The meeting was chaired by Nin Bajaj (Nottingham) who gave an overview of the aims of the SWEDD-UK group. The meeting was funded as a working party of the Dementia and Neurodegenerative Disease Research Network (DeNDRoN). The SWEDD-UK group is open to all UK researchers and clinicians working on the area of “scans without evidence of dopaminergic deficit” (SWEDDs). The aims of this meeting were to come to a greater understanding of the type of patients that might be mistaken clinically for Parkinson’s disease (PD), but have SWEDDs, and to discuss ideas for future network research studies on this group of patients.

Background

The acronym SWEDD, which stands for a “Scan Without Evidence of Dopaminergic Deficit” was first introduced to describe patients who had been entered into therapeutic trials on the basis that they had normal presynaptic dopaminergic imaging. This was the original use of the term, without evidence of dopaminergic deficit” (SWEDD). The aims of this meeting were to indicate the broader usage of the term that has subsequently developed: namely the situation in a clinical practice scenario where a patient suspected to have Parkinson’s disease and subsequently has normal presynaptic dopaminergic imaging.

Clearly, the nature of SWEDD is an evolving subject and further work is necessary to more fully understand the diagnoses and natural histories of these patients.

Presentations

1. Overview of SWEDD – Definition of term; Types of SWEDD; Frequency in Clinical Studies – Dr Donald Grosset (Institute of Neurological Sciences, Glasgow)

The term SWEDD was initially coined by John Seibyl to refer to a normal putaminal presynaptic dopaminergic scan in a patient clinically considered to have Parkinson’s disease. Subsequent usage of the term SWEDD has broadened to describe any patient with a tremor and/or parkinsonism phenotype, in whom such imaging shows a normal result.

The Benamer et al study of 2000 involved patients apparently fulfilling diagnostic criteria for idiopathic Parkinson’s disease (IPD), multiple system atrophy (MSA), progressive supranuclear palsy (PSP), or essential tremor (ET). Patients were included from early to later disease stages. Among the 158 patients with a clinical diagnosis of degenerative parkinsonism, 4 (2.5%) were identified as having SWEDD.

Within this study, patients with a clinical diagnosis of early (hemip-) Parkinson’s disease showed bilaterally abnormal FP-CIT SPECT scans in all but one case. This patient had a clinical diagnosis of PD and was on L-dopa therapy. Later clinical observations allowed complete withdrawal of antiparkinson medication and he was re-classified as dystonic tremor.

The rates of SWEDDs in the clinical studies (ELL-DOPA, REAL-PET, CALM-PD, European FP-CIT) of patients diagnosed as having PD have varied from just over 2% of 103 cases (European FP-CIT study) to 14.7% of 142 cases (ELL-DOPA). The rate of SWEDD was high-
er when studies recruited patients with a shorter diagnosis duration.

Discussion

NQ: It would be interesting to know who has seen these patients’ videos. How many were tremulous and how many non-tremulous? There has been no systematic review of patients’ clinical diagnoses, so it would be helpful to re-review these videos, ideally in a double-blinded video assessment.

PB: The whole diagnostic term SWEDD is dependent upon the reporting of a normal scan. Therefore this requires some standardisation as to what a normal scan constitutes. What type of scan is needed? Does the scan need to be visually or quantifiably normal? Should there be a requirement for two individuals to report the scan? If so, should they be blinded? And does there need to be a consensus between the two for the reporting of an abnormal/normal scan?

2. Are many SWEDDs adult onset dystonic tremor patients? Professor Niall Quinn, UCL Institute of Neurology, London

The purpose of scans looking for dopaminergic deficit is to reveal, when it is not clinically obvious, whether an individual has a lesion in their nigrostriatal tract. Theoretically almost the entire population potentially have SWEDDs, but only become a subject with a SWEDD when a presynaptic dopaminergic scan is performed and deemed to be normal.

The entry of patients into the SWEDDS arena can occur for various backgrounds and amongst these are patients with tremor syndromes in whom there is uncertainty whether they have PD instead of, or in addition to, essential tremor (ET) or dystonic tremor (DT). In the Movement Disorder Society Consensus Statement (1998), dystonia is an exclusion criterion in the diagnosis of ET. However, Jankovic et al. (1991) had earlier reported dystonia in 47% of his clinical population with a diagnosis of ET (21% spastic tremor, 14% writer’s cramp, 4% segmental dystonia) and today many patients with DT are mis-diagnosed with ET.

Adult onset dystonic tremor (AODT) is also sometimes mistaken for PD. The original paper on AODT included 10 patients. Clinical features included asymmetric resting arm tremor, including thumb tremor, reduced arm swing, hypotonia, jaw tremor and leg tremor. However, there was no fatigue or decrement of alternating movements and a normal F–CIT SPECT scan was obtained in all 10.

Subjects with classical ET would not merit an FP–CIT scan, but those with ‘ET’ or DT in combination with jaw tremor, rest tremor, leg tremor, very asymmetric or unilateral tremor, reduced arm swing or facial hypotonia may merit a scan if there is a suspicion of PD, but the scan will not differentiate ET from DT. How many subjects with SWEDDS have DT depends upon a physician’s clinical experience and acumen, and their threshold for ordering scans. All one can say is that DT patients more frequently than ET patients have atypical features that may hint at PD, but still most of these should not need scans to formulate a diagnosis. The lower the threshold for ordering FP–CIT scans, the more SWEDDS with DT there will be.

Patients with unusual tremor features but no evidence of overt dystonia e.g. isolated head/vocal tremor, jaw tremor, unilateral tremor etc probably do not have ET. Some may later turn out to have DT, when evidence of dystonia subsequently develops. These individuals should, at present, be called “indeterminate tremor”.

Chouxard et al. (1997) conducted a survey of movement disorder specialists’ views on the diagnosis of ET. 70% would diagnose ET in a patient with isolated voice tremor, and 81% with isolated head tremor. It would be interesting to repeat a similar questionnaire study amongst movement disorder specialists today. The MDS certainly needs to revisit and revise its definitions for both ET and DT.

Discussion

NQ: I would suggest that the term dystonic tremor should encompass both tremor in a body part that is affected by dystonia and tremor associated with dystonia (tremor in a body part not affected by dystonia but the patient has dystonia elsewhere). Essential tremor is a bilateral, largely symmetrical postural or kinetic tremor involving hands and forearms that is visible and persistent. Additional tremor elsewhere may occur but should follow, and be less severe than, the arm tremor. Exclusion criteria include dystonia, parkinsonism, other known causes of tremor e.g. neuropathy or isolated position–or task-specific tremors, or isolated tremor sparing the arms. Indeterminate tremor is the presence of postural or kinetic tremor (sometimes with additional rest tremor) accompanied by other neurological signs of uncertain significance e.g. mild extrapyramidal features, but without sufficient parkinsonism or dystonia to make a diagnosis of PD or dystonic tremor. Monosymptomatic rest tremor is rest tremor without sufficient parkinsonian or dystonic features to entertain a diagnosis of PD or dystonic tremor. Benign tremulous PD is part of tremor–dominant PD, but cannot be diagnosed in the absence of true bradykinesia or the presence of a normal FP–CIT scan.

HM: Many PD patients, especially those with a younger age of symptom onset have dystonia in addition to tremor. Rather than looking at some of the older videos used as examples of each tremor type, there is a good case for developing a new teaching library indicating the typical features of essential and dystonic tremor with consensus between movement disorders experts across the world.

3. The definition of dystonic tremor, revisiting the definition of essential tremor (can ET patients ever present as SWEDDs? re-defining atypical Tremor and monosymptomatic tremor – Dr Peter Bain

Tremor can be classified as rest, postural or kinetic, the latter including simple kinetic, intention, task specific, position specific and intention tremor or by aetiology according to the underlying disease. Currently the most widely used definitions are those in the ‘Consensus Statement of the Movement Disorder Society on tremor’, which proposed the following definitions:

Classic essential tremor: defined by inclusion and exclusion criteria. Inclusion criteria: bilateral, largely symmetrical postural or kinetic tremor involving the hands and forearms that is visible and persistent. Additional or isolated tremor of the head may occur but in the absence of abnormal posture, although inclusion of this has been heavily disputed.

Exclusion criteria: presence of other neurological signs (e.g. dystonia), known causes of enhanced physiological tremor (e.g. drugs), historic or clinical evidence for psychogenic tremor or convincing evidence for a stepwise onset or deterioration of tremor. The presence of primary orthostatic tremor, isolated voice tremor, isolated position specific or task specific tremor, isolated tongue or chin tremor or isolated leg tremor.

Tremor syndromes to have a bimodal age of onset similar to that of essential tremor. Approximately 49–60% have a first degree relative with a form of tremor. In terms of treatment, these patients tend to have a negative response to levodopa and approximately 70% showing a response to alcohol.

Marsden’s dystonic tremor

Referred to by Marsden as dystonic tremor, and consisting of a jerk tremor often occurring in flurries without overt dystonia. This form of tremor was not included in the MDS consensus statement.

Monosymptomatic rest tremor

Characterised by:

a. Pure or predominant rest tremor of at least 2 years duration

b. No additional signs of bradykinesia, rigidity, or problems with stance/stability sufficient to make a diagnosis of Parkinson’s disease.

c. Features of the tremor component of this group are essentially identical to parkinsonian tremor

d. Postion emission tomography (PET) scans of some patients in this group show evidence of dopaminergic deficit

Indeterminate Tremor Syndrome

These patients satisfy the criteria for classical essential tremor but also exhibit other neurological signs of uncertain significance, but insufficient to make a specific diagnosis. This term also allows clinicians to remain open minded about the diagnosis and avoids making an incorrect diagnosis and prevents the possibility of conflicting diagnoses. This category also includes the ‘possible ET type IB’ category from the TRIG criteria.

Unclassified Tremor

Those tremors that cannot be classified should be labelled unclassified and described phenomenologically.

Discussion

NQ: The bimodal age of onset distribution described in the dystonic tremor syndromes is reminiscent of that of dystonia, where DYT1 and DYT6 mutations are found predominantly in younger, but not in older, subjects.

DG: Although much discussion of the differences between essential and dystonic tremor has taken place, it must be noted that ultimately both of these patient groups could be classified as SWEDDS.

SPECIAL FEATURE

ACNR > VOLUME 10 NUMBER 4 > SEPTEMBER/OCTOBER 2010 > 33
4. Mis-diagnosis in tremulous PD – Dr Nin Bajaj

Two pairs of videos were shown and the group asked to comment on whether they felt the individuals had Parkinson’s disease or not. The assembled panel of experts performed poorly in their clinical ability to predict which patient had PD or not on the basis of the videos shown. The clinical diagnosis of PD had been assigned by NB based on FP-CIT scan result; prolonged clinical follow-up (3 years) and in all PD patients and many non-PD patients, response to dopaminergic therapy.

A study by Hughes and Lees suggested that movement disorder specialists had a sensitivity of 91.1% and specificity of 98.7% in diagnosing PD. However, Meara et al found a diagnostic accuracy of only 53% when examining this at a community level.

Bajaj et al showed two blinded experienced movement disorder experts videotaped examinations of 15 TDPD and 23 SWEDDs patients. Both experts had high false positive rates (70% to 76.1%) and negative rates (6.7 to 20%) for the diagnosis of PD.

5. The Queen Square Brain Bank Criteria in the age of SWEDD – Professor Andrew Lees (UCL Institute of Neurology, London)

Recent suggested criteria for diagnosing Parkinson’s disease have included the triad of:

a. Impaired sense of smell
b. Rapid Eye Movement (REM) sleep behaviour disorder
c. Refractory constipation

Referring to the original QSBBC, bradykinesia is arguably the most important feature, especially in younger patients where it may be the only feature.

Within the initial Brain Bank series for PD there were 730 cases, of which only 7 were found to have no evidence of neurodegenerative disease related to PD. Are these individuals pathological correlates of SWEDD? Reviewing the clinical data, all 7 patients had tremor as a dominant feature.

In the modern era, with use of FP-CIT scans, there is much variability in reporting methods; with some preferring a visual assessment system and others quantitative analysis. This in itself can lead to diagnostic uncertainty, especially when the scan result conflicts with the clinically expected outcome.

6. Offaction in SWEDD patients – Dr Laura Moriyama, UCL Institute of Neurology

The causes of smell loss are multifactorial, including:

- Decline with age
- Gender (women outperform men)
- Damage to epithelium from previous cold/flu
- Head trauma: fracture of axons passing through the cribriform plate
- Neurodegeneration: severe deficit in Alzheimer’s Dementia (AD) and PD, with mild/moderate deficit in various other conditions

In PD, 70-90% of patients have objective smell loss and although self-reporting is often reliable, smell tests may help in the early detection of PD. The severity of failure of smell identification is not related to disease duration, disease severity or PD treatment.

Smell tests conducted upon patients with ET showed a possible mild deficit in the earlier papers, but with no deficit reported in more recent papers.

Silveira-Moriyama et al reported smell testing in 21 SWEDD patients. University of Pennsylvania Smell Identification Test (UPSIT) scores within this group differed significantly from those with idiopathic PD and more comparable with controls. ET and dystonia.

UPSIT tests were also performed on 41 SWEDD patients from the Nottingham area, with mean disease duration of 16 years, mean age 64.8yrs and mostly tremor dominant in terms of clinical symptoms. Again in this cohort the SWEDD group outperformed PD group in terms of offaction.

When the results of the London and Nottingham cohorts were combined, age and gender had a statistically significant load. Statistical analysis of UPSIT scores showed the SWEDD group to differ significantly from PD and control groups, but without significant difference between ET and ET groups.

Future directions for smell testing within the SWEDD cohort:

a. Smell test more subjects with tremors (ET, DT, SWEDD) cost of a UPSIT test is approximately 10 times less than that of a FP-CIT scan
b. Go back to the SWEDD cohort and use clinical insight to determine if SWEDD patients are a heterogenous group i.e. those with smell deficits and those without.
c. Carefully collect clinical/phenomenological data on SWEDD patients: might they also be neurodegenerative?
d. UPSIT tests may be more sensitive than Sniffin’ Sticks, especially in those with milder deficits.
e. Develop a database of UPSIT scores for control and PD subjects, also very important to test local controls.

7. Handwriting and Spiral Analysis in SWEDD patients – Dr Peter Bain

As clinical distinction of SWEDD patients from PD, especially in early disease stages, can be challenging, careful analysis of the phenomenology of both conditions is called for. With this in mind, comparisons of handwriting samples and spiral drawings were carried out between SWEDD patients and PD cohorts. Results by Bajaj et al compared handwriting samples from 8 tremor dominant PD patients and 20 dystonic SWEDD patients (diagnosis based upon FP-CIT SPECT, longitudinal clinical data and response to dopaminergic treatment). Handwriting examples were then reviewed by 3 individuals, blinded to clinical details, and asked to diagnose PD or non-PD in each case. The results showed mean sensitivity of 33.5% and specificity of 83.1%.

Micrographia, in the tremor dominant PD cases, was diagnosed in 1 patient by all 3 reviewers, 2 patients by 2 reviewers, 2 cases by 1 reviewer, and deemed not present in 3 cases. Eight of 20 cases (40%) of the SWEDD cases were described as having large jerky childish writing. Overall these results suggest that visual inspection of handwriting is not a good method of discriminating between these two conditions. Previous work comparing spirals drawn by PD and ET patients showed those drawn by PD patients to be significantly smaller in diameter, denser and less tremulous than those drawn by patients with ET. As the neural cause is unclear, a true comparison of both the PD and ET cases, was diagnosed in 1 patient by all 3 reviewers, 2 patients by 2 reviewers, 2 cases by 1 reviewer, and deemed not present in 3 cases. Eight of 20 cases (40%) of the SWEDD cases were described as having large jerky childish writing. Overall these results suggest that visual inspection of handwriting is not a good method of discriminating between these two conditions.

Previous work comparing spirals drawn by PD and ET patients showed those drawn by PD patients to be significantly smaller in diameter, denser and less tremulous than those drawn by patients with ET. Using similar criteria, Bajaj et al compared 65 tremor dominant PD and SWEDD patients. This found no significant difference in tremor severity however, those drawn by tremor dominant PD patients were significantly smaller in diameter and denser than SWEDDD patients. The most sensitive method was the spiral 3 turn-diameter (75%) and spiral density the most specific (83%), thus suggesting that spirography may have some role in distinguishing between the two.

8. Tremulous patients misdiagnosed as PD – clinical and physiological characteristics of tremulous SWEDD patients – Dr Mark Edwards (UCL Institute of Neurology)

There are multiple differential diagnoses for both rest tremor and action tremor e.g. Parkinson’s disease, benign tremulous Parkinson’s disease, DT for the former and ET, cerebellar tremor, and tremor associated with dystonia for the latter.

The main problems are that clinical features of tremor syndromes overlap and there is disagreement over which features are valid. In addition simple tremor parameters overlap and do not distinguish patients on an individual level. On one level it could be thought that this argument was academic, however, it does have an impact upon clinical care as it causes a stagnation of pathophysiological understanding and a contamination of clinical trials.

34 | ACPN | VOLUME 10 NUMBER 4 | SEPTEMBER/OCTOBER, 2010
The predominant questions surrounding tremulous SWEDDs patients are:

a. How can we stop diagnosing these patients as having PD?
b. What is the underlying cause of their tremor?

Recent work by Schwingschuh et al. attempted to answer some of these questions. They attempted to define the clinical characteristics, both motor and non-motor, of 25 SWEDDs and 25 tremor dominant PD patients. There was then an assessment of the tremor itself using accelerometry comparing PD patients with SWEDDs, dystonic tremor and essential tremor. There was a further assessment using a specialised electro-physiological method (paired associative stimulation) which assesses the ease with which one can cause plastic changes within the motor system. Previous studies using this technique have found that patients with PD (off treatment) show a very limited response whereas patients with dystonia show an exaggerated response. It had not previously been applied to people with ET.

Results of the clinical investigation suggested:

- Hypomimia, re-emergent postural tremor, decreased and fatiguing of repetitive hand movements, main tremor at rest were discriminating features in favour of tremor dominant Parkinson’s disease.
- Head tremor and the presence of dystonia favoured a diagnosis of SWEDDS.
- Non-motor symptoms (scores, were more prevalent amongst PD patients. PD patients tended to respond better to medical therapy with levodopa treatment performing the best. The best group of drugs amongst the SWEDD cohort were anticholinergics.

Accelerometry results suggested an overlap amongst both groups and did not readily distinguish SWEDD patients from TDPD.

The paired associative stimulation test confirmed previous studies with an exaggerated response in patients with dystonic tremor and a subnormal response in patients with PD. Patients with ET were not different from normal controls. However, tremulous SWEDDs patients showed an exaggerated response to paired associative stimulation similar to that seen in patients with dystonic tremor.

Therefore overall tremulous SWEDDs patients have a clinical overlap with TD PD patients but lack re-emergent tremor upon posture, have a dominant tremor upon posture, involvement of head with tremor, lack true bradykinesia and lack non-motor symptoms. Using simple accelerometry, it is not possible to differentiate tremulous SWEDDs patients from other causes of tremor such as PD or ET. However, their response to an experimental plasticity protocol clearly separates them from the response seen in ET and PD and is similar to the abnormal response seen in dystonic tremor. This is additional evidence that a major cause of SWEDDs in tremulous patients could be adult-onset primary dystonia.

In contrast SWEDDs patients were found to have a significantly greater incidence of:

- Subtle dystonic features e.g. thumb or little finger hyperextension
- Positive family history of either tremor or PD
- Head tremor
- Flurries

10. Tremor Genetics – Where is Dystonia tremor Genetics? – Dr Huw Morris, University Hospital of Wales, Cardiff

Mendelian tremor conditions subgroups defined on Online Mendelian Inheritance in Man (OMIM). Under the term ‘tremor genetics’ include: familial myoclonic cortical tremor with epilepsy (FCMTE), gerstmann- straussler-scheinker, Myoclonic Dystonia Syndrome, Fragile X tremor ataxia syndrome, Essential tremor (ETM 1, 2, 3 & 4), familial dystonia, etc.

Mendelian tremor conditions subgroup defined on Online Mendelian Inheritance in Man (OMIM). Under the term ‘tremor genetics’ include: familial myoclonic cortical tremor with epilepsy (FCMTE), gerstmann-straussler-scheinker, Myoclonic Dystonia Syndrome, Fragile X tremor ataxia syndrome, Essential tremor (ETM 1, 2, 3 & 4), familial dystonia, etc.

Although there is now a well replicated common risk association in essential tremor (LINGO1) it seems surprising that to date no progress in identifying Mendelian ET genes has been made. This may relate to the overlap and diagnostic confusion with dystonic tremor. The main difficulties with research to date is ascribing to the differing degrees of variation in penetrance and the existence of phenocopies within families and variation in allelic transmission possibly playing a role. The identification of SWEDDs patients within Parkinson’s disease clinics highlights the diagnostic uncertainty in some patients, and the identification and characterisation of Mendelian families with dystonic tremor will clarify the situation, and provide insights into pathogenesis.

Discussion

NB: What is the definition of SWEDDs?

AL: Response: a patient suspected of having parkinsonism has gone on to have a nuclear imaging scan, usually FP-CIT, which has subsequently been reported as normal. This group of patients could then be subdivided into tremulous and non-tremulous forms.

NQ: Using a scan result to make a clinical diagnosis appears to be moving in the wrong direction. Instead we should begin by characterising the tremor and attempting to differentiate TD/PD/ET/DT on clinical grounds, and using scans only in clinically uncertain cases.

DG: Clinical differentiation is often very difficult and FP-CIT scans have opened a new arena where patients

have an unexpectedly normal scan. Therefore we have a need to try and analyse these cases and work out why this may be the case.

PB: SWEDDs patients are likely to be a heterogeneous group. In addition there may be medicolegal implications of the diagnosis of SWEDD in terms of prognosis versus PD.

NB: We need to consider formal drug trials in dystonic tremor which can be a very debilitating condition. There is a need for large scale trials assessing the effects of e.g. propranolol, primidone, benzodiazepines, anti-cholinergics and newer drugs such as levetiracetam. There are also anecdotal reports of deep brain stimulation surgery being helpful in case studies- again we need formal trials to decide which surgical target might be best.

ME: We could consider a trial of alcohol substitutes e.g. l-octanol.

NB: I often find the tremor component of tremor dominant PD does not respond well to L-dopa whereas the bradykinesia does. What is the experience of others?

NQ: I think virtually all PD patients with tremor will respond to L-dopa, but some will need unacceptably high doses.

AL: It will often take more than 1 year of treatment at high doses before any improvement to the tremor component is seen in tremor dominant PD. However, I agree with NQ that the rest component of the PD tremor responds better to L-dopa than the postural or kinetic components.

AL and NQ: Neither have seen DT respond to L-dopa, nor even the rest component of DT.

ME: In addition to the suggestions above there is also need for an epidemiological study to determine who is being misdiagnosed with PD and why. We should begin by attempting to correlate all reported SWEDDs cases thus far and attempt to determine their clinical features. Their clustering of numbers may reflect a referral bias to specialist centres.

NB: Access to FP-CIT scan is very variable throughout the country and the approaching decade of austerity may further lessen its availability. Instead, maybe we should be focusing upon re-learning of clinical skills to improve diagnosis.

DG: We should aim to provide reassurance to other neurologists that diagnosis of PD and differentiation from SWEDDs cases can often be difficult and mistakes will be made even by the most experienced movement disorders experts.
HM: Patients with PD should have bradykinesia but this can be difficult to determine in the presence of tremor. A normal FP-CIT scan makes the diagnosis very unlikely and should prompt the consideration of other diagnoses including dopa responsive dystonia and psychogenic tremor, in addition to dystonic and essential tremor.

ME: What is the aim of clarifying the issues surrounding SWEDDs cases? It is for clinical reasons e.g. review of patients within 6 months of initial consultation and a trial of treatment? Is it research i.e. for accurate classification of tremor disorders when carrying out therapeutic or genetic studies? Or is it a question of health economics and not giving expensive PD treatments to patients who do not have the disorder?

NB: We need to address the issue of variability in the techniques used for FP-CIT scan reporting. Visual methods using a 0-3 scale are prevalent, alternatively quantitative analysis is used in some centres. We need to standardise how scans are read and reported. We should possibly introduce blinded reading of other centre’s scans. There should also be a system of regular external audit for quality assurance purposes.

HM: Scans should be interpreted as part of the overall clinical picture. All FP-CIT scans should be reviewed as standard, followed by an additional blinded reader. There should also be a system in place to deal with questionable scans. Nuclear medicine experts should also be blinded to the clinical features of the case.

NB: What is everyone’s view on serial FP-CIT scans? If so, how many? And at what frequency? Should part of the criteria include consistent abnormality and should degree of abnormality be graded?

DG: Current evidence suggests approximately 1 in 200 scans are difficult to interpret. Generally it is suggested that these scans should be repeated 1 year later if it is clinically indicated. Our own approach is to defer repeat scanning for longer, to maximise the chance of detecting a change between sequential studies; we generally use an 18 month interval.

Consensus amongst the group: significant clinical heterogeneity amongst TDPP patients. Some TDPP patients progress with dystonic tremor over decades.

AL: Is monosymptomatic rest tremor a forme fruste of PD?

NB: Do we believe that ET can lead to PD? Statistically there must be patients with ET who also have PD.

NQ: There is inherent bias in the patients who attend clinic. We are much more likely to see those with ET who then develop PD than those who don’t.

NB: Generally the ET definition from 1998 has stood the test of time and should be adhered to.

NQ: Would disagree with component regarding isolated head tremor, which I don’t consider as ET. However, this argument may simply be tautological. If it is decided that ET constitutes a family of separate conditions, then this may be one of them.

AL: Predominant problem is that people are not using the criteria appropriately.

ME: Concerns with the number of people being labelled with dystonic tremor, often when they have very little dystonia that is visibly clinically.

HM: Future research should include further delineation and study of dystonic tremor as a clinical entity; a prospective review of diagnoses and outcomes in patients with parkinsonism/tremor and SWEDDs, evaluation of the assessment of bradykinesia in challenging clinical situations.

Conclusions

The use of new clinical diagnostic techniques has a tendency to broaden recognised clinical phenotypes, something that has already been seen with the use of molecular genetic techniques. In a similar way, the widespread use of presynaptic dopaminergic imaging has allowed us to recognise and start to categorise syndromes resembling PD. The use of these imaging techniques has not only increased our awareness of the variability within the phenotype of PD but also has made us re-examine the tremulous syndromes that can resemble PD and hopefully re-define these in a more systematic way.

These other tremulous syndromes, although often more benign in outlook, can also be more difficult to treat symptomatically than PD itself, and future directions for the study of SWEDDs should include drug trials and surgical therapy trials investigating better treatment options in SWEDDs cases. Furthermore, the high prevalence of a positive family history in these benign tremulous disorders should lead to genetic studies giving further insight into the aetiopathogenesis of these disorders.

The high prevalence of SWEDDs across clinical trials to date should also raise the question as to whether to incorporate presynaptic dopaminergic imaging into all PD clinical trials, with scan abnormality as an obligatory inclusion criteria. This may also help ensure trials more representative of PD as a whole perhaps increasing the inclusion of more tremulous PD patients that have always represented more of a clinical challenge. They may therefore have been referred for trial inclusion less regularly than their akinetic-rigid counterparts. The identification of all SWEDDs cases is of great importance in the future and across clinical departments, in order to go beyond the registry/database of SWEDDs patients allowing other external review of these subjects and further research in this fascinating and important area of movement disorder research.

REFERENCES


