

Non-motor signs and symptoms in Parkinson's disease

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ABSTRACT

Motor symptoms are cardinal clinical features of Parkinson's disease (PD). Progress in drug therapy and rehabilitation has been presenting beneficial effect for motor symptoms. However, non-motor symptoms and signs in PD have been accumulated growing attentions and its amelioration may also give beneficial effect for PD patients' and their care givers' quality of life. In this mini-review, I overviewed non-motor symptoms and signs in PD.

Keywords: Parkinson's Disease (PD); Non-Motor Signs and Symptoms; Activities of Daily Livings (ADL); Quality of Life (QOL)

1. INTRODUCTION

James Parkinson described in his historical essay, "Involuntary tremulous motion, with lessened muscular power, in parts not in action and even when supported; with a propensity to bend the trunk forwards, and to pass from a walking to a running pace: the senses and intellects being uninjured" [1]. From then, Parkinson's disease (PD) has been classified as "Movement Disorders" and its clinical diagnosis requires existences of tremor, akinesia, muscle rigidity, and loss of right reflex and has been treated mainly to improve these "motor syndromes" [1-3]. Advent of drug therapy for PD can improve motor function and activities of daily livings (ADL) from their early stages [4-7]. Recently, however, not motor syndrome but non-motor syndrome accumulated attention, because non-motor syndrome such as fatigue, sleep disorders, and dysautonomia closely relate with improvement of their quality of life (QOL) [8-12]. In addition, some researchers consider nonmotor syndrome as an initial signs and symptoms in PD [13].

In this mini-review, I overviewed non-motor symptoms and signs in PD.

2. NON-MOTOR SIGNS AND SYMPTOMS IN PD

Numbers of non-motor symptoms and signs in PD constantly increase with accumulation of information of PD clinical pathogenesis. To investigate non-motor symptoms scale for Parkinson's disease (NMSSPD), we preliminary investigated overall frequency of non-motor symptoms and signs using questioner sheets [11,12]. We investigate neuropsychological signs (depression, apathy, anxiety, anhedonia, cognitive dysfunction, attention deficit, hallucination, delusion, dementia, delirium, panic disorder), sleep disorders (restless leg syndrome, abnormal behavioral disorders in REM period, insomnia, excessive day time sleep, sleep apnea), dysautonomia (orthostatic hypotension, dysuria, impotent), digestion disorders (drooping, incontinence, dysphagia, dysosmia, visual disorder), behavioral disorder (hypersexuality, compulsive behavior, pathological shopping, pathological gambling), and others (fatigue, weight loss, weight gain) [11-16]. Based on results [14], we found that drooping, dysosmia, dysphagia, incontinence, bowel disorder, forgetfulness, inattention, depression, sleep disorder, and abnormal sweating) in PD were significantly increased comparing with those in controls.

These foregoing investigations indicate that non-motor signs and symptoms in PD have been known to affect their motor syndromes and QOL.

2.1. Neuropsychological Syndromes

PD patients may develop neuropsychiatry syndromes such as hallucination [17,18] or depression [19], which interfere their treatment, care, ADL.

Unless hallucination affects ADL, full explanation to patients and their caregivers may lighten their burdens. If hallucination in PD needs immediate integrative treatment with psychosocial interventions, antipsychotic medication and adjustment of anti-PD medication are prescribed, however leaving an adequate L-dopa dose to prevent severe off-states [20].

For people with PD, depression is quite common. Up to 60 percent of people with PD experience mild or

moderate depressive symptoms. Research suggests that PD itself causes chemical changes of dopamine, serotonin, and norepinephrine in the limbic system that may lead to depression. Dopamine and dopamine agonist are used for treatment of depression [20-23]. In addition, depression in PD has close relationship with motor dysfunction. Thus, improvement of motor syndrome is the key factor for improvement of depression in PD.

Anxiety and apathy are dependent syndromes to depression. These signs and symptoms may be found with depression, but may be found without depression unless full drug therapy for motor syndrome conducted [24,25].

James Parkinson firstly described that PD patients never developed dementia. However, we know that PD patients may develop frontal lobe dysfunction such as forgetfulness [26-28]. PD patients have difficulty planning and carrying through tasks. When facing a task or situation on their own, a person with PD may feel overwhelmed by having to make choices. They may also have difficulty remembering information, or have trouble finding the right words when speaking. To some degree, cognitive impairment affects most PD patients. The same chemical changes that lead to motor symptoms can also result in slowness in thinking [28]. Cognitive impairment in PD is different from dementia, which is a more severe loss of intellectual abilities that interferes with daily living so much that it may not be possible for a person to live independently. Causes cognitive changes in PD remain unclear, but a possible cause is a decreased level of dopamine. However, the cognitive changes associated with dopamine declines are typically mild and circumscribed. It should be noted that PD patients have deep stigma that impairs their cognitive function and increases burden of caregivers.

2.2. Sleep Disturbances

Up to 60% of PD patients have been reported to claim sleep disturbances. PD patients may have difficulty turning over in their sleep due to increased muscle tonus, may be ceased their sleep by pollakisuria, or may have depression [29]. Although non-ergotic dopamine agonists are ropinirole, pramipexole, and rotigotine which have been known to induce day time or sudden insomnia [30], PD itself induces sleep disturbances such as restless leg syndrome (RLS), abnormal behavioral disorders in REM period (RBD), insomnia, excessive day time sleep, and sleep apnea [31-35] PD patients are reported to develop RBD at high frequency up to 40% and have considered these sleep disturbances in their early stage. Thus, diagnosis and treatment of sleep disturbances is a key factor for PD treatment [9,29].

2.3. Autonomic Failure (Dysautonomia)

PD patients frequently show dysautonomia such as

orthostatic hypotension [36] and bowel disorders [37]. Unlike patients with multiple systemic atrophy (MSA), PD patients rarely lose their consciousness due to orthostatic hypotension. However, light-headedness or dizziness due to orthostatic hypotension may be a risk factor for accidental falls and injuries after falls [3,8,9]. Since PD patients are tended to have disused syndrome that impairs their ADL and QOL, rehabilitation using tilt table and elastic stockings is needed [15,36]. If their environments require, reform of houses is also planned [38-41].

PD patients may show pollakisuria, dysuria, feeling of residual urine, or incontinence of urine. Even the same man may develop a wide variety of urinary disorders. PD patients may have sleep disorders due to nocturia [9,33]. These urinary signs are improved after adequate dopamine therapy, but anticholinergic agent such as oxybutynin hydrochloride can improve these [39,41].

2.4. Digestive Disorders

PD patients frequently develop incontinence without antiparkinsonian agents, but antiparkinsonian agents themselves have some effect on developing incontinence. [42,43] Braak *et al.* pathologically found Lewy bodies in the Auerbach neural plexus that may be result in incontinence in PD [44]. Incontinence has possibility to result in ileus and should be treated with drugs, diet and exercise [45].

PD patients increasingly show drooping with progression of disease, but patients do not have increased amount of saliva sputum but slowing of swallowing may be a cause [46]. Although some drugs can reduce amount of saliva sputum that increases decayed tooth and periodontal disease, wiping or postural drainage therapy may be useful to prevent aspiration pneumonia.

To treat dysphagia in PD, nutrition support team (NST) may be useful in daily clinic [47,48].

2.5. Sensory Disturbance

James Parkinson described that PD patients never showed sensory disturbances [1], but many of patients may experience pain or dysesthesia [49] PD patients also demonstrate dysosmia [50,51] and dysgeusia [52] in their early stages. Dopamine is an agent to modulate pain in spinal cord, thalamus, basal ganglia and cingulate gyrus. [53,54] Because of dysregulation of dopamine, PD patients show sensory disturbances. Up to 29% of PD patients complain pain that impedes their QOL [11].

2.6. Behavior Disorders

Disinhibition including hypersexuality, compulsive behavior, pathological shopping, and pathological gambling are also reported as behavior disturbances in PD

[11,12]. In our study in Japan, we less frequently observed these behavior disturbances and considered this is because in Japan relatively small amount of antiparkinsonian drugs are used. Amantadine may be effective for disinhibition [54].

2.7. Fatigue

Fatigue is the most trouble but less familiar syndrome in PD [55-60]. Fatigue can be distinguished from depression. Depressions in PD have some relation with motor syndrome, but fatigue does not. Depression also troubles patients' caregivers [57-60]. Although pathogenesis of fatigue in PD remains uncertain, we hypothesize that it may have some relation with cognitive dysfunction, especially frontal lobe dysfunction (**Figure 1**) [56,61].

2.8. Others

PD patients show respiratory dysfunction which results in speech disturbances, dysphagia, and aspiration pneumonia [62,63]. We develop an exercise for PD including respiratory exercise and could improve respiratory dysfunction (**Figure 2**).

3. CONCLUSION

Since PD patients are admitted neurological clinic be-

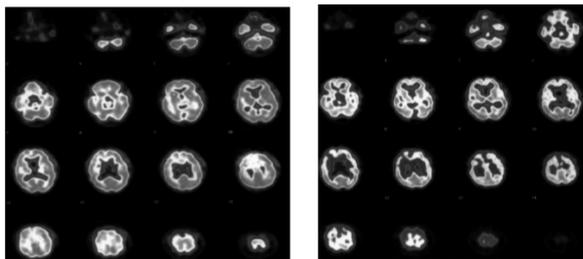


Figure 1. A single emission computed tomographic image using Tc-99m-HMPAO (hexamethyl propylamine oxime, Ceretec™) showed decreased isotope uptakes in the frontal lobe of PD patients with fatigue (right) but not in the frontal lobe of PD patients without fatigue.

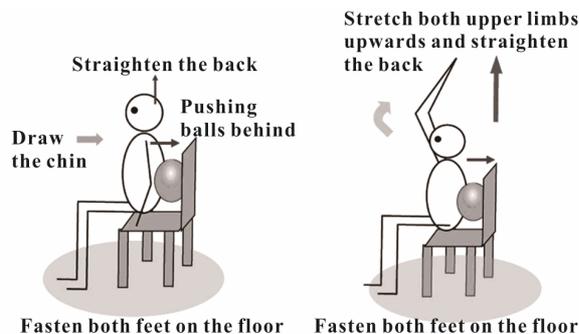


Figure 2. An exemplified exercise program for Parkinson's disease.

cause of their motor signs and symptoms such as bradykinesia, tremor, or dystonia, we neurologists mainly pay attention to improve these motor syndrome. However, with advent of PD therapy improve, in some extent, motor syndrome, but nonmotor syndrome has increasingly known to be a crucial factor to improve patients' and their care givers' QOL [9,14,57,58]. Pathological examinations mainly by Braak *et al.* hypothesized that nonmotor syndrome might result from initial pathological changes in PD [44]. Validation of this hypothesis is open for discussion, but for their QOL we should pay more attention for nonmotor syndrome in PD.

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