Genetic testing in adult epilepsy patients: a call to action for clinicians

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To the editors:

We thank Lewis-Smith and Thomas for their interest in our paper and for their interesting comments on the prevalence of molecularly diagnosable genetic epilepsies in the Danish population of young adults with SCN1A-associated Dravet syndrome (SCN1A-DS).

In their letter, they calculate the actual prevalence in adulthood of SCN1A-DS in Denmark based on the lifetime risk ascertained in the prospective Scottish study by Symonds et al.\textsuperscript{1}, concluding that there currently should be 50 young adult patients (18-30 years old) affected by SCN1A-DS. In our study we diagnosed eight adult patients with SCN1A-DS, corresponding to 16\% of their estimate of 50 patients, and thus Lewis-Smith and Thomas speculate that the remaining patients might have been diagnosed in childhood, elsewhere or have not been recognized. Following their reasoning, we investigated our SCN1A database to find out how many SCN1A-DS patients we have collected at present and found five additional young patients (same age range, 18-30 years old), who were diagnosed with SCN1A-DS in childhood, increasing the number from eight to 13 adult patients in our cohort or 26\% of the estimated 50 patients.

In our previous publication\textsuperscript{2}, we reported 17 patients born with SCN1A-DS in years 2004-2009, resulting in a prevalence of 1:22,000 births with SCN1A-DS per year. We have reviewed the SCN1A-DS birth rate between 2004-2009 and found three additional patients who were diagnosed after the initial study was completed. Therefore, the updated birth rate between 2004-2009 was 20 patients with SCN1A-DS, equaling an incidence of a 1:19,400 SCN1A-DS patients born per year. This number is still lower than that reported in the Scottish study, which is 1:15,400\textsuperscript{1}. This discrepancy might partially depend on the fact that Symonds et al.'s (2019) paper investigated only three consecutive years (in our studies both analyzed 6 years-intervals). This short time span might expose to the risk of one (or two) year(s) with a birth rate well above or below the average birth rate, which might significantly affect the calculation of the cumulative incidence rate in the three year interval. This hypothesis is supported by the observation in Denmark of a relatively high variability of the SCN1A-DS birth rate per year, ranging from zero (in 2011) to six (in 2012) and averaging three per year (unpublished data).
These observations show once again how the ascertainment of the prevalence of genetic epilepsies in adulthood can be challenging and they indicate the need of well-designed, possibly population based, studies.

Nevertheless, we believe that our findings, even though limited to the population of patients with epilepsy and intellectual disability, should alert the physicians treating these patients on the opportunity to offer them genetic testing not only for diagnostic but possibly also for treatment purposes.

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