Designing Personalized Freezing of Gait Interventions for Freezers and Non-Freezers with Parkinson Disease Based Upon Insights from Pathophysiological Mechanisms

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Website

References
Videos

Background

- Freezing of gait (FOG) in Parkinson disease (PD) has a complex pathophysiology that begins with abrupt episodic shortages of dorsal striatal dopamine and over inhibition of brainstem locomotor regions. Over time, compensatory networks breakdown, limbic dysregulation and extra-striatal pathology further strain processing, and FOG worsens.
- The diversity of freezing episodes, triggers, alleviators, and their occurrence in non-gait motor effectors and tasks (e.g., speech, crawling, handwriting, finger/foot tapping) further suggests that the underlying pathophysiology is not limited to dopaminergic circuits, but is more complex, involving multiple and variable circuits at different levels of the CNS. Since 2011, experts in the field have hypothesized mechanisms to help explain the clinical and pathophysiological differences in freezers vs. nonfreezers. To date, the integration of these mechanisms into a clinical reasoning framework for the design of personalized FOG rehab or exercise interventions has not been formalized.
- FOG can occur in 26% of persons with denovo PD to > than 80% in advanced PD. Improved clinical detection tools and the identification of at-risk predictors has increased the ability to screen for FOG onset, assess FOG severity, and to capture the benefits of behavioral interventions.
- A systematic review that included “freezers only” showed that a broad range of exercise and physical therapy interventions aimed at: 1) allocating more attention to gait for alleviating FOG episodes or preserving gait quality, and 2) targeting the motor / nonmotor correlates of FOG, reduced subjective FOG severity, but retention was short-lived (compared to nontargeted interventions).
- While it is unknown if exercise can put off or delay the onset of FOG, healthy populations at-risk for PD with a history of habitual exercise, have less severe motor and nonmotor symptoms at diagnosis, and progress at a slower rate than non-exerciser peers. In newly diagnosed PwP (nonfreezers) moderate to high intensity aerobic interventions are associated with attenuation of motor symptoms and potential disease modifying effects despite a significant loss of dopamine neurons. For example, these studies have shown increased functional connectivity of the “spared” striatal sensorimotor circuits for locomotion, of the frontoparietal cognitive networks for oculomotor control, and improved functionality in the remaining dopaminergic neurons (DAT/neuromelanin).
- We suggest these data support a proactive intervention model for FOG that could begin in at-risk/prodromal or early PD. The goal is to maximize neuroplasticity across the CNS to build resilience of underlying circuits by overtraining “**proposed mechanisms**” before FOG emerges. This has the potential to put-off PD onset and deterioration, reduce the future risk of FOG or delay its’ onset, reduce FOG severity in freezers, and finally, sustain the benefits after FOG-focused interventions.

Theoretical Framework

- To guide implementation and increased personalization and FOG specificity over time we propose a proactive clinical reasoning framework for PD-specialized therapists that starts with an understanding of five pathophysiological mechanisms: Interference, Perceptual Processing Dysfunction, Gait Incoordination Threshold, Abnormal Coupling, and Executive Dysfunction.
- This knowledge may help therapists identify “probable freezers” earlier; and inform novel FOG-relevant interventions to “train resilience” in those potential circuits prior to the emergence of FOG.
- When FOG emerges, therapists can use their clinical expertise to prioritize mechanisms and integrate them with a clients’ personal factors, clinical characteristics, triggers, and preferred compensations.
- Personalized FOG-specific interventions may be selected from existing evidenced-based FOG interventions or created to address each person’s “prioritized” theoretical underpinnings, vulnerabilities and goals.
- For each model, video examples of representative interventions are available for viewing using the “barcode” on this poster.

A strong understanding of the underlying rationale can help guide clinical reasoning, inform trial-and-error problem-solving, and shape future interventions.

A Proactive Clinical Reasoning Framework for Designing Personalized FOG-Relevant and FOG-Specific Interventions Over Time

Maximize Neuroplasticity
Prodromal / Nonfreezers / Freezers

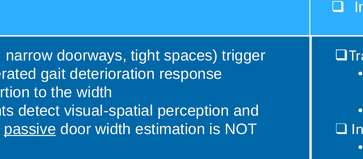
- ❑ **Start with Rehab Consultation**
  - Screen for at-risk conditions (FOG / Falls / Health)
  - Identify barriers to physical activity
  - Establish personal goals and a plan as needed
- ❑ **Train for fall prevention**
- ❑ **Educate and Empower**
  - Sustain functional mobility and participation
  - Address stress management
  - Optimize lifestyle / Holistic care
- ❑ **Initiate evidenced-informed PD-relevant exercise (in rehab or community)**
  - Address multiple motor and nonmotor symptoms
  - Emphasize aerobics/strength and functional agility training (everyday balance and coordination)
  - PD-specialized Therapists/Instructors/Trainers
- ❑ **Add FOG-relevant exercise**
  - Train FOG mechanisms proactively to delay onset of FOG in “nonfreezers”

Perform Routine FOG Screenings at Least Annually to Detect Early or Emerging FOG

- ❑ **History**
  - Types of falls, PIGD dominant, Response to meds
- ❑ **Standardized PD-Specific assessments to inform rehab goals for PD (nonfreezers)**
- ❑ **Assessments for FOG screenings**
  - NFOG-Q PwP/Partner; TUG; 360-Turns, fast & safe, alternating R/L; Four Square Step Test (Add dual tasks to gait, turning or stepping tests); Trail-making Part B; Mini-BESTest (dynamic balance/gait)
- ❑ **Motor symptoms**
  - Sequence deterioration, reduced dynamic balance, decline in step length at turning onset, general decline in gait kinematics
- ❑ **Executive dysfunction –** impaired conflict resolution set-shifting, divided attention, and prioritization
- ❑ **Other Non-motor symptoms**
  - Depression, anxiety, sleep disturbances, orthostatic hypotension
- ❑ **Non-gait freezing episodes**
  - Speech, handwriting, ADL’s, car transfers

Freezer – YES
Observe / Characterize Gait Kinematics / Rate Severity of Freezing Episodes

- ❑ **Perform a FOG provoking walking trajectory** (e.g., FOGA (Zeigler et al. 2022)



- ❑ **Adapt situations** (n=4, above) for each persons’ disease severity, triggers, therapy goals and level of cognitive/motor challenge
- ❑ **Add personalized motor/cognitive challenges**
- ❑ **Rate FOG severity** for each situation and score time to complete trajectory
- ❑ **Describe Manifestations (*image/text below left)**
  - Videotape walking trajectory for characterizing when an individuals “typical stepping or continuous gait difficulties” may convert to paroxysmal episodes of ineffective stepping.

Capture the Lived Experience
Triggers, Strategies, Hot Spots

- ❑ **Rate how often triggers cause a FOG episode** from a standardized list, Add others they self-report
  - i.e., Never, Rare, Sometimes, Often

Visual Spatial / Environmental	Temporal	Attention / Executive Function	Emotional
Clutter, narrow walkways/doors, crowds, changes in flooring, reaching a destination	Being in a hurry (streets, elevators or escalators), sudden demands (phone, decision-making)	Distractions (visual, auditory, thoughts), dual tasks, set-shifting response-inhibition	Anxiety, fear, loss of self-efficacy, negative thoughts, apathy, depression, arousal levels

- ❑ **Describe strategies used to move better or avoid freezing:**
  - External Cueing, Internal Cueing, Change Balance Requirements, Alter Mental State, Motor Imagery / Action Observation, Adapt a New Walking Pattern, Alternative to Walking
- ❑ **Describe salient “Hot Spots” in home/community** where FOG most often occurs. **NOTE:** meds on/off, environment, complexity, emotions, triggers, strategies, self-rated 0-100% confidence

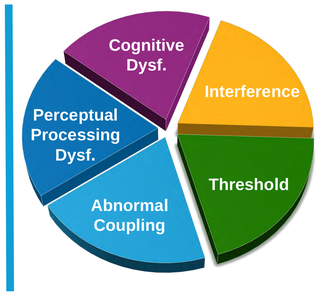
FOG Manifestations (Phenotypes) Related to the Type of Leg Movement		
Kinetic Trembling (KT)	**Kinetic No-Trembling (KNT)**	**Akinetic**
Fast oscillatory irregular lower limb movements* *Not tremor	All other ineffective** lower limb movements	No clinically discernable movement in lower limbs

UPDATED DEFINITION OF FOG 2026

Paroxysmal episodes wherein there is an inability to <u>step effectively</u>, despite attempting to do so.

- Not all FOG episodes exhibit a moment of ”distinct” cessation of movement (CORE).
- Distinguish cessation of all movement (Akinetic) vs. cessation of ineffective movement (KT or KNT)
- **Ineffective movements may include paroxysmal shuffling or festination-freezing (when accompanied by hastening)

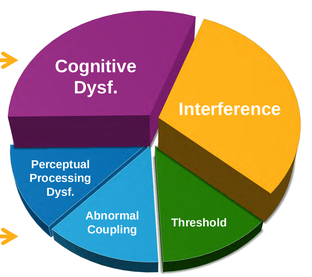
Each manifestation can occur in the same individuals, under different conditions, and at different times of the medication cycle.



Increase personalization by prioritizing mechanisms for each person

Re-assess mechanisms over time

Add more FOG specificity to interventions



Integrate Clinical Insights from History, Observations, Assessments, and Lived Experience with Knowledge of Mechanisms

Mechanism	Theoretical Principle	Supportive Observations Freezers > Nonfreezers	Intervention Video Examples See QR code TOP RIGHT
INTERFERENCE LOSS OF AUTOMATICITY & ALTERED MENTAL STATE	❑ Habitual actions become replaced by conscious, goal-directed control that requires dynamic integration of compensatory inputs (cognitive, sensory, emotional) ❑ The amount of integration (too much or too little) is determined by the arousal system (overall alertness/energy). Its’ early degeneration in PD disrupts this balance, interfering with one’s ability to adapt ❑ Overtime, relying on conscious control results in information overload and limbic dysregulation, further compromising the success of compensations.	❑ FOG is induced by complex, high-stress environments • Increased motor difficulty, environmental demands, executive challenges (response inhibition, set-switching, divided attention) • Increased stress/anxiety/fear/expectations/time pressure ❑ Supra or sub-optimal arousal influences the success of compensations	❑ Train conscious self-regulation of arousal • Decrease - Mindfulness/breathing, salience, slow rehearsal • Increase – empower, vigor/acceleration, push/pull/jump/throw/hit ❑ Augment the most relevant strategies to reduce cognitive processing • External cues (targets, music, visual); focus of attention • Internalize/vocalize self-cues, Prioritize use of vision ❑ Incorporate action observation and mental imagery
PERCEPTUAL PROC ESSING DYSFUNCTION	❑ Visuospatial processing deficits disrupt self-motion perception and online motor planning. Proposed mechanisms: • distracts attention from gait - triggering FOG • cues (inappropriately) for adaptation – triggering FOG ❑ As for ALL PD; Ineffective multimodal sensory integration may also contribute to successful navigation in complex environments	❑ Visuospatial constraints (clutter, narrow doorways, tight spaces) trigger ineffective stepping and exaggerated gait deterioration response • e.g., slowing of gait in proportion to the width ❑ Neuropsychological assessments detect visual-spatial perception and reasoning deficits > FOG; while <u>passive</u> door width estimation is NOT different	❑ Train the use of visual-spatial perceptual processing during self-motion • Navigate complex environments with intent and exploration around obstacles of varying widths, orientation and complexity while problem solving • Incorporate visual searching games; Increase use of vision ❑ Increase overall sensory integration and motor planning • Vary positions and directions during floor transfers and floor mobility • Augment proprioception, reflect on self-action
GAIT INCOORDINATION THRESHOLD	❑ Gait kinematic abnormalities accumulate until an incoordination threshold is reached and FOG occurs. o 2 or more gait abnormalities trigger FOG > greater than either alone ❑ Gait features most susceptible to breakdown: step scaling, symmetry, bilateral coordination	❑ Turning poses the greatest demand simultaneous on the most gait features and is the most provoking trigger of FOG (standing or walking) ❑ Voluntary attempts to exaggerate one of more susceptible gait features can provoke FOG • Instructions to decrease step size, increase cadence, or coordination complexity (rapid/narrow/alternating turns)	❑ Augment / Optimize baseline gait performance for <u>multiple</u> gait features at once ❑ Personalized focus by ‘overtraining” the <u>most</u> susceptible components of “their” gait to alleviate FOG severity ❑ Create a rescue plan to improve “online performance” & train fall recovery and prevention
ABNORMAL COUPLING OF POSTURE AND GAIT	❑ A failure to decouple postural preparation (APA’s) for protective stepping, or for goal-directed release of a step for gait initiation. ❑ Suggests that axial motor impairments contribute to FOG and may be associated with the inherent fall risk in freezers. ❑ The inability to inhibit unwanted APA’s may be related to dysfunctional response inhibition (see below)	❑ Voluntary attempts to accelerate weight-shifting in standing without stepping • Triggers fast oscillation of lower limbs • Reports “feels glued to the floor’ ❑ May occur during gait transitions (turns, sit to stand to walk), crawling, or non gait transitions like floor to stand transfers or all 4’s to side-sit	❑ Over-train weight-shifting (M/L & A/P) while progressing instability and motor load in all positions and directions with varying BOS ❑ Enhance the release of the APA’s (e.g., step rehearsal, visual scanning, attentional strategies, external cues, amplitude, go/no go training) ❑ Connect voluntary step to an anticipatory signal (startle stimuli, auditory or internal cueing strategy)
EXECUTIVE DYSFUNCTION	❑ Executive dysfunction in freezers is a paradox. The loss of automaticity (interference) in the striatum increases the demands for executive compensations (DLPFC), while the compensations diminish general cognitive resources in freezers, and further exaggerate the demand for executive compensations! This interplay is most evident when task requirements are ambiguous or highly challenging.	❑ FOG is worse when imposing faster response decisions (selection or inhibition), incongruence (Stroops), and complex environments. ❑ Set-shifting – Reduced ability to switch rules/tasks ❑ Impaired divided attention (dual tasks) and attention switching (prioritization) ❑ Impaired conflict resolution – Freezers show stronger activation of incorrect responses (overaction of conscious control); and less efficient inhibition of conflicting responses (failure to mute automatic control processes)	❑ Cognitive/Motor Training • Dual tasks + attention shifting (prioritization) • Selective attention + inhibition (go/nogo punching) • Incorporate real-world challenges (MD movements, dynamic balance) ❑ Progress challenge - speed, difficulty, incongruence (i.e., Stroops) ❑ Augmented reality games – complex demands ❑ Combine with aerobic priming and stress management