Movement Disorders
CLINICAL PRACTICE

REVIEW

Freezing of Gait in Parkinson's Disease: Its Pathophysiology and Pragmatic Approaches to Management

Robert Iansek, OAM, PhD, FRACP,[1,2,*] *Mary Danoudis, PT, MPT*[1]

Abstract: **Background:** Freezing of gait (FOG) in Parkinson's disease (PD) is poorly understood; however, with the established understanding of basal ganglia function, its manifestations should be more easily interpretable. This review examines freezing of gait (FOG) from such a perspective.
Methods: A search of the MEDLINE and EMBASE databases from the year 2000 onward for review articles, focused on the pathophysiology of FOG, was used to determine current concepts. A previously established model of basal ganglia function was used to determine the concepts' validities. At the core of the model are deficits in motor set maintenance and timing cue production for automatic movement. It includes the shift between attention and automation to the predominant attention control of gait in PD.
Results: The difficulties of the found concepts to explain FOG stem from failure to characterize different FOG components, from the assumption that all components share a similar pathophysiology, from a failure to separate basic deficits from compensatory mechanisms, and from the assumption that cognitive deficits are the cause of FOG rather than representing an inadequate compensation to FOG. Pragmatic approaches to management use the attention shift, with the provision of visual information about correct amplitude of step to correct initiation deficits, and motor blocks during gait. It also emphasizes the need to prevent step length reduction on turns, environmental situations, and cognitive overload.
Conclusion: The concept of automatic deficits in set maintenance and cue production best describe FOG manifestations in PD and, with the use of attention, the concept also provides pragmatic strategies for management.

A large body of literature exists on the clinical phenomenon of freezing of gait (FOG) in Parkinson's disease (PD) with a common theme of poor understanding of its pathogenesis. Several factors may underpin this ongoing uncertainty about the pathogenesis of FOG. These factors include: (1) a failure to relate the phenomenon of FOG to what is known about basal ganglia (BG) function and malfunction in PD; (2) the consideration of FOG as a single entity, rather than consisting of a variety of different manifestations; (3) the view that the pathology of FOG is consistent across all manifestations; (4) the failure to separate the compensatory mechanisms associated with FOG from basic pathophysiology; (5) the failure to take into account disturbance in motor referencing in automatic gait control; and (6) the view that cognitive deficits in patients with FOG are directly responsible for the motor deficits rather than impairing adequate compensation.

In this review, we examine FOG with a focus on BG function and malfunction in PD. Much is already known, published, and accepted in this area, and it seems to us that the clinical template for manifestations of FOG already exists; thus, it may prove useful to use this perspective to examine current theories of FOG to try and determine why such theories may not

[1]Clinical Research Centre for Movement Disorders and Gait, The National Parkinson Foundation Center of Excellence, Kingston Centre, Monash Health, Cheltenham, Victoria, Australia; [2]School of Clinical Sciences, Monash University, Clayton, Victoria, Australia

***Correspondence to:** Dr. Robert Iansek, Clinical Research Centre for Movement Disorders and Gait, Kingston Centre, 400 Warrigal Road, Cheltenham, Victoria, Australia 3192; E-mail: robert.iansek@monash.edu
Keywords: freezing of gait, gait control, Parkinson's disease, pathophysiology, rehabilitation.
Supporting information may be found in the online version of this article.
Relevant disclosures and conflicts of interest are listed at the end of this article.
Received 1 August 2016; revised 27 October 2016; accepted 9 November 2016.
Published online 26 December 2016 in Wiley InterScience (www.interscience.wiley.com). DOI:10.1002/mdc3.12463

doi:10.1002/mdc3.12463

provide adequate explanations for its manifestations. We undertook a search of the MEDLINE and EMBASE databases from the year 2000 onward for review articles focused on the pathophysiology of FOG to determine current theories and ideas. The theories identified included abnormal gait pattern generation, disturbed central drive, disturbed automaticity of gait, mismatch between anticipatory postural adjustments and step initiation, perceptual dysfunction, and frontal executive dysfunction.

The results of this review suggest that a simple concept of BG function and malfunction in PD has the capacity to explain not only most aspects of FOG manifestations but also some of the discrepancies in the examined theories. Furthermore, an extension of this concept can also provide pragmatic approaches to short-term management.

Characteristics of FOG

Definition

FOG has been defined as "a brief, episodic absence or a marked reduction of forward progression of the feet despite the intention to walk."[1] However, after this review, we recommend that this definition needs to be extended to include "the intention to walk with a predetermined stride length in automatic mode." We suggest this change in definition to emphasize that the manifestations of FOG occur only under these circumstances. Clinically, these 2 requirements exist when walking is performed without any concentration. These are important aspects of FOG that help explain some of its manifestations, as demonstrated below.

FOG Types

The transient interruption to walking in FOG can occur at initiation of gait, during gait (motor block), or in both situations.[2] In addition, the interruptions are usually associated with other motor phenomena. These include hypokinetic gait (small steps),[3] the sequence effect (sequential decrement in step size),[4] festination (hurrying slowly),[3] mismatch between anticipatory postural adjustments and step initiation,[5] and tremor in place or trembling knees (repeated but ineffective movement of the feet).[3] The latter 2 disturbances are usually associated with initiation disturbances, and the former 3 are associated with transient interruption to stepping while walking. FOG is not a single entity but rather it refers to an umbrella term that encompasses these differing motor disturbances. It is interesting that past publications frequently failed to define the above-described motor disturbances of the FOG population under study.[5–9] Few studies have attempted to define the FOG types recorded[10]; instead, many have categorized the FOG episode according to the precipitant event rather than its motor manifestations. This lack of specificity in the description of motor disturbances makes comparison between studies difficult and tends to create uncertainty of their interpretations.

FOG Pathology

The overlap between the motor manifestations of FOG and the underlying pathological abnormalities complicates the interpretation of pathophysiological mechanisms, because FOG is not specific for PD. The different motor manifestations of FOG are also seen in Parkinson-related conditions, such as progressive supranuclear palsy, progressive supranuclear palsy variants, multiple systems atrophy, and corticobasal degeneration.[11,12] Higher level gait disorder can also present with FOG.[13]

The lack of pathological identification is of most relevance for publications dealing with deep-brain stimulation surgery of the pedunculopontine nucleus (PPN). Several publications have attempted to outline the role of the PPN in FOG,[14–18] but the nature of the underlying pathology of the subjects has not been identified.

Theories of FOG

Several theories have been put forward to explain FOG but, again, under its umbrella term. *Abnormal gait pattern generation*, presenting as poor control of rhythmicity, impaired bilateral coordination of stepping, and increased asymmetry, has been associated with FOG.[8,9] It was hypothesized that FOG occurred most commonly at gait initiation and on turning, because these tasks require intact coordination of leg movements.[9] More recently, Plotnik and colleagues[19] suggested that FOG may present when more than 1 gait deficit is present, such as the sequence effect, asymmetry, and hypokinesia. However, the concept of leg-to-leg incoordination does not take into account the fact that none of the experiments that underpinned this concept controlled for the different background stride lengths between the control group and the FOG group. Danoudis et al.[20] showed that, after adjusting for preferred step length, swing time asymmetry did not differ between individuals with PD who experienced FOG and those who did not. Similarly, when participants in these 2 PD groups walked at varying normalized step lengths, their swing time asymmetry did not differ. In addition, shortening step length was found to increase asymmetry of swing time in both PD groups and in healthy controls. These findings suggest that asymmetry measures are an epiphenomena of walking with small steps[20] and have no relationship to motor blocks during walking.

An alternate suggestion has been that FOG occurs because of a *disturbed central drive and disturbed automaticity of gait*.[1] This theory is based on the role of the BG in controlling automatic movements and the presence of FOG with the performance of a secondary task. It has also been suggested that competing central BG connections with higher centers can lead to temporary interruption of brainstem outputs and thus to FOG.[14] These 2 theories fail to separate the basic deficits of BG malfunction with cortical compensatory mechanisms.

The mismatch between anticipatory postural adjustments and step initiation has also been suggested as a reason for FOG.[5] Although this theory may explain the clinical observation, it does not explain why there are repeated unsuccessful attempts

doi:10.1002/mdc3.12463

at initiating the right amplitude step (tremor in place) for the anticipated postural adjustment. Furthermore, although this may explain initiation deficits to a limited degree, it does not explain motor blocks during gait.

It has also been argued that *perceptual dysfunction* may explain FOG, because visual precipitants commonly lead to motor blocks during walking.[7] It has been shown that both healthy adults and individuals with PD who experience FOG reduce their stride length when approaching a narrow doorway, although the perceptual assessment of the doorway was normal in both groups.[21] Again, this idea merely describes the clinical manifestation without providing an adequate explanation for the observation.

Frontal executive dysfunction has been described as a common feature among individuals who have FOG with deficits in attention, problem solving, and incapacity to set change.[22–24] Studies that have examined these attributes have indeed demonstrated difficulty in cognitive multitasking among individuals with FOG. Certainly these deficits may be associated with motor blocks while walking, and they also may contribute to initiation difficulty in conflict situations, such as crossing a road; however, the relationship of these deficits to the programmed stepping mechanisms is not understood or described.

BG Function

To better understand the clinical manifestation of FOG, it is important to review BG function and malfunction in PD. The BG, in conjunction with the supplementary motor area (SMA), runs automatic movements.[25,26] Automaticity refers to motor skills that can be executed without the need to pay attention to the details of the motor action. The selection of the motor skill presets the amplitude of the movement, which the BG maintains through its interaction with the SMA. This is referred to as "motor set,"[25,27] or the maintenance of a specified motor parameter by a characteristic neuronal discharge pattern. In gait, this parameter is stride length (movement amplitude).[28] At a neuronal level, this is represented as sustained neuronal activity, which is maintained until the selected motor skill terminates.[29] The motor plan, once selected and maintained, needs to run through its subcomponents to completion. Automatic control requires precise timing from 1 component to the next. This is achieved by the BG providing a timing cue, which signals the end of a current submovement that is then used by the SMA to release the next submovement.[30,31] These timing cues are phasic bursts of neuronal discharge generated online while the motor skill or plan sequence is read out within the SMA. This is a programming process, and the programming instructions are relayed to the executive mechanisms to produce the movements. Within the instructions are embodied the amplitude and timing of the submovements.

In PD, the reduced dopamine in the striatum leads to a mismatch between the intended amplitude and the performed amplitude. This mismatch occurs during the BG processing, not at the cortical control level, which still assumes no mismatch has occurred.[32] Therefore, movements are smaller, and their amplitude reduction is directly proportional to the amount of dopamine loss in the striatum.[33]

In more advanced PD, the capacity to generate phasic neuronal bursts becomes disrupted, leading to uncertain termination of submovements, with subsequent imprecise duration of the next submovement, which further impacts on the phasic burst and the duration of the following submovement. This imprecision compounds down the sequence, resulting in smaller and smaller submovements, termed the sequence effect.[4]

The amplitude mismatch and the sequence effect are the characteristics of the motor disturbance in PD and are evident in all movements, including gait, manipulative tasks, as well as speech.[4,32] It is interesting that the Movement Disorder Society Task Force on Clinical Diagnostic Criteria emphasized the same clinical manifestations for BG malfunction in PD that we used for this review.[34]

In summary, the BG runs automatic movements in conjunction with the SMA by the provision of motor set and motor cues. In PD, the motor set is reduced, leading to hypokinesia; and, in the later stages, the timing cues are corrupted, resulting in the sequence effect.

Central Gait-control Mechanisms

Central gait-control mechanisms are involved in the programming of gait according to the environmental situation in which walking takes place. In this regard, it requires flexibility to continually update the programming through the use of 2 options: attention and automatic control.[35]

Attention control uses several cortical motor areas, including the premotor area, the cingulate motor area, the dorsal frontal motor area, and the precuneus.[36] It has been demonstrated that attention to an "automatic" motor task in healthy adults does not change the automatic activity pattern in the striatum but results in greater activity in the central attentional networks like the pre-SMA as well as motor cortex regions.[35] Attention control when walking is very dependent on visual information to guide each step, the amplitude of which can vary according to the upcoming impediment.

Automatic control uses the BG-SMA interaction, which translates the intention to walk with a particular speed and stride length into automation. This programming removes the need for attention, and walking can proceed without change in unencumbered environments. In automatic control, there appears to be a very tight relationship between the stride length and the associated cadence across all age groups. Support for this concept comes from correlations between gait parameters and magnetic resonance imaging-detected white-matter disturbances, which indicated that only stride length regulation, and not cadence, was affected by white-matter changes.[37]

Innumerable numbers of plans are continuously processed simultaneously through the BG in its role of automating motor skills. This represents automatic motor working memory. The translation of the motor command into gait from either of these

doi:10.1002/mdc3.12463

programming options requires the instruction to be directed to the brain executive components, which include the mesencephalon and spinal gait-control mechanisms. These include the cerebellum, midbrain, pons, and spinal cord. The role of these mechanisms is to maintain the command of the specified step length, irrespective of unforeseen changes in the environment, such as walking uphill or against the wind.

In PD, attention to automatic movement results in changes to the pattern of activity in the striatum, decreased activity in the SMA, and greater activity in attention areas of the motor cortex compared with healthy controls.[35] This disturbance to automatic control sees a mismatch between intention and automation, resulting in a smaller step or stride. The sequence effect may also manifest. The mismatch is not recognized at the cortical level, because it is caused by a BG processing deficit (disturbed internal referencing), and the working motor memory of the BG shrinks with fewer plans processed through the BG. The resultant effect is that programming shifts to attention control.

Although attention can improve 1 or 2 tasks through the disturbed BG, it is not able to normalize movements, because it is unaware of the existing motor mismatch.[32] Furthermore, the focus of attention control to 1 or 2 motor skills results in deterioration of other skills, which are left to be processed by the disturbed BG. In this context, the variables relate to the amount of dopamine loss and replacement benefits from medication, so some movements may be more affected than others.

Step length can be improved by the person concentrating on their walking, but it deteriorates if a secondary task is performed.[38] However, if some visual indication (steps or floor lines) is available, then the step length will greatly improve, because the attention control now can use visual information to control stepping, bypassing the BG-SMA interaction.[29] Attention is unable to improve the sequence effect by concentrating on gait, and medication is similarly unsuccessful.[4] However, external visual cues can eliminate the sequence effect, because internal BG cues are no longer needed.[4]

Pathophysiology of FOG Components

We now wish to review the theories on FOG in light of the information provided above on BG function and gait-control mechanisms. It is well established that FOG is more prevalent in severe PD and in PD of longer duration.[39] Advanced PD typically leads to end-of-dose slowing, which is associated with slower gait and shortened step lengths. Where end-of-dose slowing is resistant to medication adjustments, shortened step length may persist for increasingly longer periods throughout the day. This feature of advanced PD may be a factor in the increasing incidence of FOG in patients with advanced disease.

The severity and distribution through the striatum of the levodopa (L-dopa) loss varies and may impact more on 1 movement than another in each individual and across individuals in the reduction of step length. In severe L-dopa loss, step length may be extremely small, and the capacity of the BG to provide appropriate motor set for gait may be quite impaired. In addition, with more advanced PD, it is more likely that the sequence effect will be present during gait.[4]

Advanced PD is also associated with more severe cognitive deficits, particularly executive dysfunction, and the capacity to multitask becomes more and more impaired.[40] With advanced disease, dyskinesia becomes more prominent and, when present, can disrupt attention-control processes, making it difficult to use attention adequately.[2]

These developments are at the foundation of FOG: On the 1 hand, there is the physical template of disturbed motor set and motor cues, which predisposes to FOG; and, on the other, there is the cognitive status, which fails to compensate for the physical tendency. This failure in compensation manifests with a gait of reduced stride length.[38] Alterations in either area can lead to FOG.

Motor blocks during walking have been found to occur only if the sequence effect is present.[41] Whether the block occurs is very dependent on the background step length. If the background step length is small enough to approximate the sequence effect amplitude, then the sequence effect dominates control of stepping, and the steps become smaller and smaller until a stop occurs.[41] The decrement with each step in the sequence effect is usually small, so its relevance only occurs when the step length is also reduced. Variations occur with the slope of the sequence effect in individuals and across individuals, so that the step-to-step decrement can be much greater in some situations than in others. This variability can lead to motor blocks with even larger stride lengths. The basis for this variability is currently unclear. Possible reasons for the variability of the background stride length are multiple and include disease severity, wearing-off effects, distracted attention with multitasking, shortened attention span, or dementia.

When the sequence effect controls step length, a step-by-step reduction in step length occurs, which can terminate in a sudden block. In some individuals, this process is associated with an increasing hastening before the block. The hastening (festination) may be because of a slightly bigger original step length that has to fit into an increasingly smaller step. This can only be achieved by increasing the speed of the step time, which creates the audible speeding. In part, this explanation may underpin the accelerometer changes described before a motor block with instrumented detection techniques.[10]

Whereas reduced set and defective timing cues can explain FOG during walking, they do not provide an explanation for initiation difficulties. The inability to initiate walking with a specified step length may be due to the complete absence of motor set from the BG to the SMA. We previously demonstrated that step length is coded in the premovement potential (PMP) slope amplitude, as recorded during walking in patients with PD.[28] We observed that a smaller step length was associated with reduced PMP recorded for the SMA. The implication of this finding is that an absent PMP would be associated with an absent movement. In fact, patients with PD who had initiation difficulties demonstrated a disrupted association between step length and the

doi:10.1002/mdc3.12463

PMP.[28] It is thus feasible that gait-initiation disturbances are caused by the inability of the BG to provide the correct background set to enable automatic initiation of gait.

The capacity of the BG to initiate automatic motor plans would depend on the correct amount of motor set delivered to the SMA and the pre-SMA. It is well known clinically that certain plans are affected more than others.[42] It is not unexpected then that the plan for anticipatory postural adjustments may be initiated, but the plan to initiate step generation with appropriate set is not activated. This discrepancy may underlie the manifestation of tremor in place, wherein gait is not initiated but the postural change has occurred. This combination is associated with an imminent fall, placing further stress on the initiating step.

The perceptual dysfunction theory relates to the precipitant effects of external visual information, which may precipitate a FOG event, such as approaching a doorway, with the implication that the perceptual problem is leading to the FOG episode. However, it has been shown that the FOG episode is due to the sequence effect and a reduced background step length. The reduced step length in this context has been demonstrated in prior publications and relates rather to the fact that the step length is maintained at larger amplitude because of the shift to attention control as individuals concentrate on their walking.[21] An approaching doorway distracts attention, the step length reverts to uncompensated automatic control, and, as a result, the step length reduces.[38] If the sequence effect is present, then it can lead to a motor block. In a similar manner, planned turns require a reduction in the background step length on the second step in the turn on the order of 30% to enable the turn to occur.[43] Again, we have a forcible reduction in the step length and, if the sequence effect is present, it can lead to a motor block.

Numerous groups using differing techniques have examined the role of the brainstem locomotor region (BLMR) in medication-resistant FOG. These techniques have included fMRI, fractional anisotropy and electrophysiological studies in postoperative patients.[16–18,44,45] Studies using imagined walking have found that the SMA in patients with FOG can no longer code for step amplitude and that the BLMR is hyperactive.[45] Functional anisotropy suggests a structural attenuation of the BLMR in cortical and brainstem regions with a right hemisphere predominance.[44]

Analyses of gait in the PPN region among stimulated individuals demonstrate a variable functional benefit, but the information suggests that this benefit is via an increase in cadence without a concomitant increase in stride length.[16] Recordings from PPN neurons demonstrated wide multiple sensory inputs, including the signaling of an attention-controlled command.[18] By contrast, neurons of the subthalamic nucleus signaled movement-related events.[18]

The model of FOG outlined in this report would include the BLMR as part of the executive structure for gait and, as such, it would have the capacity to regulate the neurophysiological control of stepping; but the model indicates that the instructions for purposeful stepping would come from higher control and that this would consist of step amplitude and step timing for automatic control of gait. In attention control, the BLMR may be bypassed, because cortical attention mechanisms would control each step separately, and there would be no need to modulate a stepping center (BLMR) for the performance of a single step. In automatic control, a decoupling may occur between the BG-SMA and the BLMR.[45] This may manifest as absent disinhibition, with the lost capacity of the SMA to regulate step length and a resultant increase in BLMR activity, as demonstrated by Snijders and colleagues.[45] This would result in low cadence and low-amplitude, unregulated gait. Whether this is a structural or functional decoupling needs to be determined.

It appears that the benefit of PPN stimulation improves only cadence in a nonspecific manner with variable improvement in FOG events.[16] Interestingly, our own data in higher level gait disturbance suggest that, in severe disease, stride length becomes uncoupled with cadence, and cadence can no longer be modulated, being "fixed" at about 100 steps a minute. This is similar to the poststimulation cadence benefits observed by Thevathasan and collegues.[16]

A more recent theory has suggested that FOG may involve a fundamental disruption to the brain's inhibitory control system, which has been identified as the inferior frontal cortex and the subthalamic nucleus.[46] However, the paradigms used in those investigations employed an attention task with a high cognitive load, suggesting that circuitry may not involve automatically controlled motor skills, such as gait in PD.

In summary, all aspects of FOG can be explained by the malfunction of motor set and motor cue because of BG malfunction. In the total absence of motor set, a motor plan cannot be automatically activated, leading to initiation deficits. Reduced motor set can initiate and run plans, but at a reduced stride length. Dysfunction of motor cues leads to the sequence effect. The combination of sequence effect and severely reduced step length can lead to a motor block during gait. Precipitants of FOG events all impact on the background step length by diverting attention. It is apparent from the above description that all theories of FOG can be incorporated under this explanation. "*Abnormal gait pattern generation*, *disturbed central drive,* and *disturbed automaticity of gait*" encompass the motor set and cue disturbances. The "*mismatch between anticipatory postural adjustments and step initiation*" relates to differences in motor set to motor plan selection and initiation. "*Perceptual dysfunction* and *frontal executive dysfunction*" relate to the capacity of attention control to compensate for gait deficits consistently and the difficulty attention has in simultaneously controlling multiple aspects of gait. This deficit in attention control to compensate adequately is not the cause of FOG but, rather, a default situation in diseased BG-SMA–controlled automatic movement that has deficiencies in motor set and cue, as previously described.

Pragmatic Approaches to Management

A review of the literature on interventions for the management of FOG has been recently published[47]; and, as such, this section will focus purely on pragmatic approaches the clinician can use to facilitate walking in patients with FOG.

doi:10.1002/mdc3.12463

The information provided in the earlier part of this review on BG function and gait-control mechanisms forms the basis for therapeutic intervention. Only 1 of the 2 mechanisms for gait control is impaired in PD, and that is the automatic mechanism because of dopamine loss in the striatum.[25,26] In PD, attention tends to predominate the control of gait, but the capacity to compensate for the defective automatic control is inadequate. This is because it appears to still use the BG-mediated output. This is best illustrated by asking patients to walk faster or slower; it can be done, but it is still inadequate compared with unaffected individuals.[29] It is only when external sensory information is available regarding speed or amplitude that attention has the capacity to restore gait toward normal.[29] This is because attention control then bypasses the BG-SMA interaction. The best example is the improvement in a reduced step length with the use of visual ground cues or steps on stairs.[29] Here, the visual information guides the step length, and the movement is performed normally. This fact forms the basis of movement strategies that can be developed to normalize all movements in PD, but particularly gait.[29] The limiting factor with the use of attention is that it can only control 1 or 2 motor events at a time and requires constant concentration. In this regard, it is not a feasible approach in the long term.

Gait-initiation disturbance, as seen in PD, always occurs in automatic control. If information is provided regarding the amplitude of the first step, then attention control will be able to normally initiate the first step. Attention control is not effective until step size information is provided. This information can be 2 visual cues signaling the correct amplitude, or it can simply be a verbal prompt that specifies the distance (e.g., "take a 12-inch [30 cm] step"). Once the person is made aware of the amplitude, then it does not need to be repeated, and the visual information is no longer necessary.

Auditory cueing does not use attention control but rather automatic control via the stride length-cadence relationship.[48] However, we have demonstrated that there is significant variability in the consistency of eliciting an appropriate step length for any given cadence, thereby limiting the clinical usefulness of auditory rhythmic cues in the treatment of FOG.[48] From a practical point of view, attentional strategies are immediate and easier to apply than waiting for cues from auditory devices. In a similar way, the provision of visual information regarding step length can restore hypokinetic gait back to normal; and, as long as the individual concentrates on the specified amplitude, step length will remain normal until attention is distracted.[29] It then reverts to the mismatched size generated by automatic control.

Medication has a similar effect on restoring automatic motor set for both gait initiation and hypokinetic gait.[33] However, its capacity to return both to normal may not be as good as attention.[33] Both medication and the use of attention fail to normalize the sequence effect, despite the fact that both increase the background step length.[4] The only strategy that effectively eliminates the sequence effect is the use of visual floor cues.[4] Here, the subject is instructed either to walk over each line or to use the interline distance as a measure of step size. Whatever the instruction, each step will be visually controlled by attention and thus will bypass the defective automatic control. Because a motor block during walking is caused by a small step length in conjunction with the sequence effect, increasing the background step length to normal will eliminate the motor block completely.[41] However, the sequence effect will still be present, but it is not of sufficient amplitude to cause a motor block. In this regard, auditory cueing has the capacity to reduce motor blocks only if the cadence chosen is high enough to increase the step length outside the sequence effect amplitude range. Again, clinically, attention is a much more powerful and easily used strategy that works immediately.

Variations on these strategies can be used to deal with specific environmental situations.[49] Swivel turns need to be avoided, because, in automatic mode, the reduced step length invariably will result in a motor block. Rather, it is best to perform an arc turn with sustained bigger step length round the turn using attention control. Crowded environments, such as a shopping center, require attention control of gait, focusing on a large step length but with a specific destination within the complex. If the individual has to stop for whatever reason, it is important to start again with the appropriate step-length amplitude. Talking and window-shopping needs to be done while standing or sitting. Home environments need to be de-cluttered to eliminate obstacles and minimize stops and turns. Walking toward doorways needs a shift to attention control, with a specific step-length amplitude and with focus on the step length and not on the door surround. Alternatively, the focus on an object in the room beyond the door can help distract attention enough not to impair the step length. Ideally all of these scenarios need to be addressed with each individual and family by skilled allied health professionals who are experienced in PD and aware of the background theory described above.

In summary, pragmatic approaches to overcoming FOG phenomena are best achieved clinically with the use of attention and the provision of visual information regarding correct amplitude or velocity. These strategies are immediately effective, are not demanding on equipment, and are extremely useful for short periods. However, long-term management is not currently feasible, and alternate approaches may need to be used.

Author Roles: 1. Research Project: A. Conception, B. Organization, C. Execution; 2. Statistical Analysis: A. Design, B. Execution, C. Review and Critique; 3. Manuscript Preparation: A. Writing the First Draft, B. Review and Critique.

R.I.: 1A, 1B, 3A, 3B.

M.D.: 1B, 3A, 3B

Acknowledgments

We thank the patient for agreeing to be videoed for the purposes of this paper.

Disclosures

Ethical Compliance Statement: We confirm that we have read the Journal's position on issues involved in ethical publication and affirm that this work is consistent with those guidelines.

doi:10.1002/mdc3.12463

Funding Sources and Conflict of Interest: The authors report no sources of funding and no conflicts of interest.

Financial Disclosures for the previous 12 months: The authors report no sources of funding and no conflicts of interest.

References

1. Nutt JG, Bloem BR, Giladi N, Hallett M, Horak FB, Nieuwboer A. Freezing of gait: moving forward on a mysterious clinical phenomenon. *Lancet Neurol* 2011;10:734–744.
2. Okuma Y. Practical approach to freezing of gait in Parkinson's disease. *Pract Neurol* 2014;14:222–230.
3. Schaafsma JD, Balash Y, Gurevich T, Bartels AL, Hausdorff JM, Giladi N. Characterization of freezing of gait subtypes and the response of each to levodopa in Parkinson's disease. *Eur J Neurol* 2003;10:391–398.
4. Iansek R, Huxham F, McGinley J. The sequence effect and gait festination in Parkinson disease: contributors to freezing of gait? *Mov Disord* 2006;21:1419–1424.
5. Jacobs JV, Nutt JG, Carlson-Kuhta P, Stephens M, Horak FB. Knee trembling during freezing of gait represents multiple anticipatory postural adjustments. *Exp Neurol* 2009;215:334–341.
6. Alice N, Fabienne C, Anne-Marie W, Kaat D. Does freezing in Parkinson's disease change limb coordination?. A kinematic analysis *J Neurol* 2007;254:1268–1277.
7. Lebold CA, Almeida QJ. Evaluating the contributions of dynamic flow to freezing of gait in Parkinson's disease [serial online]. *Parkinsons Dis* 2010;2010:732508.
8. Peterson DS, Plotnik M, Hausdorff JM, Earhart GM. Evidence for a relationship between bilateral coordination during complex gait tasks and freezing of gait in Parkinson's disease. *Parkinsonism Relat Disord* 2012;18:1022–1026.
9. Plotnik M, Giladi N, Balash Y, Peretz C, Hausdorff JM. Is freezing of gait in Parkinson's disease related to asymmetric motor function? *Ann Neurol* 2005;57:656–663.
10. Moore ST, MacDougall HG, Ondo WG. Ambulatory monitoring of freezing of gait in Parkinson's disease. *J Neurosci Methods* 2008;167:340–348.
11. Giladi N, Kao R, Fahn S. Freezing phenomenon in patients with parkinsonian syndromes. *Mov Disord* 1997;12:302–305.
12. Browner N, Giladi N. What can we learn from freezing of gait in Parkinson's disease? *Curr Neurol Neurosci Rep* 2010;10:345–351.
13. Giladi N, Huber-Mahlin V, Herman T, Hausdorff JM. Freezing of gait in older adults with high level gait disorders: association with impaired executive function. *J Neural Transm (Vienna)* 2007;114:1349–1353.
14. Lewis SJ, Barker RA. A pathophysiological model of freezing of gait in Parkinson's disease. *Parkinsonism Relat Disord* 2009;15:333–338.
15. Thevathasan W, Coyne TJ, Hyam JA, et al. Pedunculopontine nucleus stimulation improves gait freezing in Parkinson disease. *Neurosurgery* 2011;69:1248–1253.
16. Thevathasan W, Cole MH, Graepel CL, et al. A spatiotemporal analysis of gait freezing and the impact of pedunculopontine nucleus stimulation. *Brain* 2012;135(Pt 5):1446–1454.
17. Thevathasan W, Pogosyan A, Hyam JA, et al. Alpha oscillations in the pedunculopontine nucleus correlate with gait performance in parkinsonism. *Brain* 2012;135(Pt 1):148–160.
18. Lau B, Welter ML, Belaid H. Fernandez Vidal S, Bardinet E, Grabli D, Karachi C. The integrative role of the pedunculopontine nucleus in human gait. *Brain* 2015;138(Pt 5):1284–1296.
19. Plotnik M, Giladi N, Hausdorff JM. Is freezing of gait in Parkinson's disease a result of multiple gait impairments? Implications for treatment [serial online]. *Parkinsons Dis* 2012;2012:459321.
20. Danoudis M, Iansek R, Simpson P. Freezing of gait in Parkinson's disease: further insights into pathophysiological mechanisms. *Parkinsonism Relat Disord* 2012;18:543–547.
21. Cowie D, Limousin P, Peters A, Day BL. Insights into the neural control of locomotion from walking through doorways in Parkinson's disease. *Neuropsychologia* 2010;48:2750–2757.
22. Amboni M, Cozzolino A, Longo K, Picillo M, Barone P. Freezing of gait and executive functions in patients with Parkinson's disease. *Mov Disord* 2008;23:395–400.
23. Heremans E, Nieuwboer A, Spildooren J, et al. Cognitive aspects of freezing of gait in Parkinson's disease: a challenge for rehabilitation. *J Neural Transm (Vienna)* 2013;120:543–557.
24. Naismith SL, Shine JM, Lewis SJ. The specific contributions of set-shifting to freezing of gait in Parkinson's disease. *Mov Disord* 2010;25:1000–1004.
25. Iansek R, Bradshaw J, Phillips J, Morris ME, Cunnington R. Review article: the functions of the basal ganglia and the paradox of stereotaxic surgery in Parkinson's disease. *Brain* 1995;118(Pt 6):1613–1617.
26. Wu T, Hallett M. A functional MRI study of automatic movements in patients with Parkinson's disease. *Brain* 2005;128(Pt 10):2250–2259.
27. Cunnington R, Iansek R, Bradshaw JL, Phillips JG. Movement-related potentials in Parkinson's disease. Presence and predictability of temporal and spatial cues. *Brain* 1995;118(Pt 4):935–950.
28. Shoushtarian M, Murphy A, Iansek R. Examination of central gait control mechanisms in Parkinson's disease using movement-related potentials. *Mov Disord* 2011;26:2347–2353.
29. Morris ME, Iansek R, Matyas TA, Summers JJ. Stride length regulation in Parkinson's disease. Normalization strategies and underlying mechanisms. *Brain* 1996;119(Pt 2):551–568.
30. Berardelli A, Rothwell JC, Thompson PD, Hallett M. Pathophysiology of bradykinesia in Parkinson's disease. *Brain* 2001;124(Pt 11):2131–2146.
31. Cunnington R, Iansek R, Johnson KA, Bradshaw JL. Movement-related potentials in Parkinson's disease. Motor imagery and movement preparation. *Brain* 1997;120(Pt 8):1339–1353.
32. Ho AK, Bradshaw JL, Iansek R, Alfredson R. Speech volume regulation in Parkinson's disease: effects of implicit cues and explicit instructions. *Neuropsychologia* 1999;37:1453–1460.
33. Morris M, Iansek R, McGinley J, Matyas T, Huxham F. Three-dimensional gait biomechanics in Parkinson's disease: evidence for a centrally mediated amplitude regulation disorder. *Mov Disord* 2005;20:40–50.
34. Postuma RB, Berg D, Stern M, et al. MDS clinical diagnostic criteria for Parkinson's disease. *Mov Disord* 2015;30:1591–1601.
35. Wu T, Liu J, Zhang H, Hallett M, Zheng Z, Chan P. Attention to automatic movements in Parkinson's disease: modified automatic mode in the striatum. *Cereb Cortex* 2015;25:3330–3342.
36. Wu T, Chan P, Hallett M. Effective connectivity of neural networks in automatic movements in Parkinson's disease. *NeuroImage* 2010;49:2581–2587.
37. de Laat KF, Tuladhar AM, van Norden AG, Norris DG, Zwiers MP, de Leeuw FE. Loss of white matter integrity is associated with gait disorders in cerebral small vessel disease. *Brain* 2011;134(Pt 1):73–83.
38. O'Shea S, Morris ME, Iansek R. Dual task interference during gait in people with Parkinson disease: effects of motor versus cognitive secondary tasks. *Phys Ther* 2002;82:888–897.
39. Bartels AL, Balash Y, Gurevich T, Schaafsma JD, Hausdorff JM, Giladi N. Relationship between freezing of gait (FOG) and other features of Parkinson's: FOG is not correlated with bradykinesia. *J Clin Neurosci* 2003;10:584–588.
40. Aarsland D, Andersen K, Larsen JP, Lolk A, Kragh-Sorensen P. Prevalence and characteristics of dementia in Parkinson disease: an 8-year prospective study. *Arch Neurol* 2003;60:387–392.
41. Chee R, Murphy A, Danoudis M, Georgiou-Karistianis N, Iansek R. Gait freezing in Parkinson's disease and the stride length sequence effect interaction. *Brain* 2009;132(Pt 8):2151–2160.
42. Snijders AH, Bloem BR. Images in clinical medicine. Cycling for freezing of gait [serial online]. *N Engl J Med* 2010;362:e46.
43. Huxham F, Baker R, Morris ME, Iansek R. Footstep adjustments used to turn during walking in Parkinson's disease. *Mov Disord* 2008;23:817–823.
44. Fling BW, Cohen RG, Mancini M, Nutt JG, Fair DA, Horak FB. Asymmetric pedunculopontine network connectivity in parkinsonian patients with freezing of gait. *Brain* 2013;136(Pt 8):2405–2418.
45. Snijders AH, Leunissen I, Bakker M, Overeem S, Helmich RC, Bloem BR, Toni I. Gait-related cerebral alterations in patients with Parkinson's disease with freezing of gait. *Brain* 2011;134(Pt 1):59–72.
46. Bissett PG, Logan GD, van Wouwe NC, Tolleson CM, Phibbs FT, Claassen DO, Wylie SA. Generalized motor inhibitory deficit in Parkinson's disease patients who freeze. *J Neural Transm (Vienna)* 2015;122:1693–1701.

doi:10.1002/mdc3.12463

47. Nonnekes J, Snijders AH, Nutt JG, Deuschl G, Giladi N, Bloem BR. Freezing of gait: a practical approach to management. *Lancet Neurol* 2015;14:768–778.

48. Egerton T, Danoudis M, Huxham F, Iansek R. Central gait control mechanisms and the stride length-cadence relationship. *Gait Posture* 2011;34:178–182.

49. Morris ME. Locomotor training in people with Parkinson disease. *Phys Ther* 2006;86:1426–1435.

Supporting Information

Three videos accompanying this article are available in the supporting information here.

Video S1: Freezing of gait manifestations in Parkinson's disease. *Segment 1:* This clip demonstrates most of the components associated with freezing of gait (FOG) in Parkinson's disease in a patient with advanced disease on oral liquid Sinemet, which was ceased several hours before the video recording. The clip demonstrates: (1) the hypokinetic gait with very small background stride length; (2) the sequence effect; (3) the motor block during gait, which occurs at the end of the sequence effect; and (4) the difficulty in gait initiation. *Segment 2:* This clip illustrates the same FOG components as in Segment 1, except for the precipitation of the motor block by the visual distraction of the narrow doorway. *Segment 3:* This clip illustrates the same FOG components as in the other 2 clips. What has not been shown is tremor in place and anticipatory postural adjustments.

Video S2: Gait Freezing Strategies I. *Segment 1:* All clips in this video demonstrate the use of attention to bypass the basal ganglia automatic control of gait. Here, visual cues are used to indicate step size. Once visual information is available, attention control can continue to generate the corrected step until attention is distracted. The arc turn helps maintain the bigger step length around the turn. *Segment 2:* Here, visual information is provided more simply with a hand-illustrated distance. The same control mechanism is in play here as for Segment 1. *Segment 3:* In this clip, the same information is provided to enable attention to control gait with a bigger step as in Segment 2, but this time to avoid the motor block in the doorway.

Video S3: Gait Freezing Strategies II. *Segment 1:* In this clip, a visual target past the narrow door is used to avoid distraction of the door and to maintain the background step size without interruption. *Segment 2:* This clip illustrates an attention controlled strategy to initiate walking when stuck on the doorway.

doi:10.1002/mdc3.12463