Original Article

Depression, Anxiety, and Quality of Life in Paroxysmal Kinesigenic Dyskinesia Patients

Wo-Tu Tian[1], Xiao-Jun Huang[2], Xiao-Li Liu[1], Jun-Yi Shen[1], Gui-Ling Liang[3], Chen-Xi Zhu[3], Wei-Guo Tang[4], Sheng-Di Chen[1], Yan-Yan Song[5], Li Cao[1]

[1]Department of Neurology and Institute of Neurology, Rui Jin Hospital, Shanghai Jiao Tong University School of Medicine, Shanghai 200025, China
[2]Department of Neurology and Institute of Neurology, Rui Jin Hospital North, Shanghai Jiao Tong University School of Medicine, Shanghai 201801, China
[3]Basic Medical Science College, Shanghai Jiao Tong University School of Medicine, Shanghai 200025, China
[4]Department of Neurology, Zhoushan Hospital, Zhoushan, Zhejiang 316000, China
[5]Department of Biostatistics, Institute of Medical Sciences, Shanghai Jiao Tong University School of Medicine, Shanghai 200025, China

Wo-Tu Tian and Xiao-Jun Huang contributed equally to the work.

Abstract

Background: Paroxysmal kinesigenic dyskinesia (PKD) is a rare movement disorder characterized by recurrent dystonic or choreoathetoid attacks triggered by sudden voluntary movements. Under the condition of psychological burden, some patients' attacks may get worsened with longer duration and higher frequency. This study aimed to assess nonmotor symptoms and quality of life of patients with PKD in a large population.

Methods: We performed a cross-sectional survey in 165 primary PKD patients from August 2008 to October 2016 in Rui Jin Hospital, using Symptom Check List-90-Revised (SCL-90-R), World Health Organization Quality of Life-100 (WHOQoL-100), Self-Rating Depression Scale, and Self-Rating Anxiety Scale. We evaluated the differences of SCL-90-R and WHOQOL-100 scores in patients and Chinese normative data (taken from literature) by using the unpaired Student's *t*-test. We applied multivariate linear regression to analyze the relationships between motor manifestations, mental health, and quality of life among PKD patients.

Results: Compared with Chinese normative data taken from literature, patients with PKD exhibited significantly higher (worse) scores across all SCL-90-R subscales (somatization, obsessive-compulsive, interpersonal sensitivity, depression, anxiety, hostility, phobic anxiety, paranoid ideation, and psychoticism; $P = 0.000$ for all) and significantly lower (worse) scores of five domains in WHOQoL-100 (physical domain, psychological domain, independence domain, social relationship domain, and general quality of life; $P = 0.000$ for all). Nonremission of dyskinesia episodes ($P = 0.011$) and higher depression score ($P = 0.000$) were significantly associated with lower levels of quality of life. The rates of depression and anxiety in patients with PKD were 41.2% (68/165) and 26.7% (44/165), respectively.

Conclusions: Depression, anxiety, and low levels of quality of life were prevalent in patients with PKD. Co-occurrence of depression and anxiety was common among these patients. Regular mental health interventions could set depression and anxiety as intervention targets. Considering that the motor episodes could be elicited by voluntary movements and sometimes also by emotional stress, and that symptoms may get worsened with longer duration and higher frequency when patients are stressed out, intervention or treatment of depression and anxiety might improve the motor symptoms and overall quality of life in PKD patients.

Key words: Anxiety; Depression; Dyskinesia; Quality of Life

Introduction

Paroxysmal kinesigenic dyskinesia (PKD; MIM: 128200) is a movement disorder characterized by transient and recurrent dystonic or choreoathetoid attacks mainly triggered by sudden voluntary movements.[1] PKD is commonly a familial disease in an autosomal dominant mode of inheritance. Three episodic kinesigenic dyskinesia (EKD) loci have been identified in PKD and are defined as

Access this article online

Quick Response Code:

Website: www.cmj.org

DOI: 10.4103/0366-6999.213431

Address for correspondence: Dr. Li Cao, Department of Neurology and Institute of Neurology, Rui Jin Hospital, Shanghai Jiao Tong University School of Medicine, Shanghai 200025, China
E-Mail: caoli2000@yeah.net

Received: 06-06-2017 **Edited by:** Ning-Ning Wang
How to cite this article: Tian WT, Huang XJ, Liu XL, Shen JY, Liang GL, Zhu CX, Tang WG, Chen SD, Song YY, Cao L. Depression, anxiety, and quality of life in paroxysmal kinesigenic dyskinesia patients. Chin Med J 2017;130:2088-94.

EKD1 (16p11.2-q12.1), EKD2 (16q13-q22.1), and EKD3. In 2011, genome-wide linkage analyses confirmed proline-rich transmembrane protein 2 (*PRRT2*) as the causative gene of PKD due to its overlapping location to EKD1/EKD2 region.[2-10] During the past 6 years, a deluge of scientific articles have been published concerning the genetic and clinical features of PKD, and papers continue to appear reporting the progress in neurobiology and neurophysiology.[11-13] Appropriate anticonvulsant treatment, such as carbamazepine, has led to many of these patients controlling attacks successfully.[3,5] However, in some patients, the motor episodes could be elicited not only by voluntary movements but also by emotional stress. Under the condition of psychological burden, motor attacks of patients may get worsened with longer duration and higher frequency.[5] It was hypothesized that PKD patients had worse mental health and poorer quality of life than normal people, as well as that both psychological burden and clinical manifestations might contribute to a low level of quality of life. This study aimed to determine the psychological properties and quality of life in PKD patients using Symptom Check List-90-Revised (SCL-90-R) and World Health Organization Quality of Life-100 (WHOQoL-100) questionnaires, and disentangle the incidence of depression and anxiety in our patients using Self-Rating Depression Scale (SDS) and Self-Rating Anxiety Scale (SAS).

Methods

Ethical approval

The Ethics Committee of Rui Jin Hospital, Shanghai Jiao Tong University School of Medicine, Shanghai, China, approved the study. All participants or their legal guardians provided written informed consent.

Participants

The present study was carried out on a total of 195 patients diagnosed as primary PKD between August 2008 and October 2016 in Rui Jin Hospital. The diagnosis of PKD was established according to Bruno's criteria: (1) identified trigger for the attacks (sudden movements); (2) short duration of attacks (<1 min); (3) lack of loss of consciousness or pain during attacks; (4) antiepileptic drug responsiveness; (5) exclusion of other organic diseases; and (6) age at onset between 1 and 20 years if there is no family history (age at onset may be applied less stringently in those with a family history).[1] One hundred and eighty-six questionnaires were collected, of which 21 questionnaires were excluded due to incomplete information. Finally, a total of 165 valid questionnaires (information integrity >95%) were statistically analyzed.

Questionnaire

Symptom Check List-90-Revised questionnaire

The Chinese version of SCL-90-R questionnaire was a 90-item symptom inventory designed to screen for a broad range of psychological problems.[14] The questionnaire measured the symptoms that the study participants experienced in the past 7 days. The participant rated each item on a 5-point scale of distress, from "1 (not at all)" to "5 (extremely serious)". The nine primary symptom dimensions were labeled as somatization, obsessive-compulsive, interpersonal sensitivity, depression, anxiety, hostility, phobic anxiety, paranoid ideation, and psychoticism. The Global Severity Index (GSI), which represents the average severity score of all 90 items on the questionnaire, was considered a reliable measure of psychological distress.[14-16] To analyze the participants' scores, results were compared with Chinese normative data taken from literature.[17]

World Health Organization Quality of Life-100 questionnaire

Health-related quality of life was assessed with the Chinese version of WHOQoL-100,[18] which was a 100-item self-administered questionnaire designed for completion by patients alone. It consists of seven domains: physical, psychological, independence, social relationship, environment, spiritual, and general quality of life. These domains contained 25 facets; each facet included four items which pertained to the general quality of life value. Each of the facets was summed and each item contributes equally to the facet score and the domain score. Higher scores in WHOQoL-100 reflected a better quality of life.[19] To analyze the patients' scores, the results were compared with reported Chinese normative data.[20]

Self-Rating Depression Scale

The SDS was a 20-item self-rated scale, with each item scored on a 4-point scale (1: never or rarely, 2: some of the time, 3: frequently, and 4: most of the time). The SDS screens for and measures the severity of psychological and somatic symptoms of depression. Ten questions involve the assessment of increasing depression levels and ten questions involve decreasing depression levels. The scores were used to define four categories of depression severity: within the normal range or no significant psychopathology (<53 points), presence of mild depression levels (53–62 points), moderate depression levels (63–72 points), and presence of severe depression (>72 points). Depression symptoms were indicated by a total index score ≥53, according to the Chinese normative data.[21]

Self-Rating Anxiety Scale

The SAS measured the anxiety-related symptoms in the physicians which was developed in 1971 to assess the severity of anxiety. The SAS questionnaire includes 20 items, with each item scored on a 4-point scale (1: never or rarely 2: some of the time, 3: frequently, and 4: most of the time). Fifteen questions involve the assessment of increasing anxiety levels and five questions involve decreasing anxiety levels. The minimum raw score was 20 and the maximum raw score was 80; the integer part was retained to generate the index score (range, 25–100). In addition, the scores were used to define four categories of anxiety severity: within the normal range or no significant psychopathology (<50 points), presence of mild anxiety levels (50–60 points), moderate levels (61–70 points), and presence of severe

anxiety (>70 points). Anxiety symptoms were indicated by a total index score ≥50, according to the Chinese normative data.[22]

Statistical analysis

Statistical analysis was performed with SPSS software, version 16.0 (SPSS Inc., Chicago, IL, USA). Continuous data were given as mean ± standard deviation (SD). Differences of SCL-90-R and WHOQoL-100 scores between patients and Chinese normal population were evaluated by means of the unpaired Student's *t*-test.

Correlational analysis proceeded in two steps. First, we used univariate linear regression to assess the relationships between PKD clinical characteristics (age of onset, family history, attack duration, type of PKD, anticonvulsant treatment, and spontaneous remission), mental health symptoms (scores of somatization, obsessive-compulsive, interpersonal sensitivity, depression, anxiety, hostility, phobic anxiety, paranoid ideation, and psychoticism in SCL-90-R), and quality of life (total WHOQoL-100 score). Second, multivariate linear regression was further fitted using a step-wise variable selection method, which entered PKD clinical characteristics (age of onset, family history, attack duration, type of PKD, anticonvulsant treatment, and spontaneous remission) and mental health symptoms (scores of nine SCL-90-R subscales) with $P > 0.05$ and removes any variables added previously that had fallen below the P - removal threshold (0.10). All tests were two tailed, and the level of statistical significance was set at $P < 0.05$. Patients' accordance with the score classification of depression (SDS) and anxiety (SAS) were calculated as percentage of variable degrees.

Results

Patients

One hundred and sixty-five patients with PKD, including 138 males and 27 females, were recruited. Mean age of the participants was 24.2 ± 6.3 years (range, 11–48 years). One hundred and forty-nine participants (90.3%) had completed high school and 38 (23.0%) of them were married. The number of patients from rural and urban areas was 26 (15.8%) and 139 (84.2%), respectively. The mean age at onset of PKD was 12.9 ± 3.5 years (range, 3–27 years). A total of 109 (66.1%) patients presented with pure PKD and 56 (33.9%) with complicated PKD. Ninety-two (55.8%) patients required anticonvulsant treatment, including 67 patients with carbamazepine, 19 patients with oxcarbazepine, and six patients with other anticonvulsants (valproate, phenobarbital, and topiramate). A total of 45 (27.3%) patients reported complete or partial remission of PKD, and mean age at remission was 25.3 ± 4.2 years. The demographic characteristics of these 165 patients were all summarized in Table 1.

In the present study, 109 (66.1%) patients had more than one visit of the doctor before finally diagnosed as PKD. Of these, 26 patients had been misdiagnosed as psychogenic dyskinesia or hysteria (15.8%), 23 as epilepsy (13.9%), 17 as idiopathic dystonia (10.3%), and 43 without identified diagnosis (26.1%). Ninety-three (56.4%) patients initially obtained the knowledge of PKD from network, 42 (25.5%) from health professionals, and 31 (18.8%) from members of "Paroxysmal Kinesigenic Dyskinesia Home" (an online community and support group composed of Chinese PKD patients). For our patients, the mean time taken from the onset to finally accurate diagnosis was 8 years, ranging from 0 to 33 years. Outpatient interviews also found that 78 (47.3%) participants did not know about the prognosis and genetic features of the disease.

Table 1: Characteristics of patients with PKD (n = 165)

Characteristics	Values
Age (years), mean ± SD	24.2 ± 6.3
Sex, *n* (%)	
Male	138 (83.6)
Female	27 (16.4)
Educational status, *n* (%)	
Years of schooling <12 years	16 (9.7)
Years of schooling ≥12 years	149 (90.3)
Marital status, *n* (%)	
Married or co-habiting	38 (23.0)
Single	127 (77.0)
Residence, *n* (%)	
Rural	26 (15.8)
Urban	139 (84.2)
Age of onset (years), mean ± SD	12.9 ± 3.5
Family history of PKD, *n* (%)	
Yes	30 (18.2)
No	135 (81.8)
Response to medication, *n* (%)*	
Complete	41 (44.6)
Incomplete	51 (55.4)
Nonresponsive	0
Remission, *n* (%)	
Yes	45 (27.3)
No	120 (72.7)

*There were 92 medically treated patients. PKD: Paroxysmal kinesigenic dyskinesia; SD: Standard deviation.

Mental symptoms and quality of life

We compared PKD patients with Chinese normative data in SCL-90-R and WHOQoL-100 scores. As shown in Table 2, patients with PKD scored significantly higher (worse) across all of the SCL-90-R subscales (somatization, obsessive-compulsive, interpersonal sensitivity, depression, anxiety, hostility, phobic anxiety, paranoid ideation, psychoticism, and GSI) than the normative Chinese population ($P = 0.000$ for all).[17] The patients also showed significantly lower (worse) scores of WHOQoL-100 than normative data[20] in physical domain, psychological domain, independence domain, social relationship domain, and general quality of life ($P = 0.000$ for all). However, scores of environmental domain and spiritual domain did not differ significantly between PKD patients and the normative data ($P = 0.096$ and $P = 0.133$, respectively).[20]

Table 3 summarizes the results of linear regression models. Univariate linear regression assessed the associations between clinical features (age of onset, family history of PKD, attack duration, type of PKD,

Table 2: SCL-90-R and WHOQoL-100 scores in PKD patients and Chinese normal population

Items	PKD patients (n = 165)	Normative data in Chinese population[17,20] (n = 1890*, n = 777†)	t	P
SCL-90-R				
Somatization	1.7 ± 0.5	1.4 ± 0.4	6.5	0.000
Obsessive-compulsive	2.3 ± 0.7	1.7 ± 0.5	10.7	0.000
Interpersonal sensitivity	2.2 ± 0.8	1.5 ± 0.5	11.2	0.000
Depression	2.0 ± 0.7	1.5 ± 0.5	8.6	0.000
Anxiety	2.0 ± 0.7	1.3 ± 0.4	12.9	0.000
Hostility	1.9 ± 0.7	1.5 ± 0.5	8.0	0.000
Phobic anxiety	1.8 ± 0.6	1.3 ± 0.4	9.6	0.000
Paranoid ideation	1.9 ± 0.7	1.4 ± 0.5	8.7	0.000
Psychoticism	1.9 ± 0.7	1.3 ± 0.4	10.6	0.000
GSI	2.0 ± 0.6	1.4 ± 0.4	11.1	0.000
WHOQoL-100				
Physical domain	13.9 ± 2.3	15.1 ± 2.3	−6.0	0.000
Psychological domain	12.8 ± 1.6	13.9 ± 1.9	−7.5	0.000
Independence domain	14.4 ± 2.4	15.6 ± 2.2	−6.2	0.000
Social relationship domain	13.0 ± 2.2	13.9 ± 2.1	−5.5	0.000
Environmental domain	12.4 ± 2.2	12.1 ± 2.1	1.7	0.096
Spiritual domain	11.5 ± 3.3	11.1 ± 3.7	1.5	0.133
General QoL	12.5 ± 2.9	13.4 ± 2.9	−3.5	0.000

Data were represented by mean ± standard deviation. *: n for SCL-90-R; †: n for WHOQoL-100. SCL-90-R: Symptom Check List-90-Revised; GSI: Global Severity Index; WHOQoL-100: World Health Organization Quality of Life-100; PKD: Paroxysmal kinesigenic dyskinesia; QoL: Quality of life.

Table 3: Linear regression model for the QoL (total WHOQoL-100 score)

Items	Univariate			Multivariate (stepwise)		
	β	95% *CI*	*P*	β	95% *CI*	*P*
Age of onset	−0.7	−2.1–0.8	0.360	−0.032*		0.594
Family history						
No	Reference		–	–		–
Yes	−3.5	−8.6–1.6	0.179	−0.103*		0.080
Attack duration	−3.4	−6.3–−0.4	0.025	−0.044*		0.469
Type of PKD						
Complicated	Reference		–	–		–
Pure	10.3	6.5–14.2	0.000	0.034*		0.626
Anticonvulsant treatment						
No	Reference		–	–		–
Yes	1.0	−3.0–4.9	0.631	0.087*		0.145
Remission						
No	Reference		–	–		–
Yes	5.0	0.2–9.8	0.041	4.7	1.1–8.4	0.011
SCL-90-R						
Somatization	−10.2	−13.5–−6.9	0.000	0.028*		0.718
Obsessive-compulsive	−9.2	−11.7–−6.7	0.000	0.074*		0.460
Interpersonal sensitivity	−9.8	−11.9–−7.7	0.000	−0.118*		0.307
Depression	−12.0	−14.3–−9.8	0.000	−12.0	−14.2–−9.8	0.000
Anxiety	−9.3	−11.9–−6.8	0.000	0.069*		0.476
Hostility	−8.5	−11.0–−5.9	0.000	0.037*		0.679
Phobic anxiety	−9.8	−12.5–−7.0	0.000	0.065*		0.416
Paranoid ideation	−8.6	−11.1–−6.2	0.000	0.038*		0.674
Psychoticism	−10.7	−13.2–−8.2	0.000	−0.037*		0.728

*Variables were not significant. –: No data; QoL: Quality of life; WHOQoL-100: World Health Organization Quality of Life-100; *CI*: Confidence interval; SCL-90-R: Symptom Check List-90-Revised; PKD: Paroxysmal kinesigenic dyskinesia.

anticonvulsant treatment, and remission trend) and comorbid psychopathology (somatization, obsessive-compulsive, interpersonal sensitivity, depression, anxiety, hostility, phobic anxiety, paranoid ideation, and psychoticism) with quality of life (total WHOQoL-100 score). We found that the attack duration was negatively associated with total WHOQoL-100 score (β = −3.4, 95% confidence interval [*CI*]: −6.3–−0.4, *P* = 0.025). Nevertheless, patients with pure PKD scored 10.3 times of total WHOQoL-100 than those with complicated PKD (95% *CI*: 6.5–14.2, *P* = 0.000) and patients with spontaneous remission trend scored 5.0 times than those without remission yet (95% *CI*: 0.2–9.8, *P* = 0.041). In terms of SCL-90-R, higher (worse) scores in somatization (β = −10.2, 95% *CI*: −13.5–−6.9, *P* = 0.000), obsessive-compulsive (β = −9.2, 95% *CI*: −11.7–−6.7, *P* = 0.000), interpersonal sensitivity (β = −9.8, 95% *CI*: −11.9–−7.7, *P* = 0.000), depression (β = −12.0, 95% *CI*: −14.3–−9.8, *P* = 0.000), anxiety (β = −9.3, 95% *CI*: −11.9–−6.8, *P* = 0.000), hostility (β = −8.5, 95% *CI*: −11.0–−5.9, *P* = 0.000), phobic anxiety (β = −9.8, 95% *CI*: −12.5–−7.0, *P* = 0.000), paranoid ideation (β = −8.6, 95% *CI*: −11.1–−6.2, *P* = 0.000), and psychoticism (β = −10.7, 95% *CI*: −13.2–−8.2, *P* = 0.000) were significantly associated with a lower total score of WHOQoL-100. Other factors, such as age of onset (*P* = 0.360), family history of PKD (*P* = 0.179), and anticonvulsant treatment (*P* = 0.631), were not evidently related to total WHOQoL-100 score.

Multivariate linear regression model (stepwise) was further fitted and the results showed that remission trend (β = 4.7, 95% *CI*: 1.1–8.4, *P* = 0.011) and the score of depression (β = 12.0, 95% *CI*: −14.2–−9.8, *P* = 0.000) were most significantly affecting the quality of life.

In this study, the percentages of patients with depression and anxiety were 41.2% (68/165) and 26.7% (44/165), respectively. According to the results of SDS and SAS assessment, patients with mild, moderate, and severe depression were 12.7%, 21.8%, and 6.7%, respectively, and the percentages of patients with mild, moderate, and severe anxiety were 17.0%, 8.5%, and 1.2%, respectively [Table 4]. Among the total 83 patients with depression or anxiety, co-occurrence of both mental disorders was 34.9% (29/83).

Discussion

PKD is the most common subtype of paroxysmal dyskinesia and is considered as a movement disorder defined by dystonic or choreoathetoid attacks mostly precipitated by sudden movements or change in velocity.[23] In some patients, the motor episodes could also be elicited by emotional stress, and symptoms get worsened with longer duration and/or higher frequency under the condition of psychological burden.[5] PKD is commonly inherited in an autosomal dominant mode.[2,3] Since 2011, when the first candidate gene *PRRT2* was identified, PKD has attracted more and more attention of clinicians and geneticists.[6,7,11,12,23-26] However, it was recognized by our clinicians that, in addition, there is impairment of mood or mental health in a high percentage of outpatients with PKD, which could be even more harmful to the quality of life. These mental disorders might occur during the course of the disease and typical examples of nonmotor features of our patients were depression and anxiety.

Table 4: Patients with PKD at various levels of depression and anxiety (*n* = 165)

Parameters	SDS, *n* (%)	SAS, *n* (%)
Mild	21 (12.7)	28 (17.0)
Moderate	36 (21.8)	14 (8.5)
Severe	11 (6.7)	2 (1.2)

PKD: Paroxysmal kinesigenic dyskinesia; SDS: Self-Rating Depression Scale; SAS: Self-Rating Anxiety Scale.

It was found that more than 2/5 patients had been misdiagnosed when they visited the doctor for the first time, and less than 1/3 patients obtained the initial knowledge of PKD from health professionals. Patients usually spend years or decades going to see doctors around, longing for accurate diagnosis and appropriate treatment. During this progress, over half of the patients would switch to Internet platforms, such as web communities or chat groups composed of wardmate with similar symptoms, for extra help. These evidences underlined the value of the Internet in promoting public understanding of rare disease.

Our data demonstrated that patients with PKD had worse mental health and lower quality of life than normal controls. Moreover, the negative associations in clinical characteristics and mental health symptoms with quality of life were also detected. Specifically, patients with nonremission trend as well as higher score of depression were more likely to report lower levels of quality of life. These findings supported previous studies documenting the effect of mental health on quality of life of patients with other paroxysmal neurological disorders, such as epilepsy and migraine.[27-32] We found that depression and anxiety were prevalent among PKD patients, and co-occurrence of both is common (more than 1/3). The finding that patients with spontaneous remission (either complete or incomplete) reported higher quality of life than those without remission may reflect greater optimism regarding benign development and alleviation pattern of PKD.[2] However, the change of mental health and quality of life with the development of disease is still unknown. To investigate the relationship or the mechanism between PKD and psychological disorder, further studies will be needed with more participants, longitudinal follow-up, and mental health as a therapeutic target.

Our study suggested that clinicians should be attentive to symptoms of depression and anxiety in PKD. Comprehensive health-care services and interventions should be further enhanced based on both training of clinicians to raise diagnosis rate as well as provision of family-based health education. Moreover, regular mental health interventions could set depression and anxiety as intervention targets. Thus, interventions which encourage patients to participate

in social activities and promote meaningful relationships might be helpful from both a quality of life and development perspective. In addition, improving community-based science popularization program may help increase public's understanding of rare disease, in turn, leading patients to be better integrated in the society. It might be beneficial to establish specialized Internet communication platform for patients' counseling and sharing their experiences and stories. Collectively, to improve general support for PKD patients, many more people should be involved, including PKD patients and their families, neurologists, pediatricians, genetic counselors, psychological counselors, and community workers.

To sum up, we examined nonmotor symptoms, quality of life, and related factors of PKD patients in a large population. While the study population was a single-center convenience sample, more than 90% of the patients evaluated in this hospital were from 14 provinces, representing patients with PKD from across the Chinese mainland. Our results provide the evidence that depression, anxiety, and low levels of quality of life are prevalent in patients with PKD. More importantly, two factors, depression score and nonremission of dyskinesia episodes, were identified to significantly influence the level of quality of life among patients. Considering that the dyskinesia episodes could also be elicited by emotional stress, and that symptoms get worsened when patients experience stress, intervention or treatment of depression and anxiety might improve the motor symptoms of these patients.

This study had limitations common to self-report studies, such as response bias. There was no information on premorbid mental health, social factors (other than marital status, residence, and educational status), all of which might be confounders. Further limitation was the cross-sectional design, which did not allow us to establish the change of mental health disorders and quality of life with the development of disease. Longitudinal follow-up studies with more participants and mental health as a therapeutic target in PKD are needed.

Financial support and sponsorship

This study was supported by the grants from the National Natural Science Foundation of China (No. 81571086, No. 81271262, and No. 81600978), Shanghai Municipal Education Commission-Gaofeng Clinical Medicine Grant Support (No. 20161401), Interdisciplinary Project of Shanghai Jiao Tong University (No. YG2016MS64), Shanghai Jiao Tong University School of Medicine Undergraduate Innovation Training Program (No. 2015045), and Technology Research Project in the Public Interest of Zhejiang Province (No. 2014C33132).

Conflicts of interest

There are no conflicts of interest.

References

1. Bruno MK, Hallett M, Gwinn-Hardy K, Sorensen B, Considine E, Tucker S, *et al.* Clinical evaluation of idiopathic paroxysmal kinesigenic dyskinesia: New diagnostic criteria. Neurology 2004;63:2280-7. doi: 10.1212/01.WNL.0000147298.05983.50.
2. Chen WJ, Lin Y, Xiong ZQ, Wei W, Ni W, Tan GH, *et al.* Exome sequencing identifies truncating mutations in PRRT2 that cause paroxysmal kinesigenic dyskinesia. Nat Genet 2011;43:1252-5. doi: 10.1038/ng.1008.
3. Wang JL, Cao L, Li XH, Hu ZM, Li JD, Zhang JG, *et al.* Identification of PRRT2 as the causative gene of paroxysmal kinesigenic dyskinesias. Brain 2011;134:3493-501. doi: 10.1093/brain/awr289.
4. Ebrahimi-Fakhari D, Saffari A, Westenberger A, Klein C. The evolving spectrum of PRRT2-associated paroxysmal diseases. Brain 2015;138:3476-95. doi: 10.1093/brain/awv317.
5. Huang XJ, Wang T, Wang JL, Liu XL, Che XQ, Li J, *et al.* Paroxysmal kinesigenic dyskinesia: Clinical and genetic analyses of 110 patients. Neurology 2015;85:1546-53. doi: 10.1212/WNL.0000000000002079.
6. Hsu WY, Kwan SY, Liao KK, Chen RS, Lin YY. Altered inhibitory modulation of somatosensory cortices in paroxysmal kinesigenic dyskinesia. Mov Disord 2013;28:1728-31. doi: 10.1002/mds.25656.
7. Hsiao FJ, Hsu WY, Chen WT, Chen RS, Lin YY. Abnormal somatosensory synchronization in patients with paroxysmal kinesigenic dyskinesia: A magnetoencephalographic study. Clin EEG Neurosci 2017;48:288-94. doi: 10.1177/1550059416662575.
8. Chen YC, Lee YS, Shih CC, Wu T, Chen CM. Mutations of proline-rich transmembrane protein-2 and paroxysmal kinesigenic dyskinesia in Taiwan. Mov Disord 2013;28:1459-60. doi: 10.1002/mds.25399.
9. Wei H, Sun Y, Chen H, Wang DQ, Li LP, Ding Y, *et al*. Somatosensory disinhibition in patients with paroxysmal kinesigenic dyskinesia. Chin Med J 2012;125:838-42. doi: 10.3760/cma.j.issn.0366-6999.2012.05.020.
10. Wang HX, Li HF, Liu GL, Wen XD, Wu ZY. Mutation analysis of MR-1, SLC2A1, and CLCN1 in 28 PRRT2-negative paroxysmal kinesigenic dyskinesia patients. Chin Med J 2016;129:1017-21. doi: 10.4103/0366-6999.180529.
11. Rossi P, Sterlini B, Castroflorio E, Marte A, Onofri F, Valtorta F, *et al.* A novel topology of proline-rich transmembrane protein 2 (PRRT2): HINTS FOR AN INTRACELLULAR FUNCTION AT THE SYNAPSE. J Biol Chem 2016;291:6111-23. doi: 10.1074/jbc.M115.683888.
12. Valente P, Castroflorio E, Rossi P, Fadda M, Sterlini B, Cervigni RI, *et al.* PRRT2 is a key component of the ca(2+)-dependent neurotransmitter release machinery. Cell Rep 2016;15:117-31. doi: 10.1016/j.celrep.2016.03.005.
13. Valtorta F, Benfenati F, Zara F, Meldolesi J. PRRT2: From paroxysmal disorders to regulation of synaptic function. Trends Neurosci 2016;39:668-79. doi: 10.1016/j.tins.2016.08.005.
14. Wang ZY. Symptom check list-90 (In Chinese). Shanghai Arch Psychiatry 1984;2:3. doi: 10.1056/NEJMe0912474.
15. Pan XF, Fei MD, Zhang KY, Fan ZL, Fu FH, Fan JH, *et al.* Psychopathological profile of women with breast cancer based on the symptom checklist-90-R. Asian Pac J Cancer Prev 2014;14:6579-84. doi: 10.7314/APJCP.2013.14.11.6579.
16. Matti H. Assessment of Psychiatric Symptoms using the SCL-90. Helsingin Yliopisto 2003;15:203-11.
17. Tong HJ. A research of Vicissitude: SCL-90-R and Its Norm (In Chinese). Psychol Sci 2010;33:928-30. doi: 10.16719/j.cnki.1671-6981.2010.04.022.
18. Hao YT, Fang JQ. The introduce and usage of WHOQOL instrument in Chinese (In Chinese). Mod Rehabil 2000;4:1127-30. doi: 10.3321/j.issn:1673-8225.2000.08.002.
19. Group. The World Health Organization quality of life assessment (WHOQOL): Development and general psychometric properties. Soc Sci Med 1998;46:1569-85. doi.org/10.1016/S0277-9536(98)00009-4.
20. Fang JQ, Hao YT, Li CX. Reliability and validity for Chinese version of WHO Quality of Life Scale (In Chinese). Chin Ment Health J 1999;13:203-5.
21. Zung WW. A self-rating depression scale. Arch Gen Psychiatry 1965;12:63-70. doi: 10.1001/archpsyc.1965.01720310065008.
22. Zung WW. A rating instrument for anxiety disorders. Psychosomatics 1971;12:371-9. doi: 10.1016/S0033-3182(71)71479-0.
23. Méneret A, Gaudebout C, Riant F, Vidailhet M, Depienne C, Roze E,

et al. PRRT2 mutations and paroxysmal disorders. Eur J Neurol 2013;20:872-8. doi: 10.1111/ene.12104.
24. Heron SE, Dibbens LM. Role of PRRT2 in common paroxysmal neurological disorders: A gene with remarkable pleiotropy. J Med Genet 2013;50:133-9. doi: 10.1136/jmedgenet-2012-101406.
25. Becker F, Schubert J, Striano P, Anttonen AK, Liukkonen E, Gaily E, *et al.* PRRT2-related disorders: Further PKD and ICCA cases and review of the literature. J Neurol 2013;260:1234-44. doi: 10.1007/s00415-012-6777-y.
26. Hsu WY, Liao KK, Tseng YJ, Kwan SY, Chen RS, Lin YY, *et al.* Reduced postmovement cortical inhibition in patients with paroxysmal kinesigenic dyskinesia. Neurology 2013;81:353-60. doi: 10.1212/WNL.0b013e31829c5e61.
27. Hermann BP, Seidenberg M, Bell B, Woodard A, Rutecki P, Sheth R, *et al.* Comorbid psychiatric symptoms in temporal lobe epilepsy: Association with chronicity of epilepsy and impact on quality of life. Epilepsy Behav 2000;1:184-90. doi: 10.1006/ebeh.2000.0066.
28. Ratcliffe GE, Enns MW, Jacobi F, Belik SL, Sareen J. The relationship between migraine and mental disorders in a population-based sample. Gen Hosp Psychiatry 2009;31:14-9. doi: 10.1016/j.genhosppsych.2008.09.006.
29. Hoppe C, Elger CE. Depression in epilepsy: A critical review from a clinical perspective. Nat Rev Neurol 2011;7:462-72. doi: 10.1038/nrneurol.2011.104.
30. Yalinay Dikmen P, Yavuz BG, Aydinlar EI. The relationships between migraine, depression, anxiety, stress, and sleep disturbances. Acta Neurol Belg 2015;115:117-22. doi: 10.1007/s13760-014-0312-0.
31. Szaflarski JP, Szaflarski M. Seizure disorders, depression, and health-related quality of life. Epilepsy Behav 2004;5:50-7. doi: 10.1016/j.yebeh.2003.10.015.
32. Rong P, Liu A, Zhang J, Wang Y, Yang A, Li L, *et al*. An alternative therapy for drug-resistant epilepsy: Transcutaneous auricular vagus nerve stimulation. Chin Med J 2014;127:300-4. doi: 10.1186/s13063-015-0906-8.