Accuracy of clinical diagnosis in tremulous parkinsonian patients: a blinded video study

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► The video for this study can be viewed online. To view this file please visit the journal online (http://jnnp.bmj.com).

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ABSTRACT

Background This study examines the clinical accuracy of movement disorder specialists in distinguishing tremor dominant Parkinson's disease (TDPD) from other tremulous movement disorders by the use of standardised patient videos.

Patients and methods Two movement disorder specialists were asked to distinguish TDPD from patients with atypical tremor and dystonic tremor, who had no evidence of presynaptic dopaminergic deficit (subjects without evidence of dopaminergic deficit (SWEDDs)) according to ^{123}I-N-ω-fluoro-propyl- 2β-carbomethoxy-3β-(4-iodophenyl) nortropane ([^{123}I] FP-CIT) single photon emission computed tomography (SPECT), by 'blinded' video analysis in 38 patients. A diagnosis of parkinsonism was made if the step 1 criteria of the Queen Square Brain Bank criteria for Parkinson's disease were fulfilled. The reviewer diagnosis was compared with the working clinical diagnosis drawn from the medical history, SPECT scan result, long term follow-up and in some cases the known response to dopaminergic medications. This comparison allowed a calculation for false positive and false negative rate of diagnosis of PD.

Results High false positive (17.4-26.1%) and negative (6.7-20%) rates were found for the diagnosis of PD. The diagnostic distinction of TDPD from dystonic tremor was reduced by the presence of dystonic features in treated and untreated PD patients.

Conclusion Clinical distinction of TDPD from atypical tremor, monosymptomatic rest tremor and dystonic tremor can be difficult due to the presence of parkinsonian features in tremulous SWEDD patients. The diagnosis of bradykinesia was particularly challenging. This study highlights the difficulty of differentiation of some cases of SWEDD from PD.

INTRODUCTION

Clinicopathological correlations have improved the diagnostic accuracy of Parkinson's disease (PD); in tertiary referral movement disorder clinics there is close to 100% concordance between the final clinical diagnosis and pathological findings.[1 2] Nonetheless, patients with tremor dominant Parkinson's disease (TDPD) continue to be a diagnostic challenge and are under-represented in published post mortem studies.

In a community based study in Wales,[3] only 53% of patients, treated with antiparkinson therapy in primary care, met the Queen Square Brain Bank criteria for the clinical diagnosis of PD when re-examined by an experienced movement disorder specialist. A quarter of the cases had no signs of parkinsonism and half of these were considered to have essential tremor (ET).

It is likely that a significant proportion of the 4–15% of de novo patients recruited for recent clinical trials with antiparkinsonian drugs who have no evidence of nigrostriatal dopamine denervation on functional imaging (subjects without evidence of dopaminergic deficit (SWEDDs)) have tremulous syndromes other than PD. This is supported by long term follow-up showing minimal clinical deterioration, no response to dopaminergic therapy and in some cases no evidence on repeat functional imaging of dopamine denervation.[4 5]

In this study, the clinical features of patients with tremor and parkinsonism were assessed by two blinded movement disorder specialists (DGG and AJL). The diagnosis arrived at by this process was compared in each case with the working clinical diagnosis (derived in all cases from history and examination by a third movement disorder expert (NB), long term follow-up and ^{123}I-N-ω-fluoro-propyl- 2ß-carbomethoxy-3ß-(4-iodophenyl) nortropane ([^{123}I] FP-CIT) result).

METHODS

Participants and on site diagnosis

A consecutive group of patients with clinically uncertain Parkinson's disease were prospectively recruited from the neurology clinics in Nottingham and Derby (local ethics approval 07/Q2502/1). Patients were referred from both primary care (75%) and secondary (25%) care. Study inclusion was based on clinical diagnostic uncertainty, including the presence of prominent postural tremor, or focal, multifocal or segmental dystonia. Patients exposed to dopamine receptor antagonists or toxins such as manganese or carbon monoxide were excluded. Cases considered psychogenic, or with uncommon secondary or atypical causes of parkinsonism (eg, Huntington's disease, fragile X ataxia syndrome), were also excluded.[6–13] Neurological examination was repeated after an average of 3 years of follow-up, and structural imaging used selectively to exclude causative cerebral lesions (eg, supratentorial meningioma, extensive cerebrovascular disease) (MR/CT brain imaging conducted in 15/38 cases).

The patients were collected over a 3 year period and referred for [^{123}I] FP-CIT scan in accordance with the National Institute for Health and Clinical Excellence guidelines.[14] All patients gave written informed consent for use of their video material for research and teaching.

All patients were examined by one of the authors (NB) and a final diagnosis of PD, dystonic tremor,

Table 1 Clinical diagnosis on blinded video assessment for 38 cases for reviewer 1 and 2 versus FP-CIT result and the working clinical diagnosis

Case No	Blinded video diagnosis		FP-CIT result	Working clinical diagnosis
	R1	R2		
1	DT	PD	Normal	DT
2	ET	DT	Normal	DT
3	PD	PD	Abnormal (grade 3 JP; grade 2 JB)	TDPD
4	DT	DT	Normal	DT
5	DT	PD	Abnormal (grade 1)	TDPD
6	DT	DT	Normal	DT
7	Monosymptomatic rest tremor	DT	Normal	ET
8	DT	DT	Normal	DT
9	PD	DT	Abnormal (grade 1)	TDPD
10	DT	DT	Normal	DT
11	DT	DT	Normal	ET
12	PD	PD	Abnormal (grade 2 JP; grade 1 JB)	TDPD
13	ET	PD	Normal	DT
14	Monosymptomatic rest tremor	PD	Abnormal (grade 2 JP; grade 1 JB)	TDPD
15	ET	DT	Normal	DT
16	ET	DT	Normal	DT
17	PD	DT	Normal	DT
18	Atypical Tremor	PD	Abnormal (grade 2)	TDPD
19	DT	DT	Normal	DT
20	DT	DT	Normal	ET
21	PD/ Atypical Tremor	PD	Abnormal (grade 2 JP; grade 3 JB)	TDPD
22	DT	DT	Normal	DT
23	PD	PD	Normal	ET
24	DT	PD	Abnormal (grade 2)	TDPD
25	DT	DT	Normal	DT
26	DT	PD	Normal	DT
27	DT	DT	Normal	DT
28	PD	PD	Abnormal (grade 3 JP; grade 2 JB)	TDPD
29	ET	DT	Normal	DT
30	PD	PD	Normal	DT
31	PD	PD	Abnormal (grade 2 JP; grade 1 JB)	TDPD
32	PD/atypical tremor	DT	Normal	ET
33	PD	PD	Abnormal (grade 2)	TDPD
34	Atypical tremor	DT	Abnormal (grade 1)	TDPD
35	ET	DT	Abnormal (grade 1 JP; grade 2 JB)	TDPD
36	PD	PD	Abnormal (grade 2)	TDPD
37	ET	PD	Abnormal (grade 2)	TDPD
38	ET	PD	Normal	DT

DT, dystonic tremor; ET, essential tremor; Grades 0–3 for ^{123}I-N-ω-fluoro-propyl- 2ß-carbomethoxy-3ß-(4-iodophenyl) nortropane ([^{123}I] FP-CIT).[22]; JP and JB refer to nuclear physicians across the two sites; PD, Parkinson's disease; R1, reviewer 1; R2, reviewer 2; TDPD, tremor dominant Parkinson's disease.

atypical tremor, monosymptomatic rest tremor or ET made. This was designated the working clinical diagnosis. All patients with a working clinical diagnosis of PD were treated with L-dopa and/or dopamine agonist drugs over the 3 year follow-up period. In addition, a minority of patients who were subsequently reclassified as non-PD had undergone a trial of dopaminergic therapy prior to initial referral (nine of 23 cases, 39%).

Blinded reviewer diagnosis

Video recording of all patients was performed according to standard criteria for the Unified Parkinson's Disease Rating Scale part III (motor score) and to demonstrate the features of ET and dystonic tremor according to consensus criteria.[15] At the time the videos were taken, no non-PD patient was receiving dopaminergic therapy. A minority of PD patients on dopaminergic therapy at the time of the video were excluded from the final analysis of false negative patients with PD, in case treatment masked their clinical features.

Two movement disorder specialists (AJL and DGG) were asked to suggest the likely clinical diagnosis based on video footage. Their diagnoses took into account the Queen Square Brain Bank operational criteria for the diagnosis of PD (with the exception of rigidity), the consensus criteria for ET and clinical features suggestive of dystonic tremor.[15–17] The term dystonic tremor is used in this paper to embrace both 'dystonic tremor' and 'tremor associated with dystonia', as defined previously.[15 18]

The abnormalities observed on sequential movement testing were broadly divided into bradykinesia typical of PD (slowness with motor decrement) or atypical of PD (pure slowness, slowness with delay in initiation of fine finger/hand movements or slowness with reduced amplitude of fine finger/hand movements without decrement). The term flurry or flurries were used to describe the rapid change in tremor amplitude and frequency that is a common feature of dystonic tremor.[17 19 20] Since re-emergence of postural tremor is sometimes considered to be the postural representation of rest tremor in PD, the time to emergence of postural tremor was calculated visually by both reviewers for all 38 cases.[21]

Imaging analysis

[^{123}I] FP-CIT imaging was carried out according to standard protocols with discontinuation of agents that might interfere

Table 2 Diagnostic accuracy of PD in 38 patients, based on blinded video review compared with working clinical diagnosis

	Video diagnosis	
	Reviewer 1	Reviewer 2
False positive diagnosis of PD	17.4%	26.1%
False negative diagnosis of PD	46.7%	20.0%
False negative diagnosis of PD, after excluding five patients on dopaminergic therapy	20.0%	6.7%
Sensitivity for PD	53.3%	80.0%
Sensitivity for PD, after excluding five patients on dopaminergic therapy	72.3%	93.3%
Specificity for PD	85.2%	79.3%

PD, Parkinson's disease.

Table 3 False positive diagnosis of PD in four cases on blinded video review: reviewer 1

		Clinical features leading to diagnosis				
False Positives	Blinded video Diagnosis	FB	FH	RAS	GI	FP-CIT result
Case 17	PD	+	+	–	+	Normal
Case 23	PD	+	–	+	–	Normal
Case 30	PD	+	+	–	–	Normal
Case 32	PD/ Atypical ET	–	+	–	–	Normal

ET, essential tremor; FB, fatiguable bradykinesia; FH, facial hypomimia; FP-CIT, N-ω-fluoropropyl- 2ß-carbomethoxy-3ß-(4-iodophenyl) nortropane; GI, gait impairment; PD, Parkinson's disease; RAS, reduced arm swing.

with [^{123}I] FP-CIT striatal uptake at least 4 weeks before the scan. Thyroid blocking and single slow intravenous injections of [^{123}I] FP-CIT were administered at activities between 111 and 185 MBq. Images were acquired 3–6 h after injection using a multi-headed gamma camera.

All [^{123}I] FP-CIT scans were scored in routine clinical service, and then independently by a second nuclear medicine specialist blind to both clinical information and video footage (JP). Visual assessment graded scans as normal or abnormal (scale 0–3).[22]

Statistical analysis

We ascertained inter-reviewer agreement on video diagnosis using Cohen's κ coefficient for each pair of blinded reviewer diagnoses per video case.

The blinded reviewer diagnoses based on video were also compared with the working clinical diagnoses. This allowed calculation of a false positive and negative rate with respect to the diagnosis of PD for the two movement disorder experts by standard formulae. The clinical and imaging data were then shared with the blinded experts.

RESULTS

Blinded second read of [^{123}I] FP-CIT SPECT

The second read of all 38 FP-CIT single photon emission computed tomography (SPECT) scans of patients (JP) showed full concordance in abnormal versus normal with the initial read of scans by the local nuclear medicine specialist (JB). Of the 15 abnormal scans, there was agreement on the grade of abnormality in eight and disagreement in seven (table 1). The scale of disagreement was never more than 1 point. Only two of these six cases of disagreement of scale featured in the false negative cases (see tables 4 and 6). Scan reports in all cases showed congruence in the most affected side on the FP-CIT scan and the clinically most affected side.

Working clinical diagnosis

In the case of TDPD patients, the working clinical diagnosis was based on clinical observation for an average of 39.6 months (SD 20.7), as well as review of video recordings (nine were recorded an average of 13.9 months after the FP-CIT scan and in six others, an average of 8.3 months before the FP-CIT scan), the L-dopa/dopamine agonist response and in all cases FP-CIT scan evidence of dopaminergic deficit.

Similarly, the working clinical diagnosis for clinically uncertain PD patients was based on a normal FP-CIT scan and clinical observation for an average of 35.9 months (SD 19.3); videos were taken an average of 8.8 months after the scan in 12 cases and in 11 cases an average of 5.1 months before the FP-CIT scan. In addition, a minority of patients had a trial of dopaminergic therapy (nine of 23 cases, 39%).

Blinded reviewers' diagnosis

The blinded baseline diagnosis on video assessment for each of the 38 cases for reviewers 1 and 2 is listed in table 1.

Comparison of reviewers' diagnoses with the working clinical diagnosis

There were differences in sensitivity and specificity of the blinded diagnosis based on video assessment between the two reviewers (table 2). Reviewer 2 had a higher sensitivity for detecting PD, with an associated lower specificity, compared with reviewer 1.

Tables 3–6 illustrate the clinical features which led the reviewers to a baseline video diagnosis which was incompatible with the FP-CIT SPECT result and the working clinical diagnosis.

Analysing the false positive case errors, the clinical feature common to eight of the 10 cases was the detection of apparent bradykinesia. Only two false positives were common to both reviewers (case Nos 23 and 30).

Analysis of the 10 false negative cases is complicated by the fact that six patients were on dopaminergic therapy. Within the drug naïve false negative cases, reviewer 1 recorded slowness but no decrement in amplitude, and thumb hyperextension, in case No 5; no bradykinesia, flurries and non-pill rolling tremor in case No 14; and no bradykinesia, absence of re-emergent tremor and normal gait in case No 35. Reviewer 2's conclusions for case No 35 were similar, that bradykinesia was not present and that there was a suggestion of retrocollis.

Considering the false negative cases on dopaminergic therapy, case No 34 was the only case falsely diagnosed by both reviewers. Case No 34 was felt by reviewer 1 to have flurries of tremor and no bradykinesia and by reviewer 2 to have no bradykinesia.

Bradykinesia

Summarising the findings of reviewer 1, 12 cases were considered to have true bradykinesia. Of these 12 cases, only eight had presynaptic dopaminergic deficit on FP-CIT SPECT. For reviewer 2, 21 cases were considered to have true bradykinesia, of which only 10 had FP-CIT scans indicating presynaptic dopaminergic deficit. A total of three cases with a normal FP-CIT scan were rated as having true bradykinesia by both reviewers. True parkinsonian bradykinesia was therefore represented in both patients with normal and abnormal FP-CIT scans.

Slowness of a non-PD type is reported in dystonic tremor.[17] Of the non-PD bradykinesia types in this series, only pure

Table 4 False negative diagnosis of PD in seven cases on blinded video review: reviewer 1

		Clinical features leading to diagnosis						
False Negatives	**Blinded video Diagnosis**	**NPRT**	**NFB**	**MF**	**NGI**	**DF**	**FP-CIT result**	**Drugs at time of video**
Case 5	DT	–	+	–	–	+	Abnormal (grade 1) Congruent	Drug naive
Case 14	Monosymptomatic rest tremor	+	+	+	–	–	Abnormal (grade 2 JP; grade 1 JB) Congruent	Drug naive
Case 18	Atypical tremor	+	+	–	–	–	Abnormal (grade 2) Congruent	6 months of pramipexole (LEDD of 213 mg/day)
Case 24	DT	–	–	–	–	+	Abnormal (grade 2) Congruent	On L-dopa for 3 years 400 mg/day
Case 34	Atypical tremor	–	+	+	–	–	Abnormal (grade 1) Congruent	8 months of L-dopa (300 mg/day)
Case 35	ET	–	+	–	+	–	Abnormal (grade 1 JP; grade 2 JB) Congruent	Drug naive
Case 37	ET	–	+	–	+	–	Abnormal (grade 2) Congruent	2 months of L-dopa 300 mg/day

Congruent refers to predominant FP-CIT abnormality contralateral to most affected clinical side.
DF, dystonic features, for example collis, thumb hyperextension, shoulder elevation; DT, dystonic tremor; ET, essential tremor; FP-CIT, N-ω-fluoro-propyl- 2ß-carbomethoxy-3ß-(4-iodophenyl) nortropane; LEDD, levodopa equivalent daily dose (pramipexole daily dose x 67); MF, myoclonic flurries; NFB, no fatiguable bradykinesia; NGI, no gait impairment; NPRT, no pill rolling rest tremor; PD, Parkinson's disease.

slowness without fatiguing or reduced amplitude of movement was discriminating for patients with normal FP-CIT scan.

Re-emergent tremor

The average latency to postural tremor across the two blinded reviewers for the 23 SWEDD patients was 0.82 s (median 0 s, IQR 0–2 s) and for the 15 TDPD cases the latency was 0.79 s (median 0 s, IQR 0–0.5 s) (p=0.69, Mann–Whitney U test). There was no significant difference in latency between SWEDD and TDPD cases for re-emergent tremor.

Inter-blinded reviewer agreement on video diagnosis

The inter-blinded reviewer agreement on video diagnosis (PD or non-PD) was low (κ coefficient=0.24, 95% CI 0 to 0.48).

DISCUSSION

The patients with suspected parkinsonism used in this study were divided into those with normal (SWEDDs) or abnormal presynaptic dopamine activity. Although supranigral forms of parkinsonism can have a normal FP-CIT scan, few of these have rest tremor as the predominant feature and the differential diagnosis for the SWEDDs in this study lay mainly between dystonic tremor, ET and atypical tremor.

Of the other diagnoses proffered by the reviewers, monosymptomatic rest tremor is considered by many authorities as a forme fruste of PD and may have abnormal presynaptic dopaminergic imaging while cases labelled as 'atypical tremor' have also in some instances been associated with an abnormal FP-CIT scan.[23 24]

It remains possible that some of our cases were wrongly categorised by FP-CIT SPECT, rather than clinically misinterpreted. We consider this unlikely given the 3 year follow-up and known sensitivity of FP-CIT SPECT in early PD, and the 100% concordance in distinguishing normal from abnormal imaging results between the two scan assessors.[25]

Video diagnoses in movement disorder patients are constrained by the absence of 'hands-on' testing of rigidity and the subliminal observation of spontaneous movement and body language in real life situations rather than the recording studio. Sometimes several consultations over a number of months may be necessary before a diagnosis can be made with reasonable certainty and historical information may also be a useful distinguishing feature in the differentiation of some patients (eg, presence of rapid eye movement sleep behavioural disorder or anosmia/hyposmia in PD). Nevertheless, both reviewers had identical video material to review, and the findings allow a comparison with studies where similar methods have been used.[26]

This study focused on the ability of two blinded movement disorder experts to distinguish PD from SWEDDs without the availability of historical details on the patients, and as such tested the capability of step 1 of the Queen Square Brain Bank criteria to distinguish PD from other tremulous disorders. Information on rigidity was unavailable to the video reviewers but increased tone is also a common associated feature of dystonic tremor, and Froment's manoeuvre can also elicit cogwheel rigidity in ET.[17 19 20 27]

SPECT imaging of presynaptic dopaminergic pathways have an error rate of approximately 5% and perhaps greater depending on the expertise of the scanning centre.[28] The diagnostic difficulties in this group of patients are highlighted by the range in sensitivity (72.3–93.3%) and specificity (79.3–85.2%) for the two reviewers, which can be compared with the proportion of SWEDD patients seen in clinical trials which found that 4–15% of patients entered as having PD had normal presynaptic dopaminergic imaging (although not all of the patients in those studies had a predominantly tremulous presentation).[4 29 30] Comparison can also be made with the high error rate in the diagnosis of tremor patients where up to 37% of ET patients were misdiagnosed as PD (15%) or dystonia (8%).[31]

Table 5 False positive diagnoses of PD in six cases on blinded video review: reviewer 2

		Clinical features leading to diagnosis						
False Positives	**Blinded video Diagnosis**	**FB**	**RT**	**HV**	**FH**	**RAS**	**GI**	**FP-CIT Result**
Case 1	PD	+	–	–	–	–	–	Normal
Case 13	PD	–	+	–	–	+	–	Normal
Case 23	PD	+	–	–	–	+	–	Normal
Case 26	PD	+	–	+	–	+	–	Normal
Case 30	PD	+	–	–	–	–	–	Normal
Case 38	PD	+	–	–	–	+	–	Normal

FB, fatiguable bradykinesia; FH, facial hypomimia; FP-CIT, N-ω-fluoro-propyl- 2ß-carbomethoxy-3ß-(4-iodophenyl) nortropane; HV, hypophonic voice; GI, gait impairment; PD, Parkinson's disease; RAS, reduced arm swing; RT, rest tremor.

Table 6 False negative diagnosis of PD in three cases on blinded video review: reviewer 2

False Negatives	Blinded video Diagnosis	Clinical features leading to diagnosis					FP-CIT result	Drugs at time of video
		NPRT	NFB	MF	NGI	DF		
Case 9	DT	–	+	–	–	+	Abnormal (grade 1) Congruent	12 months on L-dopa 300 mg/day
Case 34	DT	–	+	–	–	–	Abnormal (grade 1) Congruent	8 months on L-dopa 300 mg/day
Case 35	DT	+	+	–	–	+	Abnormal(grade 1 JP; grade 2 JB) Congruent	Drug naive

Congruent refers to predominant FP-CIT abnormality contra-lateral to most affected clinical side.
DF, dystonic features, for example collis, thumb hyperextension, shoulder elevation; DT, dystonic tremor; FP-CIT, N-ω-fluoro-propyl- 2ß-carbomethoxy-3ß-(4-iodophenyl) nortropane; JP and JB refer to nuclear physicians across the two sites; MF, myoclonic flurries; NFB, no fatiguable bradykinesia; NGI, no gait impairment; NPRT, no pill rolling rest tremor PD, Parkinson's disease.

Analysis of false negative and positive cases

Analysis of the false negative observations is complicated given six of 10 patients were on dopaminergic therapy, allowing potential masking of clinical features of PD. This may explain the inability of the examiners to detect bradykinesia but fails to fully explain the examiners' conclusions given that there was only one false negative case shared by the two reviewers.

The difference in diagnosis between the two reviewers is one of the most striking features of the present study (κ coefficient=0.24, 95% CI 0 to 0.48). Such variability in clinical opinion is however consistent with studies of inter-rater reliability of Parkinson's disease.[32]

Analysis of the false positive cases in this study shows that interpretation of sequential finger movement testing is the largest contributor to diagnostic error. Despite careful grading of motor slowness, fully defined bradykinesia (including decremental delay) was observed in four SWEDD cases by reviewer 1 and in 11 SWEDD cases by reviewer 2. Possible explanations for this finding could be that bradykinesia occurs in SWEDD patients, despite the absence of substantia nigra pathology, or that motor flurries interrupt normal self-paced movement and confound the interpretation.[17] Motor disturbances reminiscent of bradykinesia from the clinical descriptions have also been reported in dystonic tremor.[17] Furthermore, of 30 patients with torticollis reported in 1976, 26 had tremor which was familial in 16, and parkinsonian features were present in 10, including masked facies, bradykinesia and rigidity. Three patients had clinical signs sufficient to entertain a diagnosis of PD.[33]

On the latency of postural tremor in TDPD cases in this series

Re-emergence of postural tremor is felt by some authors to be the postural representation of rest tremor in PD. The latency of the postural or re-emergent tremor in TDPD cases in the current series was not significantly different from the SWEDD cases, which contrasts with a report of a significantly longer latency of postural tremor in PD.[21] However, another study on ET concluded that, 'clinically and electrophysiologically the postural tremors of ET and PD are indistinguishable'.[34] Further analysis of larger TDPD cohorts would be worthwhile to validate whether long latency to postural tremor in PD is a differentiating feature from the postural tremor of ET.

Dystonic features in TDPD patients

It is apparent from this study that a number of false negative cases of untreated PD were felt by the reviewers to have dystonic clinical features such as thumb hyperextension, torticollis or flurries. Retrospective review suggests that isolated thumb hyperextension without associated 'dinner forking' or other dystonic features may be an unreliable sign.

The specificity of clinical features that suggest dystonic tremor may therefore require further consideration.[17] The combination of dystonia and parkinsonism in autosomal recessive parkinsonism and young onset PD is well established.[35 36] Focal dystonia as a feature of PD is also recognised; Lewitt reviewed 10 patients with untreated sporadic PD noting both neck and arm dystonia and dystonic features were also described in a further nine patients with untreated PD.[37 38]

CONCLUSIONS

The accurate diagnosis of predominantly tremulous PD in its early stages remains challenging. The use of FP-CIT SPECT in this study helped us to critically evaluate clinical decision making and to highlight the difficulties in distinguishing TDPD from dystonic tremor, atypical tremor, ET and monosymptomatic rest tremor.

Although the recognition of subtle dystonic features may help reclassify some SWEDD patients as adult dystonic tremor, dystonic features also occur in adult drug naïve PD patients.

A recent note by Bain commented on the difficulty in determining whether there was true bradykinesia in dystonic tremor patients.[39] We consider further motor physiological studies worthwhile to clarify the distinction between the motor abnormalities of dystonic tremor and those considered pathognomonic for parkinsonism.

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