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ORIGINAL COMMUNICATION

Thalamic versus midbrain tremor; two distinct types of Holmes' Tremor: a review of 17 cases

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Abstract

Introduction Holmes Tremor (HT) is a unique and debilitating movement disorder. It usually results from lesions of the midbrain and its connection but can also result from posterior thalamic injury. Clinical examination can help lesion localization between these two areas. We studied the clinical features and their radiological correlations to distinguish midbrain HT (HT-m) from thalamic HT (HT-t).

Methods Retrospective review of 17 patients with a HT-type presentation was conducted. Tremor characteristics, associated clinical signs and radiological findings were studied.

Results Eleven patients had a myorythmic rest tremor, large amplitude proximal tremor with goal-directed worsening, with or without mild distal dystonic posturing, representing HT-m. Six patients had slow, large amplitude proximal tremors and distal choreathetoid movements, significant proximal/distal dystonic posturing, associated with proprioceptive sensory loss, representing HT-t. Haemorrhagic lesions were the predominant cause of HT-m; whereas, ischaemia was more commonly associated with HT-t.

Conclusion When assessing patients with HT, attentiveness to the presence of associated signs in the affected limb, such as a proprioceptive sensory deficits and additional movement disorders, can aid lesion localisation, which can have implications for management.

Keywords Holmes' Tremor · Thalamic tremor · Stroke

Introduction

More than a hundred years after the original description by Gordon Holmes, Holmes Tremor (HT) remains a unique, debilitating movement disorder with a poorly understood pathogenesis [1]. HT, as it is now known, is a syndrome of rest, postural and intention tremor usually emerging from low frequency (< 5 Hz) proximal and distal rhythmic muscle contractions [2]. Over the years, this syndrome has been described in association with multiple lesion locations, primarily midbrain/brain stem lesions but also thalamic and other more diffuse lesions [3–6]. Previous labels of this tremor were based on the presumed lesion location (i.e. midbrain, rubral, thalamic tremor) [3]. Although the original localization by Holmes was centred on the brain stem and its connections, advances in imaging had led clinicians to look at this in more detail and thalamic injury has also been linked to its causation [4, 5, 7].

On the other hand, thalamic infarction-associated movement disorders have been extensively studied and amongst these disorders, tremor is described [7–9]. Indeed, thalamic injury has been reported in the literature to cause a postural and kinetic tremor as well as Holmes' tremor, with a rest component, in addition to the postural and kinetic components [6–11].

Vascular injury is the most common cause of HT followed by head trauma [5]. The pathophysiology of HT is complex. It might arise from abnormalities of the nigrostriatal system, cerebellothalamic and dento-rubro-olivary

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connections [8, 12–14]. Recently, a circuit of eight specific brain regions (red nucleus, globus pallidus pars interna, ventral oralis posterior, pulvinar nuclei of the thalamus, ponto-medullary junction, cerebellar cortex and vermis in lobule VI, and cerebellar cortex in lobule X) has been proposed as the anatomical substrate involved in the pathophysiology of HT [4] However, the involvement of nigrostriatal pathways in the development of HT has not been confirmed [4, 15].

HT usually develops weeks to years after the injury and this delay might be explained by brain plasticity [14–16]. Furthermore, this tremor may be associated with hypertrophic olivary degeneration (HOD) with or without palatal tremor [12, 14].

The therapeutic response to various medications, including levodopa, is highly variable when used to treat HT [13]. HT responds to a degree to deep brain stimulation (DBS). Ventral intermediate (VIM), Globus Pallidus interna (Gpi), and Subthalamic nucleus (STN) being the most common targets [4, 15, 17]. The main focus of DBS treatment would be to suppress the tremor component rather than any other associated deficits. There are no studies to date that investigate the difference in treatment response when the lesion is located within the thalamus in comparison to the cases caused by a midbrain lesion.

We report a series of 17 patients referred to the Walton Centre NHS Foundation Trust, Liverpool UK, highlighting their clinical and radiological features. The aim being to help clinicians in differentiating between HT of midbrain origin and HT of thalamic origin. We believe that correct localisation has a significant implication in the management of patients, since the functional improvement of treating midbrain HT may be better than that of thalamic HT where the deficit is complicated with sensory deficits and the presence of additional movement disorders that are unlikely to improve with the treatment.

Methods

A retrospective study was conducted based on the medical records and neuroimaging findings from the outpatient movement disorders clinics at a Neurosciences Centre in Liverpool, UK in the period from 2011 to 2020. We included all the patients with a HT-type presentation. Patients with no available imaging data were excluded from the study. The clinical diagnosis of HT was accepted if it were in keeping with the Consensus Statement of the International Parkinson and Movement Disorder Society [2]. However, patients in whom an action tremor was predominant but in whom the rest component could not be excluded, because of associated involuntary movements in the hand, were also included.

All patients of the study had been examined by a movement disorder specialist; fifteen of the patients were examined and diagnosed by the senior neurologist SHA, one by MB and one by RJBE. However, all the neurologists amongst the authors agreed on the final diagnosis.

The abnormal movements were defined as follows: tremor as an involuntary, rhythmic, oscillatory movement; here termed myorhythmic if the movement was repetitive, slow 1–4 Hz and rhythmic but jerky; dystonia as a movement disorder characterised by sustained or intermittent muscle contractions causing abnormal, movements, postures, or both; choreo-athetosis as rapid (chorea) or slow (athetosis) involuntary movement of the fingers or toes (flexion–extension, adduction–abduction, writing, sometimes piano-playing movements) which are irregular, non-rhythmic and purposeless [9, 18].

In line with prior experience with Holmes' tremor in association with midbrain pathology and those with thalamic injury, the authors subdivided the patients' group into those with HT with brain stem signs including cranial nerve involvement and no joint position (JP) sense loss, clinically suggestive of a midbrain lesion, termed here HT-m and those that have a tremor in keeping with a posterior thalamic injury HT-t. HT-t was defined as a Holmes' tremor associated with other involuntary movements (dystonia, chorea, athetosis, and pseudoathetosis) as well as proprioceptive sensory loss in the same limb. In patients where the rest component of the tremor could not be excluded because of the complexity of the movement disorder, but a low frequency, large amplitude postural and kinetic tremor was present, the term HT-t was still used. We then asked three neuro radiologists, who were blinded to the clinical tremor diagnosis to report the images.

The following data were collected: sex, age at the time of presentation, neurological findings, and radiological features.

Results

Patients demography

17 patients with HT-type tremor were identified (7 men and 10 women). The average age at the time of diagnosis was 45 years, range (17–77); age at the time of brain injury was 42.6 years, range (8–68 years). The date of the brain insult could not be defined in 6 patients. The latency between the time of the CNS injury and the development of the movement disorder ranged between 8 weeks and 14 years (Table 1).

Table 1 The patients' clinical characteristics

Case no	Age	Latency (duration from insult to onset of tremor)	Aetiology and imaging findings	Description of abnormal movement	Power affected	Sensation affected	Other neurological findings	Clinical diagnosis	Good response to Levodopa
1	39 F	6 weeks	Posterior circulation infarction due to postpartum haemorrhage. Bilateral thalamic infarcts, right tegmentum and inferior collis and abnormal hyper-intense signal in both middle Cerebellar peduncles	Right sided myorythmic tremor at rest, on posture and further increased on movement. Left-sided cerebellar tremor	No	No	–	HT-m	Yes
2	17 F	3 weeks	Midbrain AVM affecting the right cerebral peduncle, substantia nigra and right red nucleus—extending into the left cerebral peduncle and involving the posterior aspect of the left red nucleus, where there is a small haemorrhagic cavity	Left hand myorythmic tremor at rest, worse on posture and on movement	Yes	No	Partial ptosis and ophthalmoplegia CNIII palsy on right	HT-m	Yes
3	77 F	2 months	A large transtentorial meningioma with mass effect on the left cerebellar hemisphere, left side of the medulla and pons, left middle and superior cerebellar peduncles	Left-sided myorythmic tremor at rest, on posture and on movement	No	No	–	HT-m	Yes
4	48 M	N/A	Left midbrain cavernoma affecting the left cerebral peduncle and medial left thalamus, extending into the subthalamic and left red nucleus	Right arm severe rest tremor which increases on posture and further on movement	No	No	–	HT-m	No

Table 1 (continued)

Case no	Age	Latency (duration from insult to onset of tremor)	Aetiology and imaging findings	Description of abnormal movement	Power affected	Sensation affected	Other neurological findings	Clinical diagnosis	Good response to Levodopa
5	27 M	25 months	Right midbrain AVM involving the right superior and both middle cerebellar peduncles, right superior colliculus and pons. Subsequent imaging shows olivary hypertrophic degeneration	Mild myorhythmia of L hand, postural tremor on both arms but worse on the left where the tremor also worsens on movement	No	No	Ataxic gait, no–no head tremor	HT-m	No
6	47 M	8 months	Bilateral superior cerebellar peduncle cavernomas; that on the right involves the right inferior colliculus, while that on the left involves the left tectum, left superior colliculus, left superior and middle cerebellar peduncles on the most recent imaging due to haemorrhage. Bilateral hypertrophic olivary degeneration	Right sided resting myorythmic tremor, mild postural tremor and worse on movement also an obvious cerebellar component bilaterally	No	No	Left CN VI/VII, cerebellar dysarthria	HT-m	No
7	54 M	7 months	RTA injury age 8. Evidence of old infarct in the left cerebellar hemisphere. The left middle cerebellar peduncle is atrophied when compared to its counterpart	Right sided myorhythmic irregular tremor of the right hand at rest persisted on posture more distally than proximally and increased on finger/nose movements abnormal dystonic posturing of the right hand	Yes—Mild hemiparesis on right	No	Moderate cognitive dysfunction, mild ataxia of gait	HT-m	No

Table 1 (continued)

Case no	Age	Latency (duration from insult to onset of tremor)	Aetiology and imaging findings	Description of abnormal movement	Power affected	Sensation affected	Other neurological findings	Clinical diagnosis	Good response to Levodopa
8	34 M	N/A	AVM involving midbrain and thalamus	Rest myorhythmic tremor. When the arm was lifted with the elbow extended; the distal component of the tremor remained but he also developed proximal large amplitude slow tremor. The tremor further enhanced on finger/nose movement	No	No	Parinaud's syndrome, deviated right eye. Visual acuity reduced markedly. Right optic disc atrophy	HT-m	No
9	49 F	UN	RTA at age 8. White matter signal abnormality in the right superior frontal gyrus, extending along the right corona radiata, right centrum semiovale and right caudate nucleus. There are smaller areas of signal abnormality in the right thalamus, particularly medially. SWI demonstrates microhaemorrhages in these regions. Appearances are in keeping with prior right thalamotomy	Jerky tremor of left arm at rest, the rhythmical involuntary movement increased on action and persisted on finger/nose movements	No	No	Mild cognitive dysfunction. Left CN III partial palsy, mild facial asymmetry	HT-m	No

Table 1 (continued)

Case no	Age	Latency (duration from insult to onset of tremor)	Aetiology and imaging findings	Description of abnormal movement	Power affected	Sensation affected	Other neurological findings	Clinical diagnosis	Good response to Levodopa
10	59 F	4 months	Right tectal AVM with haemorrhage. The AVM involves the posterior midbrain and right sup cerebellar peduncle, with bilateral hypertrophic olivary degeneration	Myorythmic tremor at rest spreading up the whole arm, persists on posture and further increased on movement	Yes—Lower limb 4+/5 power	No	Dysarthria, diplopia in all directions, 'no–no' head tremor, ataxia in all 4 limbs, left more than the right	HT-m	Yes
11	52 M	N/A	Normal MRI head scan presumed neurodegenerative genetic disorder	Right arm ataxia and left arm tremor at rest, increased on posture and on movement	No	No	Optic atrophy, saccadic abnormality in reduced initiation, cerebellar ataxia	HT-m	No
12	44 M	9 months	Hemosiderin deposition in the left midbrain (tegmentum, red nucleus, cerebral peduncle) and left superior cerebellar peduncle. There is also thalamic involvement on the left. Bilateral hypertrophic olivary degeneration is also present	Proximal postural tremor in the right arm which increased further on finger/nose movements, the tremor was present at rest but was not myorythmic, considerable dysmetria and incoordination. There was associated dystonic posturing as well	Yes—mild hemiparesis on right	Yes—significant joint position sense loss to the wrist on the right	Diplopia, increased tone on right arm	HT-m/HT-t	Yes

Table 1 (continued)

Case no	Age	Latency (duration from insult to onset of tremor)	Aetiology and imaging findings	Description of abnormal movement	Power affected	Sensation affected	Other neurological findings	Clinical diagnosis	Good response to Levodopa
13	62 M	15 years	Extensive encephalomalacia of the right frontal and temporal lobes, secondary to trauma	Irregular tremor at the wrist with some dystonic jerks. A proximal tremor persisted on posture and did not increase on goal-directed movement. Left arm abnormal dystonic posturing in a flexed position even when he walked and there was dystonic posturing of the thumb	Yes—mild hemiparesis on right	Yes—Joint position sense loss in left hand up to the middle IP joint	-	HT-t	Not taken
14	69 M	2 years	Mature haemosiderin deposition within the left thalamus, posterior limb of the left internal capsule and body of the caudate nucleus which corresponds to the site of previous haemorrhage	Large amplitude, side to side, proximal tremor of the right arm, which increased further on finger/nose movement and associated with dystonic posturing. No myorhythmic rest tremor observed	No	Joint position sense loss	Increased tone mainly in a dystonic fashion on action	HT-t	No
15	41 F	6 years	Right vertebral artery dissection following RTA, there is large mature infarct within the right thalamus (including the pulvinar)	Slow proximal tremor of the left arm. Dystonic posturing of the left arm and leg as well as pseudoathetosis and writhing movements at rest	No	Joint position sense loss distally up to the wrist on the left	-	HT-t	No
16	25 F	UN	There are two mature areas of encephalomalacia within the right thalamus, one related to the PCA infarct and the other related to previous thalamotomy	Left-sided dystonia of the left arm with jerky movements at rest and a proximal postural tremor which increases on finger nose movements	No	No, but has central pain syndrome	Severe left sided mobile dystonia	HT-t	UN

Table 1 (continued)

Case no	Age	Latency (duration from insult to onset of tremor)	Aetiology and imaging findings	Description of abnormal movement	Power affected	Sensation affected	Other neurological findings	Clinical diagnosis	Good response to Levodopa
17	32 F	UN	Large infarct within the right thalamus and ischaemic changes involving the fornix and hippocampal tail	Myorhythmic irregular movements at rest at the left wrist and left hand associated with a rhythmic tremulous movement at the shoulder both at rest and on posture which also increased on movements, choreiform movements distally and dystonia	No	Sensation to cold temperature heightened in the L arm	Left homonymous hemianopia, mild spasticity on the left, cerebellar signs and incoordination of the left leg	HT-t	No

HT-m HT likely to result from a midbrain involvement, *HT-t* tremor in keeping with a posterior thalamic injury, *M* male, *F* female, *HOD* hypertrophic olivary degeneration, *SN* substantia nigra, *CN* cranial nerve, *AVM* arteriovenous malformation, *UN* unknown, *N/A* nonapplicable, *CP* cerebellar peduncle

Aetiology

Haemorrhagic lesions (cavernoma, arteriovenous malformations and traumatic brain injury) were the main cause of HT in our series. Haemorrhage from an AVM accounted for 6 cases. Ischaemic injuries were the second most common aetiology in our series. Other causes included meningioma (patient 3) and neurodegeneration (patient 11, developing optic atrophy and cerebellar ataxia in his 20 s).

Clinical manifestation and radiological correlations

Patients 1–11

These eleven patients had a similar clinical pattern in that they all had a myorythmic tremor at rest which increased in amplitude on posture and further on goal-directed movement. They had no additional abnormal movements in the affected limb, beyond mild distal dystonic posturing observed in patient 7 and none of them had any joint position sensory loss.

Five of these patients showed mild hemi- or mono-paresis on the same side as the tremor. Other neurological findings included residual cranial nerves abnormalities in six patients and cerebellar features in five.

In seven of these eleven patients, there was clear radiological involvement of the contralateral midbrain region and its cerebellar connections and in three of these patients 1, 4, and 8, thalamic abnormalities were also present.

In one patient (3), there was no lesion in the contralateral midbrain but mass effect on the brain stem as well as involvement of the superior and middle cerebellar peduncles on the ipsilateral side.

In patient 7, there was extensive atrophy resulting from an old injury without midbrain or thalamic lesions. However, there was significant atrophy of the middle cerebellar peduncle on the contralateral side. Similarly, in case 9, there was extensive atrophy secondary to an RTA with no obvious damage to midbrain. Thalamic changes were seen but were thought to correlate with changes from a previous thalamotomy.

Finally, in patient 11, where the aetiology is likely to be an inherited neurodegenerative disorder, standard MRI head imaging was normal.

We have classified these as Holmes' tremor of midbrain origin HT-m.

Patients 12–17

These patients had a more complex pattern, in addition to the tremor, other involuntary movements were present, and a significant JP sensory loss was associated in the majority.

We have classified this syndrome as Holmes' tremor of thalamic origin HT-t.

Patient 12 had sustained a brainstem haemorrhage, which resulted in right-sided spastic hemiparesis, a mild irregular rest tremor in the right hand, which increased on posture, proximally, and further on goal-directed movement. He had cerebellar signs in the right arm. There were involuntary chorea-like movements of the thumb and significant joint position sense loss up to the wrist. His MRI head scan demonstrated previous bleeding involving the contralateral midbrain and thalamus as well as bilateral olivary hypertrophy. This patient was difficult to classify as he had features in keeping with what we classified as HT-m and HT-t.

Patient 13 had a history of head injury requiring subdural clot removal 15 years prior to his presentation. Examination revealed abnormal dystonic flexed posturing of the left arm and left thumb. Power was intact but joint position sense was lost in the left hand up to the proximal interphalangeal joint, agraphesthesia and some change in temperature sensation. There was an irregular rest tremor at the wrist, with some dystonic jerks. A proximal tremor persisted on posture and on goal-directed movement. Imaging showed extensive encephalomalacia and atrophy but no direct thalamic or midbrain abnormality could be confidently commented on.

Patient 14 presented with large amplitude, side to side, proximal tremor which increased further on goal-directed movement and was associated with significant dystonic posturing. No myorythmic rest tremor was observed. There was significant joint position sense loss up to the wrist of the same arm with pseudoathetosis. Imaging showed evidence of bleeding involving the contralateral thalamus.

Patient 15 presented with writhing movements of the left arm associated with dystonic posturing of the left arm and left leg as well as pseudoathetosis and joint position sensory loss. A slow large amplitude proximal tremor was present in the same arm and that persisted on goal-directed movements. The writing movements in the hand made a rest component to the tremor difficult to exclude. She had presented six years earlier with right vertebral artery dissection causing a large infarct in the left thalamus including the pulvinar.

Patient 16 presented years after an unsuccessful thalamotomy for left arm incapacitating movement disorder and pain. She had sustained a 'cryptogenic' posterior circulation stroke in her twenties which resulted in tremor and dystonia of the left arm. Botulinum toxin injections were partially helpful for her discomfort. Examination demonstrated flexed dystonic posturing of the forearm and wrist, associated with jerky movements and a postural proximal tremor. There was no rest component to the tremor; the amplitude increased on goal-directed movements. MRI head scan revealed previous infarct involving the right temporal and occipital lobes as well as an infarct in the right thalamus.

The movement disorder in patient 17 started 6–8 weeks after a posterior circulation stroke with left sided proximal dystonic posturing, distal choreiform movements associated with tremulous movements at the shoulder present at rest, on posture and increased on movement.

Four of these six patients (12, 13, 14, and 15) had associated proprioceptive sensory loss.

Treatment

Levodopa therapy was tried in most patients. A good response was reported by 5 of them. It is interesting to note that among the cases with HT-t, only one (patient 12) reported an improvement with levodopa, two did not report improvement, one did not take it and one had side effects.

Deep brain stimulation was performed in six cases (The surgical targets were VIM in 2, Zona inserta (ZI) /STN in 2 and two lead GPi and ZI in two) and they all reported significant improvement.

Discussion

This study sought to establish whether the clinical features associated with HT syndrome can aid the localization of the causative lesion to inform the management of patients with this disabling movement disorder.

It is now well accepted that the term Holmes' Tremor is used to describe a syndrome rather than a single clinical entity and HT clinical criteria have changed over time [2]. Some heterogeneity is accepted by many. Indeed, even when Gordon Holmes first discussed this in his 1904 paper, he drew attention to this clinical variation in the tremor and its associated signs [1]. He postulated that such tremors result from 'negative lesions in the midbrain or rather of the cerebello-rubral system'. He emphasised that the nucleus Rubor is phylogenetically and developmentally part of the thalamoencephalon and that 'a direct injury to it must frequently result from disease which is described as limited to the thalamus' [1]. The concept of thalamic lesions causing a low frequency, large amplitude postural and kinetic tremor that is similar to the tremor resulting from injury to the midbrain has been demonstrated by a number of studies [8, 10, 11]. Reina et al. [5] reported a thalamic lesion in isolation or part of a wider involvement in nearly half of their HT patients. Other areas involved in HT causation have also been reported in the literature [4, 5]. Investigators have studied the neurophysiology and lesion localisation of the movement disorders associated with thalamic injury. However, to our knowledge, there have been no studies looking at classifying the HT clinical syndrome in relation to where the lesion is.

Here, the authors tried to investigate whether the two broad patterns observed in our series of patients correlated with the suspected causative lesion by looking at the radiological findings. The first pattern was that of a tremor syndrome consisting of a myorhythmic rest component, a postural and kinetic component with or without residual cranial nerve involvement but with no other movement disorder, except for mild distal dystonic posturing, and no deafferentation, termed by us here as Holmes' Tremor of midbrain origin (HT-m). The other broad clinical pattern observed was associated with other movement disorders, in particular significant dystonia, choreo-athetosis and pseudoathetosis from joint position sensory loss. This pattern was termed as Holmes' Tremor of thalamic origin (HT-t). It is important to point out that cerebellar features other than the kinetic component of the tremor were not used to help the classification as they did not seem to distinguish between the two groups. There are two limitations in this approach in that some mild distal dystonia was observed with HT-m and could not be reliably used in the differentiation. Also, in three of HT-t patients, the rest component of the tremor was either absent or could not be assessed accurately as the movement disorder is mixed and includes distal jerky movements as well as pseudoathetosis making the assessment difficult.

The presence of a rest component, in addition to the action tremor, is regarded as part of the HT clinical syndrome [1, 2]. The myorhythmic nature of this rest component of the tremor is also well described and is usually reported in association with lesions of the midbrain [1, 6]. Thalamic lesions tremors are not always associated with a rest component unless severe [9–11, 19, 20]. Furthermore, studies looking at movement disorders resulting from thalamic lesions have clearly shown that tremors resulting from these lesions do not occur in isolation and are associated with dystonia–athetosis–chorea [9, 20]. Kim described this as a delayed-onset mixed movement disorder and demonstrated, amongst other features, the persistence of JP sense loss in these patients [9].

There seemed to be good radiological correlation with the clinical syndrome. Most patients with HT-m were demonstrated to have midbrain involvement by a vascular lesion/insult. In patients with diffuse injuries/degeneration, no focal lesions were demonstrated. However, three patients had thalamic involvement in addition to the midbrain injury. These were assumed to be non-contributory as the mere presence of a radiological thalamic lesion does not necessarily result in tremor, as such lesions would have to be in certain areas such as the posterolateral and paramedian nuclei [8–11, 21]. This study does not address the exact topographical mapping within the thalamus which is a limitation of the study. Furthermore, it is well known that thalamic lesions do not cause tremor in isolation of other movement disorders [9, 20]. Conversely, significant thalamic injury was seen in all our HT-t group, except for one patient who had diffuse encephalomalacia. These thalamic lesions were considered as causative because of the presence of other thalamic related deficits such as severe dystonia and JP sensory loss [2].

HT is very disabling given the large amplitude and its kinetic component. Although some medications such as levodopa and anticholinergics are known to suppress the tremor in some patients, the tremor remains difficult to treat [5, 22]. Surgical options focusing on the VIM, STN and GPi have also been used for its treatment. Joutsa et al. [3] showed that all the lesions that resulted in Holmes' Tremor were connected in a common brain circuit with nodes in the red nucleus, thalamus, globus pallidus, and cerebellum. They postulated that a second hit in this circuit is required to treat it successfully and that that may be the reason behind the observation that GPi is a better target for DBS than VIM and STN which are outside this circuit [3]. These pathophysiological findings may explain why the diffuse injury in our two patients with head injury and the neurodegeneration in patient 11 could be responsible for HT by pathological involvement of the tracts in this brain circuit.

It is interesting that most of the Levodopa responsiveness was reported by patients in the HT-m group and in patient 12 who had features of both HT-m and HT-t. It is possible that this is linked to the involvement of the striatonigral pathway in the HT-m group. However, given the small numbers of patients in this study, this conclusion remains speculative.

The response to DBS seemed to be significant in all patients in reducing the tremor component. However, the authors noticed that the functional gain in the HT-t group was not as good as that in the HT-m group. This is attributed that to the persistent sensory deficit/ deafferentation as well as the intrusion of other involuntary movements such as chorea and dystonia. This highlights the importance of the distinction between the two clinical entities.

There are some limitations in this study. First, the numbers studied were relatively small; larger studies may be helpful in confirming these findings. Second, no detailed mapping of the thalamus was carried out to define the exact lesion localisation within the thalamus. Third, the study was retrospective and hence, the information regarding the levodopa responsiveness was limited to what had been subjectively reported by the patients. However, despite these limitations, the authors believe that the study was successful in highlighting that when faced with a HT-type presentation, paying particular attention to the associated neurological signs would help the localisation of the causative injury which may in turn affect the clinical management.

Conclusion

Holmes' tremor could be subdivided into two distinct clinical types, delineating the aetiology to be within the midbrain or the posterior thalamus. This clinical distinction has implications on the clinical management, given that the pharmacological and surgical tremor treatments are unlikely to help the deficits associated with the tremor of a thalamic origin.

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Declarations

Conflicts of interest On behalf of all authors, Sundus Alusi states that there is no conflict of interest.

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