Periventricular nodular heterotopia (PNH) is a cortical malformation commonly found in epilepsy patients caused by the failure of neurons to migrate. Patients with PNH present with various clinical manifestations and genetic mutations. Despite their remarkable structural malformations, PNH patients generally have no neurological deficits or cognitive disabilities. However, particularly in patients with abnormal cortical development, the systematic abnormalities can also be severely delayed. About 70% of PNH patients suffer from epilepsy, typically presenting with seizures in the second decade of life. Here, we described the phenotypic picture of PNH in a cohort of Chinese patients, including clinical features, neuroimaging, and extracerebral findings to characterize the differences between patients with PNH and healthy controls (HCs). In addition, we reported on their access to social support and the impact, PNH has on their educational and economic status.

Patients with PNH-related epilepsy were enrolled if their structural magnetic resonance imaging (MRI) showed at least one visible nodule of gray matter signal intensity lining the lateral ventricular walls. Finally, thirty-seven right-handed participants with PNH (age presented as mean ± standard deviation [SD]: 27.2 ± 9.8 years; range: 9–56 years) were enrolled in the study, with a mean time of 6.9 ± 7.3 years (range: 1–33 years) since their first seizure. All patients were receiving antiepileptic drugs treatment (21 on monotherapy and 16 on polytherapy), with mean treatment duration of 5.7 ± 7.1 years. Filamin A (FLNA) mutations were identified in 11 patients, affecting eight female and three male patients (female-to-male ratio, 8:3). About half of the patients with FLNA mutations (5 out of 11) were also diagnosed with cardiovascular abnormalities. An example of one nonsense mutation in exon 30 (c.5184, C>T) at the mutation site p.gly1728 is presented in Figure 1. Thirty-seven HCs (25 females, 12 males; age [mean ± SD]: 27.1 ± 9.9 years, education years [mean ± SD]: 11.5 ± 3.3 years) were also included; patients and controls were gender- and age-matched (±1 year). Statistical analysis was performed using SPSS 20.0 software (IBM, Armonk, New York, USA).

Most patients reported experiencing monthly or yearly seizures, although five patients had daily to monthly seizures and eight patients were seizure-free. Two patients with PNH suffered from depression in addition to epilepsy. Based on MRI results, nineteen patients were with classic bilateral PNH, eight patients with bilateral asymmetric PNH, and ten patients with unilateral nodules. Two patients had mild cognitive impairments. Neurologic examination results were also normal in all cases. Epileptic status was also observed in one patient. We found no significant difference between PNH group and HCs group in their level of education (10.1 ± 4.2 years vs. 11.7 ± 2.9 years, respectively; \(P = 0.059\)), domicile (urban vs. rural), marital status, or family income \(P > 0.05\). However, individuals with PNH-associated epilepsy were less likely to be employed \(20/33, 61.0\%\) vs. \(29/33, 87.9\%\); \(P = 0.013\); those who were employed had a lower mean personal income \(1486.5 ± 1479.5\) RMB, Yuan/month; \(P = 0.042\) than HCs \(2095.2 ± 1015.9\) RMB, Yuan/month;

The results indicate that the most common feature of patients with PNH is the development of epilepsy during the second decade of life. This research was supported by the Sichuan Science and Technology Program (2015JY0343) and the Sichuan Key Lab of Neurogenetics and Neurodevelopment Disease. This is an open access article distributed under the terms of the Creative Commons Attribution-NonCommercial-ShareAlike 3.0 License, which allows others to remix, tweak, and build upon the work non-commercially, as long as the author is credited and the new creations are licensed under the identical terms.
decade of life, but in many aspects, it is a highly heterogeneous disease that can present with various clinical pictures. A comparison of the demographic factors showed that compared to HCs, patients with PNH and epilepsy did not tend to receive less education, but more of them were out of work, indicating that their social functions were partly impaired. The normal range of cognitive and neurological findings in these patients is likely one reason for this, but perhaps more importantly, the average age of seizure onset in PNH patients is during early adolescence, which is relatively late compared to other epilepsy patients and most likely means the majority of their education is complete before symptoms appear. However, we still noted a lower mean of education years compared to HCs (10.1 vs. 11.7); possibly because of academic underachievement and economic burdens from the high costs of medical care.\textsuperscript{[3]}

As for the employment problem, few other studies have also reported the low employment rate in PNH, and we supposed that epileptic seizure was an important factor affecting the employability of patients with PNH. However, while patients with PNH did not receive less education than age- and gender-matched HCs, they were more likely to be out of work. Other studies have reported similar findings, possibly because epileptic seizures may partially impair social function and negatively affect the employability of patients with PNH.\textsuperscript{[4,5]} Conversely, a higher unemployment rate, lower income, and even depression were associated with weaker social support in patients with PNH-related epilepsy.

In summary, the results indicate that the majority of PNH patients exhibit a normal range of cognitive development, neurological findings, and also have similar education and marital outcomes compared to controls. However, in the long-term, they were more likely to be unemployed or have lower incomes. A larger sample of patients with PNH in clinical characteristics with high-resolution MRI and electroencephalograph test is required for further research.

Declaration of patient consent
The authors certify that they have obtained all appropriate patient consent forms. In the form, the patient(s) has/have given his/her/their consent for his/her/their images and other clinical information to be reported in the journal. The patients understand that their names and initials will not be published and due efforts will be made to conceal their identity, but anonymity cannot be guaranteed.

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Conflicts of interest
There are no conflicts of interest.

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