

supported robust cellular growth, while the p.A397T-*MARS* insert did not support cellular growth confirming deleterious effect of this variant. **Conclusions:** Our patient's phenotype was similar to children with motor-predominant *GARS* mutations. Functional data notes this *MARS* variant to be damaging and predictive of a severe, early-onset phenotype.

## P.071

### Novel mutations in *SPG7* identified from patients with late-onset spasticity

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doi: 10.1017/cjn.2018.173

**Background:** Hereditary spastic paraplegia (HSP) is a group of genetic diseases that cause progressive degeneration of the corticospinal tract. Historically, this disease was divided into two types: the classic subtype, with leg weakness and hypertonic bladder, and the complicated subtype, with features such as cerebellar ataxia or optic atrophy. Mutations in *SPG7* (encoding paraplegin) leads to complicated HSP causing cerebellar ataxia, progressive external ophthalmoplegia in addition to the classical symptoms. *AFG3L2* is a binding partner of paraplegin and mutations in *AFG3L2* cause a similar syndrome. **Methods:** From a neurogenetic clinic, we identified 11 patients with late-onset HSP. Sequencing of *SPG7* and *AFG3L2* was performed using a customised assay, and/or clinical diagnostic sequencing panels. *SPG7* transcript level quantification was performed from whole blood RNA on a digital droplet qPCR system. **Results:** We identified 4 patients with pathogenic variants or variants of unknown significance in *SPG7*. No *AFG3L2* mutations were identified. We provide evidence for pathogenicity for three mutations that were not previously associated with *SPG7*-related disease, based on their occurrence in context of the correct phenotype, and the reduction of transcript levels measured with RT-qPCR. A curious association of the heterozygous p.Gly349Ser mutation in association with an ALS-like syndrome is reported. **Conclusions:** *SPG7* mutations sequencing has high diagnostic yield in late onset paraparesis

## P.072

### Agreement between children and their parents' ratings of the health-related quality of life of children with Duchenne Muscular Dystrophy

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doi: 10.1017/cjn.2018.174

**Background:** When measuring young Duchenne Muscular Dystrophy (DMD) patients' health-related quality of life (HRQoL), parent-proxy reports are heavily relied on. Therefore, it is imperative that the relationship between parent-proxy and child self-report HRQoL is understood. This study examined the level of agreement between children and their parent-proxy rating of the child's HRQoL. **Methods:** We used FOR-DMD clinical trial baseline data. HRQoL, measured using the PedsQL inventory, was reported by 178 parent

and child (ages 4 to 7 years) dyads. Intracorrelation coefficients (ICC) measured absolute agreement while paired t-tests determined differences in the average HRQoL ratings between groups. **Results:** The level of agreement between child and parent-proxy ratings of HRQoL was poor for the generic PedsQL scale (ICC: 0.29) and its subscales; and, similarly low for the neuromuscular disease module (ICC: 0.16). On average, parents rated their child's HRQoL as poorer than the children rated themselves in all scales except for psychosocial and school functioning. **Conclusions:** Child and parent-proxy HRQoL ratings are discordant in this study sample, as occurs in other chronic pediatric diseases. This should be taken into account when interpreting clinical and research HRQoL findings in this population. Future studies should examine reasons for parents' perception of poorer HRQoL than that reported by their children.

## P.073

### Cardiac dysfunction in mitochondrial disease: systematic review and metaanalysis

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doi: 10.1017/cjn.2018.175

**Background:** Cardiac dysfunction has significant impact on morbidity and mortality in patients with mitochondrial disorders. Cardiac screening tests are generally recommended because cardiac dysfunction can occur at any point in the disease course, and is amenable to treatment. However there is no clear evidence indicating the best screening strategy in patients with mitochondrial myopathy. **Methods:** Systematic review of the literature for cardiac investigations in adult patients with mitochondrial myopathy. We considered 1303 relevant abstracts, from which 58 full-length articles were reviewed. Seventeen articles including 701 total participants met inclusion criteria. Data extracted included age, diagnosis, and results from ECG, echocardiogram, cardiac MRI, nuclear medicine studies, and Holter monitor. **Results:** We identified echocardiogram and ECG as the principal screening modalities, that identify cardiac structural (26%) and conduction abnormalities (37%) in patients from various mitochondrial myopathy syndromes. Holter monitor was not a high yield investigation and limited studies were identified using cardiac MRI or nuclear medicine. **Conclusions:** We recommend screening with ECG and echocardiogram every 1-2 years in MERRF/MELAS, and every 3-5 years in milder syndromes when cardiac symptoms are not present. Only five of the included studies provided any follow-up data. We recommend studies of natural history, therapeutic response, and of cardiac MRI as areas for future study.

## P.074

### Clinical features of a family with distal myopathy and rimmed vacuoles due to a digenic interaction

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doi: 10.1017/cjn.2018.176

**Background:** The interaction between mutations in two or more genes is increasingly recognised as an important contributor to the phenotypic variability in genetic disorders. Co-occurrence of variants in *SQSTM1* and *TIA1* is reported as a cause of myopathy