

Case Report

## Analyzing clinical and electrophysiological characteristics of Paroxysmal Dyskinesia

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**Abstract**

The classification, clinical and electrophysiological characteristics, treatment outcome and pathogenesis of paroxysmal dyskinesia were summarized and analyzed. Paroxysmal dyskinesia was classified into three types. Different types had different incentives in clinical practice. Patients were mostly male adolescents, and the attacks, which were in various forms, manifested as dysmyotonia of choreoathetosis, body torsion and facemaking; no disturbance of consciousness during attacks. Electroencephalogram and other examinations showed no specific abnormalities during both the attacks and interictal period. Paroxysmal dyskinesia was an independent disease and different from epilepsy.

**KEYWORDS:** Ocular Motility Disorders, Chorea.

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**P**aroxysmal movement disorders are rare series of paroxysmal nervous system diseases, characterized by sudden and recurrent episodes of abnormal movement, but normal during the interictal period. Sometimes, movement disorders are present only intermittently, which is referred to as 'paroxysmal dyskinesia' (PxD).<sup>1,2</sup> PxD is further divided into three categories: paroxysmal kinesigenic dyskinesia (PKD), paroxysmal non-kinesigenic dyskinesia (PNKD) and paroxysmal exercise-induced dystonia (PED). In order to further acknowledge such disease and contribute to early diagnosis and differential diagnosis, as well as to reduce misdiagnosis and missed diagnosis, this study has analyzed the clinical data of 38 patients with PxD treated in the Department of Neurology, the First Affiliated Hospital, Sun Yat-sen University, since 1997.

**Cases**

There were a total of 38 PxD patients (29 males

and 9 females) in the age range of 9-34 years at the visiting time. The onset age was 8 to 28 years; 11 patients were younger than 10 years old, 19 patients were between the age of 10-20 years and 8 patients were older than 20 years. The average course of the disease was 6.9 years. Five patients had a history of premature birth, four had a history of dystocia (fetal distress requiring abdominal delivery), three had experienced febrile convulsion, 2 cases could not walk on their own until about two years of age and one had a suspected family history: while squatting in between class to play, the patient's seven year old sister suddenly got up to run when heard the class bell ringing, but found that she was unable to act (The exact form of the manifestations were unknown). The sister had no further attacks after taken to the hospital for general treatment. There was not any neurological abnormalities in the patients with past history of delivery diseases and no positive family history of epilepsy.

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## Results

Thirty-three PKD patients including 26 males and 7 females with the onset age of 8-27 years were studied. PKD, manifesting as flexion, torsion or choreoathetosis of unilateral limbs or a single limb or even limbs, was triggered by suddenly performing/changing a movement or posture from a stationary state (such as suddenly standing up to walk or doing other movement after sedentariness). Some patients had the manifestations of involuntary movement of wink and pout, and some appeared to twist their body as the axis, which were in various forms. Duration of the attack ranged from ten seconds to a few minutes, most continued for 10-30 seconds. Regardless of the severity and scope of the attack, patients were still conscious but unable to speak, which did not affect the sphincter and they could recall afterwards. The attachment was triggered in 13 patients when they were told to repeat the 'triggering movement' at the clinic. No abnormality was observed during the interictal period. The attack frequency varied from a few times per day to per month. Some patients with longer duration knew how to reduce or even avoid the attack by taking certain measures such as performing some mild and slow gestures prior to the 'triggering movement.'

All three PNKD patients were male with the onset age of 9, 17 and 21 years. The three patients with PNKD were triggered by fatigue, tiredness with anxiety, and alcohol, respectively, but not by a sudden movement. The clinical manifestations were the same as those of PKD, but with slower ease and usually endured 10 minutes to hours.

Both two PED patients were male with the onset age of 28 and 22 years. PED could be repeatedly triggered by long-time and continuous driving in a crowded and noisy environment with polluted air. The manifestations included sudden stiffness and extension of upper limbs, being unable to turn the steering wheels, which were relieved by immediate stop of the car or having the window open, for a few minutes by someone else.

## Electrophysiological Examination

All 38 patients received electroencephalogram (EEG) examination; the result was normal for 33 (86.49%) and gently abnormal for 5 patients (13.51%), who mostly had scattered wave  $\square$  in bilateral frontal lobes (3 cases), parietal lobe (1 case) or occipital lobe (1 case), with sometimes a high amplitude and occasionally a sporadic little sharp wave. These 13 patients whose clinical seizures could be repeatedly triggered received EEG examination during the triggered attack, but no specific abnormality was found. Video electroencephalogram (VEEG) was performed in 4 patients for their special previous history (dystocia or febrile convulsion, and so on), but showed nothing special. With normal results, Electromyogram and somatosensory evoked potential examinations were performed in 14 patients who occasionally had intermittent distal anaesthesia (To exclude the peripheral neuropathy).

## Imaging Examination

Head CT scan was performed in 32 patients, showing normal results. Head MR was performed in 18 patients, showing normal results except 1 case with right frontal lobe dysplasia and 1 case with white matter dysplasia. SPECT was performed in 5 patients, finding 4 with normal results and 1 with decreased blood flow in unilateral basal ganglia. PET was performed in 2 patients showing no abnormality. (The last two examinations were conducted to exclude the secondary dyskinesias caused by brain organic diseases.)

## Laboratory Examination

Liver function, blood sugar, renal function, electrolytes, serum copper and copper-protein were examined in all patients, showing no abnormal results.

## Treatment and Clinical Outcome

Thirty-three PKD patients received antiepileptic drug (24 taking carbamazepine 100-500 mg per day, 9 taking phenytoin 100-300 mg per day). Their symptoms improved fairly after taking medicine for a week. The effective rate

achieved 93.8%. The attack was reduced less than 50% in only 2 patients, while it was reduced to less than 50% in 17 patients, and to less than 25% in 10 patients, and was totally eliminated in 4 patients. Being followed up for more than 2 years, 27 patients who adhered to medicine achieved completely attack free. The attack of the remaining 6 cases were still 1-4 times per year, among which 4 did not adhere to the medicine. These 3 PNKD patients and 2 PED patients had no response to antiepileptic medication, which was then changed for low dose of benzodiazepines (2 PNKD patients and 1 PED patient taking clonazepam 1-1.5 mg per day) and SSRI agents (1 PNKD patient taking Zoloft 50 mg per day and 1 PED patient taking Seroxat 20 mg per day). After about two weeks of treatment, it began to show effects. Observed for 6 months, the attacks were reduced to less than 50%. It was a pity that 3 PNKD and 2 PED patients afterward could not be traced for the treatment results.

## Discussion

Paroxysmal movement disorders are rare in clinical practice. Due to its unique clinical manifestations, which are prone to be confused with that of epilepsy, Extrapyramidal diseases or dyssomnia, coupled with clinicians' lack of understanding these disorders, it often results in missed diagnosis and misdiagnosis.

The disease was first described by Mount and Renback in 1940. Due to the clinical and genetic heterogeneity, the classification of PxD had always been controversial. In 1977, Lance first classified PxD into three categories. The classification was modified by Demirkiran and Jankovic in 1995.<sup>3</sup> Currently, the following is the widely-used classification: 1) paroxysmal kinesigenic dyskinesia (PKD), 2) paroxysmal non-kinesigenic dyskinesia (PNKD), 3) paroxysmal exercise-induced dystonia (PED). There have been great advances recently with insights into genetics for all three forms of PxD. Despite the existence of several PKD genetic loci, no PKD gene has been identified so far. As to the PNKD, mutations in the non-ion channel gene MR1 have been found in several

families.<sup>4,7</sup> For instance, Bruno MK has recently identified mutations in the MR1 gene causing familial PNKD.<sup>8</sup> The mutations in the glucose transporter (GLUT1) gene have been recently identified by Weber et al, as a cause in some patients with autosomal dominant PED.<sup>9,10</sup>

The pathogenesis of paroxysmal kinesigenic dyskinesia (PKD) remains unclear. The patients are typically male children or adolescents with a family history, while the sporadic cases are also not rare.<sup>11</sup> The pathophysiology of PKD remains controversial so far: Is PKD an epileptic syndrome or a nonepileptic dyskinesia secondary to dysfunction of the basal ganglia? Some people regard PKD as a reflex epilepsy involving the thalamus and the basal ganglia,<sup>12</sup> while most scholars believe that PKD is associated with dysfunction of the dopamine system,<sup>11,13</sup> according to its characteristic manifestations and normal EEG during the attack, as well as the SPECT results showing significantly increased blood flow in contralateral basal ganglia during the attack, which suggests over-activity of basal ganglia.

The present data showed that PKD was the most common type of PxD, accounting for 86.8% in the three categories of PxD. The patients were mostly male under 20 years old, with a male-female ratio of 26:7, which was consistent with the literature.<sup>14</sup> Sudden movement was the most important trigger. Other triggers included sudden scare and hyperventilation. The attack usually lasts for seconds to minutes. Bruno MK reported that the duration of attacks in his clinical criteria was short (less than one minute).<sup>15</sup> No unconsciousness or urinary and fecal incontinence were observed during the attack. No epileptic discharge was shown on EEG, not during the attack nor in interictal period. The cases in the present study were mostly sporadic with only one case having a suspected family history, and secondary paroxysmal kinesigenic choreoathetosis (PKC) was excluded by auxiliary examination. The attack could significantly be reduced or even terminated in 93.8% (31/33) of the patients by using anti-epilepsy drugs such as carbamazepine and phenytoin acting on sodium

ion channels. The negative synchronous EEG results, which valued a lot during the attack, suggested that it was not a sort of reflex epilepsy but an independent disease.

Studies have demonstrated that the ability of synthesis and storage of dopamine in patients with PNKD is decreased, leading to chronic upregulation of the amount and affinity of postsynaptic dopamine receptors.<sup>16</sup> For PNKD patients, excessive release of dopamine in nigrostriatal system can be stimulated by alcohol and coffee. Excessively released dopamine acts on the upregulated acceptors, causing the attack of PNKD. The attack has the manifestations similar to that of PKD, with a relatively longer lasting time. It is mostly triggered by fatigue, tiredness with anxiety and alcohol, but not by sudden movement. PED is as rare as PNKD. The attack of dysmytonia lasting for up to tens of minutes usually occurs after continuous motion, which can be relieved by stopping the 'triggering movement.'

In the present study, patients with PNKD or PED were responsive to benzodiazepines or SSRI agents, which act on the  $\gamma$ -aminobutyric acid (GABA) ergic system, indicating that the pathogenesis might be associated with the abnormality in the GABA system. However, considering the small sample size of these two cat-

egories of PxD, further studies are required to provide more evidences.

## Conclusions

According to our data and related literature, we conclude that the diagnosis of PKD should meet the following criteria: 1) the onset age is in the adolescence, mostly under 20 years old; 2) usually clinical attacks are triggered by movement, such as a sudden movement or change of certain movement or posture; 3) the attack is characterized by choreoathetosis, body torsion or facemaking. The symptoms vary a lot, but for each individual, the manifestations are reduplicated and stereotyped; 4) there is no unconsciousness, tongue biting or urinary and fecal incontinence during the attack which can be recalled thereafter; 5) physical examination and auxiliary examinations show normal results during the interictal period and EEG shows no specific abnormality during both the attack and interictal period; 6) the antiepileptics which block the voltage-dependent sodium channel are effective. In the diagnosis of PKD, particular attention should be paid to whether the attack can be induced by movement and whether the patient loses consciousness during the attack. Negative synchronous EEG during the attack is of the most diagnostic value.

## Conflict of Interests

Authors have no conflict of interests.

## Authors' Contributions

ZJ designed the research and had the overall responsibility for the study. ZL did the quality control and wrote the manuscript. FZ assisted in preparation of the manuscript and collection of data. WQ, CZ, YL, CS, CX assisted in data collection. All authors have read and approved the content of the manuscript.

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