The CDKL5 disorder is an independent clinical entity associated with early-onset encephalopathy.
European Journal of Human Genetics 2012.

This is a study from Australia, which reports on the phenotypes of 86 individuals with a pathogenic or potentially pathogenic CDKL5 mutation. These individuals are located in Australia, Europe and the USA. The clinical aspects studied included seizures and motor function, hand function and speech, Rett-like features and co-morbidities, and dysmorphism. New criteria for the diagnosis of atypical Rett syndrome, including the early-onset seizure variant (ESV RTT) have recently been published and this study also looks the fulfilment of these in those studied.
There were 86 individuals studied with a variety of mutations. There were 77 females with an average age of 6.1 years (range 6 months to 22.4 years) and 9 males, average age 5.2 years (range 1.1 to 14.9 years). The main findings were that early-onset epilepsy, severe developmental delay and severely impaired gross motor function are key features of CDKL5. In this study, 90% of children with a CDKL5 disorder developed their seizures by 3 months of age. At the time of the study, 52 females were having daily seizures, 5 were having weekly seizures and 10 were having monthly seizures. Severe gross motor development was reported in all but 3 females with just over half able to sit. There were 8 females who had achieved independent walking and 9 who could walk with assistance. Males tended to be more severely affected, all had seizures and none could walk. There was a shared physical resemblance between affected females, and an overall spectrum of similar features in males and females. The majority of patients in this study did not meet the new criteria for ESV RTT. This was mainly because of the absence of regression in all males and 67.5% of females. A comparison between females with a CDKL5 disorder and Rett syndrome, identified that females with a CDKL5disorder were more likely to have seizures, sleep disturbances, and less likely to have breathing disturbances, a spinal curvature, gastrointestinal problems, hand stereotypies, or to lose hand and speech skills. In summary, the authors point out that although in some instances, mutations in the CDKL5 gene have been found in individuals with Rett-like features , the majority of cases of CDKL5 are different. They therefore advocate that the CDKL5 disorder should be considered as a distinct clinical entity.

Note - This is the first study to undertake a detailed clinical analysis of a large group of individuals affected by a CDKL5 mutation. As such it provides the first meaningful information about the spectrum of the CDKL5 disorder. One interesting point is that data for some of the study came from the InterRett database. It is not a great leap of imagination to think that a similar register for CDKL5 could and should be established - this study might act as a basis for such a register. One might hope that the various international genetic societies could co-operate in developing an international database or registry to capture all known cases of CDKL5 - there are said to be less than 300 known cases so far - and future cases as they present. This would then provide a wealth of data that could be used for future research projects. There is always going to be an issue with funding, but I would refer you to the European Commission website on rare diseases, as one such potential source. This study, at last, establishes the CDKL5 disorder as an distinct clinical entity which is an excellent starting point. The hard task is now to move this forward. Thank you Stephanie!