



## Autism in patients with propionic acidemia

Peter Witters<sup>a</sup>, Eric Debbold<sup>b</sup>, Kea Crivelly<sup>b</sup>, Kristel Vande Kerckhove<sup>a</sup>, Karen Corthouts<sup>a</sup>, Brett Debbold<sup>b</sup>, Hans Andersson<sup>b</sup>, Lena Vannieuwenborg<sup>c</sup>, Sam Geuens<sup>c</sup>, Matthias Baumgartner<sup>d</sup>, Tamas Kozicz<sup>b,e</sup>, Lisa Settles<sup>f</sup>, Eva Morava<sup>a,b,\*</sup>

<sup>a</sup> Department of Pediatrics, Metabolic Center, University Hospitals Leuven, Leuven, Belgium

<sup>b</sup> Hayward Genetics Center, Tulane University School of Medicine, New Orleans, LA, USA

<sup>c</sup> Department of Psychology, Metabolic Center, University Hospitals Leuven, Leuven, Belgium

<sup>d</sup> Division of Metabolism, Children's Research Center, University Children's Hospital Zurich, Zurich, Switzerland

<sup>e</sup> Donders Institute for Brain, Neuroscience, Radboudumc, Nijmegen, The Netherlands

<sup>f</sup> Department of Psychiatry, Tulane University School of Medicine, New Orleans, LA, USA

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### ABSTRACT

Certain inborn errors of metabolism have been suggested to increase the risk of autistic behavior. In an animal model, propionic acid ingestion triggered abnormal behavior resembling autism. So far only a few cases were reported with propionic acidemia and autistic features. From a series of twelve consecutively diagnosed cases with propionic acidemia, we report on eight patients with autistic features.

The patients were followed 2–4 times a year and underwent regular clinical, dietary and laboratory investigations. Psychological evaluation was performed every second to fourth year.

All patients were compliant with the standard diet and carnitine supplementation. None of the patients had frequent metabolic decompensations. From the metabolic factors known to impact neuropsychological outcome we detected chronically decreased valine levels and altered valine to leucine ratios in five out of the eight patients. Recurrent lactic acid elevations were present in six out of the eight patients. Five of the eight patients were diagnosed with Autism Spectrum Disorder, four of them had pathogenic variants in *PCCB*. Disorder according to DSM-IV and/or DSM-5 criteria. One of the patients diagnosed with propionic acidemia by newborn screening had the most significant behavioral features and another was diagnosed with Autism Spectrum Disorder prior to propionic acidemia.

We hypothesize that chronic suboptimal intracellular metabolic balance may be responsible for the increased risk for autistic features in propionic acidemia. We propose that patients diagnosed with propionic acidemia should be screened for Autism Spectrum Disorder.