EDITOR'S CHOICE

Peripheral trauma and movement disorders: a systematic review of reported cases

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ABSTRACT

Objective To perform a systematic review of cases reported in the literature in which a peripheral trauma preceded the onset of a movement disorder (MD).

Methods Two reviewers independently searched Medline and EMBASE. Data regarding patient characteristics, type of MD and type of injury were collected, as well as information on the spread of MD, predisposing factors, psychological characteristics, presence of nerve lesions and treatment.

Results 133 publications presenting findings on 713 patients with peripherally induced movement disorders (PIMDs) were included. MDs were more frequent in women. The most commonly reported PIMD was fixed dystonia, which was often associated with pain and sensory abnormalities of the affected body part. In 26% of patients, a nerve injury was identified. More than one-third of patients had complex regional pain syndrome; these patients were younger, had a shorter interval before developing MDs and more often showed spread of MD to other body parts. Nearly 15% were diagnosed with a psychogenic movement disorder (PMD). PMD was associated with higher frequencies of fixed dystonia and tremor. In general, response to various treatments, including botulinum toxin administrations, was disappointing.

Conclusions While there is overlap in clinical characteristics between PIMDs and PMDs, the current review indicates that there are many well documented organic cases of PIMDs. This suggests that MDs, such as dystonia, tremor, myoclonus and tics, may under certain circumstances (eg, nerve lesions or genetic predisposition) be triggered by peripheral trauma. Potential mechanisms that may explain the underlying pathophysiology are addressed.

INTRODUCTION

Movement disorders (MDs) are a well recognised sequelae of brain injury secondary to head trauma[1] but MDs associated with peripheral injury have not been well characterised. The first reports of such cases date back to 1888 when Gowers described two patients with abnormal involuntary movements that followed a local injury of the neck and thumb.[2] Thereafter, this topic received little attention for almost a century. Over the last three decades, however, numerous reports on peripherally induced movement disorders (PIMDs) revived interest in this group of neurological disorders.[3] The phenomenology of PIMDs often overlaps with otherwise typical dystonia, tremor, myoclonus, tics and other hyperkinetic and hypokinetic MDs of central origin.[3–5]

To facilitate research in this area, diagnostic criteria for PIMDs were developed[5] and subsequently refined.[6] These criteria defined requirements with respect to the severity of the trauma, its anatomical relation to the site of the MD and to the interval between time of injury and onset of MD. The criteria stimulated further research, but the pathophysiological mechanisms underlying PIMDs remained poorly understood and the topic has been a subject of some controversy.[7–9] In order to explain the relatively rare occurrence of PIMDs compared with the frequency of peripheral injuries, it has been suggested that a peripheral trauma could trigger a PIMD in genetically or otherwise susceptible subjects with a pre-existent or subclinical MD.[5 9 10] Another view suggested a predominantly psychogenic origin of PIMDs.[11] The latter was based on several premises. Firstly, currently accepted theories on the pathogenesis of MDs have assumed a central origin of most MDs which could not be identified or supported in patients with PIMDs. Secondly, some characteristics related to onset, progression, phenotype and associated sensory problems in patients with PIMDs were different from those in patients with more typical MDs that arose without preceding peripheral trauma. Finally, some patients with PIMDs had coexistent psychological problems, a history of psychiatric disease or other clinical features that supported the 'psychogenic' basis of PIMDs.

One of the difficulties in studying PIMDs is their relative rarity, which impedes the application of epidemiological studies to this group of MDs. Cohort studies may not be appropriate if diseases are uncommon whereas case control studies are only applicable for identifying frequent risk factors. Another challenge is the heterogeneous nature of PIMDs and the lack of large, well characterised series. Against this background, we conducted a systematic review of the characteristics of published PIMD cases. Additionally, mechanisms underpinning potential causality of peripheral trauma in the development of MDs are discussed.

METHODS

Search strategy

A literature search was performed in Medline and EMBASE in order to identify potentially relevant studies. The search strategy was designed together with a specialist in information retrieval methods of the Leiden University Medical Centre library, and comprised a combination of controlled vocabulary (MeSH terms) as well as free text terms related to peripheral injuries combined with (types of)

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movement disorders (see supplement 1, figure 1, available online only). The results were limited to articles in English, German and Dutch. The most recent search was performed on 31 December 2009.

Selection criteria

The eligibility of the reports, as identified by the search strategy, was independently assessed by two authors (DvR, EG). This assessment was not blind with respect to authors or institution. The identified studies were first screened by title and abstract, after which the full text of potential relevant articles was studied. Reports were only included if the onset of the MD was preceded by a peripheral trauma. We defined peripheral trauma as a tissue or peripheral nerve injury (NI) evoked by an external physical stimulus (ie, mechanical, electrical, thermal or radiation). The MDs were required to have an onset at or in close proximity to the anatomical site of the precipitating trauma.[5 6] We set no limits on the severity of the injury because it is known that even mild trauma may evoke an MD, or on the duration of the interval between injury and onset of the MD because theoretical background for any cut-off is lacking.[12] Patients with hemifacial spasm, an MD with an accepted peripheral causative origin, were excluded. Additionally, in order to rule out the possibility of CNS pathology as a cause of MDs, cases with head trauma or spinal cord injury were excluded. Other exclusion criteria were primary dystonia (including task related dystonia) and prior neuroleptic use. Additionally, reference lists of all included publications as well as reviews on this topic were tracked following the same review procedure as described above. Discrepancies between the reviewers were resolved by a consensus agreement.

Data extraction

Data regarding patient characteristics, type of MD, type of trauma preceding the onset of the MD, potential spread of the MD, potential predisposing (psychogenic and non-psychogenic) factors, psychological characteristics, other signs and symptoms (eg, sensory and autonomic changes), nerve lesions and treatment was extracted using a standard form. Neurophysiological evidence indicative of peripheral nerve lesions included: slow nerve conduction, fasciculations, sharp waves and fibrillations. In addition, nerve specific deficits on examination, as well as nerve compression revealed by imaging studies or detected during surgery, were considered as NI.

No quality assessment for each report was performed since, to the best of our knowledge, no appropriate scales exist for this type of research.

Statistical analysis

Standard descriptive statistics were calculated using SPSS (V.17.0)—that is, means or medians (as appropriate) and percentages. For studies in which only group means were described for certain characteristics, weighted means (with the number of involved patients used as weight) were calculated and used for further analysis. Differences between groups were assessed with Mann–Whitney U tests and χ^2 tests. A p value <0.05 was considered statistically significant.

RESULTS

Preceding events and patient characteristics

A total of 47 full reports and 86 case reports met the criteria for inclusion (see supplement 1, figure 2; and supplement 2, available online only). Together, these reports included data from 713 PIMD cases. Most MDs occurred after soft tissue injuries (43%), followed by fractures (10%) and surgery (10%) (table 1). Median age of the cases was 38 years (IQR 30–53) and the majority involved women (64%).

Table 1 Peripherally induced movement disorder characteristics

Total No of patients (% females)	713 (64)
Age at onset of movement disorder (years) (median (IQR)) (n=571)	38 (30–53)
No of patients with CRPS	260 (36)
No of patients with PMD	103 (14)
Trauma (n (%))	
Soft tissue injury	310 (43)
Fracture	71 (10)
Surgery	74 (10)
Other	87 (12)
Nerve entrapment	130 (18)
Amputation	12 (2)
Not described	29 (4)
Time to onset of movement disorder (days) (median (IQR)) (n=264)	21 (2–183)
Type of movement disorder (n (%))	
Dystonia	513 (72)
Type of dystonia	
Fixed (% of dystonia cases)	317 (62)
Mobile	102 (20)
Both	56 (11)
Not specified	38 (8)
Sensory trick	
Yes/no	29/110
Tremor	176 (25)
Myoclonus	95 (13)
Spasms	79 (11)
PLMT/F	46 (6)
Other (chorea, parkinsonism, tics)	26 (4)
Location (n (%))	
Face	1 (0)
Oromandibular/vocal cords	44 (6)
Neck/shoulder	176 (25)
Trunk	14 (2)
Arm	162 (23)
Leg	177 (25)
Unknown extremity	125 (18)
Multiple sites	14 (2)
Spread of movement disorder to other body regions (n (%))* (n=138)	
Ipsilateral	15 (11)
Contralateral	16 (12)
Segmental	14 (10)
Generalised	35 (25)
Multifocal	51 (37)
Unknown	7 (5)

n, indicates the number of patients on which this information was available; (%) refers to the whole group unless otherwise specified.
*Percentage calculated for the number of patients on which the information was available.
CRPS, complex regional pain syndrome; PLMT/F, painful limbs and moving toes or fingers; PMD, psychogenic movement disorder.

Movement disorders and locations

The most frequently reported MD was dystonia (72%). In cases where the type of dystonia was not specifically labelled (94%), we categorised the type of dystonia as 'mobile' if dystonic movements were reported (20%) and 'fixed' if the MD was described as a 'fixed', 'tonic' or 'dystonic' posture (62%). The remainder had either a mixed type (11%) or the type of dystonia was not specified (8%). The presence or absence of sensory tricks was described in 27% of all dystonia patients and were effective in 6% (5% (4/80) of patients with fixed vs 33% (14/42) of patients with mobile dystonia). Other reported MDs were

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tremor (25%), myoclonus (13%), spasms (11%) and painful limbs moving toes or fingers (6%) while another 4% had parkinsonism, chorea and tics (table 1). The total number of MDs exceeded 100% because of the coexistence of different MDs in some patients (160 cases, two MDs; 62 cases, three MDs).

In 66% of the cases the MD started in a limb, in 25% in the neck and shoulder region, in 2% in the truncal region and in 6% in the oromandibular region. In 2%, the MDs started simultaneously in multiple regions. Spreading of MD from the original site to other body parts was described in 19% of all cases.

Time interval

The interval between peripheral trauma and onset of MDs showed a large variability across studies, with most studies (95%) reporting latencies of less than 1 year. Median time interval was 21 days (IQR 2–183 days). In 29 cases (4%), the reported interval was more than 1 year; the clinical characteristics of these cases did not differ from the cases that developed the PIMD within 1 year.

Nerve injury

Overall, 182 patients (26%) showed evidence of an NI (table 2) which was demonstrated by neurophysiological examination (7%), imaging studies (2%), neurological examination (3%) or revealed by an operation (3%). In another 10% of patients, the presence of nerve injury was reported although the means by which this was established was not specified.

Pain and other sensory disturbances

Pain was reported in the majority of patients (86%) and preceded the onset of MD in 19% of cases. Sensory impairments of the affected body parts were noted in 42% of all patients. Positive (ie, hyperalgesia, allodynia) and negative (ie, hypoalgesia, hypoesthesia) sensory symptoms were equally distributed. Complex regional pain syndrome (CRPS) was diagnosed in 36% of patients and their characteristics were compared with those of non-CRPS patients (see supplement 3, table 4, available online only). Only 8% of the CRPS patients had an NI (CRPS type II) compared with 36% in the non-CRPS group. The proportion of females was higher in CRPS patients than in non-CRPS patients (80% vs 55%). CRPS and non-CRPS patients differed on types of trauma and locations of the MD. Dystonia was the most frequently reported MD in both groups and was almost always of a fixed type in CRPS patients (91%) while a more equal distribution of fixed and mobile type was found in non-CRPS patients. Spread of MDs was more frequently reported for CRPS patients compared with non-CRPS patients (34% vs 11%).

Psychogenic movement disorders

Fourteen percent of the patients were diagnosed with a psychogenic movement disorder (PMD). The other 86% (n=610) of PIMD cases were considered non-psychogenic, either because the original authors explicitly stated this or because potential psychogenic causes were not discussed. In 59% of the PMD patients the diagnostic criteria for documented or clinical established PMD were fulfilled. The most common psychiatric diagnosis was a somatisation disorder (7%) or conversion disorder (18%), while in 18% a psychiatric assessment could not establish a diagnosis. Other features that were frequently documented in this group were abrupt onset (47%), inconsistency over time (12%), multiple somatisations (12%), false neurological signs (31%) and distractibility (28%).

Cases with and without PMDs are compared in table 3. In cases without PMD, psychological features were described in 30% of all cases but only formally evaluated by a psychologist or psychiatrist in 9%. Twenty-seven of these patients (4%) showed symptoms of depression and anxiety associated with onset of the MD while two patients had a medical history of anxiety or psychosis. Patients with PMD more often had fixed dystonia (90% vs 58%) and tremor (38% vs 22%), and less often mobile dystonia (6% vs 22%), myoclonus (6% vs 15%), painful limbs and moving toes or fingers (0% vs 7%) or miscellaneous MDs (10% vs 3%). There were differences between PMD and non-PMD cases in the distribution of affected body regions and eliciting events. Patients with PMD were also more involved in lawsuits or received worker's compensation (notably, information on these topics was more often available for PMD patients, 63% vs 22%).

Table 2 Additional information on peripherally induced movement disorders

Nerve lesion identified by (n (%))* (n=182)	
Electrophysiology	50 (27)
Imaging	17 (9)
Neurological examination	21 (12)
Operation	24 (13)
Unspecified	70 (38)
Pain (n (%))* (n=568)	
Before start of movement disorder	132 (23)
Simultaneous with start of movement disorder	225 (40)
Present, but time unknown	186 (33)
Not present	25 (4)
Sensory signs (n (%))* (n=301)	
Hypo (hypalgesia)	94 (31)
Hyper (allodynia, hyperalgesia)	83 (28)
Both	45 (15)
Altered sensation, type deficit not described	79 (26)
Psychological aspects (n (%))* (n=258)	
Present	84 (33)
Not present	174 (67)
Litigation (n (%))* (n=200)	
Involved in litigation/worker's compensation	66 (33)
Not involved in litigation	134 (67)
Treatment with BoNT (n (%))* (n=133)	
Successful	26 (20)
Partly successful	75 (56)
Passive successful	3 (2)
Unsuccessful	29 (22)
Predisposing factors (n (%))* (n=265)	
Family history of similar movement disorder	15 (6)
Family history of other movement disorder	6 (2)
Drug abuse	1 (0)
Premature birth	1 (0)
Developmental delay	1 (0)
Other	27 (10)
No predisposing factors	214 (81)

n, number of patients on which this information was available; (%) refers to whole group unless otherwise specified.
*Percentage calculated for the number of patients on which the information was available.
BoNT, botulinum toxin.

Predisposing factors

Potential predisposing factors of MDs were addressed in 265 cases and identified in 51 (19%). A family history of an MD, similar to the one that occurred in the index case (although not peripherally induced or in the same region), was described in 15 patients. In 27 cases it was not possible to exclude other factors that may have contributed to the onset of the PIMDs (eg, HIV, previous peripheral trauma or radiotherapy). In two cases, more than two predisposing factors were reported.

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Table 3 Characteristics of patients with and without psychogenic movement disorder*

	PMD	Without PMD	p Value
Total No of patients (n (% females))	103 (61)	610 (64)	0.59
Age at onset (years) (median (IQR))	37 (28–47) n=102	39 (31–54) n=469	0.03
No of patients with CRPS (%)	10 (10)	250 (41)	<0.001
Trauma (n (%))			<0.001§
Soft tissue injury	45 (44)	265 (43)	
Fracture	5 (5)	66 (11)	
Surgery	14 (14)	60 (10)	
Amputation	1 (1)	11 (2)	
Nerve entrapment	1 (1)	129 (21)	
Other	37 (36)	50 (8)	
Not described		29 (5)	
Time to onset (days) (median (IQR))	14 (7–61)	21 (2–183)	0.54
Type of movement disorder (n (%))			
Dystonia	67 (65)	446 (73)	0.09§
Type of dystonia (% of dystonia cases)			
Fixed	60 (90)	257 (58)	<0.001
Mobile	4 (6)	98 (22)	
Both	1 (1)	55 (12)	
Unknown	2 (3)	36 (8)	
Tremor	39 (38)	137 (22)	<0.001
Myoclonus	6 (6)	89 (15)	0.015
Spasms	15 (15)	64 (10)	0.22
PLMT/F	–	42 (7)	<0.001
Other (chorea, parkinsonism, tics)	10 (10)	16 (3)	<0.001
Spread of movement disorder to other body regions (n (%))	33 (32)	118 (19)	0.004
Location (n (%))			<0.001§
Face	–	1 (0)	
Oromandibular/vocal cords	–	44 (7)	
Neck/shoulder	20 (19)	156 (26)	
Trunk	–	14 (2)	
Arm	40 (39)	122 (20)	
Leg	34 (33)	143 (23)	
Extremity not specified	–	125 (21)	
Multiple sites	9 (9)	5 (1)	
PMD criteria† (n (%))‡			
Documented/clinically established	61 (76)	–	
Probable/possible	16 (20)	–	
Not fulfilled	3 (4)	–	
Psychiatric diagnosis† (n (%))‡			
Conversion/somatisation disorder	26 (35)	–	
Multiple diagnoses	7 (9)	–	
Malingering	2 (3)	–	
Other	20 (27)	10 (5)	
No psychiatric diagnosis established	19 (26)	54 (29)	
Clinical psychological features (eg, depression)	–	19 (10)	
No clinical psychological features	–	101 (59)	
Litigation/worker's compensation† (n (%))‡	39 (60)	27 (20)	<0.001
Nerve lesion† (n (%))‡	2 (50)	180 (68)	<0.001
Pain† (n (%))‡			
Present	50 (98)	493 (95)	<0.001

n, number of patients on which this information was available; (%) refers to whole group unless otherwise specified.
*Differences between groups should be interpreted with caution: if variables were not described it was assumed that these variables were not present. This could lead to distortion of the p values, especially in features reported in less than 50% of the cases (indicated by †).
‡Percentage calculated for the number of patients on which the information was available.
§p values indicate omnibus tests; p values without a symbol are comparisons of one variable.
CRPS, complex regional pain syndrome; PLMT/F, painful limbs and moving toes or fingers; PMD, psychogenic movement disorder.

Treatment

The applied treatments differed greatly across studies and included oral pharmacotherapy (anticholinergics, baclofen, benzodiazepines, levodopa), botulinum toxin (BoNT), physical therapy, deep brain stimulation and nerve decompression surgery. BoNT was the most frequently applied therapy (19%) but was found to be successful in only 20% of these cases (table 2). There were two reports describing single CRPS patients who underwent brain surgery. One patient with fixed dystonia was treated with thalamic and pallidal deep brain

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stimulation without any improvement of the MD or pain. In the other patient, stereotaxic thalatomy abolished the muscle spasms and reduced the pain.

DISCUSSION

Clinical features

In this systematic review, we identified 133 studies that recorded information on 713 cases with PIMDs. Our findings show that both the nature and severity of a peripheral trauma preceding the onset of an MD may vary considerably. In almost half of the patients, the occurrence of an MD was preceded by soft tissue trauma, but in other cases, various types of trauma, such as surgery, were reported. The median time interval between peripheral trauma and the onset of MD was 21 days. In order to explain the obvious discrepancy between high frequency of peripheral trauma and very low occurrence of PIMDs, it has been suggested that genetic susceptibility and other predisposing factors may play a role.[5 13] In one series, peripheral trauma played a role in idiopathic torsion dystonia in 16% of the cases.[10] In a case control study, neck or trunk trauma was found to be associated with an increased risk of developing cervical dystonia while ocular diseases increased the risk of developing blepharospasm.[14] In most cases of dystonia, such as writer's cramp[15] and DYT1 dystonia,[16–18] however, no prior peripheral trauma had been documented. In contrast, trauma is commonly reported prior to the onset of DYT12 dystonia, also known as rapid onset dystonia parkinsonism.[19] Although a confounding influence of recall bias cannot be completely ruled out in some of the reported cases of PIMDs, our thorough review of the literature suggests that peripheral trauma indeed may play a role in triggering the onset of an MD or in exacerbating pre-existing idiopathic or genetic dystonias.

Dystonia was the most frequent PIMD encountered in this review, with fixed dystonia being more common than mobile dystonia. Although peripherally induced dystonia may be phenomenologically indistinguishable from idiopathic dystonia, the former is more commonly manifested by fixed dystonia.[13] More than one-third of patients with PIMDs were also diagnosed with CRPS. Compared with dystonia patients without CRPS, those with associated CRPS were usually women, younger at onset and more often showed a spread of symptoms. Only 8% of patients with CRPS had an identified NI and, by definition, thus actually suffered CRPS type II. When fixed dystonia is associated with CRPS it generally has a poor prognosis.[20] In the absence of a clear and generally accepted pathophysiological or anatomical substrate for a disease, non-organic explanations, including psychological causes, are often advanced as potential mechanisms.[11] The criteria for diagnosing PMD were first described by Fahn and Williams (1988) and classified as documented, clinically established, probable and possible PMD. The distinction between PIMDs and PMDs is complicated as about a third of PMDs are also preceded by a physical injury.[21] Furthermore, a psychiatric diagnosis is absent in one-third of cases with PMD, and PMDs may have a similar phenotype as PIMDs.[11 22] This especially holds for fixed dystonia,[23] a finding that is confirmed by the results of this review. Pending litigation or secondary gain has been found to be associated with PMDs although there is no evidence that the outcome of litigation influences the prognosis of the MD.[6 24] The results show that PMD patients were more involved in lawsuits and worker's compensation than patients without this diagnosis. However, it is difficult to draw firm conclusions from comparisons between PMDs and non-PMDs as the description of features may largely depend on the researcher's perspective.

Research on the topic of PIMDs is also hampered by the lack of objective physiological or other markers that can reliably discriminate between MDs of organic and psychogenic origin.[25] Nuclear imaging and neurophysiological investigations may be helpful in detecting psychogenic parkinsonism, tremor and myoclonus.[26–28] Transcranial magnetic stimulation was used to evaluate patients with organic and psychogenic dystonia.[26] This method showed similar short interval cortical inhibition in patients with organic and fixed dystonia[29] and in patients with organic and psychogenic dystonia.[30] However, patients with organic dystonia exhibited abnormal motor cortical plasticity measured by a paired associative stimulation protocol compared with patients with psychogenic dystonia.[31] Notably, there is still some debate regarding the methodology and the interpretation of the results emerging from this paradigm.[32 33]

Possible pathogenesis of PIMDs

Studies of the pathophysiology of hemifacial spasm have generated hypotheses for the mechanisms of other PIMDs. Vascular compression of the facial nerve at its root exit zone from the brainstem is demonstrated in most cases, and microvascular decompression is usually effective in relieving this MD.[34] A few cases of torticollis associated with neurovascular compression of the accessory nerve have been reported with remission of symptoms after decompression surgery. Further studies are needed to better understand the possible relationship between torticollis and this form of 'peripheral injury'.

Given the fact that PIMDs are usually preceded by peripheral tissue damage or NI (present in approximately 30% of all patients) and are commonly associated with pain (80%) and sensory abnormalities of the affected part of the body (37–50%), we postulate that the initial insult interferes with normal sensory processing, which eventually leads to spinal or supraspinal reorganisation.

There is a growing body of evidence from animal models that experimentally induced peripheral NI is associated with cell death of axotomised neurons as well as prominent manifestations of neuroplasticity, including reorganisation of afferent projections, involvement of glia cells[35] and changes in synaptic efficacy.[36] These latter changes have been studied mainly in the context of chronification of pain; little is known about their role in the development of MDs. Interestingly, a rat model of neuropathic pain showed clawed postures after lesions of the sciatic and tibial nerve. The prevalence of postural abnormalities that resemble dystonia in these rats correlated with the degree of nerve damage. However, contrary to the situation in humans, the majority of these postures disappeared within 2 weeks.[37]

Information on the presence or absence of NI was available in less than half of the patients in our review. One-third were diagnosed with CRPS type I and may have had pathology of the small diameter afferents, which goes unnoticed on clinical examination or standard electrophysiological testing.[38] However, the role of small diameter afferents in the pathogenesis of dystonia is uncertain as CRPS patients with and without dystonia show similar reduced cold and warmth detection thresholds.[39]

In CRPS, central sensitisation of spinal neurons underpins the occurrence of allodynia, chronification of pain and spread of pain hypersensitivity beyond the area of tissue damage.[36 40] Although research on central sensitisation has hitherto focused on sensory features, animal models show that this process may also influence spinally mediated motor behaviours such as enhancement

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of nociceptive withdrawal reflexes.[41] Furthermore, central sensitisation is associated with loss of inhibition along the neuraxis, as demonstrated in CRPS patients with dystonia.[42 43] Dystonia in CRPS patients may respond to the $GABA_B$ agonist baclofen, which enhances spinal GABAergic inhibition.[41 44] Baclofen specifically stimulates $GABA_B$ receptors, which inhibit sensory input on neurons of the spinal cord.

In primary dystonia, abnormalities of higher order sensory processes, including sensory temporal–spatial discrimination, multisensory integration and movement representation, are common and are assumed to be related to dysfunction of the basal ganglia cortico-striatal-thalamo-cortical motor circuits.[45] Cortical reorganisation may occur after changes in sensory input[36] where maladaptive changes may lead to the development of dystonia in susceptible individuals.[46] Collectively, the available evidence suggests that peripherally initiated conditions may change anatomical and functional connectivity of spinal and supraspinal sensorimotor circuits, which in turn may lead to chronification of pain, sensory impairments and abnormal centrally mediated motor responses.

Treatment of PIMDs

Responses to various treatment interventions are generally disappointing in PIMD patients. BoNT was the most commonly used treatment, administered in one-fifth of all patients. Contrary to the marked beneficial effect of BoNT in typical focal or segmental dystonia, application of this treatment in patients with PIMDs was found to be satisfactory in only 20%, which corroborates with previous observations.[47] The poor response to BoNT can be due to the fixed nature of dystonia, as the development of contractures may limit the usefulness of BoNT. Another explanation may lie in the fact that it is generally more difficult to obtain a satisfactory response in PIMD, as they mainly occur in (particularly distal) limbs, with often many muscles involved in the dystonic posturing. As these patients represent primary non-responders, immunoresistance due to blocking antibodies, detected in less than 2% of patients repeatedly treated with BoNT, is an unlikely explanation for the lack of response.[48]

There are several limitations of our review that must be acknowledged. Firstly, even though two authors independently searched the literature, potential relevant articles may have been missed. Secondly, as PIMD is a controversial issue, under-reporting may have occurred. Moreover, the quality of reported data differed considerably between studies, with some articles providing insufficient information on the characteristics of interest (or were not evaluated for all features) and the data are subject to recall bias. As prospective studies are very difficult to perform in this type of disorder, it is important that future studies report detailed information on all characteristics related to the MD, the results of additional neurophysiological examinations, psychological or psychiatric assessment, potential predisposing factors and the long term outcomes.

In conclusion, based on our review of more than 700 cases of PIMDs reported in 133 articles, we show that psychological factors may have played a role in a proportion of the patients. However, in a substantial number of patients in whom psychological features were not present or could not be identified, peripheral trauma indeed may have triggered a central process which underpins the subsequent onset of MDs. Objective tools are needed to improve sensitivity and specificity for the diagnosis of PMDs in order to optimise treatment strategies. We postulate that aberrant peripheral input, possibly in combination with genetic and other predispositions, leads to disturbed connectivity in spinal and supraspinal sensorimotor circuits associated with central reorganisation and subsequent development of MDs. The poor response to BoNT and other treatment modalities in patients with PIMD argues for future research to further explore the potential mechanisms of PIMD so that effective, pathogenesis targeted therapies can be eventually developed.

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