Handbook of Clinical Neurology, Vol. 139 (3rd series)
Functional Neurologic Disorders
M. Hallett, J. Stone, and A. Carson, Editors
http://dx.doi.org/10.1016/B978-0-12-801772-2.00021-7

Chapter 21

Functional jerks, tics, and paroxysmal movement disorders

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Abstract

Functional jerks are among the most common functional movement disorders. The diagnosis of functional jerks is mainly based on neurologic examination revealing specific positive clinical signs. Differentiation from other jerky movements, such as tics, organic myoclonus, and primary paroxysmal dyskinesias, can be difficult. In support of a functional jerk are: acute onset in adulthood, precipitation by a physical event, variable, complex, and inconsistent phenomenology, suggestibility, distractibility, entrainment and a Bereitschaftspotential preceding the movement. Although functional jerks and tics share many similarities, characteristics differentiating tics from functional jerks are: urge preceding the tic, childhood onset, rostrocaudal development of the symptoms, a positive family history of tics, attention-deficit hyperactivity disorder or obsessive-compulsive symptoms, and response to dopamine antagonist medication. To differentiate functional jerks from organic myoclonus, localization of the movements can give direction. Further features in support of organic myoclonus include: insidious onset, simple and consistent phenomenology, and response to benzodiazepines or antiepileptic medication. Primary paroxysmal dyskinesias and functional jerks share a paroxysmal nature. Leading in the differentiation between the two are: a positive family history, in combination with video recordings revealing a consistent symptom pattern in primary paroxysmal dyskinesias.

In this chapter functional jerks and their differential diagnoses will be discussed in terms of epidemiology, symptom characteristics, disease course, psychopathology, and supportive neurophysiologic tests.

INTRODUCTION

Jerky movements, including functional jerks, tics, and paroxysmal movement disorders, refer to a heterogeneous category of hyperkinetic movement disorders. The diagnosis of these jerky movements forms a true challenge for the clinician at the borderland between neurology and psychiatry (van der Salm et al., 2013). Over the last decade a paradigm shift has occurred towards a positive diagnosis of functional neurologic disorders instead of diagnosing by default after exclusion of all other possible diagnoses. More consensus seems to have been reached between psychiatrists and neurologists. First, the editors of the newest (fifth) edition of the *Diagnostic and Statistical Manual of Mental Disorders* (DSM-5, the standard psychiatric classification system) has incorporated "functional neurological symptom disorders" as a subcategory in the category of "conversion disorders," in line with the neurologic terminology (American Psychiatric Association, 2013). Second, the well-known diagnostic criteria of functional movement disorders (FMDs) by Fahn and Williams have been modified, leaving out psychologic disturbance, psychogenic signs, or multiple somatizations as a requirement for high diagnostic certainty (Fahn and Williams, 1988; Shill and Gerber, 2006; Gupta and Lang, 2009). Still, there is no pathognomonic sign or test, and diagnostic agreement between

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clinicians in cases with lower diagnostic certainty (probable or possible) is poor to moderate (Morgante et al., 2012).

In a recent study the clinical decisions and accuracy of clinicians to establish the diagnosis of a jerky movement were tested (van der Salm et al., 2013). Interrater agreement on diagnoses of jerky movements was moderate (kappa = 0.56 ± 0.1) between international movement disorder specialists. Remarkably, it appeared that best consensus was reached on the diagnosis of tics, and least consensus on the diagnosis of organic myoclonus, with FMDs scoring in between.

When can a jerky movement be considered as "functional"? How can FMD be discerned from tics on the one hand, and from myoclonic jerks on the other? In this chapter the differential diagnosis between functional jerks, myoclonus, tics, and primary paroxysmal dyskinesias (PxDs) is discussed, based on epidemiology, symptom characteristics, disease course, psychopathology, and neurophysiologic tests. We will start our chapter by defining functional jerks, myoclonus, and tics. In addition, functional paroxysmal movement disorders and their organic counterpart will be addressed.

EPIDEMIOLOGY AND CLINICAL PICTURE

Functional jerks

Epidemiology

Prevalence and incidence rates of functional jerks are largely unknown, due to diversity in the use of diagnostic criteria. Prevalence rates of FMD range between 0.24% and 3%, depending on whether they have been assessed in clinical or population-based samples (Factor et al., 1995; Stone et al., 2010). The higher prevalence rates at the upper end of this estimation are derived from specialized movement disorder clinics and are therefore an overestimation of the population prevalence. After functional tremor and dystonia, functional myoclonus or jerks represent the third most common diagnosis, comprising about 15% of all patients with FMDs (Factor et al., 1995; Hinson et al., 2005; Lang, 2006; Shill and Gerber, 2006). FMD (including functional jerks) can manifest at all ages, but mostly in adulthood, with mean age of onset ranging between 37 and 50 years (Factor et al., 1995; Williams et al., 1995). Women are more often affected than men, with female-to-male ratios ranging from 57% to 90% for females, although the male-to-female ratio seems to differ in specific subcategories of functional neurologic symptoms (Stone et al., 2010). For instance, functional jerks affecting the trunk (axial jerks) seem to affect men more often than women (van der Salm et al., 2014). Finally, little is known about clinical course. There is a clinical notion that the course is unfavorable (Gelauff et al., 2014), but this might be due to ascertainment bias, since all nonremitting cases are referred to specialized movement disorder clinics and the majority of spontaneously remitting cases are not seen.

Clinical picture

Consistent clinical features have been identified with respect to disease history and physical examination in functional jerks (Table 21.1) (Monday and Jankovic, 1993; Williams et al., 1995). Illness history often reveals an abrupt onset of symptoms, frequently preceded by a (minor) physical event (e.g., injury) or psychologic stressor, and subsequent rapid deterioration to maximal symptom severity (Monday and Jankovic, 1993; Factor et al., 1995; Williams et al., 1995; Pareés et al., 2014). The disease course is variable, with some patients experiencing a static course while others reveal fluctuations with complete remissions and sudden relapses. Often patients tend to overestimate the severity of their symptoms (Pareés et al., 2012). Previous episodes of somatization might be mentioned when interviewing on disease history and are of additional support in the diagnosis, but do not have high specificity, since functional and organic movement disorders seem to occur more often simultaneously than expected by chance (Ranawaya et al., 1990; Onofrj et al., 2010; Pareés et al., 2013a).

Clinically, functional jerks come in all shapes and sizes and can manifest everywhere in the body with focal, multifocal, segmental, axial, and generalized presentations (Monday and Jankovic, 1993; van der Salm et al., 2014). The localization of the jerks is an important factor in the differential diagnosis with tics and myoclonus. As a general rule of thumb, we find that axial jerks are likely to represent functional jerks, facial and neck jerks point more often towards tics, while limb and generalized jerks are more likely to reflect myoclonus (see below). Jerks might be present continuously or episodically (Monday and Jankovic, 1993; Ganos et al., 2014; van der Salm et al., 2014).

Functional jerks can increase with attention and decrease or disappear with (mental or motor) distraction or when patients are unobserved (Gupta and Lang, 2009); this feature is not specific for functional jerks though, and can occur in other movement disorders as well. The examiner, when asking the patient to perform a specific rhythmic task, might induce adaptation of the patient's jerks to the imposed frequency, a phenomenon called entrainment.

Abnormal stimulus sensitivity can be observed in FMDs, e.g., exaggerated tendon reflexes or excessive startle reactions. Other clinical signs frequently co-occur with FMD, including unexplained loss of muscle strength, sensory loss that is unexplained by any

Table 21.1

Clues in illness history, clinical examination, and additional features of functional jerks, tics, myoclonus, and primary paroxysmal dyskinesias

	Functional jerk	Tic	Myoclonus	Paroxysmal Dyskinesias
Clues in history				
Childhood onset	–	+	+/–	+
Positive family history	–	+	+/–	+
Acute onset	+	–	–	–
Precipitating physical event	+	–/+	–	–
Waxing and waning	+/–	+	–	–
Course characteristics	Static	↓ Adolescence	Static	↓ Adulthood
Premonitory urge	+/–	+	–	+/–
Persistence during sleep	–	+	+/–	–
Clinical examination				
Inconsistent	+	+/–	–	–
Rhythmic	+/–	–	+/–	–
Typical localization	Axial	Head/neck	Focal/segmental/axial/ generalized	Unilaterally
Entrainment	+	–	–	–
Temporal suppression	+/–	+	–	–
Suggestibility	+	+	–	–
Stimulus–sensitivity	+	–	+	+/–
Additional features				
Comorbid functional symptoms	+	–	–	+
Response medication	–	Antipsychotics	Benzodiazepines	Carbamazepine
Drastic response placebo	+	–	–	–
Psychopathology	+	+	+/–	–
Bereitschaftspotential	+	+/–	–	–

somatotopic organization, and pain (Monday and Jankovic, 1993; Gupta and Lang, 2009). Further supportive clues include marked response to placebo or suggestion, although, again, this is also observed in other movement disorders (Monday and Jankovic, 1993; Williams et al., 1995).

Since the frequency of functional jerks might vary and the nature of symptoms could be paroxysmal, it can be difficult to collect clues supportive of functional jerks during neurologic examination alone. Additional neurophysiologic testing, including a polymyographic electromyogram (EMG) and (if possible) electroencephalogram (EEG)-EMG with jerk-locked backaveraging in order to demonstrate a Bereitschaftspotential (BP) preceding the jerks, might be of particular use (Shibasaki and Hallett, 2006; van der Salm et al., 2012). This will be elaborated below.

Tics in the scope of Tourette's disorder

Epidemiology

The epidemiology of tics, i.e., movements seen in Tourette's syndrome and related disorders (denoted hereafter as "tics"), is well known: tics originate in most cases in childhood, with a mean age of onset of 5 years and male preponderance (male-to-female ratio 3:1) (Cath et al., 2011). This is in contrast with functional jerks, which usually start in adulthood (Monday and Jankovic, 1993; van der Salm et al., 2014). Tics are common in children, with prevalence estimates between 6% and 12%, but there is a sharp decline during adolescence in intensity and frequency of tics associated with maturation of the frontal lobes in adolescence (Singer, 2011). In sum, the prevalence (lifetime) of full-blown Tourette's syndrome ranges between 0.3% and 1%, depending on age of the study sample and rigor of sampling method used (Robertson et al., 2009). In contrast, functional jerks have unknown prevalence rates but are considered to be less common, and rare in children (Ferrara and Jankovic, 2008; Canavese et al., 2012). Most tics in adults do not cause much disability or the need to visit a physician. In contrast, functional jerks tend to increase in frequency in adults, causing distress and disability. Of note, tics in combination with functional tic-like jerks co-occur more often than expected by chance, and form a considerable diagnostic challenge for the treating physician (Barry et al., 2011). Patients with both functional jerks and tics are likely to be seen at movement disorder clinics.

Clinical picture

Tics are defined as sudden, rapid, repetitive, nonrhythmic, inapposite, irresistible muscle movements (motor tics) or vocalizations (vocal tics), which can be classified as simple or complex (Cath et al., 2011; Singer, 2011). Diagnosis of a tic disorder is solely made based on clinical examination, and with the aid of the Diagnostic Confidence Index (Robertson et al., 1999) or Yale Global Tic severity scale (Leckman et al., 1989). The fourth and fifth DSM (DSM-IV and DSM-5: American Psychiatric Association, 2000, 2013) and the 10th International Classification of Disease (ICD-10: World Health Organization, 2010) formulated diagnostic criteria for tic disorders, with Tourette's disorder (requiring at least two motor and one vocal tic) at the most severe end of the spectrum. The specific differentiation of a functional jerk from a tic can be challenging because of their overlapping clinical features (van der Salm et al., 2012, 2014); however, we will discuss clues supporting one or the other diagnosis below (Table 21.1).

The disease course in both tics and functional jerks is generally waxing and waning (Monday and Jankovic, 1993; Cath et al., 2011). Functional jerks often have abrupt onset and are precipitated by a physical event; this is not typical for tics (Tijssen et al., 1999; Cath et al., 2011).

Phenomenologically, motor tics are either simple – eye blinking, grimacing, nose/mouth twitches, and neck/shoulder jerks – or complex, portraying a sequence of movements, difficult to discern from more goal-directed compulsive movements (Fibbe et al., 2011). In general, motor tics are more stereotyped and less variable compared to functional jerks. Further, patients with tics sometimes tend to camouflage the movement by assimilating it into a purposeful movement, whereas patients with functional jerks are not inclined or able to hide their movements (Anderson et al., 2007; Cath et al., 2011; Pareés et al., 2013b).

Another important clinical feature of tics entails their localization: tics tend to develop following a rostrocaudal spread, usually starting in the face, with the face, neck, and shoulder region being mostly affected, as opposed to functional jerks that, except for axial jerks, lack a preferential localization (Monday and Jankovic, 1993; Cath et al., 2011; van der Salm et al., 2012, 2014).

Most patients with functional jerks are unable to voluntarily suppress symptoms, whereas patients with tics can usually suppress their tics for short periods of time. In adults, tics are usually experienced as intentional, self-directed movements performed in order to relieve inner tension, whereas functional jerks are characterized by their involuntary nature and lack of agency (Voon et al., 2010; Cath et al., 2011). As with functional jerks, tics might worsen due to emotional stress or fatigue but also with relaxation or excitement (e.g., while watching television). Decrease in intensity of functional jerks during a distracting arithmetic task supports the diagnosis. However, this can be seen in tic disorders as well (Cath et al., 2011).

Many adult patients (over 90%) experience a premonitory urge preceding the tic, which is often relieved by carrying out the tic (Cath et al., 2011). Although these premonitory urges have also been described in functional jerks (van der Salm et al., 2010, 2014), they are believed to be much less common. Moreover, tics are in up to 20% of cases accompanied by echophenomena such as echolalia and echopraxia (repetition of sounds or actions), and coprolalia (involuntary swearing). Echophenomena are usually not seen in functional jerks (Ganos et al., 2014).

To make things more complicated, "functional tics" have been described in a small group of patients (Baizabal-Carvallo and Jankovic, 2014; Demartini et al., 2015). Estimated to account for 2% of FMDs, functional tics are among the rarest phenomenologic expressions of FMD (Lang, 2006). The exact definition of a functional tic and its clinical differentiation from a functional jerk is not well established, and the diagnosis is solely based on illness history and assessment by movement disorder specialists. Typical tic features, such as premonitory sensations preceding the tic, childhood onset, rostrocaudal distribution, suppressibility, and positive family history, are lacking in functional tics. Moreover, there may be features in concordance with a functional origin, such as the inability to suppress the tic, striking disruption of normal movement – a.k.a. "blocking tics" – and the presence of other comorbid FMDs (Baizabel-Carvallo and Jankovic, 2014; Demartini et al., 2015). Finally, as described here above, the combination of tics and (tic-like) FMD seems to co-occur more often than expected when these disorders would be unrelated (Barry et al., 2011). To summarize, considering the scarceness of the occurrence of "pure" functional tics, this option is that this functional tic subtype is not considered as an independent phenotype but as an alternative expression of functional jerks, or as a phenomenon co-occurring with actual tics.

In terms of treatment and prognosis, tics and functional jerks differ. Outcome with respect to physical and psychologic disability is on average poorer in FMD (Gelauff et al., 2014) than in tics, since in the latter group a substantial proportion of patients (those with predominantly simple tics that have decreased in intensity during adolescence) has actually an excellent long-term prognosis (Cath and Ludolph, 2012). Prognosis of treatment in tics is favorable, both for behavior therapy (either habit reversal or exposure to premonitory urges with response prevention) (van de Griendt et al., 2013), with medium to large effect sizes (McGuire et al., 2013), as

well as medication (dopamine D2-receptor antagonists), with small to medium effect sizes (Weisman et al., 2013). In our experience functional jerks usually do not react as well to behavior therapy, although evidence to support this statement is lacking.

Myoclonus

Epidemiology

Due to the very heterogeneous etiology of myoclonus, epidemiologic data are scarce. Myoclonus has a lifetime prevalence of 8.6 cases per 100 000 persons (Caviness et al., 1999). However, transient forms of myoclonus (e.g., drug-induced) are not included in these numbers (Yoon et al., 2008). In general, causes of myoclonus include physiologic, posthypoxic, toxic-metabolic, drug-induced, epileptic, neurodegenerative, and hereditary forms (for extensive overview, see Fahn, 2002; Dijk and Tijssen, 2010).

Clinical picture

Organic myoclonus (denoted hereafter as myoclonus) has to be considered in the differential diagnosis of functional jerks. The definition of a myoclonus is a brief, sudden, shock-like involuntary movement as the result of a muscle contraction (positive myoclonus) or the short interruption of tonic muscle activity (negative myoclonus) (Fahn et al., 1986).

To differentiate myoclonus from functional jerks, symptom onset provides a clue; myoclonus has an insidious symptom onset, whereas functional jerks often commence abruptly, possibly precipitated by a physical event (Table 21.1) (Factor et al., 1995; Williams et al., 1995; Dijk and Tijssen, 2010; Pareés et al., 2014). The disease course of myoclonus depends on its etiology. Generally, disease course is progressive (Dijk and Tijssen, 2010). This is in contrast with the course in functional jerks, where spontaneous remissions and abrupt re-emergence of symptoms are not uncommon (Monday and Jankovic, 1993). An exception with respect to progressiveness of disease course in myoclonus is formed by the metabolic and toxically induced forms of myoclonus. A positive family history in the hereditary forms of myoclonus (e.g., myoclonus-dystonia or hyperekplexia) is a strong positive clue.

At neurologic examination, myoclonus is usually a simple movement with a fixed pattern, lacking signs of distractibility or suggestibility (Dijk and Tijssen, 2010). This is in contrast with functional jerks, where complex movements, pattern variability, suggestibility, and alteration or decrease of symptoms with distraction are key features (Monday and Jankovic, 1993). In tics, distractibility and suppressibility play a substantial role, in contrast to myoclonus. Further, myoclonus does not show entrainment (adaptation of jerks to imposed rhythm), whereas entrainment (if present) is a very strong, almost pathognomonic feature of functional jerks. Both syndromes often reveal arrhythmic jerks, although there are some rare forms of myoclonus, e.g., segmental myoclonus (see below), revealing rhythmicity (Esposito et al., 2009).

Stimulus sensitivity, as well as triggering of symptoms by startling stimuli (visual, tactile, auditory), is seen in myoclonus and functional jerks. In myoclonus stimulus sensitivity is usually located in the limbs, whilst in functional jerks tactile stimulation of the trunk or testing of the tendon reflexes elicits the movements (Thompson et al., 1992; Williams et al., 1995; van der Salm et al., 2014). Further, premonitory urges form a clue: in functional jerks, sensations prior to the movement might be felt, whereas in myoclonus, premonitory urge is not a feature (van der Salm et al., 2010).

Functional jerks can manifest at different localizations and this strongly influences the approach and differential diagnosis of the jerks. The localization of the myoclonus – focal, segmental, axial, or generalized – strongly depends on the anatomic origin of the myoclonus and therefore, we will discuss the different forms of myoclonus shortly below with their differentiation from functional jerk.

Cortical myoclonus

When jerks manifest differentially in the limbs and in the face, especially if present simultaneously in hand and face, myoclonus of cortical origin should be considered. Causes of cortical myoclonus include posthypoxic, epileptic, and neurodegenerative diseases (Dijk and Tijssen, 2010). The jerks in cortical myoclonus are very brief and can be focal, multifocal, or generalized (Lozsadi, 2012). This is in contrast with functional jerks, which lack typical localization and have a longer burst duration (Brown and Thompson, 2001). Jerks in cortical myoclonus are stimulus-sensitive, e.g., myoclonus can often be triggered by movement, such as tapping the fingers (Dijk and Tijssen, 2010). Whereas functional jerks can be elicited by similar stimuli in some cases, they lack a typical stimulus-sensitive localization and show inconsistent patterns of movement.

With respect to treatment response, cortical myoclonus often responds well to levetiracetam or piracetam, although this is mainly based on expert opinion and small observational studies (class IV evidence) (Dijk and Tijssen, 2010).

Subcortical myoclonus

One of the most important forms of subcortical myoclonus is myoclonus-dystonia (DYT11), characterized by

jerks of the proximal or distal upper limbs and trunk accompanied by mild dystonia (Foncke et al., 2006). This syndrome is caused by a SGCE gene mutation in 50% of cases (Peall et al., 2014). The onset of symptoms in childhood, alcohol-responsiveness, and often positive family history seen in myoclonus-dystonia can help distinguish it from functional jerks, but is similar to onset of tics. The high rate of comorbid psychiatric disorders in patients with myoclonus-dystonia, including anxiety, depression, and obsessive-compulsive disorder (OCD), might wrongly be considered as suggestive of a functional origin, although this pattern of psychiatric comorbidity would be in line with tic and not FMDs (van Tricht et al., 2012). The abundance of psychiatric comorbidity in myoclonus-dystonia might put the clinician on the wrong track of an FMD (Peall et al., 2015).

Brainstem myoclonus could be considered when generalized, synchronous, axially located myoclonus is seen (Dreissen and Tijssen, 2012). This form of myoclonus can be acquired, usually due to a cerebral hypoxic event, and is characterized by stimulus sensitivity over the limbs and elicitation by startling stimuli (Hallett, 2000; Beudel et al., 2014). A specific form of myoclonus originating in the caudal brainstem is hyperekplexia. This syndrome is caused by different gene mutations (e.g., GLRA1, Glyt2) engaged in the glycine neurotransmission pathway (Bakker et al., 2006; Davies et al., 2010; Dreissen et al., 2012).

Differentiation of hyperekplexia from functional startle-induced jerks can be helped by illness history evaluation: generalized (transient) stiffness at birth, and exaggerated nonhabituating startle reflexes followed by short-lasting generalized stiffness elicited by unexpected stimuli – both cardinal features in hyperekplexia. Further distinction between hyperekplexia and FMD can be made from neurophysiologic examination. As opposed to a physiologic startle response, seen in hyperekplexia, which is generated in the caudal brainstem and has a distinct recruitment pattern with short onset latencies ($<$100 ms), onset latencies of functional startle are generally $>$ 100 ms, compatible with voluntary mimicking of a startle reaction (Thompson et al., 1992). Although there is little formal evidence, hyperekplexia is thought to respond well to clonazepam (Tijssen et al., 1997b; Bakker et al., 2009a).

Spinal myoclonus

Spinal myoclonus can be divided into spinal segmental myoclonus and propriospinal myoclonus. Jerks of one limb can be regarded as a manifestation of (segmental) spinal myoclonus. Herein muscles innervated by one or two contiguous spinal segments are affected, often as a consequence of a spinal lesion. As opposed to functional jerks, spinal segmental myoclonus is continuous, often rhythmic, and persists during sleep.

Propriospinal myoclonus is of particular interest, since an important paradigm shift has recently taken place in the diagnosis of this disorder. The majority of cases of idiopathic propriospinal myoclonus have recently been determined to be of functional origin, either because a BP (see below) was found preceding the jerks or the clinical course was strongly suggestive of a functional origin (van der Salm et al., 2010; Erro et al., 2013). Further, it was shown that the typical recruitment pattern as seen in propriospinal myoclonus could be mimicked voluntarily (Kang and Sohn, 2006). Moreover, the pathophysiology of symptomatic propriospinal myoclonus is poorly understood and heavily debated, since the correspondence between imaging and the neurophysiologic findings was not clear in most cases (Esposito et al., 2014). Yet the label propriospinal myoclonus, suggesting an organic origin in the propriospinal pathways of the spinal cord, is still widely used; therefore the descriptive term (functional) axial jerks might be better suited.

Axial functional jerks often start abruptly during middle age, with men being slightly more often affected than women (van der Salm et al., 2014). Phenomenology includes nonrhythmic flexion jerks of the trunk, hips, and knees, mostly present when supine. In a substantial proportion of patients, jerks are multifocal, with involvement of the face and/or neck, lacking the classic propriospinal stereotyped pattern (Erro et al., 2014b; van der Salm et al., 2014).

Disease course is variable, including spontaneous remissions, relapses, and complete resolution of symptoms in a substantial part (22%) of patients (van der Salm et al., 2014). Moreover, jerks show a high degree of inconsistency and variability over time and might show distractibility. Tactile stimulation of the abdomen can elicit jerks and patients are able to voluntarily suppress jerks in some cases (van der Salm et al., 2014). Premonitory urge is reported by some patients, together with vocalizations, resembling tics. However, they differ in disease history, including age at onset (middle age), lack of family history, and waxing and waning disease course, which is typical for a tic origin.

Red flags to suspect a very rare diagnosis of (secondary) propriospinal myoclonus due to a structural lesion of the spinal cord are clinical signs indicating a myelopathy such as urinary urgency, gait problems, abnormal reflexes, and sensory changes of the thorax wall. If a functional disorder is not considered based on clinical signs combined with neurophysiologic tests (see below) and a myelopathy is excluded, the diagnosis of idiopathic propriospinal myoclonus (or rather, axial jerks) remains. This term should be reserved for patients without a BP or any other signs of a

functional cause (Shibasaki and Hallett, 2006; van der Salm et al., 2012).

Paroxysmal movement disorders

Epidemiology

Paroxysmal attacks of jerks sometimes elicited by triggers (e.g., loud noise) have been described as a specific entity together with other phenomenologies as functional paroxysmal movement disorders (FPMD) (Bressman et al., 1988; Fahn and Williams, 1988; Williams et al., 1995; Baik et al., 2009; Ganos et al., 2014). This distinction, however, might be arbitrary, since a paroxysmal nature and stimulus sensitivity in itself are typical characteristics of FMD.

Epidemiologic data on FPMD are scarce. In the largest case series, FPMD accounted for 10% of all patients referred with FMDs at a specialized movement disorder clinic (Ganos et al., 2014). The mean age at onset was 38.6 years, with a female predominance. FPMDs have also been reported in children (Bressman et al., 1988; Ferrara and Jankovic, 2008; Canavese et al., 2012), although caution is required, as potential non-FMDs may not have fully developed and one should be aware that organic movement disorders such as PxDs have sometimes been misdiagnosed as functional because of their bizarre and paroxysmal nature.

Differential diagnosis should include PxD, a rare, clinically heterogeneous group characterized by episodically occurring involuntary movements of brief duration (Bhatia, 2011; Erro et al., 2014a). They have been reported to account for 0.76% of all movement disorders and can either be inherited (largest group) or acquired (Blakeley and Jankovic, 2002). In this chapter we will only focus on inherited forms of PxDs, including paroxysmal kinesigenic dyskinesia, paroxysmal nonkinesigenic dyskinesia, and paroxysmal exercise-induced dyskinesia (Bhatia, 2001; Erro et al., 2014a). The primary PxDs all have their onset in the first or second decade of life and are caused by different gene mutations (PRRT-2 gene, MR-1 gene, GLUT-1 gene) (Erro et al., 2014a). PxDs can be differentiated from FPMDs based on a few features, which will be discussed below (Table 21.1).

Clinical picture

At clinical examination phenomenology can help distinguish between FPMD and PxD; attacks in FPMD include a broad range of involuntary movements, including dystonia, tremor, jerks, and complex movement disorders. FMPD symptoms often show great variability in symptom characteristics and attack duration, both between and within subjects (Ganos et al., 2014), in contrast to the PxD presentation with a consistent pattern of short-lasting attacks of dystonia, chorea, or ballism, or a mixture of these. For instance, tremor has never been described in primary PxD.

Usually FPMDs are not familial, in contrast to PxD. Coexistence, however, with organic movement disorders is described in a substantial proportion of patients (Ranawaya et al., 1990; Ganos et al., 2014).

Other features suggestive of a functional disorder are seen in FPMD as well, such as distractibility, entrainment, and aggravation during examination (Ganos et al., 2014). When symptoms manifest after age 20, this nearly always indicates a functional cause, since all forms of primary PxD manifest in the first two decades of life (Bhatia, 2011; Erro et al., 2014a). FPMDs, however, do occur in children, so age at onset is not always discriminating.

Precipitating physical or emotional events triggering symptoms have been reported in FPMD, including stress, but also loud noises, walking, and "feeling frightened" have been reported (Baik et al., 2009; Ganos et al., 2014). Not a trigger as such, but premonitory sensations or auras are reported in the majority of PxD patients and have been described as "butterflies in the stomach," "electricity in the head," or numbness or a tingling sensation in the limbs (fingers) (Bruno et al., 2004). Additionally, patients with FPMD might present with odd relieving maneuvers, such as focusing on the affected limb or exerting pressure on it. It is, however, not uncommon that functional and organic paroxysmal movement disorder co-occur, especially in the same or adjacent body part (Ranawaya et al., 1990; Ganos et al., 2014).

Further, the prognosis in FPMD is suggested to be favorable, in comparison with other FMDs, with strong responses not just to placebo and hypnotherapy but also physiotherapy and cognitive behavioral therapy. However, this is based on small sample sizes and low levels of evidence (Bressman et al., 1988; Baik et al., 2009; Ganos et al., 2014). The prognosis of PxD is static, disease is managed by avoiding triggers and treatment with anticonvulsive medication or ketogenic diet, and attacks tend to diminish with age.

If, despite clinical clues, there is still well-founded doubt, it can be helpful to perform video recordings to review the phenomenology and consistency of the attacks. Additionally, laboratory investigation, including genetic testing, can be performed (for further details, see Erro et al., 2014a).

Psychiatric comorbidity and psychopathology

Functional jerks

Psychiatric disturbances, traumatic life events, and their pathophysiologic meaning in FMD, and more

specifically in functional jerks, have not been thoroughly investigated. This topic will be covered in a separate chapter and, therefore, we will focus on the differences in psychiatric disturbances between functional jerks, tics, and myoclonus.

Differential diagnosis with tics and myoclonus based on psychiatric comorbidity

When trying to distinguish a functional jerk from a tic or organic myoclonus, assessment of comorbid psychiatric disorders could be of help. In tic disorders, the two most prevalent psychiatric comorbidities, OCD and attention-deficit hyperactivity disorder (ADHD) occur most frequently (Cath et al., 2011), apart from impulsive disorder, sleep problems, and anxiety and depression (Freeman et al., 2000). OCD or obsessive-compulsive behavior is reported in 20–89% of tic disorder cases (Singer, 2011), and ADHD in up to 60% of patients (Stewart et al., 2006). These high rates of ADHD and OCD are not seen in functional jerks and the presence of these disorders actually makes it more likely that the movement disorder is organic. Other psychiatric disorders in tic disorder are less distinctive and encompass, amongst others, anxiety, depression, and sleep disorder (Robertson, 2000; Freeman, 2007), of which specifically depressive disorders might well be the consequence of suffering from a debilitating health condition.

In organic myoclonus, one distinct form of hereditary myoclonus, myoclonus-dystonia (DYT 11) is specifically associated with psychiatric comorbidity, such as OCD, anxiety disorders, and alcohol dependence (Foncke et al., 2009; van Tricht et al., 2012; Peall et al., 2013, 2015). Depression is also more prevalent, but appears to be secondary rather than primary in patients with myoclonus-dystonia (van Tricht et al., 2012; Peall et al., 2014).

Thus, although there is some overlap in comorbidity patterns between tics and myoclonus-dystonia, the psychiatric profile of patients with functional jerks is quite different from both tics and myoclonus and might be of additional value in the diagnosis.

PATHOPHYSIOLOGY OF FUNCTIONAL JERKS

The fascinating and yet incomprehensible feature of FMD and of functional jerks in particular is the discrepancy between several features (entrainment, distractibility, suppressibility, suggestibility, presence of a BP) of the movements, suggesting at least some intentional control on the one hand, and the uncontrollable and involuntary perception by patients on the other hand. Unraveling this mystery would be the key to understanding the pathophysiology of this disorder. It has been hypothesized that a discrepancy between predicted and actual information processed by the brain plays a key role in this matter (Edwards et al., 2012). Some functional imaging studies concerning functional tremor have been performed in which the temporoparietal junction, an area associated with the comparison of actual information and what is internally expected, is suggested to play a key role (this topic is covered in further details in Chapters 7 and 11) (Voon et al., 2010). However, no imaging studies have been performed so far in functional jerks, and therefore future studies need to elucidate whether similar mechanisms play a role in the neurobiology of functional jerks.

THE NEUROPHYSIOLOGIC EXAMINATION

Additional electrophysiologic investigation can be of particular help in the diagnosis of functional jerky movements (for an overview, see Table 21.2).

Since it is easily performed and can be distinctive in the differential diagnosis between functional jerks, tics, and myoclonus, recording the jerks with surface EMG is advised as a first step in order to establish the burst duration of the jerk. Contractions of less than 75 ms are generally considered unlikely to be of functional origin (Thompson et al., 1992; Edwards and Bhatia, 2012). The jerks in cortical myoclonus are very brief (<50 ms) (Lozsadi, 2012). All other forms of jerks, including subcortical myoclonus, tics, and functional jerks, reveal a longer burst duration, therefore it is of less distinctive value in the differential diagnosis.

A more extensive EMG registration, polymyographic EMG, enables evaluation of the pattern of muscle activation during a movement. It may aid in mapping the different characteristics in support of a functional jerk, such as an inconsistent recruitment pattern, entrainment, distractibility and stimulus sensitivity (Apartis, 2014). It can be especially helpful in the diagnosis of axial jerks. Typical electrophysiologic characteristics of axial jerks of propriospinal origin include a fixed pattern of synchronous muscle activation starting at the spinal generator (without involvement of the face), spreading up and down the spinal cord with slow conduction velocity (5–15 m/s) and burst duration of < 1000 ms (Chokroverty et al., 1992). The sensitivity and specificity of these findings are unknown. One should keep in mind that this pattern can even be mimicked by healthy volunteers (Kang and Sohn, 2006; van der Salm et al., 2014). However, most patients with functional axial jerks do not show this pattern.

Polymyography can also be used to study the stimulus-sensitive startle reflex. In order to differentiate between different startle disorders, measuring the whole-body auditory startle reflex is of value (Bakker et al.,

Table 21.2

Clinical neurophysiologic test characteristics in support of different jerky movement disorders

Neurophysiologic test	Characteristics	In support of
Surface EMG	Burst duration < 75 ms	Cortical myoclonus
	Burst duration > 75 ms	Tic, subcortical myoclonus, functional jerk
Polymyography	Inconsistent recruitment pattern, entrainment, distractibility	Functional jerk
Startle reflex	Inconsistent recruitment pattern, long-onset latencies (>100 ms)	Functional jerk
C-reflex	Long-loop reflex with latency of 40–45 ms	Cortical or subcortical reflex myoclonus
EEG-EMG with backaveraging	Cortical spike (latency 10–40 ms)	Cortical myoclonus
	Bereitschaftspotential (latency 1000–2000 ms)	Functional jerk*
EEG-EMG coherence analysis	Significant coherence between EEG and EMG	Cortical myoclonus
SSEP	Giant SSEP	Cortical myoclonus

*Can also occur in a minority of tic cases with shorter onset latencies (500–1000 ms) (van der Salm et al., 2012).
EMG, electromyogram; EEG, electroencephalogram; SSEP, somatosensory evoked potential.

2009b). Here, a fixed rostrocaudal recruitment pattern with short onset latencies (<100 ms) and habituating responses with repeated stimuli can be measured. Functional startle jerks are assumed to be characterized by extended onset latencies (>100 ms) and a variable recruitment pattern. However, except for one older study by Thompson et al. (1992), the auditory startle response has not been assessed in a systematic fashion in functional jerks so far. In hereditary hyperekplexia the startle reflex shows enlarged startle responses with normal onset latencies (Tijssen et al., 1997a). Reticular (brainstem) myoclonus shows a somewhat similar pattern as the startle reflex except for shorter latencies in the deep hand muscles (Brown et al., 1991; Beudel et al., 2014).

To classify reflex myoclonus of cortical or subcortical origin one could also study the so-called long-loop reflexes or C-reflex. The C-reflex is a discharge of the EMG 40–45 ms after stimulation of the median nerve in the same limb. Its presence is associated with hyperexcitability of the sensorimotor cortex and is often seen in cortical reflex myoclonus (Brown and Thompson, 2001; Cassim and Houdayer, 2006). However, enhanced long-loop reflexes can also be found in reticular reflex myoclonus. Further onset latencies show great intraindividual variability. Here again, distinction from stimulus-induced functional jerks can be made based on longer onset latencies (>100 ms).

EEG-EMG co-registration with backaveraging of the EEGs time-locked to the onset of the jerk might reveal a BP, or pre-movement potential (Shibasaki and Hallett, 2006). The BP is a slow negative cortical potential, with maximal amplitude over the central areas (Cz) starting about 2000–1000 ms prior to the jerk (Fig. 21.1). It is associated with self-initiated movement (Shibasaki and Hallett, 2006; van der Salm et al., 2012). A BP is not found in subcortical myoclonus (van der Salm et al., 2012), and therefore EEG-EMG registration with jerk-locked backaveraging is a good option to differentiate between myoclonus and functional jerks. A drawback of this procedure is that it is a time-consuming and technically difficult procedure, requiring at least 40 jerks for a good-quality recording. Although clinicians hardly ever use the BP to differentiate between the various movement disorders, and BP is not a diagnostic test as such, it is a strong positive clue in support of a functional jerk. In a small study assessing the presence of a BP preceding

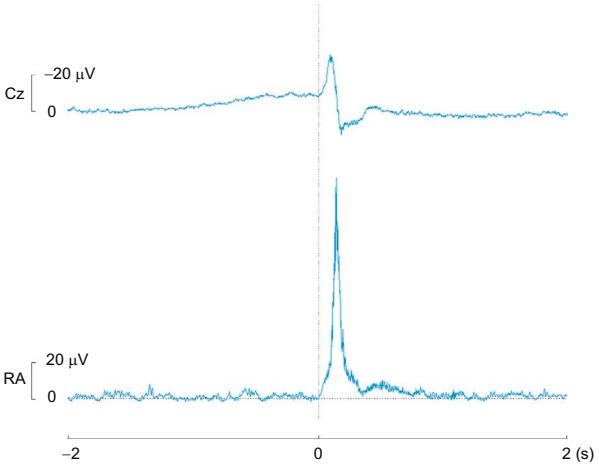

Fig. 21.1. Example of Bereitschaftspotential (BP) recording of a patient with axial jerks. The electromyogram was triggered at the onset of the rectus abdominis (RA) muscle. A premovement potential (BP) is seen starting about 1500 ms prior to the jerk, with maximal amplitude at the central cortical areas (Cz).

jerky movements, a BP was found in 25 of 29 patients with functional jerks, with a sensitivity and specificity of 0.86 (van der Salm et al., 2012). A BP was also found in a small proportion of patients with tics (6 of 14 patients), although it had a much shorter onset latency (500–1000 ms). These findings should be interpreted with caution, since a golden standard of functional jerks is lacking and clearcut criteria of a BP are absent.

In patients with cortical myoclonus, EEG-EMG back-averaging can also show a cortical correlate: a so-called cortical spike preceding myoclonus – with much shorter time delay (10–40 ms) than a BP (BP delay 1500–2000 ms) (Shibasaki and Hallett, 2005). Additional supportive electrophysiologic tests for cortical myoclonus include a giant somatosensory evoked potential, and with high frequent myoclonus, significant coherence between EEG-EMG can be found (Shibasaki and Hallett, 2005).

SUMMARY AND CONCLUSION

In this chapter we aimed to clarify different clinical jerky functional syndromes. Functional jerks show distinct positive clinical phenomena that we tried to highlight. Knowledge of the clinical and electrophysiologic characteristics of functional jerks, tics, myoclonus, and PxD helps to differentiate between the different types of jerks. In our opinion, FMDs and tic disorders represent movement disorders on the line between voluntary and involuntary movement. The exact etiologic relationship in this borderland between neurology and psychiatry needs to be further elucidated, i.e., does this comorbidity reflect one disorder being the consequence of the other, or shared multifactorial causes? Clinical neurophysiologic studies can be helpful in discriminating the different kind of jerks, although the sensitivity and specificity of these tests are largely lacking.

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