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Review

"Thermoregulation-dependent component" in pathophysiology of motor disorders in Parkinson's disease?

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Abstract

Parkinson's disease (PD) is a neurodegenerative disorder characterised by motor symptoms (resting tremor, brady- or akinesia and muscle rigidity), and also by postural problems gait disorder and fatigue as well as behavioural and autonomic symptoms, including thermoregulatory impairment. These symptoms are strikingly similar with some motor phenomena, evoked by the whole body cooling, though the primary cause of PD and cold-induced symptoms are apparently different. The review is focused on the hypothesis that thermoregulatory mechanisms are involved in pathophysiology of motor disorders in PD. The comparative analysis provides some examples of analogy between PD and the state of cooling in respect with tremor, muscle hypertonus, postural reactions and impairment of gross and fine muscle performance. This analogy cannot be considered as specific, because in some normal conditions the motor system utilises identical strategy to compensate for motor deterioration, e.g. at fatigue and ageing. However, such motor phenomena, as neuroleptic malignant syndrome and paired discharges of motor units indicate that the "thermoregulation-dependent component" exists in the pathophysiology of PD. Data on the influence of the whole body cooling and heating on muscle performance, rigidity and tremor in PD patients also provide evidence for the involvement of thermoregulatory mechanisms in PD.

Keywords: Parkinson's disease; Thermoregulation; Motor disorders; Cooling; Heating; EMG

Contents

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1. Introduction

Parkinson's disease (PD) is a progressive degenerative disorder of the nervous system. PD is caused by progressive loss of *substantia nigra* neurones. It is characterised by motor symptoms, such as resting tremor, hypokinesia, bradykinesia and/or akinesia, muscle rigidity, gait disorder, postural instability and fatigue. Non-motor behavioural reactions and autonomous functions, including thermoregulation, are also affected in PD. Muscular performance and manual dexterity are strongly deteriorated at PD, thus evoking in some cases a total disability of PD patients.

The classical symptoms of PD (resting tremor, deficit and slowness of movement, muscle rigidity) formally resemble motor phenomena evoked in normal subjects by cooling, such as cold shivering, slowed and weakened muscle contraction and elevated muscle tone. It is also common to define some PD symptoms in thermal terms, e.g. "frozen movement", "freezing of gate" or insufficient "energising" of muscles. Cold affects motor performance either due to shivering thermogenesis or to a decrease of muscular temperature. Behavioural reactions on cold may also contribute to the decrement of motor performance.

Some of the motor disorders in PD may reflect a process of *adaptation*, or *compensatory disorder* rather than be direct consequences of the "primary disorder" [1]. Compensatory mechanisms may reflect a *new order* in attempt to minimise the consequences of the primary disorder [1], or *a new pathophysiological system* of PD [2]. The motor deficits in PD patients and in the cooled subjects have apparently different primary causes. However, the motor system in PD patients and subjects in the state of cooling utilise identical compensatory strategy for motor deficits.

We hypothesise that thermoregulatory mechanisms may be involved in the pathophysiology of motor disorders in PD. This paper reviews studies, which suggest a contribution "thermoregulation-dependent component" in PD pathophysiology.

2. Formal analogy between cold-induced motor phenomena and PD symptoms

2.1. Muscle tone and tremor

Both cooling and PD evoke elevated muscle tone and tremor. Rigidity in PD is manifested as resistance to movement due to elevated muscle tone. It often has a cogwheel quality. In PD the resting tremor has a well-documented frequency of approximately 3.5–7 Hz.

Shivering thermogenesis aims to prevent hypothermia by increasing heat production, and it comprises of *thermoregulatory muscle tone* and *cold shivering* itself [3]. According to the "glossary of terms for thermal physiology" [4] thermoregulatory muscle tone is "the increase in electrical activity of the skeletal musculature of a resting tachymetabolic regulator during moderate cooling". During more intensive cooling, thermoregulatory muscle tone is superimposed by microvibrations and eventually by shivering tremor. Cold shivering is defined as "involuntary tremor of skeletal muscles as a thermoeffector activity for increasing metabolic heat production" [4].

In human investigations cold shivering can be subdivided into the burst-like and clustering patterns of EMG. The bursts of cold shivering occur from 6 to 12 min^{-1} and they reveal slow amplitude modulations on EMG [5]. The EMG clustering in the man occurs with the frequency of 4–8 Hz [6]. The clustering of EMG coincides with the most intensive tremor, and it probably corresponds with "shuddering" or "shaking", first described by Denny-Brown et al. [7] as a "maximum development of shivering". These two different patterns of cold shivering (with burst-like EMG and grouping discharges on EMG) have also been documented in animals [8].

2.2. Velocity and force of muscle contraction

Both PD and cooling are characterised by muscle weakness and slowed muscle contraction. There is a direct dose-dependent relationship between velocity, force and power and intramuscular temperature. The velocity of muscle contraction decreases by 4.7% [9] and maximal dynamic force and anaerobic power decreases by 4–6% per 1 °C decrease of intramuscular temperature [10]. Cooling to a larger degree, than the *isometric* one impairs the *dynamic* exercise. The faster movements are more susceptible to cooling than the slower ones. Thus, during jumping muscle performance decreases by 16–17% per 1 °C, while in slower movements the decrease is 2–10% per 1 °C [9,11–14]. The functional properties of skeletal muscles and nerves, peripheral force regulation, and impaired muscle co-ordination, i.e. "braking effect" may account for the decreased force and velocity of movements in cold (for review see [9]).