Reply to: "MRI Linear Measurements in Normal Pressure Hydrocephalus Versus Progressive Supranuclear Palsy"

We thank Ugga and colleagues for their interest and positive comments[1] on our recent article.[2] We agree that differentiating between idiopathic normal pressure hydrocephalus (iNPH) and progressive supranuclear palsy (PSP) is often challenging and that simple imaging biomarkers are needed for the differential diagnosis between these two diseases in clinical practice.

The Magnetic Resonance Parkinsonism Index (MRPI) and its new version, including also the measurement of the third ventricle width (MRPI 2.0), are well known and accurate biomarkers to distinguish PSP from other degenerative parkinsonism.[3] However, as demonstrated in our article[2] and discussed by Ugga et al,[4] these biomarkers were not able to differentiate PSP from iNPH because of the overlap of some radiological features between these diseases.

In our recent article published in *Movement Disorders*,[2] we proposed a new imaging linear biomarker, termed Magnetic Resonance Hydrocephalic Index (MRHI), which showed very high accuracy in differentiating iNPH from PSP. In our article, we also validated the performance of MRHI in a training and a testing cohort obtaining similar accuracy values, thus demonstrating the potential usefulness of this biomarker also in patients from new sites. Ugga et al[4] investigated the potential role of the interpeduncular angle (IPA), which showed higher divarication of the cerebral peduncles in iNPH compared to PSP patients. The IPA values were significantly higher in iNPH with respect to PSP but showed some overlap between the 2 patient groups. Thus, we retain that the IPA could be a promising new biomarker, but further studies are needed to evaluate and validate its accuracy in differentiating iNPH from PSP.

Finally, we agree on the use of imaging biomarkers in the differential diagnosis between iNPH and PSP to reduce misdiagnosis and avoid ineffective shunt procedures.

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Relevant conflicts of interest/financial disclosures: Nothing to report.

Funding agencies: None.

Received: 21 September 2020; **Accepted:** 23 September 2020

Published online in Wiley Online Library (wileyonlinelibrary.com). DOI: 10.1002/mds.28337

Letter to the Editor on "A Randomized, Controlled Trial of Exercise for Parkinsonian Individuals With Freezing of Gait"

In a recent issue of *Movement Disorders*, Silva-Batista and colleagues reported the results of a randomized, controlled trial on adapted resistance training with instability (ARTI) compared with traditional motor rehabilitation (TMR) in people with Parkinson's disease (PD) and freezing of gait (FOG).[1] The authors found that ARTI significantly improved several outcomes of symptom severity, including FOG, compared with TMR. Nonpharmacological interventions are essential in managing FOG, and we commend the authors for aiming to increase the scientific evidence in this field. We further realize such intervention studies take tremendous amounts of effort to conduct. However, we are concerned about the safety of the reported training and about several methodological issues, which may cloud accurate data interpretation.

Key Words: freezing of gait, Parkinson's disease, rehabilitation, excercise

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Received: 9 July 2020; **Revised:** 23 July 2020; **Accepted:** 27 July 2020

Published online in Wiley Online Library (wileyonlinelibrary.com). DOI: 10.1002/mds.28294

Both groups contained a select group of unusually severe freezers based on NFOG-Q scores at baseline (TMR, 22.3 ± 6.0; ARTI, 21.6 ± 5.7), some of whom must have had FOG episodes lasting >30 seconds.[2] Moreover, the Hoehn and Yahr stages in both groups ranged from 3 to 4, indicating a moderate to severe degree of postural instability. Considering this severe level of disability, our concern relates to the requirements and feasibility of the ARTI intervention in such an extremely fall-prone cohort. Patients were asked to perform high-level balance exercises, that is, weighted lunges and squats on unstable surfaces, which could lead to falls and should therefore not translate to self-administration without expert supervision. Notably, adherence rates were exceptionally high (100% for 612 ARTI sessions) and adverse events scarce for such high-risk activities, although it remains unclear how these were monitored.

The primary outcome was the New Freezing of Gait Questionnaire (NFOG-Q). Recent work comparing consecutive measurements in 2 independent PD populations without intervention showed that the NFOG-Q has a minimal detectable change (MDC) of 9.95 points.[3] This is larger than the reported effect of ARTI (4.7 points). The authors did not refer to this work, but calculated the MDC using pre- and postassessments of their own active control intervention (2.7 points). Thus, although the ARTI intervention seemed to significantly improve several outcomes, the conclusion that the intervention effectively reduced FOG is likely confounded by test-retest error.

Furthermore, the FOG ratio, an objective measure of FOG severity, strongly deteriorated in controls (12.8 preintervention vs 20.9 postintervention), which is unexpected during this brief trial duration (3 months), particularly because controls received an active intervention. This unexplained worsening in controls may have inflated the effect of the ARTI intervention on this outcome. Also, participants had abnormal FOG-ratio values (average of 20.9), whereas they were ON medication, which is much higher than those reported in patients OFF medication in the initial FOG-ratio validation article (0-13).[4]

Inconsistencies also exist between the trial registration and the reported outcome measures, including those for gait, balance, and fMRI analyses, hinting toward selective reporting. Further, the statistical analyses did not account for baseline performance, although the TMR group seemed to have scored worse on multiple metrics. Last, the original trial registration targeted a sample of n = 32 (albeit without power calculation), but it is unclear why the investigators proceeded to include n = 40.

Given these issues, we caution the clinical interpretation of this article. PD patients with FOG typically have severe balance impairment, which greatly amplifies their fall risk.[5] The described intervention seems hazardous, based on images provided in the supplementary material, whereas the efficacy for reducing FOG appears uncertain. Therefore, we believe that caution and further studies are warranted before advocating the ARTI intervention for people with FOG. ■

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Reply to: 'Letter to the Editor on "A Randomized Controlled Trial of Exercise for Parkinsonian Individuals With Freezing of Gait"'

We read with interest the comments of Nonnekes et al[1] on the safety of our adapted resistance training with instability (ARTI) for people with Parkinson's disease(PD) and freezing of gait (FOG [freezers]) and the methodological issues related to our trial.

We are confident that ARTI is safe if implemented with expert supervision and the strict safeguards we suggested. Challenging interventions, safely implemented, have been suggested to decrease FOG severity.[2,3] ARTI is challenging and complex, but it has a hierarchical progression strongly based on the safety and motor abilities of each participant (see Supplementary File). ARTI was implemented in a one-to-one fashion with constant supervision of experienced physical therapists to ensure the safety of theparticipants. Adverse events were monitored by the first author (C.S.B.) during each session and in the time period

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Received: 20 August 2020; **Accepted:** 21 August 2020

Published online in Wiley Online Library (wileyonlinelibrary.com). DOI: 10.1002/mds.28292