Neuroimaging in Parkinsonism: Insights and Challenges

The diagnosis of different forms of Parkinsonism is primarily based on clinical evaluation and differentiating them can be challenging.[1,2] Although various ancillary tests can aid in the diagnosis, no current test can reliably differentiate between different Parkinsonian disorders. Significant advances have been made across neuroimaging modalities to develop imaging markers for these disorders,[3] and among these modalities, magnetic resonance imaging (MRI) of the brain is widely available and commonly used in clinical practice.

Both qualitative and quantitative MRI markers have been investigated for different Parkinsonian disorders. For example, the loss of dorsolateral nigral hyperintensity ("swallow tail") on susceptibility-weighted MRI has been observed in Parkinson's disease and atypical parkinsonism. In MSA-parkinsonism, the putaminal rim sign and putaminal hypointensity on T2-weighted images have been described, while in the MSA-cerebellar subtype, the "hot cross bun" sign due to cruciform pontine hyperintensity on T-2 weighted images can be present. Radiological markers such as "hummingbird" and "morning glory" signs due to midbrain atrophy are useful to differentiate PSP from other Parkinsonian disorders. Recently, magnetic resonance parkinsonism indices (MRPI) and MRPI 2 have been introduced to distinguish PSP from PD based on brain imaging.[3] These indices use MRI to measure the degree of atrophy in specific areas of the brain, which can help differentiate between the two disorders. Similarly, for idiopathic normal pressure hydrocephalous (iNPH), multiple radiological markers have been investigated to differentiate it from other Parkinsonian syndromes, including the Evans Index (EI), narrowing of callosal angle (CA), magnetic resonance hydrocephalous Index (MRHI) and disproportionate enlarged subarachnoid space (DESH) score.[4] These radiological markers could be utilized to support the diagnosis of Parkinsonian disorders in conjunction with their clinical symptoms.

Despite the advances, the utility of radiological markers in clinical diagnosis is currently limited, as these findings may not be present in all patients, particularly in the early stages of the disease. Also, overlapping imaging findings across different disorders can create diagnostic challenges.[5,6] Studying the overlapping MRI markers among different disorders has the potential to identify markers that could enhance diagnostic accuracy and provide insight into underlying commonalities in pathophysiology.

In this issue of the journal, Önder *et al*.[6] conducted a study to compare MRI parameters between patients with probable PSP and iNPH. The authors retrospectively identified 19 patients with a clinical diagnosis of probable PSP and 18 patients with a diagnosis of iNPH from the database and analyzed different MRI markers. The study found no significant differences in the MRI parameters for PSP (MRPI, $P = 0.630$ and MRPI 2, $P = 0.946$) between the two groups. Upon comparing radiological parameters for iNPH, the authors identified an overlap in imaging findings between the two groups. Specifically, they found that all patients with iNPH and 90% of patients with PSP had an EI >0.3, narrowing of CA in 53% of patients with iNPH and 16% with PSP, and a DESH score ≥ 3 in 82% of patients with iNPH and 68% with PSP. Although there were differences in the radiological parameters for iNPH, such as CA and DESH score, the ROC analysis did not demonstrate high diagnostic accuracy. These findings suggest that MRI parameters may not accurately distinguish between the two conditions.

Both PSP and iNPH can present with similar clinical features, such as gait difficulty, freezing of gait, and falls. Therefore, clinical differentiation between these two conditions can be challenging, especially in the early stages of PSP when patients may not exhibit significant oculomotor abnormalities. While imaging markers can aid in distinguishing between these disorders, the study by Önder *et al*. highlights the challenges of utilizing radiological markers to differentiate between PSP and iNPH. These findings can have implications for clinical practice and may influence therapeutic approaches. The current study found overlapping parameters in the majority of the patients, although the small sample size warrants further investigation of these findings in a larger patient population to determine what percentage of patients with PSP and iNPH can have significant overlap in MRI parameters.

Another interesting aspect discussed by the authors is that these findings support the possibility of co-occurring pathology of PSP and iNPH in some patients. Similarities in imaging findings between PSP and iNPH were also observed previously in another study based on which authors proposed a new PSP phenotype with hydrocephalous.[7] This is an important observation as it suggests that these patients may share common pathophysiological mechanisms, leading to overlapping imaging findings. Understanding the commonalities between these disorders could have implications for the diagnosis and management of patients with these conditions. However, further studies and clinicopathological data are needed to investigate the co-occurrence of these disorders and to determine the frequency and clinical significance. Additionally, it will be important to follow patients with overlapping imaging findings who undergo shunt surgery over time to understand the long-term response and guide clinicians in the management of these patients.

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Submitted: 04-Apr-2023 **Accepted:** 11-Apr-2023
Published: 22-May-2023

DOI: 10.4103/aian.aian_292_23