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Dysphagia

Pharyngo-Esophageal Dysphagia in Parkinson's Disease

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Abstract. The radiologic characteristics of pharyngo-esophageal (PE) dysfunction in Parkinson's disease (PD) are not well established, partly because most previous studies have examined only small numbers of patients. We administered a dynamic videofluoroscopic swallowing function study to 71 patients with idiopathic PD. Using the Hoehn and Yahr disease severity scale, patients were subdivided into those with mild/moderate disease, subgroup I (n = 38), and advanced PD disease, subgroup II (n = 33). From pharyngeal ingestion to gastric emptying, bolus transport was normal in only 2 patients. The most common abnormalities occurring during pharyngeal ingestion included impaired motility, vallecular and pyriform sinus stasis, supraglottic and glottic aspiration, and deficient epiglottic positioning and range of motion. Esophageal abnormalities were multiple but most commonly included delayed transport, stasis, bolus redirection, and tertiary contractions. Typical aberrations of lower esophageal sphincter (LES) function included an open or delayed opening of the LES and gastro-esophageal reflux. A pathogenesis linking PE with the pathology of PD is proposed.

Key words: Pharyngoesophageal dysfunction — Parkinson's disease — Radiologic evaluation — Gastro-esophageal reflux — Deglutition — Deglutition disorders.

Dysphagia is becoming increasingly recognized as a complication of Parkinson's disease (PD). Although Parkinson described dysphagia in his 1817 description of the illness [1], the first English citation documenting related radiologic abnormalities did not appear until 1945 when Penner and Druckerman [2] reported esophageal dysmotility. Over the next five decades, many investigators have focused on pharyngo-esophageal (PE) transport in PD, reporting slowed peristalsis, pharyngeal retention, cricopharyngeal sphincter abnormalities, and esophageal dilation [3–16].

Recent advances in the radiologic evaluation of the dysphagic patient have expanded our knowledge of bolus transport during the pharyngeal stage of ingestion of PD. Using a variety of substances that modify test bolus viscosity, Robbins et al. [13] and Bushmann et al. [14] confirmed some pharyngeal abnormalities reported previously and described additional disorders of motility including pyriform sinus bolus retention, showed laryngeal elevation, and laryngeal penetration or aspiration [13,14]. Their investigations did not observe anomalous cricopharyngeal motility witnessed by others or include esophageal function with its potential interplay with preceding stages of ingestion.

In our recent evaluation of dysphagia in patients with PD, we observed multiple prepharyngeal motor abnormalities considered secondary to disease-related bradykinesia and rigidity [17]. This cohort completed a dynamic videofluoroscopic swallowing function study. We herein report the results of the PE component of that study.

Methods

A Crozer-Chester Medical Center Dysphagia Center evaluation was completed on 72 patients with idiopathic Parkinson's disease. This included dysphagia history and clinical assessment of oral motor and sensory system functions, the results of which have been reported previously [17]. A dynamic video-fluoroscopic swallowing function study (DVSFS) was performed on all patients. The prepharyngeal results, reported previously, showed that one patient from the original cohort was unable to complete the DVSFS [17].

The videoradiography results were reviewed in 71 patients, 50 men and 71 women (Table 1). Ages ranged from 50 to 88 years (mean age = 73.0) (Table 1). The group mean disease severity score using the Hoehn and Yahr (H&Y) scale [18] was 3.5 (range II-V); the disease duration was 8.65 years (range 2–30). All but 2 patients were receiving

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Table 1. Demographic data

	Parkinson's disease	Subgroup I	Subgroup II
	(n = 71)	(n = 38)	(n = 33)
Age (±SEM)	73.0 (1.18)	73.7 (1.50)	72.18 (1.87)
Disease duration (±SEM)	8.7 (0.72)	5.5 (0.72)	12.4 (1.0)
Hoehn & Yahr score (SEM)	3.4 (0.8)	2.7 (0.07)	4.18 (0.08)
Sex (M/F)	50/21		

a variety of antiparkinsonian medications when first evaluated, the majority (70.4%) on an inpatient basis.

Dynamic Videofluoroscopic Swallowing Function Study

All patients underwent a DVSFS to confirm the location, severity, type, and cause of overt dysphagic symptoms, and to identify covert abnormalities in the pharyngeal and esophageal stages of deglutition. Two patients, both H&Y stage IV, were unable to complete the esophageal portion of the study due to severe aspiration or positioning problems. Each DVSFS used a video positioning chair (VPC), designed by one of the authors (MCK), specifically to ensure focused erect lateral and anteroposterior (A-P) observation during all stages of deglutition.

Motility functions were assessed with barium-impregnated foods of varying textures, ranging from pureed to solids, introduced in teaspoon amounts. Thin liquids followed, from regulated straw and cup sips to continuous drinking of unregulated amounts. Pharyngoesophageal transport and emptying functions were analyzed in both the lateral and A-P projections.

Statistics

Because our patient samples with H&Y stages II and V were small, patients with mild/moderate or more severe PD were grouped together for exploratory statistical purposes: subgroup I—H&Y stages II, III (n = 38); subgroup II—H&Y stages IV, V (n = 34). X2 was used to test the hypotheses about categorical variables.

Results

For descriptive purposes, pharyngeal transport function was divided into anterior and posterior segments. The former includes epiglottic and laryngeal motility and the latter, movement of the pharyngeal constrictors. Normal pharyngeal bolus progression was encountered in only 8 of the studied patients. The most involved patients manifested several aberrant pharyngeal stage abnormalities (Fig. 1).

Abnormalities of the epiglottis dominated anterior pharyngeal segment dysfunction. Epiglottic malpositioning, dysmotility, or enlargement was noted in 41/71 patients; most patients had multiple abnormalities. Epiglottic dysmotility, defined as restricted or limited movement through its normal range, occurred in 40/71. Of

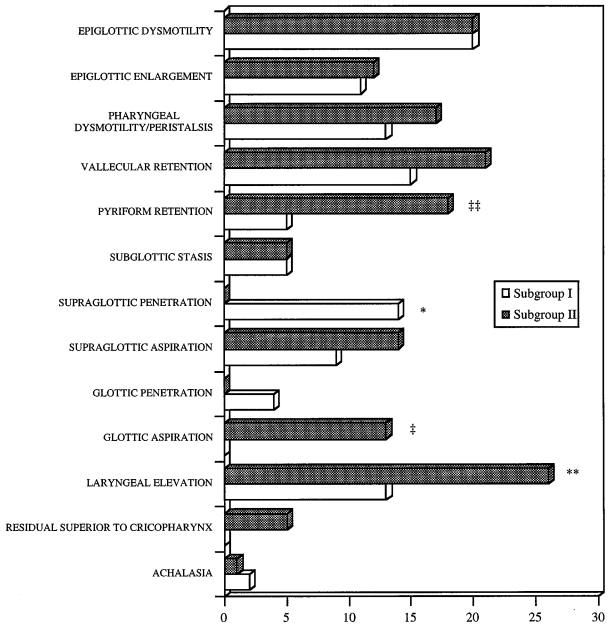

Fig. 1. Occurrence of abnormalities during pharyngeal ingestion in patients with Parkinson's disease (n = 71). *p:* * < 0.0003; ** < 0.0004, ‡ < 0.00007, ‡‡ < 0.0005.

these, a vertical resting position with incomplete inversion was observed in 10/40, a horizontal resting position with no movement during the swallow in 20/40, and vertical resting position with no subsequent movement in 10/40 patients. A slowed return to the preswallow resting position was seen in 12/71 patient. Epiglottic enlargement was noted in 23/40 of these patients; 5 patients displaced the epiglottis only to the transverse position and 15 patients had no movement from a transverse resting position. All patients with epiglottic enlargement also had confirmed GE reflux and an enlarged velum.

Vallecular sinus retention was observed in 36/71 patients. (Fig. 1) Of those with vallecular stasis, 23/36 patients also had pyriform sinus retention ($x2 = 11.99$, $df = 1$, $p < 0.00005$) Subepiglottic stasis was noted in 10 patients. Cricopharyngeus dysfunction and a cervical osteophytic spur each resulted in residua superior to the cricopharynx in 2 patients with no displacement to the pyriform sinuses. Vertical laryngeal movement was evaluated during the DVSFS. Vertical excursion was slowed in 39/71 patients, with a significant majority in subgroup II ($x2 = 12.43$, $df = 1$, $p < 0.0004$).

Posterior segment dysmotility included pharyngeal constrictor dysfunction in 30/71, with all but 4 patients being concordant for dysmotility and pharyngeal stasis. Supraglottic aspiration via the aryepiglottic folds was witnessed in 23 patients, 13 of whom also had glottic aspiration via the pyriform sinus. Only subgroup II patient were glottic aspirators. ($X2 = 15.79$, $df = 1$, $p < 0.0007$) Of our 23 patients with supraglottic aspiration,

20 aspirated before and 3 during the swallow. All patients with glottic aspiration did so both during or after the swallow. Supraglottic (X2 = 12.90, df = 1, $p < 0.0003$) and glottic penetration with increased aspiration risk were seen in an additional 18 patients.

By dividing structural dysfunction at the level of the vallecula, four clusters of aberrant bolus transport emerged (Fig. 2). Above the vallecula, superior pharyngeal or epiglottic dysmotility risked supraglottic aspiration; below the vallecula, inferior pharyngeal or cricopharyngeus dysfunction risked glottic aspiration.

Esophageal motility was normal in only 6/69 patients. Dysmotility with delayed transport function was observed most frequently (39/69) (X2 = 5.90, df = 1, $p = 0.02$) (Fig. 3). Other aberrations included stasis (16/69), tertiary contractions (17/69), reverse peristalsis (27/69) (X2 = 9.98, df = 1, $p < 0.002$), reduced peristalsis (9/69), aperistalsis (1/69), and esophageal tortuosity (7/69) or patulency (7/69). Each of the three cluster profiles illustrated in Figure 5 reflect potential airway exposure from the deleterious effects of GE reflux disease, post-swallow thoracic esophageal residua, and transport dysmotility.

Lower esophageal sphincter (LES) function was normal in only 10 patients (Fig. 4). Confirmed GE reflux was present in 40 patients, 10 of whom also had hiatal hernia; the LES failed to close in an additional 21 patients. Delayed distal thoracic esophageal emptying (60/69) and nonoptimal esophageal alignment (54/69), either excessive vertical (36/69) or excessive horizontal displacement (18/69), were also noted. Vomiting during the DVSFS occurred in 2 patients. Abnormalities of esophageal and LES function also tended to cluster. Mid- and distal esophageal dysmotility and LES incompetency risked reverse penetration and aspiration (see Fig. 5).

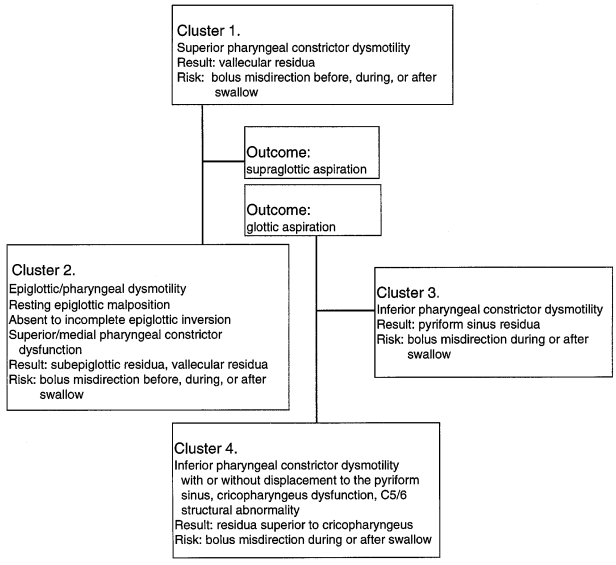

Fig. 2. Radiologic abnormalities during pharyngeal deglutition in Parkinson's disease.

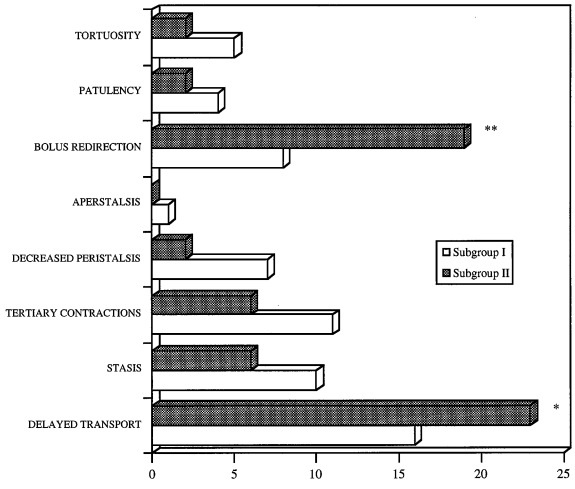

Fig. 3. Occurrence of abnormalities of esophageal motility in patients with Parkinson's disease (n = 69). *p:* * < 0.02; ** < 0.002.

Discussion

The PE swallow completes the ingestive process by transporting a liquid or food bolus to the stomach. In patients with PD, the inherent rhythm of PE function deteriorates resulting in multiple abnormalities during these stages of ingestion. Consequently, delayed or misdirected bolus transit frequently causes dysphagic symptoms including choking and coughing [17].

Normal pharyngeal ingestion directs the bolus into the esophagus while protecting the rostral and caudal portions of the pharyngeal airway, the nasopharynx and larynx. Before the pharyngeal swallow, the tongue prepares to forcibly expel the bolus into the oropharynx. The velum and pharynx then elevated while the pharynx contracts to accept and surround the bolus [19,20]. Preprogramed by a medullary swallowing central pattern generator (CPG), a series of sequential automatic movements also elevates the hyoid bone and laryngeal cartilages, depresses the epiglottis, and closes the laryngeal vestibule. In PD patients, incompetent posterior lingual retraction before the swallow and labored, uncoordinated lingual motility at swallow onset dampen the bolus propulsive force into the pharynx [17]. Bolus transit through the pharynx falters as evidenced by vallecular and pyriform sinus stasis and reduced pharyngeal motility and peristalsis [6,8,11–15,21]. Concurrently, laryngeal elevation slows; epiglottic depression incompetently hoods the laryngeal vestibule [14,21]. As a result, any food or liquids retained in the vallecular and pyriform sinuses

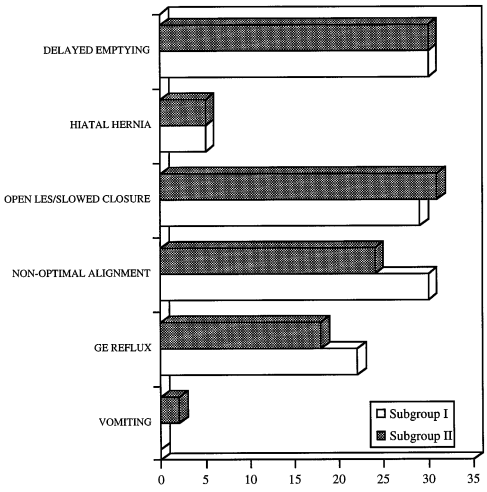

Fig. 4. Occurrence of abnormalities of lower esophageal functions in patients with Parkinson's disease (n = 69).

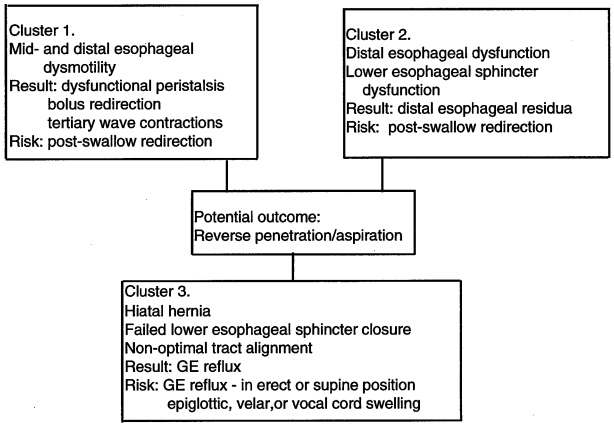

Fig. 5. Radiological abnormalities during esophageal deglutition in Parkinson's disease.

seep into the tracheal space to risk aspiration. We observed in our cohort these and other signs of dysmotility during pharyngeal ingestion. Only 9 patients had normal pharyngeal function on DVSFS.

Epiglottic movement, anomalous in many dysphagic patients, has received little attention in PD [22,23]. Ekberg and Nylander [22] classified epiglottic movement during deglutition into resting, transverse, and inverted positions. They described ''anatomic dysfunction'' of the epiglottis when it fails to completely invert, leaving its tip in the transverse, displaced position resting against the posterior pharynx. However, Ekberg and Sigurjonsson [24] reported that 7 of 150 volunteers had no epiglottic movement. Although none of this cohort had dysphagic symptoms, their neurologic status was not reported. Feinberg et al. [25] evaluated 144 elderly patients, 25 of whom manifested epiglottic dysmotility. The authors did not specifically address the prevalence of epiglottic dysmotility in their subgroup of 30 patients with PD. Perlman et al. [21] observed epiglottic dysmotility in 52.4% of 21 PD patients, approximating the 56.3% noted in our cohort. Although we observed a vertical epiglottis with no motion during ingestion in all patients with H&Y stage V disease, patients with H&Y stage II disease, several of whom had mild midline or appendicular rigidity and bradykinesia, also manifested this aberration. The pathophysiology of epiglottic immobility in PD is unknown.

Lying at the anatomic transition between the pharynx and esophagus, the upper esophageal sphincter (UES) is, like all pharyngeal muscles, composed of striated muscle. Because motor deficits of PD interfere with simultaneous and sequential contraction of striated muscles, such as those associated with other movements during oropharyngeal deglutition, UES dysmotility might be expected frequently. Yet, only several reports mention dysfunction in this area [7,9,26,27]. Using a variety of radiologic techniques, other studies have not confirmed these results [28]. Only 1/71 of our upright-positioned cohort had cricopharyngeus dysfunction and none of 46 supine-positioned patients, studied by Eadie and Tyrer [4], had cricopharyngeus dysfunction. Ali et al. [29] reported increased manometric pressure immediately above the UES in 30% of their PD patients despite normal motility of this region during videofluoroscopy. Additional studies combining videofluoroscopy and PE manometry are needed.

The pharyngeal swallow helps generate the primary esophageal peristaltic wave. A local sensory feedback neural network stimulates secondary peristalsis. Together, synergistic peristaltic contractions push the bolus distally through the LES. In PD patients, both primary and secondary peristalsis are often slow, uncoordinated, and inefficient [28]. Esophageal spasm has also been reported [2,4,27]. Edwards et al. [30], reviewing gastrointestinal function in PD, estimated that almost 7% of patients had esophageal dysmotility. Other investigators detail a range of esophageal abnormalities from minor peristaltic slowing to patulency and aperistalsis [5,10]. In our experience, aberrant esophageal peristalsis and motility are commonplace, regardless of disease severity. However, bolus transport delay is mild in patients with H&Y stage II but severe in those with stage V disease.

The LES governs the termination of esophageal bolus transport. Eadie and Tyrer [4] observed GE reflux in 30.4%of their patients with parkinsonism, more than three times as frequent as their control population. Gibberd et al. [10] recorded similar abnormalities in 14% of their studied patients. We noted hiatal hernias in 14.7% but confirmed GE reflux in 57.9% of our patients. We observed an open LES, delayed distal esophageal emptying, and nonoptimal alignment of the distal esophagus

with the LES and gastric fundus in an additional 21 patients. Patients with this cluster of radiologic signs, particularly those manifesting laryngeal aspiration or penetration during the pharyngeal videofluoroscopy, face an increased risk for GE reflux and reverse aspiration. For safety reasons, we did not position these patients supine to confirm GE reflux.

We introduce the PD-related pharyngeal and esophageal ingestion profiles with clusters (Figs. 2, 5) to alert dysphagia clinicians to specific problematic areas and their potential consequences. For each stage of ingestion studied, the cluster profiles are arranged in order of observed frequency and severity, such that cluster 1 is seen most frequently. In addition to predicting dysphagia performance patterns, these profiles may suggest compensation procedures that reduce patient and clinician radiation exposure, and assist the dysphagia clinician to develop prescriptive, individualized dysphagia treatment plans.

Many previous reports of dysphagia in PD examined either small numbers or insufficient number of patients across the clinical spectrum of PD [13,14,27,31]. What emerges is an unclear relationship between PE motility and disease severity. Eadie and Tyrer [4] observed an increased prevalence of GE reflux with its potential for reverse aspiration in patients with more advanced disease. Although Bushmann et al. [14] stated disease severity could not predict the presence of dysphagia, they commented that most of their patients with H&Y stages III or IV had severe dysphagia; their study group included no stage V patients. None of our patients had H&Y stage I disease. The absence of H&Y stage I patients from our cohort and the rarity of dysphagia as an early symptom of PD support a correlation between disease progression and pathologic ingestion [18,32]. Orolingual ingestion in PD patients also deteriorates coincident with disease progression [17]. Regardless of disease stage, patients share many radiologic features. However, our data suggest that those with more advanced disease manifest more severe radiologic abnormalities of ingestion, particularly epiglottic immobility, pyriform sinus retention, glottic aspiration, and reverse esophageal bolus movement.

Although impaired PE deglutition in PD is undisputed, there is no consensus as to its pathogenesis. Because PD onset is generally during senescence, some deglutitory abnormalities reported in PD, particularly esophageal dysmotility, may relate partly to normal aging. However, qualitative and quantitative studies of PE ingestion in a normal, aged population are few. Of those pertinent studies reviewed by Shaker and Lang [33], most focused on PE manometry. Using videofluoroscopy, Robbins et al. [34] examined pharyngeal motility in men over age 60. They reported laryngeal penetration in 22% of this cohort, none of whom aspirated. Vallecular or pyriform sinus retention without underlying disease is not a reported feature of ingestion in normal aging [34,35]. Similar to our PD cohort, esophageal dysmotility in the aged includes tertiary contractions, delayed esophageal emptying, and esophageal patulency [33]. However, accurate frequency estimates of defective esophageal motility in normal aging based on a DVSFS or similar methodologies are not available.

Prepharyngo-esophageal stages of ingestion are clearly under voluntary control. Aberrations during these stages can readily be ascribed pathology that results in PD-related bradykinesia and rigidity [17]. By diminishing oral bolus propulsive forces and slowing contraction of lingual-related hyoid muscles, deficient lingual stage movements link basal ganglia pathology to impaired pharyngeal bolus transport. Indeed, Ali et al. [29] recorded normal pharyngeal pressure wave amplitude originating from lingual propulsion rather from pharyngeal constrictors in a majority of their PD patients.

Pharyngeal peristalsis in PD has been described as weak [26,28]. However, patients with PD or other parkinsonian syndromes are not inherently paretic, but instead are akinetic, bradykinetic, and rigid. In addition, impaired oral sensorimotor integration reported previously in PD may have some pharyngeal equivalent [36]. These abnormalities, alone or in concert, may disturb the normal harmony between pharyngeal and laryngeal elevation, epiglottis tilting, and pharyngeal motility and peristalsis. The resulting motor dissonance discourages direct delivery of the bolus to the cervical esophagus.

In addition to basal ganglia influences on prepharyngeal ingestion, pathologic changes in PD have suggested other contributing sites. Lewy bodies, the neuropathologic marker of PD, appear in central nervous system (CNS)-pigmented nuclei as well as in other CNS and peripheral nervous system nuclei [37]. Their presence in the dorsal motor nucleus of the vagus (DMNV), other nuclei of the medullary reticular activating system, and the esophageal myenteric plexus [38,39] has generated speculation that these regions are responsible for some aspects of the pharyngo-esophageal dysmotility in PD [4,13,30]. However, the significance of these intraneuronal inclusions is unknown. Lewy bodies may be present without coincidental neuronal loss or absent in regions with neuronal loss [40]. Finally, in PD, the nucleus ambiguus (NA), the dominant medullary motor nucleus governing deglutition, is devoid of Lewy bodies and cell loss is insignificant. However, the more sensitive technique of ubiquitin immunocytochemistry for Lewy body identification [41] has not been applied systematically to this nucleus.

Of the medullary nuclei, the DMNV is of particular interest in PD. In addition to Lewy bodies, this

nucleus is significantly depopulated [37]. The DMNV helps modulate both the LES and esophageal smooth muscle contraction [42,43] and may help explain some of the esophageal motility and LES disturbances in PD mentioned previously. However, in several animal models, LES function is shared in part with the NA [44,65]. Noting that DMNV neuronal loss was diffuse, Eadie [37] questioned its clinical significance in PD. His reservations are supported by the rarity of DMNV pathology in progressive supranuclear palsy [46,47], a parkinsonian syndrome characterized in part by severe dysphagia and, in our experience, DVSFS abnormalities similar to PD. Consequently, DMNV pathology in dysphagic PD patients is of enigmatic significance.

The cardinal signs of parkinsonism arise primarily from deficient dopamine activity in the basal ganglia complex. To date, there is meager evidence to support a role for DA influences on deglutition. Dopamine may either inhibit or enhance ingestion, depending on the investigative method [48–52). In animals, DA injected into the dorsal medullary region adjacent to the tractus solitarius inhibits swallowing [52]. On the other hand, subcutaneous apomorphine, a DA receptor agonist, may improve esophageal motility in PD patients [51]. Finally, other basal ganglia diseases, such as Wilson's disease [53] and drug-induced parkinsonism [54], in which parkinsonism is not governed by DA depletion but by reduced striatal dopamine D-2 receptor activity, are associated with dysphagia and PE dysmotility [55,56].

Despite the appeal of a parsimonious explanation for a bradykinetic disorder of deglutition based on impaired DA activity, one clinical observation deserves consideration. Levodopa, an effective therapy for the cardinal signs of PD, provides relief of dysphagia for only a minority of PD patients. Several anecdotal reports mention such symptomatic benefit [12,26,36,57], but only Bushmann et al. [14] evaluated their dysphagic PD patients prior to and after levodopa treatment. Levodopa improved some aspects of pharyngeal function in 40% of their cohort, a result that might be partly attributed to improved lingual stage efficiency. Other neurotransmitters of the basal ganglia and surrounding structures are deficient in PD [58,59] indicating that PE dysphagia in PD may not be linked solely to a reduction in basal ganglia DA activity.

Without diminishing the role of DA in PD, it may be more appropriate to consider dysphagia in this and other akinetic-rigid extrapyramidal syndromes a consequence of defective output via the efferent basal ganglia pathways. These include well-described connections ascending through the ventral thalamic relay nuclei to the supplementary motor cortex. Less well-delineated descending paths, possibly via the substantia nigra pars reticulata to lower brainstem nuclei including the pedunculopontine nucleus (PPN), may also affect ingestion [60–63]. The PPN, a relay nucleus with projections to the trigeminal and hypoglossal nuclei and from the nucleus tractus solitarius [64–67], suffers significant neuronal loss in PD [68,69]. Morgan [60] also reported a striofugal tract from the globus pallidus to the nucleus ambiguus (NA). These descending basal ganglia efferents may be the unifying structures that link oral, pharyngeal, and esophageal dysphagia in PD.

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