Editor's comment: The paroxysmal movement disorders are a group of etiologically and clinically heterogeneous conditions, that include secondary (symptomatic), primary (genetic), and psychogenic forms. In the absence of biomarkers or supportive ancillary examinations, the diagnosis of a psychogenic movement disorder remains based on clinical grounds, and it should only be made after the secondary and genetic forms are carefully excluded. In this context, the recent availability of genetic diagnostic tools for the three main categories of primary paroxysmal dyskinesias (PRRT2, MR-1, and GLUT-1 gene mutations cause kinesigenic, non-kinesigenic, and exercise-induced dyskinesias, respectively) has renewed interest into the phenomenology and the differential diagnosis of the different genetic as well as the psychogenic forms. In this issue of the journal, Ganos and colleagues describe a considerable number of patients diagnosed with psychogenic paroxysmal movement disorders, and compare their clinical features with those of patients with different, genetically proven, primary forms. Keeping in mind some limitations, mainly concerning the retrospective nature of the case-ascertainment, and the comparisons made with previously published genetic series, this novel study offers a number of clinical clues that might help the neurologists in making a correct diagnosis of psychogenic paroxysmal movement disorder. This exercise has practical implications, because a correct diagnosis leads to therapeutic approaches that are efficacious in many of these patients.

Vincenzo Bonifati, Associate Editor, Erasmus MC, P.O. Box 2040, 3000 CA Rotterdam, The Netherlands

Psychogenic paroxysmal movement disorders—Clinical features and diagnostic clues

Christos Ganos a, b, Maria Aguirregomozcorta a, Amit Batla a, Maria Stamelou a, c, d, Petra Schwingenschuh a, e, Alexander Münchau i, Mark J. Edwards a, Kailash P. Bhatia a,*

a Sobell Department of Motor Neuroscience and Movement Disorders, UCL Institute of Neurology, University College London, Queen Square, London WC1N 3BG, UK
b Department of Neurology, University Medical Center Hamburg-Eppendorf (UKE), Hamburg, Germany
c Second Department of Neurology, Attiko Hospital, University of Athens, Greece
d Neurology Clinic, Philipps University, Marburg, Germany
e Department of Neurology, Medical University of Graz, Graz, Austria
f Department of Paediatric and Adult Movement Disorders and Neuropsychiatry, Institute of Neurogenetics, University of Lübeck, Lübeck, Germany

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Abstract

Background: The diagnosis of psychogenic paroxysmal movement disorders (PPMD) can be challenging, in particular their distinction from the primary paroxysmal dyskinesias (PxD) remains difficult.

Methods: Here we present a large series of 26 PPMD cases, describe their characteristics, contrast them with primary PxD and focus on their distinguishing diagnostic features.

Results: Mean age at onset was 38.6 years, i.e. much later than primary PxD. Women were predominantly affected (73%). Most subjects (88.4%) had long attacks, and unlike primary PxD there was a very high within-subject variability for attack phenomenology, duration and frequency. Dystonia was the most common single movement disorder presentation, but 69.2% of the patients had mixed or complex PxD. In 50% of PPMD cases attack triggers could be identified but these were unusual for primary PxD. 42.3% of patients employed unusual strategies to alleviate or stop the attacks. Response to typical medication used for primary PxD was poor. Precipitation of the disorder due to physical or emotional life events and stressors were documented in 57.6% and 65.3% of the cases respectively. Additional interictal psychogenic signs were documented in 34.6% and further medically unexplained somatic symptoms were present in 50% of the cases. 19.2% of patients had a comorbid organic movement disorder and 26.9% had pre-existing psychiatric comorbidities.
1. Introduction

The spectrum of paroxysmal dyskinesias (PxD) encompasses different conditions characterized by sudden episodes of involuntary movements (e.g. dystonic, choreatic, ballistic) lasting for brief (but variable) periods of time and triggered by different factors [1]. They are divided into primary, which can be familial or sporadic and where routine clinical examinations are unrevealing, and secondary, where structural lesions are typically identified linked to the onset and phenomenology of the presenting symptoms [1]. Depending on the type of PxD, treatment and prognosis vary.

Familial clustering of primary PxD has been recognised since their original description [2] and clinical cohort and genetic studies have led to their aetiological delineation and clear genotype–phenotype correlations. Thus, the clinical characteristics of the three major primary PxD, i.e. paroxysmal kinesigenic dyskinesia, (PKD), paroxysmal non-kinesigenic dyskinesia (PNKD) and paroxysmal exercise-induced dyskinesia (PED) due to respective mutations in the Proline-rich transmembrane protein 2 (PRRT2), Myo-inositol monophosphatase (IMMP), and Glucose transporter 1 (GLUT-1) genes are now very well described [3–16]. This helps to guide treatment selection and diagnostic differentiation of other causes of paroxysmal movement disorders.

Numerous causes for secondary PxD have been reported [17–19]. However, psychogenic (or functional) PxD have received limited attention in recent literature [20–24], in particular after the genetic delineation of the primary forms. In view of the sparse information on the phenomenology of psychogenic paroxysmal movement disorders (PPMD) and treatment options [20–24], we sought to explore their explicit clinical characteristics and aimed to identify clinical features which help distinguishing them from primary PxD. Therefore, here we present a large series of 26 cases of PPMD illustrating their diverse phenomenology, associated features and clinical course. We compare them to the classic phenotypic characteristics of primary PxD and propose a list of red flags that can aid clinicians in the diagnosis of PPMD.

2. Patients and methods

We retrospectively reviewed medical records of patients who were diagnosed with psychogenic movement disorders (PMD) between 2006 and 2013 in the movement disorders clinic of the National Hospital for Neurology and Neurosurgery, Queen Square, London. All cases were seen either by K.B. or M.L. or both. Diagnosis of PMD was made based on the criteria proposed by Fahn and Williams [21] and only cases with documented or clinically established PMD were included. We selected those cases where paroxysmal attacks of abnormal movement were the main clinical presentation. In addition, cases where “altered consciousness” was the predominant feature bearing resemblance to non-epileptic attacks were excluded from further analysis.

Investigations relevant to the clinical presentation, including brain and/or spinal imaging (24 cases), electroencephalography (EEG) and/or video-EEG (17 and six cases respectively), biochemical investigations (e.g. cerebrospinal fluid, serum copper and ceruloplasmin levels in five cases) were performed as part of the diagnostic work-up.

Supplementary video related to this article can be found online at http://dx.doi.org/10.1016/j.parkreldis.2013.09.012.

We specifically collected information on age at onset, attack phenomenology, attack duration and frequency, as well as specific triggers of attacks. We also examined the presence of precipitating factors preceding the first attack, environmental stressors, the profile of comorbidities and family history for neurological disorders. Where possible, we also examined the clinical course of the disorder and its response to treatment. This study was performed with permission of the local ethics committee.

3. Results

Within the selected timeframe 245 PMD cases were identified. Twenty-six (10.6%) presented with a PPMD (individual patient characteristics are given in supplementary Table 1). According to published diagnostic criteria [21], a documented PMD was diagnosed in seven patients, whereas the remaining 19 were categorized as clinically established. Clinical characteristics of all patients are summarized in Table 1.

Mean age at onset was 38.6 years (range 16–82 years; SD 15.6 years). Nineteen (73%) patients were female (F:M = 2.7:1). Eight patients (30.7%) had one type of movement disorder during episodes, with dystonia being the most common (n = 4; 15.3%). Isolated paroxysmal tremor or jerks were each seen in two patients (7.6%). Seven patients (26.9%) had a combination of two movement disorders, typically dystonia and tremor. Eleven patients (42.3%) had complex generalised movements, challenging established movement disorders classifications of hyperkinesias. Attacks commonly occurred bilaterally (n = 12) when they mainly affected the arms and legs. Only four patients presented with unilateral attacks (cases 3, 6, 15, 26). The head/face or trunk were predominantly affected in seven and six cases respectively. In seven cases (26.9%) the phenomenological characteristics between attacks varied (video segments E1–3).

Six cases also had speech disturbances during attacks (23%; cases 3, 5, 7, 9, 11, 21), four reported pain (15.3%; cases 11, 15, 19, 26) and five additional somatic complaints such as breathlessness, rapid breathing, light-headedness, drowsiness, fatigue, chest tightness or blurring vision (19.2%; cases 2, 3, 5, 6, 20).

In addition to movement disorders, three patients (cases 7, 19, 25) had rare occasions of unresponsiveness during attacks. Another four cases had episodes of “collapse” but without loss of consciousness in addition to their usual paroxysmal phenomena (cases 9, 11, 13, 14).

Five patients (19.2%) had a coexistent organic movement disorder consisting of simple motor tics (n = 2), cerebral dystonia (n = 1), writer’s cramp (n = 1) and mild unilateral postural tremor secondary to brain surgery at the age of 3 (right thalamic glioma) (n = 1). Six patients (23%) were diagnosed with depression and two (7.6%) with an anxiety disorder after formal psychiatric assessment. None of the presented cases had a positive family history of primary PxD. However in one patient (case 25) there were two family

| Table 1 |
| --- |
| Patient characteristics. |
| Number of cases | 26 |
| Criteria for diagnosis of PMD | 7 Documented/19 clinically established |
| Mean age at onset of symptoms (±SD) | 38.6 (±15.6) |
| Gender (male/female) | 7/19 |
| Type of paroxysmal movement disorder | 4 Dystonia/2 tremor/2 jerks/7 mixed/11 complex |
| Attack duration (<5 min/>5 min) | 3/23 |
| Presence of triggers | 13 (50%) |
| Presence of relieving factors/manoeuvres | 11 (42.3%) |
| Presence of unexplained somatic symptoms | 13 (50%) |
| Family history for neurological disorders | 7 (26.9%) |
| Coexistent organic movement disorders | 5 (19.2%) |

SD – standard deviation; PMD – psychogenic movement disorder.

* Diagnosis according to the Fahn and Williams criteria [21].
members with episodes of hyperglycaemic periodic paralysis. Further 6 patients had a positive family history for neurological disorders (supplementary Table 1).

Psychogenic physical signs on interventional examination were documented in nine (34.6%) patients. They included gait weakness (n = 7, cases 1, 4, 6, 11, 14, 15, 23; 23%), give way weakness (n = 4, cases 6, 7, 9, 11; 15.3%), non-anatomical sensory disturbances (n = 3, cases 6, 7, 11; 11.5%) and fixed dystonic postures of the feet (n = 2, cases 7, 14; 7.6%). These patients were included because paroxysmal symptoms were the presenting and most prominent clinical characteristic in them.

Medically unexplained somatic symptoms such as diffuse abdominal symptoms, chest pain, palpitations, swallowing difficulties, voice changes, dizziness and headaches were found in 13 patients (50%).

Only three patients reported short attacks (<5 min) (cases 18, 20, 23). Large within- and between-patient duration variability was found in all other cases. This ranged between a few minutes to several hours or even days (supplementary Table 1). In case 15, attack duration ranged from a few hours to 1 week. Attack frequency between patients ranged from several times a day to once every three months (supplementary Table 1).

Specific attack triggers were documented in 13 cases (50%). These involved “increased stress” in three patients, alcohol intake in two cases, as well as walking, loud noises, feeling frightened or thirsty in individual cases (supplementary Table 1). In one patient (case 25, video segment B) attacks were triggered by sounds of pre-recorded incantations. Nine patients (34.6%) experienced attacks of their paroxysmal movement disorder during examination.

Precipitants prior to the onset of the movement disorder could be identified in 15 cases (57.6%). These included accidental injuries, recent illness, invasive medical procedures and antibiotic intake, physical assault, giving birth, family problems, as well as changing religious beliefs (supplementary Table 1). Stressors augmenting the disorder’s manifestation were found in 17 (55.3%) cases. Common stressors were family or work problems, health-related issues of the affected individual or of close familial members. Alleviating factors were recognized in 11 (42.3%) cases and included treatment with diazepam (n = 4, cases 4, 5, 7, 26), gabapentin intake with immediate (placebo) therapeutic response (n = 1, case 11), pressure on the affected body part (n = 3, cases 9, 23,26), focussing attention to an external object (e.g. on examiners button hole, n = 1, case 21, video segment C), focussing attention to affected body parts and moving the non-affected contralateral limbs (n = 1, case 25), as well as reducing physical exercise (n = 1, case 12) or sleep (n = 1, case 26) (supplementary Table 1).

The most commonly commenced medication prior to diagnosis of a PPMD was antiepileptics (n = 7), which with the exception of one case with placebo response (case 11, see above), had been ineffective. Benzodiazepines (n = 8) had relieved symptoms in four cases. Baclofen (n = 1), trihexyphenidyl (n = 1), levodopa (n = 1), as well as risperidone and tetrabenazine (n = 1) had also been tried also unsuccessfully. Seven patients were receiving antidepressants.

Seventeen patients (65.3%) experienced significant disability due to their movement disorder, having to leave their work or college with restriction of their daily activities. Six patients (23%) had impaired mobility and used stick or wheelchair between attacks. In one case, where symptoms emerged after a car accident with a whiplash injury, there was an ongoing litigation process.

Follow-up information was available for 17 cases. The diagnosis was carefully explained to and accepted by all patients but three, who remained symptomatic at follow-up (mean follow-up period 2.3 years). In one of them (case 17) a litigation process was ongoing. Five patients showed spontaneous symptom amelioration upon diagnosis. Three patients (cases 1, 8, 16) benefited from local injections with botulinum toxin, two (cases 1, 8) had an immediate (placebo) response. One patient (case 22) improved upon restarting treatment with botulinum toxin, two (cases 1, 8) had an immediate (placebo) response. One patient (case 22) improved upon restarting treatment with botulinum toxin, two (cases 1, 8) had an immediate (placebo) response. One patient (case 22) improved upon restarting treatment with botulinum toxin, two (cases 1, 8) had an immediate (placebo) response. One patient (case 22) improved upon restarting treatment with botulinum toxin, two (cases 1, 8) had an immediate (placebo) response. One patient (case 22) improved upon restarting treatment with botulinum toxin, two (cases 1, 8) had an immediate (placebo) response. One patient (case 22) improved upon restarting treatment with botulinum toxin, two (cases 1, 8) had an immediate (placebo) response. One patient (case 22) improved upon restarting treatment with botulinum toxin, two (cases 1, 8) had an immediate (placebo) response. One patient (case 22) improved upon restarting treatment with botulinum toxin, two (cases 1, 8) had an immediate (placebo) response. One patient (case 22) improved upon restarting treatment with botulinum toxin, two (cases 1, 8) had an immediate (placebo) response. One patient (case 22) improved upon restarting treatment with botulinum toxin, two (cases 1, 8) had an immediate (placebo) response. One patient (case 22) improved upon restarting treatment with botulinum toxin, two (cases 1, 8) had an immediate (placebo) response. One patient (case 22) improved upon restarting treatment with botulinum toxin, two (cases 1, 8) had an immediate (placebo) response. One patient (case 22) improved upon restarting treatment with botulinum toxin, two (cases 1, 8) had an immediate (placebo) response. One patient (case 22) improved upon restarting treatment with botulinum toxin, two (cases 1, 8) had an immediate (placebo) response. One patient (case 22) improved upon restarting treatment with botulinum toxin, two (cases 1, 8) had an immediate (placebo) response. One patient (case 22) improved upon restarting treatment with botulinum toxin, two (cases 1, 8) had an immediate (placebo) response.

4. Discussion

Here we present the phenotypic characteristics of a large series of 26 cases of PPMD reviewed in our centre. They accounted for
10.6% of PMD during the assessed timeframe. Although there has been limited focus on PPMD in recent medical literature [20–24], their distinction from the three classic primary PxD (i.e. PKD, PNKD and PED) (Table 2) is of great importance, since management differs. Based on the presented data we have identified a number of characteristics, which may aid clinicians in differentiation of PPMD from the primary PxD leading to appropriate treatment.

4.1. Age of onset

The average age of symptom onset was 38.6 years in our reported cases, in contrast to previous reports of PKD, PNKD and PED, which classically manifest at much earlier ages (Table 2). Although, unusual cases of classic PKD and PNKD have been published with patients developing symptoms at a later age (27 and 21 respectively) [4,5] and PPMD have been described in children [25], this is very rare. Therefore, as previously noted [26], we also suggest that an adult age at onset (particularly above the age of 25 years) should be considered as a diagnostic clue pointing towards a secondary or psychogenic cause of PxD.

4.2. Phenomenology of attacks

The single most common phenotypic presentation in our cases was that of dystonia, mirroring previous data [21], followed by tremor and jerks. However, most cases presented with a combination of at least two paroxysmal movement disorders and 11 cases presented with more complex movement disorders difficult to classify. In all cases the phenomenological presentation was incongruent with primary PxD (Table 2), but also variable in 26.9% of individuals (video E1-3). Moreover, the presence of paroxysmal tremor (demonstrated as the sole phenomenon in video segment E3, and adjoined with further movement disorders in video segments C and D) has never been reported in primary PxD, and is a useful additional diagnostic clue for PPMD (Table 3).

In addition, clinical inconsistencies, such as induction of an attack or increase in severity during examination, as well as distractibility, entainment, placebo response to medication, but also other psychogenic physical signs were found in the majority of patients. These features are inconsistent and incongruent to the phenotypic presentation of primary PxD, which by virtue of the Williams and Fahn [21] criteria for PMD constitute important clues towards the diagnosis of PPMD (Table 2).

19.2% of the presented cases had a coexistent organic movement disorder, which reflects reported estimates of patients with concomitant psychogenic and organic movement disorders (“functional overlay”) [27–29]. They usually manifest on the same or contiguous body parts [28], but usually with different phenomenology [27] (e.g. case 26: writer’s cramp and paroxysmal psychogenic dystonic–choreoathetoid movements of the right arm; video segment F1–2).

Table 3: Red flags for suspecting a psychogenic paroxysmal movement disorder.

| Adult age of onset         |
|---------------------------|
| Paroxysmal tremor as predominant clinical feature | High phenomenological variability between episodes |
| Atypical and variable duration of attacks       |
| Presence of multiple atypical triggers          |
| Altered level of responsiveness                   |
| Presence of odd precipitating factors            |
| Presence of unusual relieving maneuvers          |
| Additional psychogenic physical signs and/or medically unexplained somatic symptoms |
| Atypical response to medication                     |

4.3. Attack duration

Attack durations are well defined for primary PxD (Table 2). For example a typical PKD attack lasts less then a minute in the vast majority of cases [4,11,30]; PED attacks usually occur for 15 min [12] and PNKD episodes typically last a few hours [5]. The attack duration of the psychogenic cases presented here was incongruent with these classic forms. In particular, only three cases (cases 18, 20, 23) had recurring attacks for brief periods of time (<5 min), raising the possibility of classic PKD. However, the phenomenology of the attacks in these cases is incongruent with known PKD presentations and proposed diagnostic criteria (Table 2) [4]. Furthermore, not only attack duration, but also their very high intra- and inter-individual variability (from seconds to hours or days) as reported here and previously [25], should prompt considering PPMD over primary PxD. Of note, secondary causes of PxD, can also present with great between-subject variability of attack duration (e.g. PNKD-like attacks lasting for seconds in one individual or 10–15 days in another) [17]. However, high within-subject variability does not commonly occur in these conditions [17], as in the presented cases here (e.g. case 15), and moreover, symptomatic causes have been excluded in these patients.

4.4. Triggers

Primary forms of PxD have typical triggers (Table 2); classic PKD is induced by sudden movement [4,30], PED by prolonged exercise [3,12] and PNKD usually by coffee, alcohol and emotional stress [5]. The triggers in psychogenic cases were atypical (e.g. video segments A and B) and numerous for the majority of patients. (Supplementary Table 1). Even in cases where triggers similar to those seen in PNKD were present (e.g. increased stress or alcohol intake; Table 2), the clinical phenomenology of attacks remained incongruent.

4.5. Associated features

Precipitating factors and stressors were commonly reported in our cases and involved physical and/or emotional distress. In addition, three cases (11.5%) had additional rare episodes with alterations in responsiveness during some attacks. Further four cases (15.3%) reported rare attack variations with “collapsing” events. Intercital and ictal EEG recordings were respectively available in 5 and 4 of the aforementioned cases and were normal, prompting the diagnosis of psychogenic non-epileptic seizures. Of note, even though seizures are associated features of PKD and PED [3,7,10,12,13], they occur independent to the attacks and have classic epileptic characteristics.

Of the 11 patients with alleviating strategies, odd manoeuvres (video segment C, F1 and F2), benzodiazepine intake, placebo response to gabapentin, focussing on the affected body parts and moving the non-affected contralateral limbs, exerting pressure on affected body parts as well as going to bed were documented. While patients with PxD have been reported to attempt controlling their attack symptoms usually by exerting pressure on the affected limb (“holding tight”) [1] or through benzodiazepine intake or sleep, the remarkably variable and unusual strategies seen in our patients are additional red flags pointing towards the diagnosis of PPMD.

4.6. Treatment outcome

The majority of the presented cases acknowledged the diagnosis and wished to pursue further therapy, including physiotherapy and cognitive behavioural treatment. This led to significant improvement of their symptoms. Three patients had botulinum toxin treatments, two with persistent placebo responses.
It is noteworthy that the number of PPMD patients with a significant clinical improvement is high and comparable to previous reports [21,22,31]. In particular, Bressmann et al. reported clinical remissions in five of 11 patients with PPMD upon different treatments, and a dramatic improvement in an additional case with hypnotherapy [22]. It therefore appears that PPMD might have a better overall prognosis than other PMD [27,32,33]. However, as systematic prospective data are not available, such comparisons do not allow for unequivocal conclusions and suggest the need for specific study in this area.

4.7. Study limitations

This study has several limitations. The retrospective design of our data analysis is subject to potential errors, such as ascertainment bias. Thus, the presented prevalence of PPMD among PMD may not be reflected in all clinical populations. However, the aim of the current study was to provide a diagnostic pathway for clinicians confronted with patients with paroxysmal movement disorders, concentrating on clinical features suggesting a psychogenic cause. We also acknowledge the difficulties of diagnosing PMD, in the absence of biomarkers, solely based on available clinical criteria. However, with the amount of information available on the presented cases collected in our centre by movement disorders specialists with long-standing experience in PMD (K.R., M.J.E.), including long follow-up examinations for the majority, we are confident that these patients fall within the borders of this diagnostic category. Although not all attacks were observed during clinical examination, in none of the presented cases did patients lose consciousness during their paroxysmal episodes and all could accurately provide detailed descriptions. Finally, comparisons with primary PxD were made based on existing literature and not “head to head” with patients from our centre. Given the rarity of the primary PxD, this allowed pooling existing knowledge and using well-established diagnostic criteria providing for accurate clinical inferences.

5. Conclusion

Although the phenotypic presentation of PPMD can be highly diverse, after exclusion of secondary PxD conditions certain clinical features help in distinguishing this condition from the primary forms of PxD. These characteristics include an adult age of onset, the presence of paroxysmal tremor, high within-subject phenomenological variability, marked increases in attack frequency and severity during examination, highly variable attack duration, numerous and unusual triggers, alteration of responsiveness during attacks, odd precipitating factors and relieving manoeuvres, medically unexplained somatic symptoms and atypical response to medication. The communication of the diagnosis in an appropriate manner was often useful therapeutically, and treatment with physical and cognitive behavioural therapy was helpful in a number of patients.

Author contributions

Christos Ganos
Drafting/revising the manuscript for content, including medical writing for content. Acquisition of data. Study supervision or coordination.

Amit Batla
Drafting/revising the manuscript for content, including medical writing for content. Acquisition of data.

Maria Stamelou
Drafting/revising the manuscript for content, including medical writing for content. Acquisition of data.

Petra Schwingenschuh
Revising the manuscript for content, including medical writing for content. Acquisition of data.

Alexander Münchau
Revising the manuscript for content, including medical writing for content.

Mark Edwards
Drafting/revising the manuscript for content, including medical writing for content. Acquisition of data. Study supervision or coordination.

Kailash Bhatia
Drafting/revising the manuscript for content, including medical writing for content. Acquisition of data. Study supervision or coordination.

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Appendix A. Supplementary data

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