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REVIEW/MISE AU POINT

Characterization and quantification of freezing of gait in Parkinson's disease: Can detection algorithms replace clinical expert opinion?

Caractérisation et quantification du freezing *de la marche dans la maladie de Parkinson : les algorithmes de détection automatique remplacent-ils l'expérience du clinicien ?*

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Summary Freezing of gait is a paroxysmal phenomenon that is frequently reported by the parkinsonian patients or their entourage. The phenomenon significantly alters quality of life but is often difficult to characterize in the physician's office. In the present review, we focus on the clinical characterization and quantification of freezing of gait. Various biomechanical methods (based mainly on time-frequency analysis) can be used to determine time-domain characteristics of freezing of gait. Methods already used to study non-gait freezing of other effectors (the lower limbs, upper limbs and orofacial area) are also being developed for the analysis of freezing in functional magnetic resonance imaging protocols. Here, we review the reliability of these methods and compare them with reliability of information obtained from physical examination and detailed analysis of the patient's medical history.

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MOTS CLÉS
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Résumé Le *freezing* de la marche est un trouble paroxystique souvent difficile à mettre en évidence dans un environnement médical malgré le fait qu'il soit souvent rapporté par le patient ou son entourage et qu'il ait un retentissement important sur la qualité de vie des patients parkinsoniens. Dans cette revue, nous nous sommes focalisés sur la caractérisation et la quantification du *freezing* de la marche. Diverses méthodes étudiant sa structure temporelle, basées principalement sur les analyses temps-fréquence, sont présentées. Des méthodes utilisées pour caractériser des équivalents de *freezing* sur d'autres effecteurs (membres inférieurs et supérieurs, sphère orofaciale) sont aussi développées dans le but d'étudier le *freezing* en imagerie fonctionnelle. La fiabilité de ces méthodes est évaluée et comparée à l'évaluation clinique (incluant une anamnèse précise).

Parkinson's disease (PD) is characterized by axial signs; these notably include gait impairments that worsen over the course of the disease. Patients walk more slowly, with a shorter step length, higher cadence [40] and greater step time variability [26]. These gait impairments (which are present in most patients with PD) may be associated with paroxysmal events, such as freezing of gait (FoG) and/or festination [6]. During FoG, the feet appear to be more or less ''glued'' to the ground, with a dramatic change of cadence. Signs of shaking and asynchronous movement (described as ''trembling in place'') may occur as the result of ineffective efforts to move forward, particularly during step initiation [32]. Another FoG pattern (characterized by a frozen, akinetic state) has also been described [6]. Nutt et al. [49] defined FoG as the ''absence or marked reduction of the forward progression of the feet, despite the intention to walk''. One of the strengths of this definition (based on clinical evaluation) is that it encompasses the different subtypes of FoG. Freezing is most commonly experienced during turning, step initiation and when faced with spatial constraints, stress, and/or distraction: this often corresponds to passing through a narrow doorway or reaching a destination, although FoG may also occasionally occur during walking in a straight line in open space [59,66]. Focused attention and external stimuli (cues) can overcome a FoG episode or, on the contrary, trigger it [37].

Gait festination is defined as a tendency to move forward with faster but smaller, ''tottering'' steps. It is associated with a forward displacement of the center of gravity (in front of the feet) [21]. FoG and festination often occur in the same patient, and display very similar spatiotemporal anomalies in the steps preceding the FoG phenomenon [10,45].

FoG is frequently reported in PD: in 81% of patients after 20 years of disease (in an Australian cohort) [29], and in 87% after 11 years (in a Chinese cohort) [4]. In the DATATOP cohort [22], FoG was present in early-stage disease (in 26% of L-dopa-naive patients). Furthermore, FoG is reportedly an independent risk factor for falls [52] and impairs quality of life [54]. FoG and festination are debilitating problems because of their relative resistance to treatment by levodopa [16,54] (as is the case for most axial signs). Moreover, the effects of subthalamic nucleus deep brain stimulation on FoG are subject to debate [19]. Hence, FoG is a frequent, serious problem in PD and must be closely monitored.

A detailed analysis of the patient's clinical history is necessary and will provide information on self-reported FoG and the latter's relationship with dopaminergic medication [3]. Given this context, what advantages might automated quantification methods provide in the detection of FoG and the characterization of its pathophysiological mechanism?

In the present review, we shall successively focus on:

- the clinical characterization and quantification of FoG;
- biomechanical methods for characterizing FoG;
- useful applications of these methods (e.g. for the objective detection of FoG and assessment of its pathophysiological basis).

The clinical assessment of FoG

In most publications, the classification of patients as ''freezers'' has been based on the patient's retrospective self-assessment of FoG over a period of time (often the previous week) using various questionnaires. The most frequently used tools are the Unified Parkinson's Disease Rating Scale (UPDRS) part 2, item 14 (''freezing'') [18] and item 2.13 of the more recent Movement Disorders Society (MDS)-UPDRS questionnaire [24]. Patients rate their propensity to freeze over the previous week on a scale from 0 (no FoG) to 4 (frequent falls due to freezing for the UPDRS, and the need to use a walking aid or someone's help for the MDS-UPDRS). The Freezing of Gait Questionnaire (FOG-Q) and the new FOG-Q (NFOG-Q, which includes a video showing several subtypes of FoG) [20,23,47] can be used to identify freezing behavior. Indeed, FOG-Q question 3 (''Do you feel that your feet get glued to the floor while walking, making a turn or when trying to initiate walking [freezing]?'') was at least as good as item 14 of UPDRS part 2 for distinguishing between freezers and non-freezers. Snijders et al. [64] developed a decision tree for refining the classification of freezers into three categories: (i) a ''self-reported freezer,'' (ii) a ''probable freezer'' (i.e. when FoG is confirmed by a third person, such as caregiver) and (iii) a ''definite freezer'' (when freezing is actually observed during formal, objective testing). Other less specific gait and balance scales could be useful to assess FoG and have recently proved to be able to differentiate freezers and non-freezers [15]: the Mini-BESTest and Berg Balance Scale. Both tests take