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Secondary clinical outcomes of spinal surgery and satisfaction in patients with spinal muscular atrophy (SMA) II and non-ambulant III

C. Brusa[1], J. De Graaf[1], A. Manzur[2], M. Main[2], E. Milev[1], M. Iodice[1], D. Ramsey[1], S. Tucker[2], T. Ember[2], R. Nadarajah[2], F. Muntoni[1], M. Scoto[2]
[1] *UCL GOS Institute Child Health, London, UK;* [2] *Great Ormond Street Hospital, London, UK*

Scoliosis is a highly prevalent feature of SMA and surgery is frequently required. Studies in small cohorts have reported a positive impact of spinal surgery on respiratory function, while limited data are available on motor function, weight gain, post-surgical skeletal pain and satisfaction. We retrospectively reviewed the notes of 33 patients (26 SMA II, 7 non-ambulant SMA III) who successfully underwent spinal fusion (25), magnetic (4) or traditional (4) growth rods followed by final growth spinal fusion (3) at Great Ormond Street Hospital-London. Median age at surgery was 10.9 years (4.28–16.72), median pre-operative Cobb angle 70 degrees (35–89), median follow up before and after surgery 3.9 (0.9–12.3) and 3.7 (0.4–10.5) years respectively. Mean annual rate of Forced Vital Capacity % decline improved after surgery in SMA II: -2.8 versus -7.4 ($p<0.001$). Similar trajectories were observed in SMA III. At first post-surgery assessment a median decline of 4.5 points (0-14) was observed on the Hammersmith Functional Motor Scale while the Revised Upper Limb Module's scores showed a less progressive deterioration. A temporary negative deviation from previous weight curve was observed in 17 patients requiring food supplements (5); one/4 type II with significant weight loss (>5% of total weight) needed gastrostomy. Hip pain was the most common skeletal pain documented (13/33) requiring painkillers (8), intra-articular steroids (1) or surgery (1). Ten patients/parents participated in a phone interview developed by the neuromuscular team on satisfaction. Nine/10 reported major improvements in posture, physical appearance, self-image and all rated the surgical procedure as very successful. However, 7/10 did not report significant improvements in quality of life due to reduced mobility and increased unmet care needs. This ongoing study expands the knowledge on outcomes after spinal surgery in SMA and highlights the importance of a careful post-operative multidisciplinary approach.

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General movements assessment in infants with spinal muscular atrophy: a pilot study

B. Yardımcı Lokmanoğlu, N. Bulut, G. Aydın, G. Sırtbaş, F. Kabakçı, D. Porsnok, A. Mutlu, I. Gürbüz, H. Topaloğlu, O. Yılmaz, A. Karaduman
Hacettepe University, Ankara, Turkey

Although the number of clinical studies performed in spinal muscular atrophy (SMA) has been increased in recent years, the outcome measures evaluating the functions which the initial symptoms first occur are limited. The aim of this study was to assess general movements (GMs) in infants with SMA in early stage. Eight infants aged between 9-19 weeks with SMA diagnosis were included in the study. GMs was applied to infants in fidgety period and motor optimality score (MOS) was calculated. Motor function was evaluated with Children's Hospital of Philadelphia infant test of neuromuscular disorders (CHOP-Intend) which is a SMA-specific measure. The correlation between MOS and CHOP-Intend was analyzed with spearman correlation coefficients. The mean birth week and the birth weight of infants were 38.37±1.59 weeks and 3.30±0.70 kg, consecutively. The mean MOS was 7.87±2.03 and CHOP-Intend score was 18.87±11.69. There was no correlation between CHOP-Intend and MOS ($p>0.05$). GMs, which have been started to use in many genetic diseases, have been used for the first time in neuromuscular diseases in our country by this study. Although there is no association between GMs and CHOP-Intend, it is important to identify specific movement patterns in GMs for SMA infants. Future research included more SMA infants should be conducted.

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CONGENITAL MYOPATHIES: RYR1 AND TITIN

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Electron microscopy characterisation of triads in RYR1 rhabdomyolysis-myalgia syndrome

T. Evangelista[1], C. Labasse[1], M. Beuvin[1], G. Brochier[1], A. Madelaine[1], J. Pastor[2], N. Romero[1]
[1] *GHU Pitié-Salpêtrière, Sorbonne Université, INSERM, Paris, France;* [2] *Myology Institute, Paris, France*

RYR1 gene encodes a calcium channel (RyR1) embedded within the sarcoplasmic reticulum (SR). Variants in the RYR1 gene result in a spectrum of RYR1-related disorders one of which is RYR1 rhabdomyolysis-myalgia syndrome. RYR1 mutations generate structure and post-translational modifications of the receptor impairing its function and the interaction with other components of the triad. When analysing seven cases of RYR1 rhabdomyolysis-myalgia syndrome on electron microscopy (EM) we had the impression that the number of triads was increased. With this work, we aimed to validate this hypothesis studying age matched controls and using normative values from the literature. We have studied, on EM, a group of muscle biopsies from seven patients with confirmed RYR1 mutations and RYR rhabdomyolysis-myalgia syndrome and five age-matched normal controls. We have compared our results with normative data published by Boncompagni et al. 2016. We studied deltoid muscle biopsies performed on a diagnostic setting and processed according to standard histoenzymology and EM techniques. The density of triads was determined counting the number of triads on EM micrographs at x13500 magnification. We used 16 random micrographs of non-overlapping regions/case for an area of 1120 μm2. Two patients showed structural abnormalities with the oxidative staining, eccentric or centric cores in type I fibres. On EM, one case, presented swollen SR in close relation with the sarcolemma; the dilated SR cisternae were tightly packed and rimmed with RYR1 feet. There was no significant difference in the number of triads between the two groups. Comparing with the reference values by Boncompagni, determined to assess the evolution of the triads' density in sarcopenia, we have noticed that unlike normal aging population our older patients had a higher density of triads. We hypothesize that the increased number of triads with age may be a compensatory aspect of the disease.

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Phenotype and pathological variability in RYR1-related myopathy with compound heterozygous variants in Japan

A. Ozaki, A. Ishiyama, E. Takeshita, Y. Shimizu-Motohashi, H. Komaki, S. Noguchi, I. Nishino, M. Sasaki
NCNP, Tokyo, Japan

Mutations in *RYR1* are often associated with central core disease, and are also the most common cause of other congenital myopathies (CMs) such as multi-minicore disease, CFTD (congenital fiber type disproportion) and centronuclear myopathy (CNM). There is an increasing interest in the clinical variability and pathologic overlap among these CMs due to *RYR1* mutations. In addition, it has been reported that the compound heterozygous *RYR1* mutations can cause more severe phenotype compared to the autosomal dominant cases. Here we report clinical and pathological features of the 3 patients with compound heterozygous variants in *RYR1* who were seen and received muscle biopsy at NCNP. Case 1: a 2.5-year-old girl with generalized hypotonia, swallowing and respiratory problems since her birth. She had a markedly myopathic face with extraocular muscle involvement, and required tracheostomy and gastrostomy. She was diagnosed with CNM by muscle pathology. Case 2: a 10-month-old girl with hypotonia, reduced antigravity movements, and swallowing and respiratory problems since neonatal period. Nasogastric feeding and non-invasive ventilation were needed. She was diagnosed with CFTD by muscle pathology. Case 3: a 1-year-old girl with