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Review article

Micrographia, much beyond the writer's hand

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ABSTRACT

Introduction: This review on micrographia aims to draw the clinician's attention to non-Parkinsonian etiologies, provide clues to differential diagnosis, and summarize current knowledge on the phenomenology, etiology, and mechanisms underlying micrographia.
Methods: A systematic review of the existing literature was performed.
Results: Micrographia, namely small sized handwriting has long been attributed to Parkinson's disease. However, it has often been observed as part of the clinical picture of additional neurodegenerative disorders, sometimes antedating the motor signs, or following focal basal ganglia lesions without any accompanying parkinsonism, suggesting that bradykinesia and rigidity are not sine-qua-non for the development of this phenomenon. Therefore, micrographia in a patient with no signs of parkinsonism may prompt the clinician to perform imaging in order to exclude a focal basal ganglia lesion.
Dopaminergic etiology in this and other cases is doubtful, since levodopa ameliorates letter stroke size only partially, and only in some patients. Parkinsonian handwriting is often characterized by lack of fluency, slowness, and less frequently by micrographia. Deviations from kinematic laws of motion that govern normal movement, including the lack of movement smoothness and inability to scale movement amplitude to the desired size, may reflect impairments in motion planning, possible loss of automaticity and reduced movement vigor.
Conclusions: The etiology, neuroanatomy, mechanisms and models of micrographia are discussed. Dysfunction of the basal ganglia circuitry induced by neurodegeneration or disruption by focal damage give rise to micrographia.

1. Introduction

1.1. Micrographia

Micrographia, abnormally small handwriting, is defined as an acquired reduction in handwriting size resulting in smaller than normal letter strokes [1]. Classically, micrographia is well known as a sign of Parkinson's disease (PD). However, it may occur in the context of other neurological conditions. The name was coined in 1903 by Pick [2], even before the first connotation to PD made by Froment, and was attributed to a patient with a syphilitic infarct involving the left thalamus [3]. This review aims at informing and updating the movement disorders neurologist about phenomenological clues for diagnoses other than PD, the spectrum of etiologies, motor control mechanisms and models of micrographia.

1.2. Review of literature

A systematic review of the existing literature by MEDLINE search using the keyword “micrographia” and a filter for the English language was performed. Reported patients with micrographia were reviewed and summarized using clinical, radiological or pathological information. Additional searches using the keywords “handwriting” and “levodopa” or “deep brain stimulation”

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were performed. Relevant references cited by the informative articles were also included. Literature search details are summarized in Fig. 1.

2. The phenomenon: *progressive*, *constant/consistent* and *fast* micrographia

The change in handwriting size involves several motoric elements associated with writing. Only part of these elements is apparent among all individuals demonstrating micrographia, and some may be suggestive of intricate pathologies.

"Progression" of micrographia is referred to in two senses. The first indicates changes from mild to severe micrographia along with disease worsening [4]. In a second sense, micrographia may be "progressive", showing a gradual decrement in letter stroke size during continuous writing or serial production of alphabetic characters and numbers, or remaining "constant/consistent" signifying that letter stroke size persists. In this article, we shall use the term "progressive micrographia" in the second sense. While both constant and progressive types are observed in PD, the latter is often considered a classical sign of the disease [4–6]. However, progressive micrographia may also appear following focal lesions of the basal ganglia (BG) [7,8].

The effect of writing direction may influence micrographia. For example, in Chinese, progressive micrographia may appear in vertical and horizontal writing directions [9], or only in the horizontal direction, whereas vertical handwriting from top to bottom, remains of constant size [10]. In this context, progressive micrographia was described in a Huntington's disease patient showing gradually reduced size of Chinese letters in vertical writing [11]. In the case of different writing directions in a native versus an acquired language, writing size may differ. Writing in an acquired language possibly necessitates the recruitment of more attentional resources that may influence the outcome (discussed in section 5.5). Indeed, in a case report, a Japanese PD patient exhibited micrographia in his native language, but produced normal sized handwriting in English [12]. The literature lacks references as to differential effects of left-to-right vs. right-to-left writing such as in Hebrew or Arabic. Hence, questions still unaddressed include the role of writing direction in PD and its correlation with the affected body side.

The presence of progressive decrement in writing size, versus letter size constancy, may provide a clue concerning the differential diagnosis of PD versus progressive supranuclear palsy (PSP). A recent study revealed that micrographia was more common in PSP (75%) than in PD (15%) [5]. Decrement in script size was less common in PSP than in PD. This finding parallels the one involving limb hypokinesia without decrement, observed in repetitive finger tapping of constant amplitude in PSP patients. In that study [5], the authors even suggested an increase in writing speed in some PSP patients; however, the handwriting task was not timed. This relative increase of speed differs from the concept of "fast micrographia" which is a consequence of pallidal damage [13–15]. It is characterized by microscopically small letters performed at a normal or slightly faster than normal speed.

3. Prevalence and appearance of micrographia in the course of PD

Studies suggest that micrographia may antedate additional motor signs of PD by three to four years [4]. As an early or first presenting symptom of PD, micrographia may serve for screening and diagnosis [4, 6, 16–18]. By examining the handwriting of 800 PD patients followed every 6–12 months, Mc Lennan [4] observed that 30% of patients showed micrographia in the course of PD and about 5% reported its occurrence prior to PD diagnosis. The frequency of micrographia in PD cohorts varies according to the study's methodology, such as information retrieved through verbal history (about 60% of patients), actual testing (about 50%) [16], or while copying letters [19]. Kim et al., by defining micrographia as letter size smaller than controls by two standard deviations found that, in copying, 25% of PD patients depict progressive and 44% constant micrographia, while only 3% fulfill these size criteria in free writing [19].

4. Non-Parkinsonian micrographia

Micrographia has been described in conjunction with focal lesions (Table 1) and neurodegenerative diseases of the BG (Fig. 2) such as PSP [5,20], Huntington's disease (HD) [11], corticobasal degeneration [21] and, corticobasal syndrome [22]. Distinctive properties of micrographia in PD and other neurodegenerative disorders are summarized in Table 2. These include the "constant" character lacking of progressive size reduction [5], the omission errors seen in PSP [20] and micrographia in the context of apraxic dysgraphia in corticobasal syndromes [21,22] (Table 2).

Focal lesions of the BG of diverse etiologies were described in detail as causative of micrographia (summarized in Table 1) [7,8,13,14,23–43]. In some of these reports, mainly with vascular lesions, the fact that patients do not exhibit any bradykinesia or any signs of parkinsonism is remarkable (Fig. 2). Interestingly, a cortical lesion causing micrographia was reported in a single patient with anterior cerebral artery infarction affecting premotor areas [34].

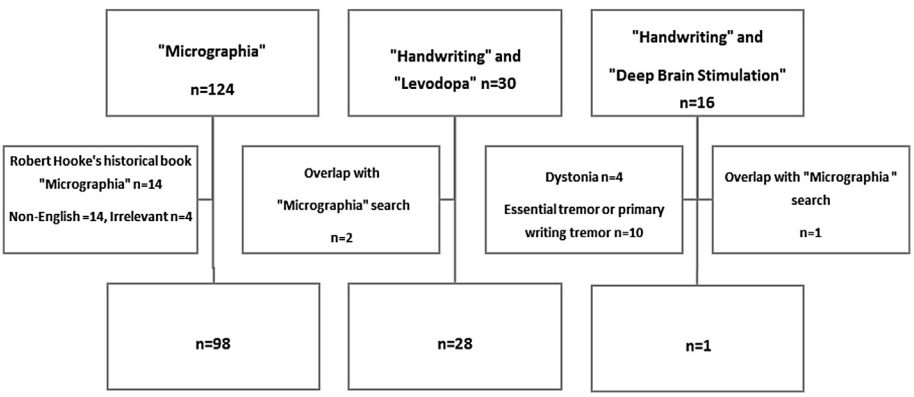

Fig. 1. Flow chart of literature search.

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