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Background: Glycogenosis type III (GSDIII) is a rare autosomic recessive metabolic disorder, due to a deficit in the debranching enzyme, encoded by the *AGL* gene, and is of both hepatic and muscular expression. Its evolution is typically two-phased: a pure metabolic impairment in childhood, improving at puberty; and later on muscular impairment characterized by exertion intolerance followed by permanent muscular weakness. Cardiac involvement is often encountered, without correlation with the severity or duration of muscular disease.
Methods / Case Report: The French registry was created in 2014, constituted by nine centers. It prospectively retrieves genetic data, muscular, cardiac and clinical features, CPK levels in blood, and glucose tetrasaccharide (Glc4) levels in urine. This allows us, in a first time, to establish a genotypical and phenotypical description of a large cohort of GSDIII patients, and, in the future, to describe the natural history of the disease.
Results: 44 patients have been included, with a mean age of 26 ± 15 [4–66]. 19 patients were under 20 years old. Molecular analysis showed a great variability, with a large majority of private mutations, except for a few ethno-geographic groups. Mean MFM score was 88.40% (± 17.07, 32–100). Mean 6-minute walking-test was 472 meters (±133, 50–677). 5 patients (11%) had difficulty walking, 3 were wheelchair-bound. Muscular involvement was more severe in older patients, but did not correlate with CPK or Glc4 dosages. Hypertrophic cardiomyopathy, the most frequent cardiologic finding (56%), was associated with higher levels of CPK and Glc4.
Discussion: This registry aims to collect epidemiologic, clinical, biological and therapeutical data on glycogenosis type III patients, and to further and better describe the disease and its evolution. Baseline analysis of the patients already allows us to identify some of the disease's characteristics, and prospective data will help us to determine its natural history.

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Further confirmation of the clinical phenotype in patients with bi-allelic mutations in *TANGO2*: a report of 6 new cases

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Background: *TANGO2* (transport and golgi organization 2) related disease is a newly delineated cause of recurrent crises with rhabdomyolysis, arrhythmias and metabolic disturbance that can also present with developmental delay. The precise function of *TANGO2* is unknown however it is hypothesized to function in loading of newly synthesized secretory proteins in the endoplasmic reticulum. Bi-allelic pathogenic variants resulting in loss of protein function is the likely cause of this disorder.
Case Report
Results:Here we present six patients with bi-allelic variants of the *TANGO2* gene. Three had homozygous, previously described exon deletions, whilst the remainder were homozygotes or compound heterozygotes for three new variants that were predicted to be pathogenic. The clinical phenotype was characterized by developmental delay and regression often associated with viral illness. Ataxia, dysarthria and signs of spastic diplegia were also present with progression during childhood.
The majority of patients had metabolic crises associated with catabolism which were characterized by decreased consciousness, ataxia and weakness. Hypoglycaemia, hyperlacticaemia and hyperammonaemia were frequently present initially with subsequent development of rhabdomyolysis. Investigations showed variably increased dicarboxylic acid excretion and abnormal acylcarnitine profiles. Cardiac evaluation during crises showed prolongation of QTc and ventricular tachycardia. Three patients died, in one of whom a diffuse disorder of neuronal migration was found on autopsy.
Discussion:We report six cases of bi-allelic mutations in *TANGO2* which both confirm the existing phenotype and expand it. This brings the total number of reported cases to 21 since 2016. New information in the form of a neuronal migration disorder indicates the developmental deficits seen are not solely related to the cumulative effects of repeated crises and instead may have an origin during development of the nervous system.

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Patients experiences are essential for improving the quality of health care

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Background: Metabolic diseases (MD) are rare and specific care for them is insufficiently developed. Because of the complexity and severity of MD, patients' opinions about care needs are essential. We inventoried the patient's perspective on health care and centres of expertise (CEs) in The Netherlands through an online survey as part of the project Expertise Mapped. This provides a picture of the organisation of care for rare diseases from the patients' perspective. From these data we have distilled shared opinions to advocate the needs of patients with MD.
Methods: Between 2013–2018 401 Dutch patients with 97 different MD filled in the online survey.
Results: 38.9% of patients experiences problems regarding their care. Their top 3 problems are: 1) a lack of knowledge among healthcare professionals regarding their disease (62.8%); 2) a lack of collaboration between specialists/healthcare professionals (42.9%); 3) the administrative burden of arranging their medical care (30.8%). Problems identified by the entire group are: insufficient support regarding the organisation/coordination of care (29.8%) and insufficient psychological support (39.8%). Of all respondents, 46.4% is aware of the existence of a CE. 57.6% is willing to travel to always see an expert.
Discussion: CEs should increase their visibility for patients, emphasize their added value and involve patients in the organisation of care. When a larger proportion of patients is seen in a CE, the knowledge of MD will increase and the quality of care will improve. Simultaneously, experts must pass along their expertise to other healthcare professionals to decrease the knowledge gap. Support for patients in the CEs in the coordination of their care is indispensable and collaboration between healthcare professionals should be stimulated. All these data suggest there is a larger role for the CEs, and possibly for the MetabERN as well, to fill the gaps that patients experience. See also www.expertisemapped.org.