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Understanding and Treating Freezing of Gait in Parkinsonism, Proposed Working Definition, and Setting the Stage

Nir Giladi, MD[1] and Alice Nieuwboer, MD[2]*

[1]*Department of Neurology, Tel-Aviv Sourasky Medical Center, Sackler School of Medicine, Tel-Aviv University, Tel-Aviv, Israel*
[2]*Departement Revalidatiewetenschappen Faculteit Bewegings- en Revalidatiewetenschappen, Katholieke Universiteit Leuven, Leuven (Heverlee), Belgium*

Although the term "freezing of gait" (FOG) was not used by early authors and notably not by Parkinson himself,[1] the typical propulsive high frequency stepping associated with this gait disturbance was described by him as a feature of Parkinson's disease (PD). Martin[2] also reported examples of an inability to initiate locomotion accompanied by disturbed stepping patterns in postencephalitic parkinsonism with a dramatic response to visual cues. It was not until the early 1970s that FOG started to get increased attention, based on the realization that its response to levodopa was more complex than that of bradykinesia and rigidity. During those early days, it was first suggested that levodopa can sometimes induce or even worsen FOG.[3] Based on those reports and the occurrence of FOG in atypical parkinsonism, it has long been considered a levodopa-resistant symptom. It took 30 years of experience with levodopa treatment to understand that this is a misconception. Schaafsma et al. demonstrated that "off"-related FOG episodes were significantly shorter in duration and markedly fewer in frequency when turning from "off" to "on."[4] However, the concept of a complex relationship with levodopa treatment still holds, as is evidenced by the continued manifestation of FOG in the "on" period, and its relationship with other levodopa-resistant symptoms such as postural instability.[5,6]

Despite its fascinating and unique nature, its common appearance among people with advanced PD, and its significant contribution to the development of major disability and frequent falls,[7] research about the pathophysiology and treatment of FOG moved slowly forward. One possible reason for that delay is the unpredictable and episodic nature of freezing, which makes it very difficult to capture true spontaneous episodes. In addition, FOG appears most frequently at home during unobserved behavior and in response to specific environmental triggers[8] and rarely in the gait lab.[9] Another difficulty that might have slowed down FOG research is its lack of definition. This is of special importance, considering the fact that FOG is very heterogeneous in nature and can frequently be confused with bradykinesia or akinesia.

Taking all those difficulties together, we thought it is time to join forces and move research about FOG forward to a better understanding of its mechanisms and hopefully with time leading to more effective treatment. This supplement is the result of a satellite symposium which was held just prior to the Kyoto International Movement Disorders Congress in late October 2006. In this meeting, a number of state-of-the-art presentations were put forward, summarizing the most recent clinical and research findings. All speakers and two additional leading figures in the field of FOG research were subsequently invited to contribute to this first ever supplement devoted to FOG in parkinsonism.

As part of the introduction to this supplement, we propose a working definition of FOG. We are aware of the difficulties inherent to this task but believe that this first step has to be taken to improve communication and upgrade the quality of scientific terminology among researchers.

The most common feature associated with FOG is the unique subjective feeling of patients describing that "their feet get glued to the ground." As suggested in one of the supplement papers on the clinimetrics of FOG,[10] this characteristic feeling may aid in accurate history

*Correspondence to: Alice Nieuwboer, Departement Revalidatiewetenschappen, Faculteit Bewegings- en Revalidatiewetenschappen, Katholieke Universiteit Leuven, Tervuursevest 101, 3001-B Leuven (Heverlee), Belgium. E-mail: alice.nieuwboer@faber.kuleuven.be
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taking. However, it cannot be used as a research or clinical definition, especially when one deals with patients who might have difficulties verbalizing their feelings. The other typical features of FOG are its episodic nature and the fact that it is a short-lasting event of either a complete arrest of gait or associated with some degree of forward progression, albeit with small, disturbed, and rapid steps. We propose that both aspects are an integral part of FOG and therefore should be included in the definition. To keep the definition as broad as possible, reflecting hesitations at the start of walking, interruptions during turning as well as freezing while walking in a straight line, we have chosen to define it as a general inability to produce effective steps. As frequently done in other clinical definitions such as of dystonia or dementia, we included the situations where FOG most commonly occurs, to stress its functional significance. It also underscores the trigger-sensitivity of FOG which is so characteristic and distinguishes it from other clinical features. The last part of the definition addresses the behavior which can improve FOG, as its distinct response to self-prompting or external stimuli can help to differentiate FOG from akinesia and as such aid in its recognition.

We define FOG as "an episodic inability (lasting seconds) to generate effective stepping in the absence of any known cause other than parkinsonism or high-level gait disorders. It is most commonly experienced during turning and step initiation but also when faced with spatial constraint, stress, and distraction. Focused attention and external stimuli (cues) can overcome the episode."

The mechanisms responsible for FOG are not well understood, posing the main challenge for future research. This being said, increasing amounts of knowledge are being gathered about abnormalities of gait in between the freezing episodes, events preceding the actual freeze, leg activation during the FOG, and brain activity differences in freezers and controls during rest conditions, all of which will be discussed in this issue.

Two papers in this supplement specifically address the neurophysiological aspects connected to FOG. By contrasting the role of intrinsic and extrinsic brain circuits, Hallett[11] conceptualizes how brain dysfunction related to the self-initiation of movement may be a factor associated with FOG. Bartels and Leenders[12] bring together the most recent finding from functional brain imaging to highlight how dysfunctional frontal lobe-basal ganglia connections may contribute to the pathophysiology of FOG.

From the perspective of gait analysis, two groups discuss how disturbances of ongoing gait may be associated with the occurrence of FOG. Morris and Iansek[13] propose that severe hypokinesia and motor instability constitute some of the underlying movement disorders. Plotnik and Hausdorff[14] speculate on how abnormalities of rhythmicity, symmetry, and bilateral coordination of gait may be predisposing factors or even causally related to FOG.

From a clinical viewpoint, Okuma and Yanagisawa[15] use the description of the broad clinical spectrum of FOG to gain insight into its origins. Factor[16] gives an overview of FOG in atypical parkinsonian conditions, providing an avenue for further pathophysiological work involving its nondopaminergic mechanisms. Snijders et al.[10] summarize the present tools used for the assessment of FOG, discussing their advantages and disadvantages for clinical and research purposes and as outcomes for intervention.

The last three papers in this supplement deal with the treatment of FOG. A common theme in this section is the often ambiguous effects of existing interventions. Giladi[17] discusses the current state of the art of the role of medications (dopaminergic and nondopaminergic) in the overall management of FOG. The positive effects as well as the limitations of cues as part of rehabilitation strategies are presented by Nieuwboer,[18] highlighting the complexity of the motor deficits inherent to FOG. The sometimes controversial role of deep brain stimulation and its relationship with levodopa is portrayed by Ferraye et al.,[19] including the preliminary results on the pedunculopontine nucleus as a potential target.

This supplement does not cover all aspects related to FOG, and important issues like the role of cognition, affect, visual perception, or postural control are outside its scope. However, we believe that this is a comprehensive scientific document that is fully devoted to FOG and as such, likely to be an instrumental tool for all those who are fascinated by its unique features. We also hope that it will help to increase the interest, improve the scientific language, and encourage additional researchers to bring this field forward. Taking into account the complexity of FOG and its heterogenic nature, as reflected in this supplement, we believe that an interdisciplinary research approach is needed to better understand and treat FOG. Furthermore, we hope that based on current knowledge, future research, and new therapeutic interventions, FOG will be prevented throughout the course of the disease.

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