

sparing of intrafusal muscle fibres and proprioceptive functions may be limited to the more slowly progressive muscular dystrophies.⁹

Troise et al. have provided an important basis for consideration of proprioceptive feedback in the assessment and

potential treatment of manual dexterity in DMD. Further exploration of the underpinnings of both sensory and perceptual control of movement across muscular dystrophies is warranted, especially considering the implications for treatment planning.

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Ketogenic diet in children with intractable epilepsy: what about resting energy expenditure and growth?

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This commentary is on the original article by Groleau et al. on pages 898–904 of this issue.

The study by Groleau et al.¹ looks at the effect of ketogenic diet treatment on resting energy expenditure (REE) and growth in children with intractable epilepsy with and without cerebral palsy (CP) over 15 months. It is an attempt to better understand the metabolic and nutritional long-term effects of the ketogenic diet in children at different degrees of risk for growth and body composition abnormalities.

In the last decade, only one study has focused on the effects of the ketogenic diet on REE² in children with intractable epilepsy without CP for over 6 months of dietary treatment. The authors stated that ketogenic diet treatment increases fat oxidation without significant changes in REE. These findings are confirmed in the present study suggesting that the ketogenic diet does not change daily basal metabolic rate both in the short- or in long-term.

From the available research it is hard to draw firm conclusions on the effect of the ketogenic diet on growth. Quite often results are confounded by ketogenic dietary management, follow-up protocol, duration of treatment exposure, and pre-existing malnutrition (as in our own previous investigation³). In this regard, the present study provides an advance in this area. In line with previous research, results show that height z-score decreased overall from baseline to 3 and 15 months, indicating height velocity deceleration, particularly in children with CP. This could suggest differential mechanisms underlying the association between the ketogenic diet and growth, possibly linked with the putative effects of ketone bodies plasma level and chronic ketosis on intermediate metabolism and hormone secretion (i.e. growth hormone and insulin-like growth factor I) according to different neurological diseases.

Moreover, the ketogenic diet could act differently on nutritional status across the different developmental ages. In adults affected by glucose transporter 1 deficiency syndrome (Glut1-DS) it was recently shown that the ketogenic diet over 5 years did not have any major negative impact on nutritional status.⁴ From this point of view, growth retardation could reflect the potential compensatory mechanisms of the neuro-endocrine axis to cope with the ketogenic diet-induced alteration in protein metabolism.

The authors found an increment of fat mass and fat free mass at 15 months, which seems in contrast to the observed growth failure. However, the validity of these results may be limited by the estimation of fat mass and fat free mass by four skinfolds thickness, using the age and sex-specific equations which were validated for healthy children. Even if, as the authors report, the skinfolds method to estimate fat mass and fat free mass has been used in several adult and child studies, including children with CP, we cannot consider it as a criterion standard. In this regard, it would be very interesting to follow up the changing body composition with dual energy X-ray absorptiometry, which could provide more information not only on the long-term effects of the ketogenic diet on fat mass and fat free mass but also on bone mineral content.

In summary, this study describes the impact of 15 months of ketogenic diet treatment on growth and

REE in children with intractable epilepsy. While there are some weaknesses in the reliability of body composition measures, its results give useful information about energy requirement during ketogenic diet treatment, alongside an indication of possible growth failure not related to changes in REE. Taking into account these considerations, it is clear that the mechanism underlying growth retardation is yet to be elucidated. Since the ketogenic diet is often discontinued after a few years of intractable epilepsy treatment, but is a lifelong therapy in some neurometabolic diseases (e.g. Glut-1DS and pyruvate dehydrogenase deficiency),⁵ future research to identify the mechanism underlying growth failure is strongly needed.

Once translated into guidance for clinical practice, these results endorse the need for continuous surveillance of nutritional status in children treated with the ketogenic diet.

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