Breathing and its rehabilitation in Parkinson's disease

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Abstract

Parkinson’s disease is underlined by insufficient neuronal dopamine (DA) content. DA is influential for breathing, particularly for hypoxic ventilatory responses, at both central and peripheral carotid body level. There are reasons to believe that breathing might be impaired in PD. We tested this hypothesis in the rat reserpine model of parkinsonism. Ventilation and its responses were recorded in a plethysmograph in conscious rats before and after the induction of parkinsonic symptoms. The findings are that the ventilatory hypoxic responses were substantially reduced in parkinsonism. The likely mechanism of reduced ventilation seems the missing stimulatory element of central DA. The study suggests that breathing rehabilitative exercise, possibly combined with home oxygen therapy, might be a potential countermeasure for deteriorating bodily and cognitive symptoms in parkinsonism.

Key words: Dopamine - Hypoxia - Oxygen therapy - Parkinsonism - Pulmonary rehabilitation - Ventilation

Introduction

Parkinson’s disease (PD) is a leading progressive neurodegenerative disease whose incidence increases steadily in persons aged 60 and more. The increased trend of PD appearance is noted worldwide and is especially noticeable in highly industrialized societies. Major symptoms of PD are characteristic and thus rather easily identifiable. They are muscle rigidity, tremor, hypokinesia or catatonia, often combined with balance problems leading to frequent falls and in consequence bone fractures. These classical motor disorders are accompanied by non-motor neuropsychological symptoms of impaired cognition, depression, or pain. Both motor and non-motor PD symptoms usually require specific rehabilitation procedures.

One of the PD features is a characteristic flexed standing and walking posture due to muscle rigidity and stiffness. This posture may cause mechanical restriction of the muscle-skeletal respiratory pump and thus may impair lung function. Ventilation has indeed been found impaired in PD by some (Serebrovskaya et al., 1998), but not studies on the subject (Seccombe et al., 2013). There are however other reasons of respiratory impairment in PD. The disease is underlined by deficiency of dopaminergic neurons in midbrain their loss, and decreased general dopamine (DA) activity. DA is an essential modulator of respiration and of the hypoxic ventilatory reactivity. The prevailing consensus is that DA is stimulatory for ventilation at the central level (Huey and Powell, 2000; Hsiao et al., 1989), although the issue is somehow debatable. However, DA is rather distinctly inhibitory for hypoxic ventilation, generated at the peripheral organ of the carotid body (Ciarka et al., 2007). The role of the carotid body in respiratory changes of PD is unknown.

Methodology

In the present study we set out to measure ventilation and its responses to hypoxia (8% O₂ balanced with N₂), with a hope to be eventually able to ascribe ventilatory changes accompanying experimentally induced parkinsonism to central or peripheral DA effect. Ventilation was recorded in a whole body plethysmography (PLY3223; Buxco Electronix Inc., Wilmington, NC) in conscious rats,

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in which parkinsonic motor and behavioral symptoms were pharmacologically modeled with reserpine (2.5 mg/kg) followed by alpha-methyl-p-tyrosine (250 mg/kg) 16 hours later both given intraperitoneally. The study was approved by a local Ethics Committee for Animal Experiments.

Minute ventilation ($V_E$) was compared before (control) and after reserpine-induced parkinsonic symptoms in the same rats. Data were expressed as mean values with standard error of $V_E$, collected every 30 sec along the course of 3-min acute hypoxic tests. Differences in $V_E$ between the control and parkinsonic conditions were compared at the corresponding time marks with a paired t-test.

**Results and Discussion**

The ventilatory response to hypoxia classically consists of the fast stimulatory phase followed by a gradual inhibition. We found that ventilation and its responses to hypoxia were appreciably decreased in the parkinsonic condition compared with the untreated healthy control. The ventilatory decreases are exemplified in Figure 1. The most pronounced decrease concerned the peak response noted at 30 sec from the onset of hypoxia, although basal resting prehypoxic ventilation also was decreased. Statistical significance was defined as $p<0.05$.

![Fig. 1. Ventilatory responses to acute 8% hypoxia in reserpine-induced parkinsonic (solid symbols) and healthy (open symbols) conditions. Parkinsonism decreased ventilation. Data are means ±SE of four rats. *p<0.05 for the differences between the two conditions at all (vertical) time points.](image)

The findings underscore the role of a lacking central stimulatory DA element in the impaired parkinsonic ventilation, rather than any major role of carotid body DA in ventilatory regulation. Since carotid body DA is inhibitory for ventilation, its deficiency, if present in parkinsonic rats, would rather tend to hold up, and not to decrease, ventilation. The study raises attention to the possibility of respiratory impairment and thus worsened oxygen supply through the lungs and tissue oxygenation in the body in parkinsonism.

There is no cure for PD as yet. The disease, however, should be managed in a multidisciplinary way to prevent progression of symptoms and to attempt to increase quality of life of patients. The impaired lung ventilation in PD offers one avenue of management, aside from known pharmacological and cognitive treatments, which is pulmonary rehabilitation consisting of specific physical and breathing exercises to improve organ oxygenation and function. Breathing exercise, through appropriate movements of the chest, is aimed at the activation of muscle spindles in the intercostal respiratory muscles, which may lead to greater chest expansion on air inhalation, better oxygen supply to the lungs, reduction of dead space ventilation, and a decrease in the feeling of breath shortness. The benefits of pulmonary rehabilitation are multiple, as they also include improved cognitive function.
(Pecyna and Pokorski, 2013; Joshi and Telles, 2008; Kang 2006; Nikolov et al., 1991). It seems a reasonable assumption that pulmonary rehabilitation could be most effective at an initial stage of PD before disability development and the need for pharmacological treatment. However, current research on non-pharmacological therapies for cognitive dysfunction in PD is, in general, very limited (Hindle et al., 2013) and regarding pulmonary rehabilitation, specifically, is non-existing.

Recently, exercise has become part of the comprehensive rehabilitation program for elderly patients, also suffering from PD. This concept recently advanced in Japan (Comprehensive Pulmonary Rehabilitation, 1995), combines exercise with proper nutrition, social activity, pharmacotherapy, home oxygen therapy, and psychosocial support for patients and their family members. Long-term home oxygen therapy is noteworthy in this context. Originally designed for severe chronic obstructive disease (COPD) patients who have hypoxemia (PaO$_2$<55 mmHg or SaO$_2$<90%) and hypercapnia (PaCO$_2$>60 mmHg), this treatment method has been increasingly extended to other diseases characterized by breathing insufficiency, including neuromuscular and neurodegenerative disorders (Kida et al., 2013). Home oxygen therapy, particularly combined with breathing exercises, holds a potential to decisively decrease the feeling of breathlessness and to improve exercise capacity, and quality of life of in PD.

In conclusion, respiration is impaired in parkinsonism due likely to central dopamine insufficiency, which may worsen body oxygenation and consequently also quality of life. The impairment of lung ventilation raises the possibility of breathing exercise, supported by home oxygen therapy if required, to improve physical and cognitive symptoms of parkinsonism; the therapy yet to be shown effective.

References


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