Supplementary materials

1. The diagnostic criteria for PKD:

All patients were diagnosed according to Bruno's diagnostic criteria (Bruno et al., 2004): (i) identified kinesigenic trigger for attacks; (ii) short duration (<1 min) attacks; (iii) no pain or loss of consciousness during attacks; (iv) normal neurologic examination and exclusion of other organic diseases; (v) control of attacks with phenytoin or carbamazepine, if attempted; and (vi) if no family history of PKD, age at onset between 1 and 20 years.

2. Genetic analysis

In PKD patients, genomic DNA was extracted from the peripheral blood using a standard phenol/chloroform extraction. Sanger sequencing was applied to detect PRRT2 mutations using an ABI 3730 automated DNA sequencing system (Invitrogen, Shanghai, China) as described in a previous report (Li et al., 2020). First, the polymerase chain reaction (PCR) products were amplified using published PCR primers specifically designed to amplify the entire exons and the intron-exon boundaries of the PRRT2 gene (Chen et al., 2011). Next, the PCR products were purified in 5 µl total volume for one cycle of 60 min at 37 °C and 15 min at 80 °C; the purified products were treated with the ABI PRISM Big Dye Terminator Cycle Sequencing Ready Reaction sequencing kit. Next, the sequencing products were purified again by ethanol/EDTA/sodium acetate precipitation. Finally, the products were analyzed on the ABI 3730 automated DNA sequencer. Comparing the DNA sequence with the genomic DNA sequence of PRRT2, PRRT2 (NM_145239), mutations were identified by numbering the nucleotide change positions that correspond to their positions in PRRT2 mRNA.

3. Network Metrics

Global parameters: Cp is defined as the average of the clustering coefficients

over all nodes and quantifies the "cliquishness", reflecting local interconnectivity. Lp measures the mean distance or routing efficiency between any pair of nodes in a network, lower values indicating higher routing efficiency. A small-world network is characterized by high Cp and low Lp (Rubinov & Sporns, 2010): normalized clustering coefficient (γ), normalized characteristic path length (λ), and small-worldness (σ) indicate the degree of small-world organization. A small world network has a similar characteristic path length but higher clustering coefficient than a random network (based on the original output 90×90 random matrix, using 100 randomized networks), i.e. $\gamma = Cp/Crandom > 1$, $\lambda = Lp/Lrandom \approx 1$, and $\sigma = \gamma/\lambda > 1$.

<u>Network efficiency parameters</u> include local efficiency (Eloc) and global efficiency (Eglob), which measure the capability of the network for information transmission at the global and local levels (Latora & Marchiori, 2001): Eglob measures the global efficiency of parallel information transfer, while Eloc reflects the network fault tolerance level, the communication efficiency among the first neighbors of a node when it is removed.

<u>Nodal centrality metrics</u> including nodal degree and nodal efficiency: nodal degree represents the number of links connected to a node, while nodal efficiency measures the ability of a node to exchange information with other nodes. They measure the importance of a node within a network from different aspects. Detailed formulae, uses and explanations of these metrics can be found in an excellent methodological review (Rubinov & Sporns, 2010).

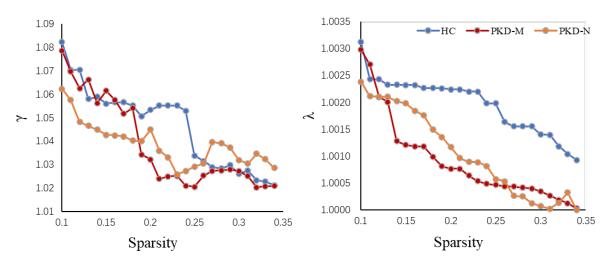
References

- Bruno, M. K., Hallett, M., Gwinn-Hardy, K., Sorensen, B., Considine, E., Tucker, S., . . . Ptacek, L. J. (2004). Clinical evaluation of idiopathic paroxysmal kinesigenic dyskinesia: new diagnostic criteria. *Neurology*, 63(12), 2280-2287. doi:10.1212/01.wnl.0000147298.05983.50
- Chen, W. J., Lin, Y., Xiong, Z. Q., Wei, W., Ni, W., Tan, G. H., . . . Wu, Z. Y. (2011). Exome sequencing identifies truncating mutations in PRRT2 that cause paroxysmal kinesigenic dyskinesia. *Nat Genet*, 43(12), 1252-1255. doi:10.1038/ng.1008
- Latora, V., & Marchiori, M. (2001). Efficient behavior of small-world networks. Phys

Rev Lett, 87(19), 198701. doi:10.1103/PhysRevLett.87.198701

- Li, L., Lei, D., Suo, X., Li, X., Yang, C., Yang, T., . . . Gong, Q. (2020). Brain structural connectome in relation to PRRT2 mutations in paroxysmal kinesigenic dyskinesia. *Hum Brain Mapp*, 41(14), 3855-3866. doi:10.1002/hbm.25091
- Rubinov, M., & Sporns, O. (2010). Complex network measures of brain connectivity: uses and interpretations. *Neuroimage*, 52(3), 1059-1069. doi:10.1016/j.neuroimage.2009.10.003

Figure S1. Normalized clustering coefficient (γ) and normalized characteristic path length (λ) as a function of chosen sparsity



In the defined threshold range, both the PKD and control groups exhibited normalized clustering coefficient (γ) substantially > 1 and normalized characteristic path length (λ) \approx 1, the typical features of small-world topology. Abbreviations: HC, healthy control; PKD-M/PKD-N, paroxysmal kinesigenic dyskinesia patients with/without PRRT2 mutations.

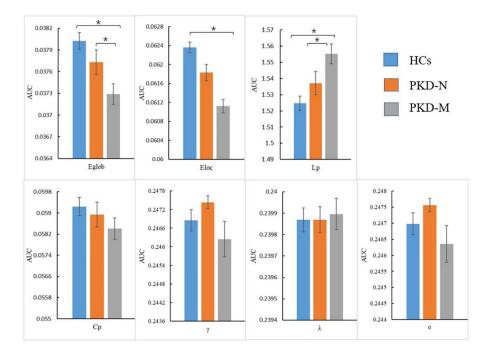


Figure S2. Differences in global topological properties between the three groups.

Note: '*' indicates a statistically significant difference between the two groups (p < 0.05). Error bars denote standard error of the mean. Abbreviations: AUC, area under the curve; Cp; clustering coefficient; Eglob; global efficiency; Eloc, local efficiency; HC, healthy controls; Lp; characteristic path length;; γ , normalized clustering coefficient; λ , normalized characteristic path length; σ , small-worldness; PKD-M/PKD-N, paroxysmal kinesigenic dyskinesia patients with/without PRRT2 mutations.