A Randomized Controlled Feasibility Trial of a Specific Cueing Program for Falls Management in Persons With Parkinson Disease and Freezing of Gait

Tara Martin, MSc, Mark Weatherall, FRACP, Tim J. Anderson, MD, FRACP, and Michael R. MacAskill, PhD

Background and Purpose: Freezing of gait (FOG) increases fall risk in persons with Parkinson disease (PD). Cueing improves gait parameters associated with freezing, but it is unclear whether a cueing program can address falling.

Methods: We used a parallel-groups delayed- (n = 12) or immediate-start (n = 9) randomized controlled trial design to evaluate a cueing exercise program for FOG and falls in participants with PD. Each group received preintervention falls monitoring, followed by a 6-month standardized, home-based, cueing exercise and education program. Participant questionnaires rated program value and compliance. Freezing was measured with the New Freezing of Gait Questionnaire (NFOGQ). Falls were recorded by weekly diaries.

Results: Self-reported adherence was high; 83% of participants reported exercising after 6 months. Participants reported that the program was beneficial (89%), walking improved (78%), falls were fewer (73%), and self-management of freezing improved (61%). Mean (standard deviation) NFOGQ scores were 14.8 (5.0), for the immediate (n = 10), and 16.0 (7.7) for the delayed group (n = 9), after 6 months (difference = −1.0 [95% confidence interval, −7.9 to 6.0; P = 0.78]). With baseline NFOGQ scores as a covariate, the estimate of difference was −0.7 (95% confidence interval, −6.1 to 4.7; P = 0.79). The relative rate of falls for immediate compared with delayed groups was 1.22 (95% confidence interval, 0.45 to 3.26).

Conclusions: The cueing program intervention is acceptable and participants feel they improve; however, this small feasibility study lacks statistical power to detect important changes in falls rates or FOG severity. A larger study is warranted to further investigate the potential to influence FOG and falls.

Video Abstract available for more insights from the authors (Supplemental Digital Content 1, http://links.lww.com/JNPT/A105).

Key words: cueing, falls, freezing of gait, Parkinson disease

BACKGROUND

Gait disorders are common in persons with Parkinson disease (PD) and are associated with disease progression. In particular, the phenomenon of freezing of gait (FOG) eventually affects about half of those with PD. Freezing of gait is associated with specific gait impairments of step length and stepping frequency, as well as cognitive and perceptual impairments. Falls are common in PD, and FOG increases the risk of falling. Certain movements or activities, such as turning or walking through doorways, are known to provoke FOG. These provocative movements are known as FOG “triggers.”

Cues can be used to enhance attention to a particular motor activity, such as gait, which improves performance. Cues can also be used to avoid or manage FOG in the presence of known “triggers.” Cueing strategies to improve gait and functional movements in PD are supported by best-practice physical therapy guidelines and current research. A systematic review of cueing for FOG in PD reports that both visual and auditory cues benefit those with FOG when used as a training tool in a functional context. Rhythmic auditory cueing (RAC) is a specific type of cueing that uses an external pacing device, such as a metronome, to improve awareness and performance of step length and step frequency in gait and functional movements. Rhythmic auditory cueing helps individuals with PD use learned movement strategies in the presence of a trigger and avoid or reduce the severity of freezing.
Although there is evidence that FOG, a risk factor for falls in PD, can be improved by physical therapy intervention with cueing strategies, there is yet no robust evidence that any intervention can reduce falls rates in PD. However, it is plausible that a cueing exercise intervention might decrease falls in those with FOG by reducing episodes of or severity of FOG.

The aims of this randomized controlled trial (RCT) feasibility study were to determine the acceptability and feasibility of a specific cueing program in PD with FOG, the changes in a FOG questionnaire with the program, and the exploration of falls in relation to such a program.

METHODS

Participants
Participants were recruited from the New Zealand Brain Research Institute database of willing volunteers for studies on PD. All participants had a diagnosis of PD confirmed by a movement disorder specialist neurologist (TJA). During the study, participants received usual ongoing care from a general practitioner and a neurologist. Of the 29 potential participants identified from the database, 21 met inclusion criteria and gave informed consent. Eligibility criteria were confirmed diagnosis of PD by a movement disorder specialist, aged over 65 years, presence of FOG as indicated by answering “yes” to question 1 on New Freezing of Gait Questionnaire (NFOGQ), independently mobile with or without walking aid, and had a stable PD medication regimen at the time of recruitment. A participant was excluded if he/she had significant cognitive impairment (Mini Mental State Examination Score of <24), had comorbidities that would prohibit safe participation in exercise, were unable to press metronome buttons, or hear a metronome adequately. Ethical approval for this study was granted by the Upper South A Regional Ethics Committee of New Zealand (Reference number URA/12/02/003). All participants provided written informed consent to participate.

Study Design and Randomization
The parallel delayed-start randomized control trial design was chosen to improve recruitment and to increase the numbers of participants who had measurements under an active treatment condition. Participants were randomized to immediate-start (IS), n = 12, or 6-month delayed-start (DS), n = 9, groups by a computerized random number generator.

Study Procedures
The IS group began the 6 month intervention after 2 weeks of waiting. The DS group began the intervention after a 6 month wait period. Falls monitoring began for both groups at the point of study entry. Mean baseline falls rates were calculated from the first 5 weeks of falls monitoring for both groups.

Intervention
The intervention (the Cued Up! program) is a home-based exercise and education program designed to address FOG and falls that may result from FOG. It was developed from best-practice guidelines14,16,19,25 and uses a metronome to provide RAC as the primary cueing strategy. The program addresses common FOG triggers through cued exercises using a metronome and practice of functional movement-associated FOG using cues (see Video, Supplemental Digital Content 2, http://links.lww.com/JNPT/A106, for examples of exercises performed with metronome). Gait impairments associated with FOG, such as short step length and high frequency of stepping, are also practiced with metronome cues. Exercises are not only standardized but also tailored for each individual on the basis of their FOG triggers, functional ability, and any expressed aims or goals. The exercises are presented in a booklet along with instructions on how to perform the exercises and how to use the metronome. Education is also provided during the program on identifying FOG triggers, using cues for overcoming FOG when it occurs, and using other types of cues such as visual cues, internal cueing strategies, or verbal cues provided by others when needed.

The format of Cued Up! is similar to that of the Otago Exercise Program (OEP),26,27 a well-known standardized falls prevention program for older people widely used in clinical practice in New Zealand, and was designed to provide efficient and cost-effective use of therapy time. Six home visits were completed within the first 4 weeks of the 6-month intervention period. This was followed by weekly phone calls for the remaining 5 months.

The home therapy sessions were provided by a physical therapist (TM) with experience in PD and FOG and the use of cues. Therapy sessions included the following: assessment of an appropriate metronome exercising frequency at approximately 10% below preferred stepping rate, instruction on metronome use, selection of appropriate exercises, progression of exercise difficulty and intensity, and education on FOG. Therapy session duration was between 30 and 60 minutes per session depending on each participant’s ability and exercise tolerance.

Participants were encouraged to complete the prescribed exercises independently on the days when the physical therapist did not visit and to continue with the exercises and metronome use “most days of the week” once visits had finished. Adherence was encouraged by the weekly telephone calls in the remaining 5 months. Telephone calls also allowed for resolution of problems with metronome use and for further discussion and participant reflection on functional use of cues and management of triggers. Participants were allowed and encouraged to continue any other usual exercise programs such as exercise groups. The flow of participants in the study is shown in Figure 1.

Outcome Measures
The participants evaluated the program’s utility, acceptability, and compliance by an anonymous questionnaire that was designed specifically for this study by the researcher TM. The questionnaire was given within 2 weeks of finishing the intervention.

Two objective outcome measures used were scores from the NFOGQ and falls, recorded as the individual mean number of falls per week per participant.

The NFOGQ is a validated, self-reported measure of the subjective experience of severity of freezing symptoms in
PD. The NFOGQ was completed at the time of consent for both groups. The IS group had another NFOGQ at completion of the 6-month intervention, and again at end of the complete study, which was 6 months after the intervention finished. The DS group had another NFOGQ after the end of the wait-list period (6 months after study entry), and at completion of their 6-month treatment phase. The instrument is scored from a minimum of 0, meaning no symptoms of FOG, to 28, meaning very severe FOG.

A fall was explained to participants as “an unexpected event in which you (the participant) come to rest on the ground, floor or other lower level.” Participants used a daily diary to record whether a fall had occurred and the number of falls that occurred each day. Family or caregivers were also instructed on use of the falls diary to help with its completion. Participants posted diaries to the researcher each month. Telephone calls were made to prompt participants if diaries were not received.

**Analysis**

The sample size was chosen to have 20 degrees of freedom, to allow reasonably precise estimate of the variances of the NFOGQ in an analysis of covariance, with the NFOGQ as the response variable and the randomized delayed or immediate start for the intervention as the explanatory variable. The achieved sample size also had a margin of error for estimating a proportion of plus or minus 20%.

NFOGQ scores were analyzed with unpaired t tests for the difference between mean scores after the wait-list time for the DS group and after the 6-month treatment phase of the IS group. Paired t tests were also used to compare within-group NFOGQ score changes. Unpaired t test was used to estimate the difference in mean NFOGQ scores for both groups combined with further analysis of covariance used to account for baseline NFOGQ scores. Falls rates were analyzed by a negative binomial regression model with an offset for time of observation to give an estimate of the relative rate of falls between the 2 randomized groups.

SPSS Statistics Software version 21 (SPSS Inc, Chicago, IL) was used for the analysis.

**RESULTS**

**Participant Profile**

The research participants are described in Table 1. All the participants in study were aged 65 years or older and had moderate disease severity.
Table 1. Participant Characteristics

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>All (n = 21)</th>
<th>Immediate Start (n = 12)</th>
<th>Delayed Start (n = 9)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Female sex</td>
<td>8 (38)</td>
<td>5 (42)</td>
<td>3 (33)</td>
</tr>
<tr>
<td>New Zealand European</td>
<td>20 (95)</td>
<td>11 (92)</td>
<td>9 (100)</td>
</tr>
<tr>
<td>ethnicity</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Past fall</td>
<td>18 (86)</td>
<td>10 (83)</td>
<td>8 (89)</td>
</tr>
</tbody>
</table>

Mean (SD)

- Age, y: 72 (5.3) 72 (5.1) 72 (5.8)
- Disease duration, y: 11 (6.6) 9 (4.6) 13 (8.2)
- Hoehn and Yahr score: 2.8 (0.6) 2.9 (0.5) 2.6 (0.7)

Abbreviation: SD, standard deviation.

End of Program Questionnaire

Two participants were not given the questionnaire to complete as one withdrew from the study because of poor health and another had died. Of the 19 participants given the questionnaire, 18 completed it. Questionnaires were completed at the end of the 6-month intervention, except for one participant who completed the questionnaire at the point of withdrawal from the study (week 8 of intervention).

Participant satisfaction with the program was high, with 89% reporting that the program was "of some benefit" (12 of the 18) or "great benefit" (4 of the 18), and the remaining 2 participants finding it of "limited benefit." Most participants reported that participating in Cued Up! "improved their walking" (78%, 14 of the 18), although 4 participants (22%) felt the program made "no difference" to their walking. None of the participants felt the program "made their walking worse." The exercises were felt to be enjoyable (50%, 8 of the 16) and easy to understand (94%, 16 of the 18). Three participants (17%) felt the exercises made no change to their freezing; however, most participants felt that the program helped them to "understand" (50%, 9 of the 18) and/or "avoid" their freezing (61%, 11 of the 18), with a further 39% (7 of 18) indicating that the program helped them learn to "overcome freezing when it occurs." None of the participants felt the program had made their freezing worse.

Participants’ attitudes about falling were mixed after the program, with 39% (7 of 18) reporting that they worried less about falling, 17% (3 of 18) indicating they worried more about falling, and 44% (8 of 18) having no change in their feelings about falling. Most (73%, 11 of 18) perceived they were falling less frequently after the program and only one participant felt they fell more frequently.

At the end of the 6-month active intervention period, 83% (15 of the 18) of participants reported that they were still doing their exercises at least 2 to 3 times per week. Only one participant reported that they were not doing the exercises any more. Most participants (15 of the 18) said they would continue to use the exercises as a way to help them manage their FOG, one participant said they would not continue with the exercises, and 2 participants did not answer this question. Most participants also said they would continue to use the metronome (67%, 12 of the 18).

FOG

The summary of NFOGQ scores by group and time of measurement is shown in Table 2. The 6-month measurement time refers to the IS group measured at the end of the intervention and the DS at the end of the wait-list period. The 12-month measurement time refers to the IS group measured a further 6 months after the RAC intervention finished and the DS group at the end of their 6-month intervention. The change in the total score for each group from baseline was −0.8 (95% confidence interval [CI], −4.4 to 2.6; P = 0.63) for the IS group and −1.9 (95% CI, −6.4 to 2.65; P = 0.36) for the DS group, indicating that in both groups participant scores did not change significantly from baseline after receiving the intervention.

The estimated difference in NFOGQ total scores at the end of intervention between the IS group and the DS group was −1.9 (95% CI, −6.4 to 2.65; P = 0.36) for the DS group, indicating that in both groups participant scores did not change significantly from baseline after receiving the intervention.

Falls

Three participants reported no falls before the study. Six participants, 3 in each group, did not fall during the baseline observation period. However, during the study all participants fell at least twice. One participant in the IS group had a very high mean falls rate during the baseline observation period of 41.2 falls per week and was considered an outlier. Other than this participant, the highest individual mean weekly falls rate at baseline in the IS group was 27 falls per week. The highest individual mean weekly falls rate at baseline in the DS group was 10 falls per week.

Table 2. NFOGQ Summary Scores by Intervention Group and Measurement Time

<table>
<thead>
<tr>
<th>Total Score</th>
<th>Mean NFOGQ Score (SD)</th>
<th>IS</th>
<th>DS</th>
<th>All</th>
</tr>
</thead>
<tbody>
<tr>
<td>Study entry (baseline)</td>
<td>15.7 (6.3)</td>
<td>16.9 (4.1)</td>
<td>16.2 (5.4)</td>
<td></td>
</tr>
<tr>
<td>n = 12</td>
<td>n = 9</td>
<td>n = 9</td>
<td></td>
<td></td>
</tr>
<tr>
<td>After 6 mos</td>
<td>14.8 (5.0)</td>
<td>16.0 (7.7)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>n = 10</td>
<td>n = 9</td>
<td>n = 9</td>
<td></td>
<td></td>
</tr>
<tr>
<td>After 12 mos</td>
<td>13.6 (7.1)</td>
<td>15.8 (8.8)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>n = 10</td>
<td>n = 8</td>
<td>n = 8</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Change in the total baseline score after intervention using paired t test</td>
<td>−0.8 (5.0)</td>
<td>−1.9 (5.4)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>n = 10</td>
<td>n = 8</td>
<td>n = 8</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

Abbreviations: DS, delayed start; IS, immediate start; NFOGQ, New Freezing of Gait Questionnaire; SD, standard deviation.

Table 3. NFOGQ Scores Comparison of Groups at the End of Intervention

<table>
<thead>
<tr>
<th>Estimate (95% CI)</th>
<th>P</th>
</tr>
</thead>
<tbody>
<tr>
<td>Unpaired t test</td>
<td>−0.1 (−7.9 to 6.0)</td>
</tr>
<tr>
<td>ANCOVA with the baseline score as a covariant</td>
<td>−0.7 (−6.1 to 4.7)</td>
</tr>
</tbody>
</table>

Abbreviations: ANCOVA, analysis of covariance; CI, confidence interval; NFOGQ, New Freezing of Gait Questionnaire.
The mean falls rate per group during the study by time period is shown in Table 4.

Using the negative binomial model to compare falls rates at the end of the 6-month intervention between groups, the estimate of relative rate of falls for the IS group compared with the DS group was 1.22 (95% CI, 0.45 to 3.26; \( P = 0.70 \)), excluding the on-going participant. With the outlier included in analysis, the estimate of relative rate of falling was 3.21 (95% CI, 1.39 to 9.38; \( P = 0.008 \)). The results (with outlier excluded) indicate that there was no significant difference in rate of falling between groups after intervention.

DISCUSSION

The standardized, individualized physical therapist-led exercise and education cueing program used in this study was very acceptable to participants with moderate PD and FOG. Participants largely felt that their walking ability was improved by intervention. Although nearly all participants felt they improved in this small feasibility study, there was no detectable difference between groups or improvement in the NFOGQ or in diary-reported falls.

Freezing of Gait

Participants in this study had severe FOG. Fourteen participants had an NFOGQ of greater than or equal to 14, which is 50% of the maximum possible total NFOGQ score. However, the duration and severity of disease for the participants in this study provide face validity for the use of the NFOGQ for measuring FOG in this study.

The NFOGQ has an advantage over its predecessor the Freezing of Gait Questionnaire (FOGQ) because it enables measurement of the impact of FOG on walking, fear of falling, and activity levels; seen in questions 7 to 9. A disadvantage is that the likely magnitude of the clinically important change in the NFOGQ is not yet established, and some aspects of its external validity and other psychometric properties need more development.\(^7\)\(^24\) The findings of this study can be compared with other research on cueing using the original FOGQ. The original FOGQ was used by Nieuwboer et al\(^16\) in the large multicentre, randomized RESCUE trial. In that study, 63 of the 153 (41%) participants had FOG. In that subgroup of participants with FOG, the change in the FOGQ score with cueing therapy was 5.5% of baseline and the paired mean change to standard deviation (SD) ratio was 1.33/3.81 = 0.35. The effect size was similar to that seen in the DS group in this study. A 5.5% change in baseline for the total group in this study, where the mean baseline score was 16.2, is an absolute change in the NFOGQ total score of 0.9 units. This is a similar magnitude of change from baseline seen in the IS group and about half the change from baseline seen in the DS group.

We suggest that future research with the NFOGQ might consider a change of one point as a clinically meaningful change, which represents about 6% of the baseline score. This would signify an effect size of about 0.2 SD based on the larger SD seen in the DS group. In this study, there are a number of potential reasons for not detecting a treatment effect of the intervention. One of these, as already discussed, is that the NFOGQ has a large SD in relation to the relatively small change that might represent a clinically important change. With a small sample size, the current study clearly lacks statistical power to detect this size difference.

Falls

This group of participants had a very high falls rate, on average 3 per week, with some participants having more than 20 falls a week. We were unable to demonstrate that the intervention improved this rate of falls and this is likely because of a number of factors. Most importantly, the sample size chosen for this study was primarily to explore the feasibility of the intervention in a realistic sample of persons with moderate PD. Because of this, the study was not adequately powered to detect even a very large difference in falls rates between the randomized groups. In addition, the falls rates described in this group of participants were extremely variable. This is in turn likely because of participant selection, namely of those with PD and FOG. We did not measure indirect assessments of the intervention, such as fear of falling or feelings of self-efficacy, and these may have shown detectable differences even if there was no difference in falls rates.

An important strength of this study was the parallel-groups delayed randomized design. This reduced the potential for bias in effect estimation. The use of the negative binomial model for analysis of the falls data was also a strength and is a model recommended for evaluating the efficacy of falls prevention programs.\(^30\) Use of this model means that all participants could be included in falls analysis, even if they had missing data or had withdrawn from the study. The use of this model also means that data from this study can be used in a meta-analysis of other fall studies.

Although participants in this study had a stable medication regimen at entry to the study, medication changes, including those relating to drug research trials, were relatively common among the participant group, with 8 of the 21 (38%) having at least one change to a PD medication during the study. This may have led to greater variability in the outcomes.

Finally, although the NFOGQ scores and falls rates remained relatively unchanged, participant responses in the end of program questionnaire indicated that they had found the program of value. This is interesting and in line with the findings of a recent Cochrane review, which highlights the need for more patient-orientated outcomes in research to “capture the difficulties experienced by patients in everyday life or their opinions on treatment acceptability and personal improvements.”\(^31\)

<table>
<thead>
<tr>
<th>Table 4. Mean Falls Rate per Group by Study Time Point</th>
</tr>
</thead>
<tbody>
<tr>
<td>Mean Falls Rate per Week (SD)</td>
</tr>
<tr>
<td></td>
</tr>
<tr>
<td>Baseline (wks 1-5)</td>
</tr>
<tr>
<td>n = 11</td>
</tr>
<tr>
<td>Mid Active (wks 9-13)</td>
</tr>
<tr>
<td>n = 11</td>
</tr>
<tr>
<td>End of Active (wks 24-28)</td>
</tr>
<tr>
<td>n = 9</td>
</tr>
</tbody>
</table>

Abbreviations: DS, delayed start; IS, immediate start; SD, standard deviation.

*Excluding outlier in the IS group.
Future Research

The Cued Up! intervention, a standardized home-based exercise program, can be delivered consistently and easily by a single therapist, which makes it generalizable to usual physical therapy clinical practice and reproducible in future studies. The similar format to the OEP for falls prevention in older people means the intervention (Cued Up!) could be compared with another standardized fall prevention program, such as OEP, in a larger RCT. Sample size calculations generated from this study suggest that to detect a clinically important difference of one point for the total NFOGQ score, on the basis of a 6% change from the baseline score and an SD of 5.4, and an effect size of 0.18, at 80% power with a type I error rate of 5%, a total of 972 participants would be needed, 486 in each group.

Outcome measure selection for future research on falls and FOG in PD should be carefully considered, as our study demonstrates that the participants’ perceptions of and feelings about their FOG and falling may not align with standardized measures or recorded falls rates. Outcome measures that evaluate fear of falling, self-efficacy, quality of life, and participation should also be considered.

CONCLUSIONS

The results of this feasibility study showed that the Cued Up! intervention is acceptable and participants feel they achieve improvement. Although this small study lacked statistical power to detect important changes in falls and FOG, the study provides insight into the measurement properties of the NFOGQ and its utility, as well as providing guidance for future larger RCT using similar interventions. Specific interventions to target FOG and falling such as Cued Up! require further research in larger studies.

REFERENCES

29. Skelton D. Definition of a fall. 2012; http://profane.co/2012/02/22/definition-of-a-fall/.