Imaging and atypical parkinsonism

Introduction
The spectrum of parkinsonian syndromes is wide and, due to the lack of specific biomarkers, their diagnosis remains largely clinical. Disorders that are most commonly referred to as 'atypical parkinsonism' comprise progressive supranuclear palsy (PSP), multiple system atrophy (MSA), corticobasal degeneration (CBD) and dementia with Lewy bodies (DLB). The characteristic features of these disorders are well recognised. However, these features may be absent or ambiguous at initial diagnosis and the clinician may be uncertain about the L-dopa response. Many atypical parkinsonism cases initially resemble idiopathic Parkinson's disease (PD).

Furthermore, clinicopathological studies have suggested varying and overlapping phenotypes between these disorders. Early diagnostic accuracy is not only important for patients and their families, particularly with respect to prognosis, but also imperative for researchers entering patients into clinical studies. Identification of patients in the pre-symptomatic phase is also essential for evaluation of potential disease modifying agents. There has been much discussion regarding abnormal imaging findings in atypical parkinsonism, but the question arises as to how useful these are in clinical practice. In this brief article we will outline how structural and functional imaging can aid the diagnosis of atypical parkinsonism.

Part 1: Atypical parkinsonism

PSP:
Pathologically PSP is characterised by neuronal loss, gliosis and the presence of microtubule-associated tau inclusions within neuronal and glial cells. A genome-wide association study in PSP has recently identified new loci potentially related to underlying disease pathogenesis. There are two main clinical subtypes: Richardson syndrome (PSP-R) and PSP-parkinsonism (PSP-P), which appear to differ pathologically as well as clinically. PSP-R is the classic phenotype: patients present with falls, executive dysfunction, eye movement abnormalities (initially with slowed saccades and evolving into supranuclear gaze palsy), dysarthria and marked postural instability. In PSP-P, there is bradykinesia, limb and axial rigidity and sometimes a jerky tremor at presentation. Signs may be asymmetric and initially be L-dopa responsive. Rarer subtypes include PSP-pure akinesia with gait freezing, PSP-corticobasal syndrome and PSP-frontotemporal dementia. The Movement Disorder Society Task Force is currently reviewing the diagnostic criteria for PSP and these should be published in 2015.

MSA:
There are two main clinical subtypes of MSA: MSA with parkinsonism (MSA-P) and MSA with cerebellar signs (MSA-C), with progressive autonomic failure and falls being common to both. MSA-P may be difficult to differentiate clinically from PD although the former's signs are usually more symmetrical. MSA-C patients present with gait ataxia, dysarthria, cerebellar and oculomotor dysfunction, often with little evidence of parkinsonism. Other features may include stridor and pyramidal signs. MSA is generally poorly L-dopa responsive and a minority of patients have cognitive dysfunction.

In common with PD and DLB, pathologically MSA is an alpha-synucleinopathy, except that oligodendrogliosis rather than neurones are affected. Although these lesions are widespread they are predominately located within olhopontoocerebellar regions in MSA-C and within striatonigral regions in MSA-P. Furthermore, the burden of these inclusions is greater with increasing disease duration and severity. Familial MSA is very rare, but variants in the alpha-synuclein gene have been associated with an increased disease risk.

CBD:
CBD is possibly the most challenging atypical parkinsonism to diagnose accurately. The classic presentation is with a corticobasal syndrome (CBS) consisting of asymmetric akinetically-rigid parkinsonism, ideomotor apraxia, dystonia, myoclonus and the alien limb phenomenon. However, post-mortem studies have shown that only 50% of CBS patients clinically diagnosed during life pathologically had CBD, with other causes of CBS including PSP, Alzheimer's disease and frontotemporal dementia (FTD). Furthermore, rarer CBD phenotypes include FTD, progressive non-fluent aphasia and Richardson syndrome. The clinical diagnostic criteria for CBD were updated in 2013 and cases can be divided into probable and possible. Pathologically there are tau-positive inclusions with cortical and striatal neuronal and glial cells with marked neuronal cell loss in frontoparietal and nigral regions.

DLB:
Like PD and MSA, DLB is an alpha-synucleinopathy: Parkinson's disease dementia and DLB are pathologically considered as a continuum with little change in the distribution or quantity of Lewy bodies and neurites. Clinically DLB is differentiated by the predominance of dementia at presentation or within 12 months of motor symptoms. In DLB the cognitive impairment is characterised by deficits in...
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temporal bone window. Furthermore, 10% of the population have abnormal substantia nigra echogenicity. In MSA a combination of striatal hyperechogenicity and normal echogenicity of the substantia nigra can distinguish MSA-P from PD.11 TS is also abnormal in PSP and CBD.

Another imaging method that has been studied in atypical parkinsonism is MIBG myocardial scintigraphy. This is usually reduced in PD and normal or slightly low in MSA-C.11 However, this technique has largely remained a research tool.

Conclusions
The importance of early and accurate diagnosis in neurodegenerative disorders cannot be overstated. The spectrum of atypical parkinsonian disorder is wide and until such time as reliable biomarkers are identified these disorders will continue to be diagnosed on clinical grounds. The challenge is greatest in early disease when characteristic clinical features may be subtle, present at all. The recognised changes on structural imaging may not be present in these early stages but can certainly inform the diagnostic process in individual cases. Functional dopaminergic imaging also has a role, and has the advantage of being abnormalities at an earlier clinical stage, but does not allow reliable differentiation between disorders.

REFERENCES

Emma Williams, Founder/CEO of Matthew’s Friends and Mum of Matthew, has been awarded an MBE for her services to Children with Epilepsy.

Julie Edwards, Trustee of the charity says “Noone is more deserving than Emma for her selfless and tireless work over the years and her continued drive and remarkable determination to help those who live with drug-resistant epilepsy. Emma’s passion and championing of Ketogenic Dietary Therapies has made a huge difference to so many affected families and her work nationally and internationally has impacted enormously on the positive awareness of these treatments. Achieving this whilst caring for her own severely disabled son Matthew and his sister Alice is truly inspirational to us all.”

Professor Nick Alderman, Director of Clinical Services, Brain Injury Services, has won the UK Acquired Brain Injury Forum (UKABIF) Stephen McAleese Award for inspiration by an individual in the field of acquired brain injury.

UKABIF Award winners were announced on 27th November in London at the organisation’s sixth annual conference.

Announcing the award, Professor Michael Barnes, UKABIF Chair said “Nick has made an outstanding contribution to neurorehabilitation and he’s a well-deserved winner of this Award”.

Chartered Psychologist and Chartered Scientist, Prof Alderman was selected for successfully reducing the need for restrictive intervention in managing recovery, through his development of observational rating scales and outcome measures now accepted as the best available, including tools called OAS-MNR, SASBA and SANSOS. He also co-authored BADS, a widely used test of executive functioning capabilities. He has also been instrumental in developing clinical interventions to reduce social handicap associated with neurobehavioural disability.

On receiving the award from John and Susan McAleese, parents of Stephen McAleese, Professor Alderman said “Stephen McAleese dedicated his life to raising awareness of acquired brain injury and to helping others; he was a truly inspirational individual. I feel honoured and humbled to be the recipient of this award from UKABIF which bears his name.”