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**Editor's comment**: Assessment of non-motor features is an important part of the routine neurological evaluation of a patient with Parkinson's disease (PD). Some of these non-motor features may be just as disabling as the classic motor signs or even more so. Among these disabling features, drooling is one that affects PD patients not only physically but also emotionally, leading to diminished quality of life. In this timely review, Srivanitchapoom and colleagues elegantly describe the prevalence of drooling in PD patients, its pathophysiology, and available assessment tools. They provide a critical review of currently utilized pharmacological and non-pharmacological therapies. They also point to the gaps in our knowledge of understanding the exact pathophysiology of drooling in PD. I am positive that our readers will find this manuscript to be of great assistance in their daily practice of movement disorders.

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Review

# Drooling in Parkinson's disease: A review

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ABSTRACT

Parkinson's disease (PD) is a neurodegenerative disease causing both motor and non-motor symptoms. Drooling, an excessive pooling and spillover of saliva out of the oral cavity, is one of the non-motor symptoms in PD patients that produces various negative physical and psychosocial consequences for patients and their caregivers. At present, the pathophysiology of drooling in PD is not completely certain; however, impaired intra-oral salivary clearance is likely the major contributor. There are neither standard diagnostic criteria nor standard severity assessment tools for evaluating drooling in PD. In accordance with the possible pathophysiology, dopaminergic agents have been used to improve salivary clearance; however, these agents are not completely effective in controlling drooling. Various pharmacological and non-pharmacological treatment options have been studied. Local injection with botulinum toxin serotypes A and B into major salivary glands is most effective to reduce drooling. Future research to explore the exact pathophysiology and develop standard diagnostic criteria and standard severity assessment tools are needed to formulate specific treatment options and improve patient care.



## 1. Introduction

Drooling may occur in many neurological disorders including neuromuscular diseases such as myasthenia gravis, amyotrophic lateral sclerosis (ALS) and oculopharyngeal muscular dystrophy, neurodegenerative diseases such as Parkinson's disease (PD), multiple system atrophy (MSA), progressive supranuclear palsy (PSP), dementia with Lewy bodies (DLB) and corticobasal degeneration (CBD), and cerebrovascular diseases. Drooling is generally defined as excessive pooling and poor control of saliva in the oral cavity that might be caused by impaired salivary clearance whereas sialorrhea refers to overflow or overproduction of saliva [1]. Regrettably, both terms are sometimes used interchangeably. If patients have drooling, they might subsequently spill saliva from their oral cavity, or might aspirate the saliva causing aspiration pneumonia. Other possible negative consequences are poor oral hygiene and social embarrassment. In PD, drooling is considered a non-motor symptom. This article focuses on the prevalence, associated factors, negative impacts of drooling, normal physiology of salivation and swallowing, pathophysiology of drooling, assessment tools, and treatment options for drooling in PD.

## 2. Methods

References for this review were identified through searches of PubMed using the search terms "Drooling and Parkinson's disease", "Sialorrhea and Parkinson's

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**Table 1**
Prevalence of drooling in Parkinson's disease.

| Year | Reference | Screening tools | Number surveyed | Prevalence (%) |
|---|---|---|---|---|
| 2012 | Damian et al. [16] | SCOPA-AUT | 62 | 81 |
| 2012 | Ozdilek et al. [15] | UPDRS part II: salivation subscore | 50 | 84 |
| 2012 | Rana et al. [14] | UPDRS part II: salivation subscore | 307 | 40 |
| 2012 | Perez-Lloret et al. [13] | UPDRS part II: salivation subscore | 419 | 37 |
| 2011 | Müller et al. [12] | UPDRS part II: salivation subscore | 207 | 42 |
| 2010 | Leibner et al. [11] | Questionnaire:7-item drooling survey questionnaire | 58 | 59 |
| 2008 | Cheon et al. [10] | PD-NMSQuest | 74 | 32 |
| 2008 | Nicaretta et al. [9] | UPDRS part II: salivation subscore | 134 | 10 |
| 2007 | Martinez–Martin et al. [8] | PD-NMSQuest | 525 | 42 |
| 2007 | Verbaan et al. [7] | SCOPA-AUT | 420 | 73 |
| 2007 | Kalf et al. [6] | Questionnaire: "Do you suffer from involuntary loss of saliva (drooling)?" | 216 | 49 |
| 2002 | Siddiqui et al. [5] | Questionnaire: rating 0–4 point for detecting severity of symptoms<br>0 = normal<br>1 = rare (one per month)<br>2 = occasional (one per week)<br>3 = frequent (one per day)<br>4 = constant | 44 | 52 |
| 2002 | Volonté et al. [4] | Questionnaire: Present or absent nocturnal sialorrhea | 65 | 15 |
| 2000 | Scott et al. [3] | Questionnaire: present or absent drooling | 943 | 40 |
| 1991 | Edwards et al. [2] | Questionnaire: rating 0–4 point for detecting severity of symptoms<br>0 = normal<br>1 = rare (one per month)<br>2 = occasional (one per week)<br>3 = frequent (one per day)<br>4 = constant | 96 | 70 |

UPDRS: Unified Parkinson's Disease Rating Scale; SCOPA-AUT: Scales for Outcome in Parkinson's disease; autonomic; PD-NMSQuest: Parkinson's disease non-motor symptoms questionnaire.

disease" and "Treatment of drooling in Parkinson's disease". We mainly selected papers that were published between January 1973 to August 2014. Only reports published in English were included. We cited references reflecting personal selection of the review authors.

## 3. Prevalence, associated factors and negative impacts of drooling in PD

Due to the lack of a standard definition and criteria for diagnosing drooling in PD patients, estimates of prevalence vary. Previous studies showed that prevalence ranged from 10 to 84% (Table 1) [2–16]. Various tools such as the Unified Parkinson's Disease Rating Scale (UPDRS) part II [12–15]; Scales for Outcomes in PD for Autonomic Symptoms (SCOPA-AUT) [7,16]; PD non-motor symptoms questionnaire (PD-NMSQuest) [8,10]; and different types of screening questionnaires [2–7,10,11] were used to screen drooling. The factors associated with drooling have been reported. However, results vary among studies and the conclusion remains unclear. Factors possibly associated with drooling were severity of PD [2,14], male gender [3,10], aging [6], hallucinations [11], duration of PD [13], the sum of the scores of UPDRS part II and III greater than 28 points, dysarthria, dysphagia, orthostatic hypotension, and a history of using antidepressants [12]. Drooling during PD can have negative impact for both patients and caregivers. Many negative physical sequelae were reported to follow the course of drooling such as perioral dermatitis, poor oral hygiene, bad breath, increased amount of intra-oral occult bacteria, eating and speaking difficulty, and an increased rate of respiratory tract infection from silent aspiration of saliva [11,17–21]. Psychosocially, drooling PD patients showed poor quality of life (QoL), i.e., social embarrassment and increasing emotional distress [6,11]. In addition, drooling patients affected their caregivers by increasing their burden, depression and anxiety, and reducing their QoL [16].

## 4. Normal physiology of salivation and swallowing

The processes of salivation are controlled by both sympathetic and parasympathetic nervous systems. However, facilitation of ingestion and swallowing are mainly contributed by the parasympathetic nervous system. The parasympathetic afferent pathways receive unconditioned reflex stimulation from the pharynx and esophagus. Then, signals are conducted via the vagus and spinal splanchnic nerves to the salivary center located in the medulla. The parasympathetic outputs are conducted via two different pathways including the glossopharyngeal nerve, which then innervates the otic ganglion, and, subsequently, to the parotid glands via the auriculotemporal nerve and the facial nerve through the chorda tympani nerve to the submandibular ganglia and then innervates the submandibular and sublingual glands via the lingual nerve [22].

The normal physiology of human swallowing is composed of three phases: oral, pharyngeal, and esophageal. The oral phase is voluntary whereas pharyngeal and esophageal phases are involuntary. When swallowing begins, the oropharyngeal phase uses more than 30 different muscles to coordinate and precisely time moving the food bolus to the esophagus. The upper esophageal sphincter (UES) subsequently opens and the bolus passes through the esophagus by peristalsis into the stomach [23]. The central motor control areas include the premotor cortex, primary motor cortex, basal ganglia, pedunculopontine nuclei, and cerebellum; they project descending motor outputs to the medullary swallowing center which includes a swallowing central pattern generator and its interneurons such as the nucleus of the solitary tract. After that, the medullary swallowing center provides the outputs to the structures involved in the swallowing process such as the tongue, larynx, pharynx, and upper esophagus. Lingual muscles are controlled by the motor output of the hypoglossal nucleus while laryngeal, pharyngeal and upper esophageal muscles are controlled by motor output of the nucleus ambiguus [24]. The oropharyngeal phase is most affected in PD patients.

## 5. Pathophysiology of drooling in PD

Drooling is more prominent during the "off" period. Two major domains possibly influencing the pathophysiology of drooling in PD have been proposed: one is an abnormality of salivary production and the other is insufficient salivary clearance. Overproduction of saliva might cause drooling. However, many studies showed that drooling PD patients produced less saliva compared to normal controls [25–27]. The exact mechanisms causing decreased salivary production are not understood [26]. A possible explanation is dopamine deficiency. Previous studies in both invertebrate and vertebrate animal models showed that dopamine modulates salivary secretion [28,29]. Experimental studies in rats demonstrated that activation of central and peripheral dopamine receptors produced salivary secretion [29]. Supportive evidence consists of