

## Commentary

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# Freezing of Gait Before Levodopa

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We have recently studied the general impression that freezing of gait (FOG) is nowadays more common than before the introduction of levodopa [1]. To this aim, we carefully reviewed historical films and medical textbooks from before 1972. In the historical footages we did not observe FOG, and in the textbooks and accompanying literature, we only found scarce descriptions of FOG, which were (with one exception) of the akinetic phenotype. We therefore postulated that the occurrence of FOG may have increased after the introduction and long-term use of levodopa, expressing itself with a shuffling and trembling phenotype.

Gilat and colleagues have challenged our contribution [2]. They first emphasize that FOG can occasionally be present in untreated patients. We do not disagree, but this sporadic presence of FOG in levodopa-naïve patients does not distract from our main message which was—and remains—that FOG was distinctly rarer prior to introduction of levodopa. As an add-on to our findings, Gilat and co-workers note that FOG may have been present during turning in a single patient filmed around 1910 [3]. We have asked nine established international movement disorders experts to rate this video. Only two of them felt that there was a clear episode of FOG (notably,

of the akinetic phenotype), whereas the seven others classified the turning hesitation as a manifestation of severely bradykinetic gait. Regardless, such sporadic observations of FOG in levodopa-naïve patients do not implicate that the incidence is the same as in levodopa-treated patients.

Gilat and colleagues [2] also challenge our interpretation that the manifestation of FOG may have changed after the introduction and long-term use of levodopa, now expressing itself with a shuffling and trembling phenotype. Their argument is that historical cinematography has technical limitations, hampering the detection of FOG, especially the trembling subtype. We disagree, as the sampling rate of historical films is typically 16–24 frames per second, which will be sufficient to observe a trembling subtype of 3–8 Hz. Interestingly, the 1910 video mentioned earlier shows a clear tremor of the hands (most pronounced on the right side), confirming that the sample rate of historical films is sufficient to detect trembling. The hesitation noted during turning in this video was clearly of the akinetic phenotype. Moreover, in the textbooks and accompanying literature, we found only scarce descriptions of FOG, which were always of the akinetic phenotype, with only one exception. We therefore maintain that the characteristic trembling variant of FOG must have been rare prior to introduction of levodopa.

Finally, the authors state that our observations may induce levodopa-phobia, but this concern is

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unfounded. Our paper never made this claim [1]. Indeed, we have repeatedly recommended levodopa as first-line therapy for persons with Parkinson's disease [4], also as the primary pharmacological treatment for FOG [5]. Instead, our main purpose was to draw attention to the possible role of non-physiological stimulation of dopamine receptors in generating FOG [6], as an incentive for development of improved pharmacotherapies that may carry a lower risk of causing this debilitating gait problem in future patients.

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