em>*</td>
<td>0.09 (0.03) (0.08–0.10)</td>
<td>0.09 (0.04) (0.08–0.11)</td>
<td>0</td>
<td>p = 0.981</td>
<td>d = −0.01</td>
</tr>
<tr>
<td><strong>Double support % gait cycle</strong></td>
<td>18.8 (2.9) (17.6–19.9)</td>
<td>20.2 (2.7) (19.1–21.3)</td>
<td>+1.4</td>
<td>p &lt; 0.001</td>
<td>d = −0.51</td>
</tr>
<tr>
<td><strong>Single support % gait cycle</strong></td>
<td>40.7 (1.5) (40.1–41.3)</td>
<td>39.9 (1.4) (39.9–40.4)</td>
<td>−0.8</td>
<td>p &lt; 0.001</td>
<td>d = 0.56</td>
</tr>
<tr>
<td><strong>Stride time (s)</strong></td>
<td>0.98 (0.1) (0.94–1.02)</td>
<td>1.02 (0.09) (0.98–1.05)</td>
<td>+0.04</td>
<td>p = 0.02</td>
<td>d = −0.38</td>
</tr>
<tr>
<td><strong>Nstride time</strong></td>
<td>0.35 (0.02) (0.34–0.36)</td>
<td>0.35 (0.02) (0.34–0.36)</td>
<td>0</td>
<td>p = 0.24</td>
<td>d = −0.26</td>
</tr>
</tbody>
</table>

* Wilcoxon sign rank test; all other tests paired t-test; N prefix = normalised.

(Kennedy R, et al. 2017)
Balance & falls
Retrospective survey of 107 people with CMT (Ramdharry et al. 2017)

Frequency of falls

- Once a day: 5.3%
- Once a week: 14.9%
- Once a month: 29.8%
- Once 6/12: 18.1%
- Once a year: 17.0%

% of respondents

- Indoors private: 36.6%
- Indoors public: 12.6%
- Outdoors: 28.6%
- On uneven ground: 13.9%
- Stairs: 4.6%
- No recollection: 2.5%
Patient Reported Falls and Balance Confidence in Individuals with Charcot-Marie-Tooth Disease

Katy Eichinger*, Karen Odrzywolski, Janet Sowden and David N. Herrmann
Department of Neurology, University of Rochester, NY, USA

• 28 adults with varying types of CMT
• 50% reported falls
• Balance confidence correlated with timed walk; 5 times sit to stand; lower extremity function; reported falls
• Reported falls correlated with timed walk
- Perturbation study
- No SLR in CMT1a
- Delayed MLR
Hand Function

Can be affected by:
• Weakness
• Reduced sensation
• Muscle fatigue
• Altered grip patterns
• Dexterity determined by the degree of weakness

Impacts on:
• Fine motor tasks
• Activities of daily living
• Quality of life

(Videler et al 2009)
REHABILITATION INTERVENTIONS
Can exercise improve primary weakness?

FAST trial

• 60 children with CMT1A

• 6 months progressive resistance training of DF >grade 4 MRC

(Burns et al. 2017)
Can exercise improve secondary/disuse weakness?

Lindeman et al 1995 Arch Phys Med Rehab 76:612:
RCT n=29 people with CMT; 24 weeks training of hip extensors, abductors and knee flexors and extensors at 60% to 80% of 1 repetition max.
Significant improvements in isokinetic knee torque and gait speed (6m TW)
Can exercise improve secondary/disuse weakness?

Chetlin et al 2004  *Arch Phys Med Rehab* 85:

N=20 people with CMT, no control group. 12 weeks of training of elbow flexors and extensors at 20-30% MVC; knee flexors and extensors 40-50% MVC.

Significant improvements in percentage of normal strength in elbow and knee flexors and timed ADL measures

Pooled data from a study of exercise and Creatine
Can exercise improve secondary/disuse weakness?

• Cross over trial of hip flexor strength training n=28
• Increased hip flexor strength
• No carry over into gait performance
• Relationship between baseline strength and change in MVC with training: $r = -0.44$, $p = 0.018$

Can exercise improve aerobic capacity?

El Mhandi et al. *Muscle Nerve* 37 601-10 2008:

N=8 people with CMT, no control group. 24 week bicycle interval interval training.

Significant improvements in oxygen uptake and fatigue
Can exercise improve range of motion?

Interventions for increasing ankle range of motion in patients with neuromuscular disease (Review)

Rose KJ, Burns J, Wheeler DM, North KN
Foot orthoses

• **Indications**
  – Pain, decreased stability, poor alignment
  – Alignment correctable manually

• **Principles**
  – Reduce and redistribute pressure under the foot
  – Increase stability
  – Realignment

• **Evidence**
Ankle foot orthoses

• Indications
  – Foot drop, reduced control of the lower leg, ankle instability

• Types
  – Off the shelf / custom made
  – Flexible / rigid

• Evidence
Gait analysis study of three types of splints, n=14:

- All AFOs reduced foot drop at ground clearance (p<0.05)
- All AFOs reduced the hip flexion angle (p<0.05)
- Stiffer AFO reduced ankle power generation
- Variability in a small group

(Ramdharry et al 2012)
Carbon fibre AFOs


Top strut
Middle strut
Bottom strut
Ankle

Left:

Right:

1 5
2 6
3 7
4 8
10
11
12
13
14
15
16
9

EMNC workshop: Timing of surgical referral

**History**
- Poor outcomes of conservative measures, injury Hx: inversion, #

**Presentation**
- Pain, instability, callosities/ulcers, falls, alignment when weight bearing, MRC, sensation

**Assessment**
- ROM, Silverskold, manual realignment, Coleman’s block,

**Explore conservative measures**

**Referral for surgical opinion**

**Yearly review**

**Surgery**

**Failure**
- inability to correct or support the deformity
- cannot be tolerated: pain or skin breakdown
- unacceptable to the patient & risk MSK injury
- limited potential to increase range of movement

**Success**
- patient satisfaction,
- improved ROM, decreased pain,
- improved skin condition,
- increased stability,
- reduced risk of falls/injury,
- functional benefits

(Reilly et al. 2017)
Further research needed

- Interventions to increase physical activity
- Hand function
- Fatigue management
- Optimal orthotic prescription
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