Supplementary Information
for
Loss of symmetric cell division of apical neural progenitors drives *DENND5A*-related developmental and epileptic encephalopathy

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1. Supplementary Methods

1a. Motor skills scoring system

Item	Scoring
Able to reach/grasp objects	**+1** if positive
Able to roll over	**+1** if positive
Able to sit with support	**+1** if positive OR is able to sit without support
Able to sit without support	**+1** if positive
Able to stand with support	**+1** if positive OR is able to stand without support
Able to stand without support	**+1** if positive
Able to walk with support	**+1** if positive OR is able to walk without support
Able to walk without support	**+1** if positive
Muscle tone or spasm problems	**+1** if negative for all (hyperreflexia, spastic tetraplegia, clonus, and current hyper/hypotonia)
Motor regression after seizure	**+1** if negative AND could perform one of the above behaviors in past
TOTAL	**10**

Scoring system used for quantifying motor abilities. A low score reflects minimal motor abilities, a high score indicates a high degree of motor capabilities. If a child's ability to do a skill is unknown, it is counted as positive.

1b. Neurological phenotype scoring system

Item	**Scoring**
Seizures	**+1** if positive
Reduced volume (cerebral or supratentorial parenchymal volume loss)	**+1** if positive
Cerebellum abnormalities (hypoplastic vermis, reduced volume)	**+1** if positive
Thalamus abnormalities (thalami fusion or reduced volume, massa intermedia prominence)	**+1** if positive
Basal ganglia abnormalities (dysplasia or reduced volume)	**+1** if positive
Calcifications	**+1** if positive
Ventricle or CSF abnormalities	**+1** if positive
White matter abnormalities (reduced corpus callosum or other white matter tract volume, delayed myelination or hyperintensity)	**+1** if positive
Hemorrhage or ischemic event	**+1** if positive
Cortical visual impairment	**+1** if positive
TOTAL	**10**

Scoring system used for quantifying neurological phenotypes. A low score corresponds to few neurological abnormalities, a high score indicates many neurological abnormalities.

1c. Communication skills scoring system

Item	**Scoring**
Smiles	**+1** if positive
Eye contact	**+1** if positive
Points at objects/people	**+1** if positive
Babbles	**+1** if positive OR if speaks in at least single words
Uses PECS board	**+1** if positive OR if speaks in at least single words
Speaks in single words	**+1** if positive OR if speaks in at least short phrases
Speaks in short phrases	**+1** if positive OR if speaks in sentences
Speaks in sentences	**+1** if positive
Language regression after seizure	**+1** if negative AND if had language skills in past
Receptive language delay	**+1** if negative AND at least babbles
TOTAL	**10**

Scoring system used for quantifying communication abilities. A low score reflects minimal communication ability, a high score reflects more advanced language and communication abilities.

1d. Comorbidities scoring system

Item	Scoring
Chronic constipation	**+1** if positive
Autism spectrum disorder (formally diagnosed or clinically suspected)	**+1** if positive
Psychiatric disorders (ADHD, anxiety)	**+1** if positive
Behavioral disorders or abnormalities (self-injury, poor sleep, hyperphagia)	**+1** if positive
Lung or breathing abnormalities (restrictive lung disease, asthma)	**+1** if positive
Cardiac abnormalities (ventricular/atrial septal defects, arrythmia)	**+1** if positive
Blindness	**+1** if positive
Obesity	**+1** if positive
Bone abnormalities (low density or osteoporosis, scoliosis, vertebral fusion, posterior fossa abnormality)	**+1** if positive
GERD	**+1** if positive
TOTAL	**10**

Scoring system used for quantifying neurological phenotypes. A low score corresponds to few comorbidities, a high score indicates many comorbidities.

2. Supplementary Notes

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