SWEDD for the General Neurologist

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A pleasant spring morning in a London Square was the setting of the first ever SWEDD-UK meeting. The event was made possible with generous support from the Dementias and Neurodegenerative diseases network (DeNDRoN).

Many of you will be forgiven for never having heard of SWEDD. This article, summarising the proceedings of the meeting, and detailing the aims of the UK consensus group, should tell you all you need to know. For those of you who want to know more, there has been a detailed recent review.[1]

What is a SWEDD and why should I care?

Scans without evidence for dopaminergic deficit (SWEDD) is the term originally coined to describe a group of patients that puzzled the movement disorder establishment. At the time this term was coming into use, a number of studies comparing post-mortem diagnosis of Parkinson's disease with the clinical diagnosis in life had already confirmed our widely held belief that our clinical skills were excellent and indeed, over the course of studies held a decade apart, were improving.[2,3]

A number of clinical trials held against this backdrop of high confidence in our clinical diagnostic skills, were attempting to use nuclear medical imaging techniques [18F-dopa PET or β-carbomethoxy-3β-(4-iodophenyl)nortropane single photon emission computed tomography (β-CIT SPECT)] as a biomarker to assess disease progression.[4-6] The use of these imaging techniques as disease biomarkers in PD has since come under considerable criticism, but the role of these techniques in distinguishing PD from benign tremor disorders has been endorsed, inter alia, by NICE.[7] These trials all sought to recruit patients with PD, either relatively early or later in the disease course, referred from movement disorder specialists in the USA, UK and Europe. The trials organisers were surprised to note a consistently high normal functional imaging scan ranging from 4% for later disease course trials to 15% for early disease course trials. Initially a number of explanations were considered to explain this anomaly, including poor diagnostic accuracy of the scans and poor diagnostic accuracy of the clinicians. Subsequent long term follow-up of these patients however was notable for no initially normal scans becoming abnormal with time and for blinded clinician review of the video-tape of patients confirming the initial clinical presumption that these patients looked like they had PD.[8,9] Furthermore, more recent olfaction studies have shown near normal olfaction scores in SWEDDs patients whereas PD patients are notable for impaired olfactory function.[10] A number of studies looking at diagnostic accuracy of SPECT scanning have also confirmed a high clinical concordance between the scan findings and clinical opinion with sensitivity (93%) and specificity (95%) of detection of the pre-synaptic dopaminergic deficit typical of PD.[11]

Although the term SWEDD is relatively recent in usage and has emerged from the clinical trial literature, clinicians have always been aware of PD mimics where the parkinsonism is not of a pre-synaptic, dopaminergic deficiency origin. Thus the term SWEDD can really be levelled at any patient that looks as if they have PD but where subsequent functional imaging assessments do not confirm this. SWEDD phenotypes will therefore vary in much the same way as PD phenotypes do. There are two broad PD phenotypes, akinetic-rigid (also known as postural instability gait disorder variant-PIGD) and tremor dominant (also known as tremulous PD).[12] In the same way, SWEDDs patients can be subdivided into tremor dominant and non-tremor dominant (or tremor absent) subtypes. These subtypes are summarised in Tables 1 and 2.

Most causes of SWEDDs are sufficiently uncommon to be rare causes of clinical mis-diagnosis outside the most specialised of units. It is the common causes of SWEDDs that the clinical readers of this article need to be most wary of. Some common causes of SWEDDs give other clues- vascular parkinsonism is relatively common but most cases of vascular parkinsonism do not look like typical PD. The classic vascular PD case may have stepwise progression (reviewed in 13), be predominately lower body, show no response (or poor response at standard doses) to leva-dopa and have an MRI brain showing extensive leukoariopathy especially in the basal ganglia. Tardive cases are common but are usually referred from concerned psychiatrists and are obviously on neuroleptic drugs – similarly a drug history of valproate exposure requires little detective work to come up with this as a diagnostic consideration.

The commonest cause of SWEDD that would trouble the general neurologist and even the movement disorder expert are those harbouring a tremulous but benign condition where parkinsonian features are a common occurrence. This is where adult onset dystonic tremor, indeterminate tremor and perhaps essential tremor (ET) need to be considered. Whether ET should be considered at all as a cause of SWEDD is controversial, and indeed was one of the topics debated by our experts in the SWEDD-UK meeting (see proceedings following), but there is sufficient reference to this in the current literature that for the moment, we have retained it. Under the 1998 Movement Disorder Consensus Statement on Essential Tremor,[14] other neurological features e.g. dystonia, are exclusion criteria for definite ET and thus ET masquerading as SWEDD should not occur, but given the prevalence of ET, dual pathology with parkinsonism secondary to the ageing process, cerebrovascular disease or concomitant medications, is likely to occur.

Table 1. Causes of non-tremor dominant SWEDD phenotype

Non-Tremor Dominant SWEDD	References
Tardive (neuroleptic) induced	18
Vascular Parkinsonism	13, 19
Brain Neoplasm	20, 21
Carbon Disuphide	22
Manganism	23, 24
Huntington's disease	25

Table 2. Causes of tremor dominant SWEDD phenotype

Tremor-Dominant SWEDD	References
Adult onset Dystonic Tremor	17
Essential Tremor	26
Psychogenic Tremor	27
Fragile X premutation	28
Valproate Toxicity	29

As a proof of principle that tremulous SWEDDs patients are the really troublesome diagnostic conundrums and to emphasise clinical diagnostic error rate, we recently assessed the ability of two of the UK's leading movement disorder experts to clinically distinguish a series of tremulous SWEDDs from TDPD on blinded videotape analysis. Many will argue that videotape analysis is not the same as seeing a patient in clinic, but we already know from the SWEDD literature that even seeing patients in person, in the clinic setting, can give a false positive error rate of up to 15% for PD. Furthermore, videotape diagnosis of movement disorder is something that we experts indulge in at numerous video Olympics sessions held around the world and there is a literature validating the diagnostic accuracy of video consultation.[15]

So how did our experts do? Well, you can soon read for yourself but with a specificity for the diagnosis of PD ranging from 79-85%, and sensitivity of 72-93%, their performance was respectable but not as good as either of them would have liked.[16] To spare the blushes of our experts, the entire audience at the British and Irish Movement Disorder Meeting in London 2009, and the assembled panel at SWEDD-UK were subjected to similar blinded analysis of tremulous parkinsonian patients. Needless to say, the diagnostic accuracy of both audiences was sub-optimal and really serves to highlight the following point: tremulous SWEDD cases are not uncommon, you will all come across them in your clinics and even the very best among you will make diagnostic mistakes. If you have diagnostic doubts, you should consider ordering an FP-CIT or PET scan for diagnostic clarification.

Making SWEDD obsolete

Having taken the time to publicise the term SWEDD for the general neurological community, one of the aims of the SWEDD-UK meeting was how to eliminate SWEDD from our practices. After all, there are clinical clues to spotting some causes of SWEDD and we have detailed these already, such as the lower body phenotype of most vascular PD cases and the very symmetrical parkinsonian appearance of tardive PD cases.

Are there clinical clues or "tells" that would make us consider an alternative diagnosis and save us from making a false positive diagnostic error of PD? This consideration was the subject of a paper from Schneider and colleagues[17] noting the frequency of dystonic features in a cohort of SWEDDs patients which would allow their re-classification as adult onset dystonic tremor. Although this paper was a real landmark in the understanding of tremulous SWEDD, it is unlikely to be the end of this story. One finding that emerged strongly from the mis-diagnosis between TDPD and tremulous SWEDD by our two movement disorder experts[16] was the frequency of dystonic features in drug naïve, adult onset TDPD, which markedly reduced the usefulness of identifying dystonia as the discriminating feature between these two conditions. Furthermore, discussions following on from the publication of the original paper,[16] have highlighted that one mans' dystonia may not be anothers', and that subtle head tilt and thumb hyperextension as hints to dystonia may lead to over-interpretation of the signs. Still, the identification of dystonic features is useful and would certainly save the more typical dystonic tremor patient from being mis-diagnosed as TDPD. Whether the lessons we have learnt from functional imaging will inform our clinical practice to such a degree as to render these scans obsolete is another matter altogether. I rather feel that SPECT scanning for the uncertain parkinsonian patient is here to stay.

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