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# Diurnal drooling in Chinese patients with Parkinson's disease

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ABSTRACT

*Objective:* The aim of this study is to explore the prevalence and clinical correlates of diurnal drooling in Chinese patients with Parkinson's disease (PD).
*Methods:* A cross-sectional analysis of 518 Chinese patients with PD was conducted. Each subject was categorized as a diurnal "drooler" or a "non-drooler" using the Non-Motor Symptoms Scale (NMSS).
*Results:* One hundred and twenty-one (23.4%) patients exhibited diurnal drooling. Diurnal drooling was reported more frequently in male and late-onset PD patients ($p < 0.05$). The levodopa equivalent daily doses, mean age and disease duration, the percentages of PD family history and levodopa or entacapone use, the incidences of dysarthria, dysphagia and fluctuation, and the Unified PD Rating Scale (UPDRS) part III, NMSS, Hamilton Depression Scale (HAMD), Hamilton Anxiety Scale (HAMA) and PD Questionnaire 39 (PDQ-39) scores in droolers were significantly greater than in non-droolers ($p < 0.05$). The percentage of benzhexol use in non-droolers was significantly higher than in droolers ($p < 0.05$). The Frontal assessment battery (FAB) and Montreal Cognitive Assessment (MoCA) scores were not different between the droolers and non-droolers. The forward binary logistic regression model indicated that dysarthria, male sex, age, UPDRS part III, sexual dysfunction and a family history of PD were associated with diurnal drooling.
*Conclusions:* Diurnal drooling is a relatively common debilitating symptom in Chinese PD patients. It is not only related to male sex, age, dysarthria and PD family history, but also correlates with motor and non-motor severity especially sexual dysfunction of PD. However, it is not related to cognition.


## 1. Introduction

Drooling (or sialorrhea), a common non-motor symptom (NMS) in Parkinson's disease (PD), is defined as the inability to control oral secretions, resulting in excessive saliva accumulation in the oropharynx [1]. It is reported by 32–74% of patients with PD [2,3].

Drooling can be classified into diurnal and nocturnal drooling. Diurnal drooling is defined as dribbling of saliva while awake, which typically appeared later in the disease course [4]. It is reported to be present in about 28% of PD patients [4]. Compared with nocturnal drooling, diurnal drooling may have a worse impact on patients, which can give rise to social embarrassment, isolation and depression, while also represents a potential cause of choking or aspiration pneumonia [5]. However, only few studies have focused on it. A case–control study on 15 Dutch patients with diurnal drooling and another 15 patients without diurnal drooling found that diurnal drooling was related to disease severity, dysphagia and male sex [6]. Another observational study on 104 Dutch patients found that involuntary mouth opening and dysphagia were the correlated factors with diurnal drooling [4]. Other studies focused on drooling including both diurnal and nocturnal drooling found that drooling was related to disease duration [7], hallucination [8], dysarthria [3,9,10] and, less commonly, cognitive dysfunction [3,11].

The relationships between diurnal drooling and other clinical factors, such as depression, anxiety or cognitive function have been inadequately investigated. Meanwhile, the clinical characteristics of diurnal drooling in the Chinese PD population have yet to be reported. The aim of this study is to explore the prevalence and clinical correlates of diurnal drooling in a large cohort of Chinese PD patients.

## 2. Patients and methods

A total of 518 PD patients from the Department of Neurology, West China Hospital of Sichuan University between June 2011 and August 2014 were consecutively recruited for this observational study. Written informed consent was obtained from all participants and the study was approved by the local Ethics Committee. PD was diagnosed according to the United Kingdom PD society Brain Bank Clinical Diagnostic Criteria for PD [12]. Atypical and secondary Parkinsonisms were excluded.

Demographic data including age, sex, age at onset, disease duration, diagnostic delay, family history of PD, history of hypertension and diabetes, dysarthria, dysphagia, years of education, handedness, treatment

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regimen and motor complications were collected by neurologists majoring in PD through face-to-face interviews. Unified PD Rating Scale (UPDRS) part III [13] and Hoehn and Yahr (H&Y) stage [14] were used to evaluate the severity of motor symptoms. PD Questionnaire 39 (PDQ-39) (8 domains) [15] was used to evaluate the quality of life (QoL) of PD. Non-Motor Symptoms Scale (NMSS) (9 domains) [16], Hamilton Depression Rating Scale (HAMD) (24 items) [17] and Hamilton Anxiety Rating Scale (HAMA) [18] were used to evaluate the severity of the NMS. Frontal assessment battery (FAB) [19] and Montreal Cognitive Assessment (MoCA) (7 domains) [20] were used to evaluate the frontal lobe function and global cognitive function respectively. All of the assessments were conducted at "on" state.

Diurnal drooling was evaluated using the NMSS. All participants were categorized as "droolers" (with the presence of diurnal drooling) or "non-droolers" (with an absence of diurnal drooling). The prevalence of diurnal drooling was calculated from the percentage of patients who obtained score $\geq 1$ in item number 19 from NMSS. Dysarthria and dysphagia were considered to be present according to the score $\geq 1$ in item number 5 or 7 from UPDRS part II. Early-onset PD (EOPD) in the current study was defined as an onset age of PD younger than 50 years, while late-onset PD (LOPD) was defined as older than 50 years. PD patients were grouped into three subtypes including tremor-dominant, akinetic-rigid and mixed based on the criteria described in a previous study [21].

## 3. Statistical analyses

SPSS 19.0 was applied for the statistical analyses and $p$-values $< 0.05$ were considered statistically significant. All of the continuous data, including age, age at onset, disease duration, diagnostic delay, years of education, levodopa equivalent daily doses (LEDD), UPDRS part III score, the total scores and each domain score for PDQ-39, NMSS and MoCA, and the total scores for HAMD, HAMA and FAB, are presented as the mean ± standard deviation (SD). The discontinuous data (H&Y stage) is presented as the median value (quartile).

The Chi-square test was used to evaluate the differences in the categorical variables between the droolers and non-droolers, while the Wilcoxon rank sum test was performed to compare the discontinuous data between the droolers and non-droolers. Student's $T$ test was used for the comparisons of the continuous variables, including age, age at onset, disease duration, diagnostic delay, years of education, UPDRS part III score and LEDD, between the droolers and non-droolers, while the one-way analyses of covariance (ANCOVA) adjusted for confounding factors, including age, sex, LEDD (or benzhexol use), disease duration and UPDRS part III, were performed to compare the remaining continuous variables, including the total scores for PDQ-39, FAB, MoCA, NMSS, HAMD and HAMA, as well as the scores for each subdomain from NMSS, PDQ-39 and MoCA, between the droolers and non-droolers. A multivariate analysis using forward binary logistic regression model with diurnal drooling as dependent variable and the above significant disease characteristics, including sex, age, disease duration, LOPD, dysarthria, dysphagia, family history of PD, LEDD, levodopa, benzhexol and entacapone application, UPDRS part III, fluctuation, the HAMD and HAMA scores, and the scores for sleep/fatigue, mood/apathy, gastrointestinal, urinary and sexual dysfunction subdomains from NMSS as independent covariables was used to explore the potential clinical factors that may be related to diurnal drooling.

## 4. Results

### 4.1. Comparison between the droolers and non-droolers

The prevalence of diurnal drooling is presented in Table 1. Of 518 patients, 121 PD patients (23.4%) reported diurnal drooling. Diurnal drooling reported more frequently in male and LOPD patients compared to female and EOPD patients ($p < 0.05$), whereas no difference was found among the PD patients with three different subtypes.

**Table 1**
Prevalence of diurnal drooling in patients with PD.

| Groups | Diurnal drooling | | $p$-Value[a] |
|---|---|---|---|
| | $N$ | % | |
| Total | 121 | 23.4 | |
| Gender | | | |
| Male | 82 | 28.7 | 0.002[b] |
| Female | 39 | 16.8 | |
| Onset age | | | |
| EOPD | 15 | 11.4 | <0.001[b] |
| LOPD | 106 | 27.5 | |
| Type of motor symptom | | | |
| Tremor-dominant | 0 | 0 | 0.152 |
| Akinetic-rigid | 80 | 24.1 | |
| Mixed | 41 | 23.6 | |

PD: Parkinson Disease. EOPD: early-onset PD. LOPD: late-onset PD.
[a] $p$-Value is calculated from Chi-square test.
[b] Significant difference.

The demographic and clinical features of the PD patients are listed in Table 2. The droolers had an older age, late onset age, longer disease duration, higher LEDD application, higher UPDRS part III score, and greater H&Y stage, as well as higher frequencies of male sex, family history of PD, dysarthria, dysphagia and motor fluctuation than the non-droolers ($p < 0.05$). The droolers had a lower percentage of benzhexol use and higher percentages of levodopa and entacapone use than the non-droolers ($p < 0.05$). The diagnostic delay, and the percentages of dopamine receptor agonist or amantadine use, as well as the incidence of dyskinesia were not different between the droolers and non-droolers.

The NMS results for the PD patients with and without diurnal drooling are listed in Table 3. After adjusting for confounding factors, the droolers presented significantly higher scores for the NMSS, HAMD and HAMA, as well as higher scores for the sleep/fatigue, mood/apathy, gastrointestinal, urinary and sexual dysfunction subdomains of the NMSS than the non-droolers ($p < 0.05$). The remaining domains of the NMSS were not different between the droolers and non-droolers. The cognitive function assessment results for the PD patients with and without diurnal drooling are presented in Table 4. After adjusting for confounding factors, no differences in the total scores for the FAB and MoCA, as well as the scores for the all subdomains of the MoCA were found between the droolers and non-droolers.

The PDQ-39 results for the droolers and non-droolers are listed in Table 5. After adjusting for confounding factors, the PDQ-39 score and the scores for the emotional well-being, cognitions and communication subdomains of the PDQ-39 in the droolers were significantly higher than the non-droolers ($p < 0.05$). No significant differences in the scores for the remaining domains of the PDQ-39 were found between the droolers and non-droolers.

### 4.2. Multivariable analysis

The potential factors related to diurnal drooling are presented in Table 6. The forward binary logistic regression model indicated that male sex, older age, higher UPDRS part III score, higher score for sexual dysfunction subdomain from the NMSS, dysarthria and a family history of PD were associated with diurnal drooling ($p < 0.05$). The remaining clinical factors including disease duration, LOPD, dysphagia, LEDD, use of levodopa, benzhexol and entacapone, fluctuation, depression, anxiety, and sleep/fatigue, mood/apathy, gastrointestinal and urinary subdomains from the NMSS were not correlated with diurnal drooling.

## 5. Discussion

To the best of our knowledge, this is the first study to investigate the prevalence of diurnal drooling and explore such a vast spectrum of clinical factors pertaining to diurnal drooling in a large cohort of Chinese