

PKD or not PKD - that is the question

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We commend Dr Gardella and colleagues for expanding the clinical and genetic spectrum of sodium channelopathies.¹ However, we would like to comment on the unusual phenomenology of the paroxysmal attacks, and its implication with regard their labelling as paroxysmal kinesigenic dyskinesia (PKD).

By definition, primary paroxysmal dyskinesias are characterised by brief, self-limiting attacks of dyskinesia, with *no change in consciousness* during attacks and normal inter-ictal neurological status differentiating them from secondary forms.²⁻⁴

Based on triggering factors and duration of attacks, three main phenotypes are recognised. PKD, the most frequent form, features brief (seconds to minutes) attacks of dystonia or chorea precipitated by sudden movement, or acceleration of ongoing movement.²⁻⁵ Proline-rich transmembrane protein 2 (PRRT2) gene mutations are the most common cause, although there is some clinicogenetic heterogeneity.^{4,5}

The five individuals reported as having PKD¹ differ significantly with regard nature and precipitants of attacks, and the fact that one had altered level of consciousness.

Three patients had generalised “shivering attacks” triggered by emotional stimuli, which is not a recognised manifestation of paroxysmal dyskinesias neither by phenomenology nor by trigger. The triggers in the two other patients with attacks of hemidystonia or choreoathetosis of the legs were prolonged stretching of the limbs and “voluntary movements”.¹ We acknowledge that “sudden whole body activity, like standing-up, or initiation of walking” were also named as precipitants, but it appears that mostly, the “kinesigenic” element is lacking. Lastly, the index case thought to have classical PKD had impaired consciousness during all events with an overt ictal EEG correlate.

Thus, from a movement disorders specialists view these do not constitute classic PKD and we think the readership should be aware of this.

The identification of other cases may help to further delineate the spectrum of paroxysmal attacks associated with the new SCN8A mutations, and if they should be indeed be ranked amongst the classic paroxysmal dyskinesias or maybe be considered as epileptic events.

We did not detect any pathogenic variant in SCN8A screening by whole exome sequencing our cohort of well defined cases with paroxysmal dyskinesias (9 PKD, 5 paroxysmal non-kinesigenic dyskinesia, 3 paroxysmal exercise induced dyskinesia) negative for mutations in PRRT2, myofibrillogenesis regulator 1 (MR-1), or glucose transporter 1 (SCL2A1), respectively.

Furthermore, none of our 72 patients with paroxysmal dyskinesias due to PRRT2, MR-1, or SCL2A1 gene mutations⁵ had shivering attacks and it is possible that this may be a clinical feature particular to SCN8A mutations.

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Potential Conflicts of Interest:

None of the authors (BB, RE, VS, HH, KPB) declares a conflict of interest.

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