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Original Article

Can loss of the swallow tail sign help distinguish between Parkinson Disease and the Parkinson-Plus syndromes?

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ABSTRACT

Purpose: To determine if loss of the swallow tail sign (STS) can distinguish Parkinson Disease (PD) from the Parkinson-Plus syndromes.
Methods: Twenty-five patients with PD, 21 with Parkinson-Plus syndromes, and 14 control patients were included. Presence of the STS was assessed.
Results: The STS was present in 79% of controls, statistically greater than the PD/Parkinson-Plus patients. There was no difference in the presence of the STS between the PD/Parkinson-Plus subgroups or when scanning at 1.5 T or 3 T.
Conclusions: Loss of the STS could not distinguish between PD and Parkinson-Plus patients. The STS can be identified at both 1.5 T and 3 T.

1. Introduction

Parkinson Disease (PD) is a progressive neurodegenerative disorder that produces characteristic motor symptoms which include tremor, hypokinesia, bradykinesia, muscle rigidity, and gait disturbance. Patients also exhibit non-motor symptoms such as dementia and depression. Parkinson-Plus syndromes are a group of disorders characterized by different causes of degeneration of the nigrostriatal system and, as such, are manifested by parkinsonism with additional distinguishing features, such as early autonomic failure, early postural instability or poor response to levodopa [1]. These syndromes include Multisystem Atrophy with predominant Parkinsonism (MSA-P), a synucleinopathy, as well as the tauopathies, Progressive Supranuclear Palsy (PSP) and Corticobasal Degeneration (CBD). Given the overlap of the clinical presentations of PD and Parkinson-Plus syndromes, accurate diagnosis of these syndromes can be challenging [2,3], with reported error rates of up to 29% [4].However, a correct, early diagnosis of a specific condition is important, since prognosis, expected disease progression, and management differ for each entity [5]. Ioflupane I-123 single photon emission computed tomography (SPECT), also known as a DaTscan, was approved by the Food and Drug Administration for the diagnosis of PD in 2011. While the DaTscan has been shown to be sensitive for the diagnosis of PD [6] versus controls, it cannot differentiate between PD and the Parkinson-Plus syndromes [7]. Additionally, this test is not widely available and requires the use of ionizing radiation. Given these limitations, researchers have looked to MRI for another method to distinguish PD from the Parkinson-Plus syndromes.

Nigrosomes are clusters of dopaminergic cells within the substantia nigra (SN) which exhibit calbindin D_{28K} negativity on immunohistochemical staining [8]. Nigrosome 1 is located within the dorsolateral SN and has been shown to be disproportionately affected in PD [9–11]. In healthy individuals, nigrosome 1 demonstrates hyperintense signal on susceptibility-weighted imaging (SWI). It is surrounded anteriorly, medially, and laterally by hypointense portions of the SN and medial lemniscus, resulting in an appearance which some have compared to that of a swallow's tail, or so-called swallow tail sign (STS) [12,13] (Fig. 1). Recently published research in patients with PD found that loss of the normal hyperintense signal within the dorsolateral SN can be reliably identified on SWI at 3 T [13,14]. These studies demonstrated high inter-observer agreement and showed that loss of the STS was both a highly sensitive and specific indicator for the presence of PD in comparison to normal controls [13,14]. Reiter et al. found similar results but also determined that loss of the STS could be seen in patients with MSA-P and PSP [15]. More recently, Frosini et al. found that loss of the STS may not be consistently seen in patients with CBD [16]. To date, no single study has compared normal patients with those diagnosed with PD, MSA-P, CBD and PSP. Similarly, no study has included examinations performed at 1.5 T. Our aim is to investigate whether loss of the normal hyperintense signal within the dorsolateral SN can distinguish between patients with PD and any of the Parkinson-Plus syndromes

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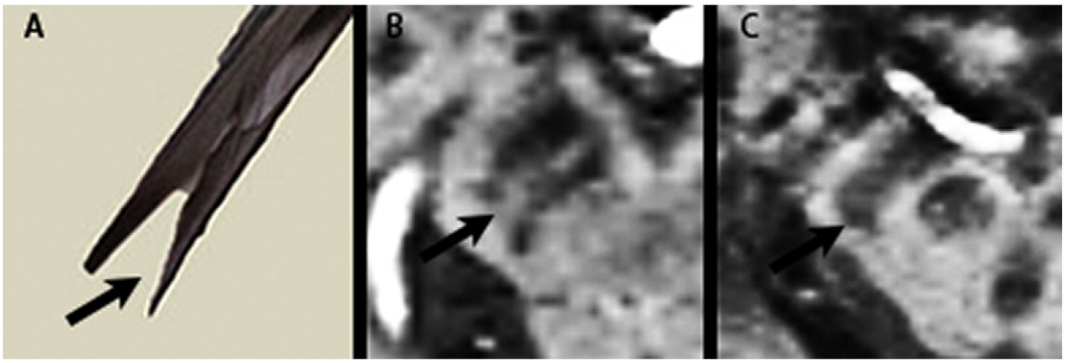

Fig. 1. A) Appearance of a swallow tail (image courtesy of Dick Daniels). The gap between the swallow tail feathers (black arrow) forms the basis of the swallow tail sign. B) SWI MRI of the brain at 3 T in a healthy patient demonstrates the hyperintense signal of nirgrosome 1 (black arrow) surrounded anteriorly, medially, and laterally by hypointense portions of the substantia nigra and medial lemniscus, the swallow tail sign. C) SWI MRI of the brain at 3 T in a patient with MSA-P demonstrates loss of the swallow tail sign (black arrow).

and to determine if this can be reliably performed on both 1.5 and 3 T MR scanners.

2. Methods

This was a retrospective, cross-sectional study which was performed following Institutional Review Board approval.

Patients were retrospectively identified utilizing the Enterprise Data Warehouse at our institution. To be included, all patients must have been diagnosed with PD, MSA-P, CBD or PSP following evaluation by a movement disorder specialist at our institution and must have also undergone MRI with SWI. Age-matched control patients were randomly selected from a pool of patients who did not carry a diagnosis of a movement disorder but who also underwent MRI with SWI. SWI is routinely included in multiple department protocols, including imaging for acute stroke, trauma, movement disorders and motor neuron diseases. In total, 25 patients with a clinical diagnosis of PD, 11 patients with a clinical diagnosis of MSA-P and 10 patients with a clinical diagnosis of the tau-related protein disorders (CBD or PSP), were included in the study. Clinical diagnoses for all patients were determined by neurologists specialized in movement disorders and were based on standard clinical criteria. The diagnosis of PD was based on UK Society Brain Bank criteria [17]. MSA-P was diagnosed by the probable presence of MSA based on American Academy of Neurology and American Autonomic Society [18]. The diagnosis of PSP was based on the probable presence of PSP based on the NINDS-PSP criteria [19]. CBD was diagnosed based on new diagnostic criteria for CBD that have been developed based on clinical phenotype predictive of CBD pathology [20]. A total of 14 age-matched, healthy controls were randomly selected and included. All patient scans occurred between January 2009 and February 2014 and were performed at either 1.5 or 3 T.

SWI is a high resolution 3D fully velocity-compensated gradient echo sequence. In SWI, both magnitude and phase images are acquired. A high pass filter is applied to the phase images in order to remove low frequency phase shifts which result primarily from background magnetic field inhomogeneities and tissue-air interfaces. A phase mask can then be generated from the filtered phase data by suppressing the signal in voxels with certain phase values. Traditionally, the phase value chosen corresponds to that of venous blood. The phase mask is then multiplied by the initial magnitude images to generate the final susceptibility-weighted magnitude image [21]. SWI studies performed at 1.5 T were performed on Avanto, Espree, and Aera scanners (Siemens, Erlangen, Germany) utilizing an 8-channel head coil, while studies performed at 3 T were performed on Verio and Skyra scanners utilizing a 16-channel head coil (Siemens, Erlangen, Germany). Scan parameters at 1.5 T included slice thicknesses between 1.6 and 2.25 mm, TR/TE 48/40, and a flip angle of 15°. Scan parameters at 3.0 T scans included slice thicknesses between 1.5 and 2.5 mm, TR/TE 28/20, and a flip angle of 15°.

MRI scans were reviewed on local radiology workstations. Scans were assessed for the presence or absence of the STS by two blinded neuroradiologists with 3 and 8 years of clinical experience, respectively. The STS was deemed absent if a normal appearing nigrosome 1 could not be visualized on one or both sides. Inter-rater reliability was assessed with the Cohen Kappa statistic. In cases where the raters disagreed, a consensus agreement was reached.

Statistical analysis for comparison of demographic variables between groups was performed using the one-way ANOVA. Statistical analysis for comparison of the presence or absence of the STS in each group was performed with the Fisher's exact test with a Bonferroni correction which set statistical significance at 0.05. All statistical analysis was performed using IBM SPSS software, Version 22.

3. Results

The PD, MSA-P, CBD/PSP, and control groups did not differ in age, gender, or magnet strength (Table 1).

There was high inter-rater agreement (58/60 cases, kappa = 0.923, $p < 0.001$). At 1.5 T, raters agreed on 24/26 cases (kappa = 0.830). At 3.0 T, raters agreed on 34/34 cases (kappa = 1.0). The STS was present in 11/14 of the healthy controls while it was absent in 19/25 patients in the PD group ($p = 0.001$), 10/11 patients in the MSA-P group ($p = 0.001$), and 10/10 patients in the CBD/PSP group ($p < 0.001$) (Fig. 2). The overall sensitivity of the loss of the STS for diagnosing PD, MSA-P, and CBD/PSP was 0.76, 0.91, and 1.0, respectively (Table 2).The overall specificity of the loss of the STS for diagnosing PD, MSA-P, and CBD/PSP was 0.34, 0.35, and 0.36 respectively. The sensitivity, specificity and diagnostic accuracy of the loss of the STS for normal patients versus all patients with movement disorders in general is 0.85, 0.79, and 0.83, respectively.

Table 1
Patient demographics.

	Controls	PD	MSA-P	CBD/PSP	p Value
Mean age (years)	65.2	66.6	62.5	72.2	0.224
Males/females	5/9 (36%)/(64%)	18/7(72%)/(28%)	4/7 (36%)/(64%)	7/3 (70%)/(30%)	0.062
Scanned at 1.5 T/3T	9/5 (64%)/(36%)	7/18 (28.0%)/(72%)	6/5 (55%)/(45%)	4/6 (40.0%)/(60%)	0.143