Effects of adaptive-tempo music-based RAS for Parkinson's disease patients

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ABSTRACT

The use of Rhythmic Auditory Stimulation (RAS) is a potential method to help Parkinson Patients improve their gait characteristics. By providing auditory stimuli such as a metronome or music, gait impairments, which characterize the illness, tend to improve without pharmacological or surgical intervention. This work evaluates three different RAS approaches: fixed-tempo metronomes, fixed-tempo music and adaptive-tempo music. 29 Parkinson Disease (PD) patients were tested in a repeated measures experiment to compare spatiotemporal gait parameters in different cueing conditions. Baseline measures without RAS were taken, followed by counterbalanced trials of the three RAS methods. Compared to the baseline, beneficial effects were found for all RAS types. Fixed-tempo metronomes resulted in the highest increase for cadence, velocity and stride length, fixed-tempo music increased velocity and stride length, and adaptive-tempo music increased stride length. However, metronomes lowered the fractal scaling value compared to the baseline, possibly increasing the risk for falling, while adaptive music increased the fractal scaling to healthy levels, reducing the risk for falling. These promising results suggest that rhythmical auditory stimuli based on music might have an advantage over metronomes that may hold benefits for treatment of Parkinson's disease.

I. INTRODUCTION

A. Parkinson's Disease

Parkinson's disease is characterised by an impaired basal ganglia function (Braak, 2003; Buhusi & Meck, 2005), which can lead to problems of movement timing and rhythm (Grahn & Brett 2009; Graybiel, Aosaki & Flaherty, 1994; Schwartze, Keller & Patel, 2010). This loss in the ability to produce a steady gait can cause gait disturbances, such as shuffling steps, start hesitation and freezing. These debilitating symptoms of Parkinson's disease (PD) have been associated with increased risk of falling (Hausdorff, 2009; Hove, Suzuki, Uchitomi, Orimo & Miyake, 2012).

Pharmacological (i.e. medication) and surgical (i.e. deep brain stimulation) can positively influence gait cadence and velocity (Chen, Wang, Liou & Shaw, 2013). In addition, patients can be helped with a non-invasive method: Rhythmic Auditory Stimulation (RAS), such as playing metronomes or marching music. RAS has been shown to be an effective method in improving gait in PD patients (Ashoori, Eagleman & Jankovic, 2015; Ashoori, 2015) and reducing costs associated with falling. Positive effects of the RAS cueing can even lead to benefits beyond gait (Benoit et al., 2014; Bella, Benoit, Farrugia, Schwartze & Kotz, 2015), such as improvement of quality of life. There are several different approaches for RAS, based on the type of stimuli (metronomes, marching songs, music) and tempo (fixed tempo, adaptive or interactive tempo).

Fixed tempo RAS has been researched the most, and has shown to improve many aspects of gait timing (Thaut & Abiru, 2010; Rubinstein, Giladi & Hausdorff, 2002; McDonough, Batavia, Chen, Kwon & Ziai, 2001). Most notably, the fixed tempo RAS can increase gait tempo and stride length (McIntosh, Brown, Rice & Thaut, 1997) and decrease the magnitude of stride-time variability (Arias & Cudeiro, 2008; Hausdorff et al., 1996). Despite these results, the use of fixed tempo RAS in Parkinson rehabilitation has limitations because it requires synchronization to a metronome or music. PD patients, however, have an impaired ability to synchronizing gait with the RAS (O'Boyle, Freeman & Cody, 1996). Synchronizing gait with auditory rhythms presents attentional demands, which can be problematic for PD patients, for example due to difficulties with multitasking (Rochester et al., 2004). The task to synchronize walking to external stimuli is sometimes even hard for healthy population (Styns, van Noorden, Moelants & Leman, 2007).

It has been suggested that RAS that adapts to patients' movements may be more effective than fixed tempo RAS (Ashoori et al., 2015). Adaptive RAS uses feedback from human walking rhythm to determine cueing or RAS rhythm. A cueing system that aligns to the patients' movements could reduce attention demand and could improve gait more than with fixed, non-adaptive cueing (Hove & Keller, 2015).

Walk-Mate (Miyake, 2009), for example, is an adaptively timed metronome used as adaptive RAS (Uchitomi, Miyake, Orimo, Suzuki & Hove, 2011; Hove et al., 2012). The results were compared to regular fixed-tempo metronomes and a control (silent) condition. In the Walk-Mate study, participants were not explicitly instructed to synchronize their steps with the beats, and often did not synchronize with the metronome, although they all synchronized with the Walk-Mate because that device also synchronized with them, having been programmed to carry out phase correction (Repp & Su, 2013). They found similar results on spatiotemporal parameters (cadence, velocity, step length) for all RAS types. Additionally, they showed that the isochronous metronome introduced unnatural random variation in the gait timings, but that the adaptive RAS raised the patients' gait timings to almost normal or healthy levels.

The aim of our study is to test if the same positive kinematic effects of using fixed and adaptive RAS are also present when used with music.

B. DFA: Fractal scaling exponent

Gait dynamics can be analysed using Detrended Fluctuation Analysis (DFA) (Peng, Havlin, Stanley & Goldberger, 1995; Goldberger et al., 2002). The resulting fractal-scaling exponent alpha is associated with gait adaptability and is one of the best measures of predicting falling (Herman, Giladi, Gurevich & Hausdorff, 2005; Bartsch et al., 2007; Hausdorff et al., 2000). The main goal of RAS is to improve gait patterns and reduce falling, therefore the alpha DFA value seems an important tool to asses RAS systems, in addition to conventional measures such as stride length, cadence, etc.

DFA analyses long-range correlations in time-series, or in this case, stride interval timings. The method, in contrast to standard variability, determines whether the gait pattern is predictable, based on previous steps. The result of the analysis is called the DFA fractal-scaling exponent or the 'alpha value' which has a useful meaning between 0 and 2.

The alpha value is an intuitive measure: based on previous steps (e.g. short, long) we should be able to predict the next step (similar, following a speedup or slowdown trend, etc). If the pattern is not predictable, a step interval could be followed by any unrelated step interval, which would seem unnatural. We note the following alpha levels (Hausdorff et al., 2000) with the interpretation to the gait:

- Alpha < 0.5: anti-persistent stride intervals: long steps are often followed by small steps and vica versa (Beran, 1994).
- Alpha = 0.5: stride intervals are random distributed and unpredictable, seemingly white noise.
- Alpha = 1.0: stride intervals represent a 1/f sequence. This is a common pattern for self-organizing systems (Bak, Tang & Wiesenfeld, 1987) and indicates long-term correlations in the data. The previous strides can be used to predict the next steps. Strides are most likely followed by strides of about the same interval; but over time the interval tends to fluctuate. This is most similar to healthy walking (Jordan, Challis & Newell, 2007).
- Alpha = 1.5: stride intervals represent a random walk process or Brownian noise.

Healthy people show a value of around 1.0 in random walks. PD patients often exhibit a fractal scaling value around 0.5 in random walks without RAS (Bartsch et al., 2007; Hausdorff et al., 2000), depending on the advancement in functional impairment.

Fixed-tempo metronome RAS has been show to decrease the alpha value away from healthy levels (Delignieres & Torre, 2009), as stride-time variability becomes organized around a single frequency. Hove et al. (2012) have shown that using adaptive metronome-based RAS, patients' alpha value increased towards healthy levels, reducing the risk of falling. However, this was only tested with metronomes.

C. D-Jogger and music alignment strategies

D-Jogger is a music player that adjusts the musical tempo to the listeners' gait rhythm (Figure 1) (Moens & Leman, 2015). The device has been tested on healthy subjects to study the synchronization of gait to adaptive rhythmic cues (Moens et al., 2014).

The detail of how music is synchronized to gait is called a music alignment strategy. Among the four proposed strategies in Moens & Leman (2015), three were used in this experiment: adaptive tempo music, fixed tempo music (similar to typical RAS at baseline tempi) and the adaptive tempo and phase strategy, where the system forces beat-footfall synchronization upon the user – allowing for uninstructed synchronization scenarios where all participants are synchronized to the music. In a literature review, Ashoori et al. (2015) stated that "results from healthy participants motivate further testing of D-Jogger on patients with PD or other movement disorders". D-Jogger is used here as a basis to implement RAS strategies.

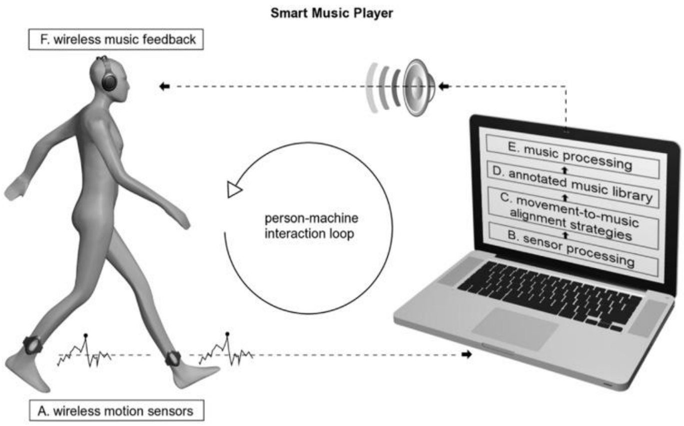

Figure 1. D-Jogger interactive cueing system

D. Synchronization and measures

RAS systems provide auditory stimulus (such as a metronome or a song) for a patient to walk on. The patient can try to synchronize his or her footsteps to the stimuli, ignore the stimuli and have an unsynchronized walk, or somewhere in between (partial phase locking). We believe that the amount of synchronization could greatly influence the efficacy of the RAS, as spontaneous or forced synchronicity with music can affect performance (Van Dyck et al., 2015) and mood or motivation (Karageorghis & Priest, 20012; Karageorghis & Terry, 1997) in healthy participants.

A global quantifiable synchronization measure over a trial is called the resultant vector length (R): it indicates the consistency of the timing differences between footfalls and beats during a trial and is related to the spread of the distribution and its circular variance. R is expressed as a number between 0 (no synchronization) and 1 (only synchronized steps, i.e. all steps coincide with a beat) (Fisher, 1993).

The resultant vector length can be an interesting measure for assessing the amount of synchronization with RAS systems. For example, is a fixed tempo RAS more efficient when patients are synchronized, or is there no need to synchronize? The resultant vector length measure is also taken into account in this study, and we expect the R-value to be high in the adaptive RAS scenario's as the D-Jogger automatically phase-corrects the music so it matches the footfalls.

II. METHODS

A. Participants

29 patients, 17 men and 12 women, (age *M* = 66.16, *SD* = 8.18) with an idiopathic form of Parkinson's disease were included. Patients' disease severity was Hoehn and Yahr Stage 2.5 to 4, nine patients reported freezing on the NFOG questionnaire and the mean duration of disease was 6.84 years (*SD* = 3.52). All patients were able to walk two minutes repeatedly. Patients with deep brain stimulation, severe gait disorders and Parkinson-plus syndromes were excluded. All patients were tested while 'on' medication.

B. Ethics

This trial was ethically approved by the Ethical Committee of the University Hospital of Ghent.

C. Design and procedure

Before the actual testing procedure began, participants completed an intake questionnaire. Afterwards, they completed the unified Parkinson's disease scale (UPDRS) part I (evaluation of mentation, behaviour and mood) and III (clinician-scored monitored motor evaluation) and the new freezing of gait questionnaire (NFOG-Q), a valuable tool for assessment of freezing (Nieuwboer et al., 2009). A Borg scale was taken to evaluate the influence of fatigue (Borg, 1982). It is a valid measurement instrument to determine the exertion intensity, showing good results with physiological criteria (Chen et al., 2002).

The participants walked around a rectangular shaped trail (15 m long and 3.02 m wide, see Figure 2) whilst allowing for big turns. Participants walked for two minutes in four different conditions, alternated with six minutes of rest. After each condition, in the moment of rest, an oral Borg scale rating was taken. After the experiment a short personal interview was taken by the experiment supervisors to gather information on participants' experience with music, three months later a second series of questions was asked by means of a telephone interview.

Figure 2. Location of the experiment

D. Conditions

The only instruction, given in the different conditions, was to walk for two minutes around the rectangle, enabling to determine the effect of RAS on their gait. No instructions or explanations about synchronization were given before or after the experiment.

First, participants walked on a comfortable pace without RAS as a baseline step rate measurement (= no RAS condition). Afterwards, there were three conditions, which were counterbalanced to exclude the influence of fatigue. A first RAS condition was walking with the use of a metronome with a tempo that matched the baseline step rate (= fixed tempo metronome condition). A second RAS condition used music with a tempo that matched the baseline step rate (= fixed tempo music condition). Finally, a third interactive RAS condition used music with a tempo and phase that matched the step rate during the walking task (= adaptive-tempo music condition).

E. Apparatus

A GAITRite mat, a sensor-augmented mat of 9 meters long, measured spatial and temporal gait parameters such as cadence, step length and gait variance (McDonough et al., 2001; Bilney, Morris & Webster, 2003) with a good test-retest reliability. This instrument was placed in the middle of one of the lengths of the rectangle.

Auditory stimuli were provided using a modified version of the D-Jogger system, a platform that automatically chooses and matches music to activities like walking or running in both tempo and phase (Moens et al., 2014; Moens & Leman, 2015). Custom music alignment algorithms were implemented to match this experiment RAS requirement. The D-Jogger software was running on a Dell Latitude i7 laptop (Dell E6520). Two iPods (4th generation) attached at each ankle were used for real-time gait analysis. The wireless connection between was provided through a Wi-Fi router (TP-Link M5360). Musical tempi were manipulated using a phase vocoder, which time-stretched the music without pitch modification. Music tempo was adapted based on the selected alignment strategy. Finally, the selected and aligned music was sent back to the participant using wireless Sennheiser HD60 headphones with the base-station connected to the computer.

F. Music Database

A music database was generated a priori based on Li et al's (2010) recommendations (based on tempo, cultural, and beat strength features). We selected popular and stimulating radio songs, which we believed to be familiar to the patients; with stable tempi in the range of 80-130 BPM. Songs were bought at iTunes, converted to wav, normalised so all songs matched the perceived loudness, and finally intro's without a clear beat were cut. Tempo's and beat timings were determined and manually verified using BeatRoot (Dixon, 2007).

G. Data capture and statistical analysis

Spatiotemporal data was captured by the GAITRite system, synchronization data was provided by the D-Jogger system. The D-Jogger system also provided step and stride times for each trial used in DFA analysis.

To calculate the DFA alpha values, the left stride times were used because this was the most complete dataset. In some cases, sensor data was corrupt (i.e. due to low batteries) and the right stride times were used instead. For each trial, the first 20 and last 5 strides were ignored, as well as outliers that indicate a missed step in the data processing. On average, 123

± 15 strides were used from each trial to calculate the alpha value. The DFA alpha values were calculated using the algorithm described by Peng et al. (1995) and Goldberger et al. (2013) implemented in Matlab with a maximum bin size of 100 and an advancement of 10 steps.

Synchronization scores were calculated using the Circular Statistics Toolbox in Matlab (Berens, 2009).

All data were processed in Matlab and analysed in SPSS using repeated measures ANOVA with post hoc test using Bonferroni corrections.

III. RESULTS

A. Population

Out of the 29 participants, four had a missing value in one of the conditions registered by GAITRite. The results of these four participants were not included in the data processing or statistical analysis, resulting in 25 participants (15 men and 10 women). Table 1 describes the population.

Characteristics	Mean (±SD)	Mean (±SD) men	Mean (±SD) women
Age (years)	66,7 (8,2)	66,9 (7,3)	65,1 (9,7)
Height (cm)	168,6 (8,6)	173,5 (5,8)	161,2 (6,5)
Weight (kg)	74,8 (16,9)	81,3 (14,7)	62,6 (13,7)
BMI body mass index	25,7 (4,2)	26,9 (3,8)	24,0 (4,4)
Years since diagnosis	6,8 (3,5)	6,2 (2,9)	7,8 (4,3)
Score UPDRS part I	2,8 (1,4)	2,7 (1,6)	2,8 (1,1)
Score UPDRS part III	41,0 (11,3)	46,5 (11,1)	32,9 (5,3)
Freezer NFOGQ (Y - N)	9 - 16	3 - 12	6 - 4
Men/women	15 - 10	15 - 0	0 - 10

Table 1. Population description used in the analysis

B. Spatiotemporal parameters: velocity, stride length and cadence

Repeated measures ANOVA tests with a Greenhouse-Geisser correction determined that mean velocity differed statistically significantly between conditions ($F(2.08, 49.98) = 4.0$, $p < .05$) and that mean stride length differed statistically significantly between conditions ($F(2.26, 54.21) = 8.63$, $p < .001$). The mean cadence did not differ significantly between conditions ($p = .057$), but indicated a trend to significance. Post hoc tests using the Bonferroni correction revealed patients walked significantly faster in the fixed metronome ($p < .05$) and fixed music ($p < .05$) condition when compared to the no RAS condition. Stride length also increased significantly (Bonferroni correction) for fixed metronome ($p < .01$), fixed music condition ($p < .01$) and adaptive music condition ($p < .05$) compared to the no RAS condition. These results are summarised in Figure 3 and Table 2.

C. BORG ratings

After each trial a BORG scale was taken. A repeated measures ANOVA with a Greenhouse-Geisser correction determined that the BORG ratings were not statistically different between conditions. This indicates that the type of RAS did not appear to have an influence on fatigue.

D. Fractal Scaling

A repeated measures ANOVA with a Greenhouse-Geisser correction determined that mean fractal scaling differed significantly between conditions ($F(2.36, 51.53) = 11.06$, $p < .001$). Post hoc tests using the Bonferroni correction revealed patients had a more natural DFA scaling value using adaptive music when compared to fixed metronome ($p < .01$) and fixed tempo music ($p < .01$). Interestingly, no significant difference was found between adaptive music and the baseline (no RAS). With the fixed metronome RAS, patients' stride had a lower fractal scaling than during the silent-control condition ($p < .05$). These results are summarised in Figure 4 and Table 2.

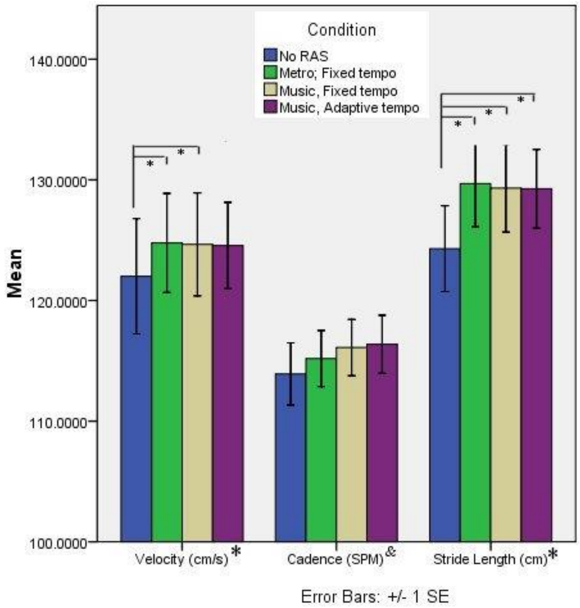

Figure 3. Results of spatiotemporal gait parameters. Significant results are indicated with a '*', trend to significance with '&'.

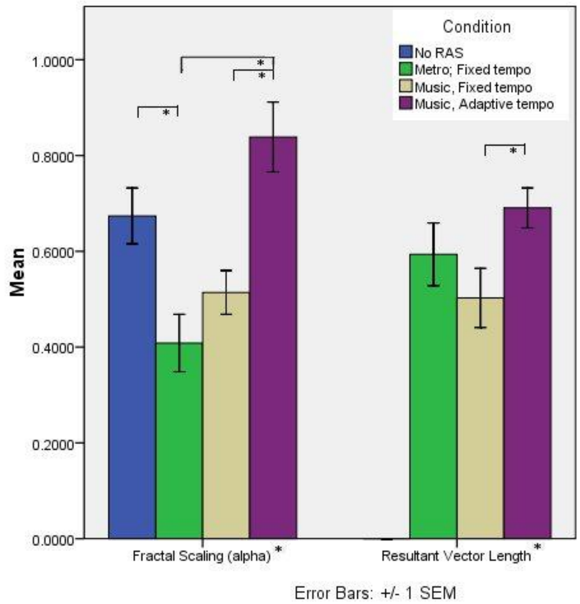

Figure 4. Results of the fractal scaling and synchronization value. Significant results are indicated with a '*'

E. Resultant vector length

The first condition does not have a valid resultant vector length, as this is a measure for synchronicity and no music/metronomes were present in this condition, hence the subsequent tests were performed on the three RAS conditions. A repeated measures ANOVA determined that mean resultant vector length differed significantly between conditions ($F(2.00,48.00) = 5.332$, $p < .01$). Post hoc tests using the Bonferroni correction revealed that there was significantly less synchronization in the fixed music condition than in the music adaptive condition ($p < .02$).

We note that, while not statistically significant, the resultant vector length for the fixed metronome condition is lower than for the adaptive music condition but higher than the fixed music condition. This indicates that the adaptive system increased step-beat synchronization (as it was designed to do); and that music at a fixed tempo is slightly more difficult or less intuitive to synchronize to than metronomes. However, spontaneous synchronization to metronomes is still lower than the adaptive system. These results are summarised in Figure 4 and Table 2.

F. Survey Results

The survey immediately after the experiment indicated that 14% of the patients did not like the music, so the majority felt that the music was good. About half of the patients had experience with walking on music, while 40% indicated that they used cueing systems before.

Three months after the experiment, patients were contacted again for a follow-up questionnaire. From the 29 participants in total, 11 could not be reached. The following data shows the result for the remaining 18 participants. We did not differentiate between the two music conditions because these detailed questions might be confusing. First, all but one patient indicated to remember the experiment very well. 61% of the patients found the music conditions the easiest; followed by 22% that found the metronome condition the easiest. 17% of the patients indicated not to have an opinion.

When asked if they noticed any difference between the two music conditions (adaptive vs. fixed tempo), 61% of the patients responded that they noticed a difference while 39% did not. 67% of the patients liked the music conditions the most, 11% the metronome and 22% did not indicate any preference.

N = 25	**Velocity (cm/s ± SD)**	**Cadence (SPM ± SD)**	**Stride Length (cm ± SD)**
No RAS	119.27 ± 20.71	113.92 ± 12.88	124.29 ± 17.76
Metro, fixed	124.77 ± 20.53	115.19 ± 11.61	129.69 ± 17.81
Music, Fixed	124.65 ± 21.35	116.10 ± 11.65	129.31 ± 18.19
Music, Adaptive	124.55 ± 17.88	116.36 ± 12.02	129.26 ± 16.27
N = 25	**BORG (cm/s ± SD)**	**R (SPM ± SD)**	**Alpha DFA (cm ± SD)**
No RAS	9.64 ± 2.66	0.00 ± 0.00	0.67 ± 0.29
Metro, Fixed	10.20 ± 2.53	0.59 ± 0.33	0.41 ± 0.30
Music, Fixed	10.20 ± 2.57	0.50 ± 0.31	0.51 ± 0.23
Music, Adaptive	10.12 ± 2.22	0.72 ± 0.19	0.84 ± 0.37

Table 2. Results

IV. DISCUSSION

The results of our study largely agree with other recent studies (Uchitomi et al., 2011; Hove et al., 2012; Rubinstein et al., 2002; del Olmo & Cudeiro, 2005). Basic kinematic measures (velocity, cadence and step length) did not differ significantly between RAS conditions. However, the addition of adaptive music together with the measurements of the DFA alpha (as a falling predictor) and the resultant vector length (as a measure of synchronicity) opened up some interesting viewpoints, especially towards the use of metronomes vs. music in a RAS system.

A. Metronomes: not as efficient as hoped?

Fixed metronome-based RAS provides a significant benefit in terms of spatiotemporal gait structure for PD, increasing stride lengths and velocity. An increasing trend was also found for the cadence. However, while these results are very positive, we noted a negative effect of metronome-based RAS: the fractal scaling value was lowered significantly, from slightly correlated inter-stride times (a ~= 0.65) to anti-persistent inter-stride times (a ~= 0.4); while optimal walking patterns show an alpha of around 1. Lower values have been linked to falling (Herman et al., 2005; Bartch et al., 2007), so this can be seen as a negative effect of metronome-based RAS. Anti-persistent means that large steps are often followed by small steps. This could be a result of humans' tendency to synchronize to rhythms close to our own (Moens et al., 2014; van Dyck et al., 2015) while walking to fixed tempo RAS: we tend to 'self-correct' so our steps match the metronome tick; even when not instructed to synchronize. The reasoning is also strengthened by the negative correlation found between the amount of spontaneous synchronization (*R*) and the alpha value.

Our results show that alpha values were inversely correlated to synchronization score: when the patient did not synchronize to the RAS, alpha values returned towards the baseline level but high synchronization scores lead to lower alphas. A Spearman's rank-order correlation was run to determine the relationship between the resultant vector length *R* and the fractal scaling values. There was a strong, negative correlation between *R* and alpha for the metronome condition, which was statistically significant ($r(26) = -.718$, $p < .001$), meaning that, if the patient spontaneously synchronized to the metronome, the fractal scaling became worse and increased the risk of falling. The negative correlation was not present with fixed music or adaptive music. Spontaneous entrainment or synchronization is only possible when gait and music cadence don't differ much (Van Dyck et al., 2015), so this could be a reason why metronome RAS is often used at +10% tempo compared to baseline (Willems et al., 2006): to avoid synchronization which reduces fractal scaling.

Furthermore, our survey data shows participants liked musical stimuli for RAS more than metronomes. So while the kinematic gait parameters such as velocity and step length do improve most when using metronome based RAS, this intervention might on the other hand increase the risk of falling and is not the preferred sound for patients to walk to.

B. Adaptive music: less efficient to influence cadence and velocity but potential decreasing the risk of falling

In this study we can confirm the positive effects of music RAS on velocity (fixed-tempo) and stride length (fixed-tempo / adaptive-tempo). However, the effects of musical RAS were less significant than fixed metronome based RAS. We note that with these results, the adaptive tempo RAS seems the least efficient: it only significantly raises stride length. The lesser efficacy of music could be partially explained by the individual preference for music, a more complex stimuli then metronomes. For example, it has been shown that the familiarity with the music has a significant effect on the changing of the gait parameters (Leow, Rinchon & Grahn, 2015; Ashoori et al., 2015).

With both music conditions, we found no correlation between the synchronization score R and the alpha value, whereas for metronomes, a negative correlation was found.

The advantage of adaptive-tempo music RAS stimuli becomes clear when looking at the alpha value. The metronome lowered the alpha value compared to the no-RAS condition, indicating an increased risk of falling; but the adaptive-tempo music significantly increased the alpha value compared to the metronome condition. This indicates that adaptive-tempo music is significantly better in reducing falling risk than regular metronome RAS. Furthermore, walking on music was the most preferred condition, which is in line with findings of de Bruyn et al. (2010) who showed that walking on cadence-matched music is feasible and enjoyable for PD Patients,

C. Synchronization to different stimuli

No explicit instructions to synchronize to the music were given. The resulting intuitive synchronization scores are the highest for adaptive music, followed by fixed metronome, whereas fixed music had the lowest R score. The adaptive tempo music RAS was designed to synchronize to the patient and also phase-correct, resulting in a high synchronization score. In the non-adaptive RAS conditions, the patient needed to synchronize (sometimes unsuccessful) to the music to obtain a high R. Music is more complex and often deviates small fractions from the mean tempo when compared to metronomes, which could explain the lower synchronization rate to music compared to metronome (yet insignificant). This might indicate that spontaneous synchronization to music induces a higher cognitive load than synchronization to metronomes, and that adaptive cueing lowers the cognitive tasks to synchronize. This can be advantageous especially for freezers. Nieuwboer (2008) concluded that freezers have less effect of cueing when attention is overloaded (e.g. during therapy).

Interestingly, the synchronization result R of the fixed metronome condition correlates with the fractal scaling alpha of all three conditions. There is a negative correlation for the fixed metronome (see earlier) but also for music ($r(26) = -0.378$, $p < .05$), while there is a positive fractal scaling correlation ($r(26) = 0.485$, $p < .01$) for the adaptive music condition. This could indicate that spontaneous 'synchronizers' (with a high R on the metronome) have the most benefit of adaptive music (a high value of alpha).

D. Limitations

We are aware of multiple limitations of this presented study. To begin with, the lack of a healthy control group makes it difficult to know if the results are generally applicable or only valid for PD patients. Second, the amount of time per participant was restricted, limiting the RAS conditions to three. Ideally, an adaptive metronome would also have been included in the study. A third constraint is that we did not differentiate between freezers and non-freezers, or gender, as the resulting groups was quite small. Finally, we dit not take into account possible carry-over effects of the different conditions (it has been shown that positive cueing effects persist for a short while after the training sessions (McIntosh et al., 1997; Hausdorff et al., 2007; Benoit et al., 2014). However, the study was counterbalanced or randomized in order to minimize the carry-over effect. The exposure to the stimuli was restricted (2 minutes) to study the immediate effect and limit carry-over effects. Apart from this, the music selection was not standardized which could have had an influence on the gait velocity of the patients (Buhmann, Desmet, Moens, Van Dyck & Leman, 2016). New experiments could benefit from using a personalized music selection of the patients in terms of familiarity (Leow et al., 2015) and motivation.

V. CONCLUSION

Metronome-based RAS appears to be the most efficient manner to increase step length, cadence and velocity, but might induce unhealthy gait timings leading to increased risk of falling. Fixed music retains most positive effects of metronome RAS, but less pronounced. Adaptive music also results in increased step length but has less influence on gait velocity. In contrast, gait timings with adaptive music RAS are restored to normal timings reducing the risk of falling. Finally, participants prefer music to metronome as a stimulus. Based on these results, it can be worth considering adaptive music as a primary stimulus type for RAS over metronomes.

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REFERENCES

Arias, P., & Cudeiro, J. (2008). Effects of rhythmic sensory stimulation (auditory, visual) on gait in Parkinson's disease patients. Experimental Brain Research, 186(4), 589-601.

Ashoori, A., Eagleman, D. M., & Jankovic, J. (2015). Effects of auditory rhythm and music on gait disturbances in Parkinson's disease. Frontiers in neurology, 6, 234.

Bak, P., Tang, C., & Wiesenfeld, K. (1987). Self-organized criticality: An explanation of the 1/f noise. Physical review letters, 59(4), 381.

Bartsch, R., Plotnik, M., Kantelhardt, J. W., Havlin, S., Giladi, N., & Hausdorff, J. M. (2007). Fluctuation and synchronization of gait intervals and gait force profiles distinguish stages of Parkinson's disease. Physica A: Statistical Mechanics and its Applications, 383(2), 455-465.

Beran, J. (1994). Statistics for long-memory processes (Vol. 61). CRC press.

Benoit, C. E., Dalla Bella, S., Farrugia, N., Obrig, H., Mainka, S., & Kotz, S. A. (2014). Musically cued gait-training improves both perceptual and motor timing in Parkinson’s disease. Frontiers in human neuroscience, 8, 494.

Bella, S. D., Benoit, C. E., Farrugia, N., Schwartze, M., & Kotz, S. A. (2015). Effects of musically cued gait training in Parkinson's disease: beyond a motor benefit. Annals of the New York Academy of Sciences, 1337(1), 77-85.

Berens, P. (2009). CircStat: a MATLAB toolbox for circular statistics. J Stat Softw, 31(10), 1-21.

Bilney, B., Morris, M., & Webster, K. (2003). Concurrent related validity of the GAITRite® walkway system for quantification of the spatial and temporal parameters of gait. Gait & posture, 17(1), 68-74.

Borg, G. A. (1982). Psychophysical bases of perceived exertion. Med sci sports exerc, 14(5), 377-381.

Braak, H., Del Tredici, K., Rüb, U., de Vos, R. A., Steur, E. N. J., & Braak, E. (2003). Staging of brain pathology related to sporadic Parkinson’s disease. Neurobiology of aging, 24(2), 197-211.

Buhusi, C. V., & Meck, W. H. (2005). What makes us tick? Functional and neural mechanisms of interval timing. Nature Reviews Neuroscience, 6(10), 755-765.

Buhmann, J., Desmet, F., Moens, B., Van Dyck, E., & Leman, M. (2016). Spontaneous velocity effect of musical expression on self-paced walking. PloS one, 11(5), e0154414.

Chen, P. H., Wang, R. L., Liou, D. J., & Shaw, J. S. (2013). Gait disorders in Parkinson's disease: assessment and management. International Journal of Gerontology, 7(4), 189-193.

de Bruin, N., Doan, J. B., Turnbull, G., Suchowersky, O., Bonfield, S., Hu, B., & Brown, L. A. (2010). Walking with music is a safe and viable tool for gait training in Parkinson's disease: the effect of a 13-week feasibility study on single and dual task walking. Parkinson’s disease, 2010.

del Olmo, M. F., & Cudeiro, J. (2005). Temporal variability of gait in Parkinson disease: Effectsof a rehabilitation programme based on rhythmic sound cues. Parkinsonism & related disorders, 11(1), 25-33.

Delignières, D., & Torre, K. (2009). Fractal dynamics of human gait: a reassessment of the 1996 data of Hausdorff et al. Journal of Applied Physiology, 106(4), 1272-1279.

Dixon, S. (2007). Evaluation of the audio beat tracking system beatroot. Journal of New Music Research, 36(1), 39-50.

Fisher, N. I. (1995). Statistical analysis of circular data. Cambridge University Press.

Goldberger, A. L., Amaral, L. A., Hausdorff, J. M., Ivanov, P. C., Peng, C. K., & Stanley, H. E. (2002). Fractal dynamics in physiology: alterations with disease and aging. Proceedings of the National Academy of Sciences, 99(suppl 1), 2466-2472.

Goldberger, A. L., Amaral, L. A., Glass, L., Hausdorff, J. M., Ivanov, P. C., Mark, R. G., ... & Stanley, H. E. (2000). Physiobank, physiotoolkit, and physionet. Circulation, 101(23), e215-e220.

Grahn, J. A., & Brett, M. (2009). Impairment of beat-based rhythm discrimination in Parkinson's disease. Cortex, 45(1), 54-61.

Graybiel, A. M., Aosaki, T., Flaherty, A. W., & Kimura, M. (1994). The basal ganglia and adaptive motor control. SCIENCE-NEW YORK THEN WASHINGTON-, 1826-1826.

Hausdorff, J. M. (2009). Gait dynamics in Parkinson’s disease: common and distinct behavior among stride length, gait variability, and fractal-like scaling. Chaos: An Interdisciplinary Journal of Nonlinear Science, 19(2), 026113.

Hausdorff, J. M., Lertratanakul, A., Cudkowicz, M. E., Peterson, A. L., Kaliton, D., & Goldberger, A. L. (2000). Dynamic markers of altered gait rhythm in amyotrophic lateral sclerosis. Journal of applied physiology, 88(6), 2045-2053.

Hausdorff, J. M., Lowenthal, J., Herman, T., Gruendlinger, L., Peretz, C., & Giladi, N. (2007). Rhythmic auditory stimulation modulates gait variability in Parkinson's disease. European Journal of Neuroscience, 26(8), 2369-2375.

Hausdorff, J. M., Purdon, P. L., Peng, C. K., Ladin, Z. V. I., Wei, J. Y., & Goldberger, A. L. (1996). Fractal dynamics of human gait: stability of long-range correlations in stride interval fluctuations. Journal of applied physiology, 80(5), 1448-1457.

Herman, T., Giladi, N., Gurevich, T., & Hausdorff, J. M. (2005). Gait instability and fractal dynamics of older adults with a “cautious” gait: why do certain older adults walk fearfully?. Gait & posture, 21(2), 178-185.

Hove, M. J., & Keller, P. E. (2015). Impaired movement timing in neurological disorders: rehabilitation and treatment strategies. Annals of the New York Academy of Sciences, 1337(1), 111-117.

Hove, M. J., Suzuki, K., Uchitomi, H., Orimo, S., & Miyake, Y. (2012). Interactive rhythmic auditory stimulation reinstates natural 1/f timing in gait of Parkinson's patients. PloS one, 7(3), e32600.

Jordan, K., Challis, J. H., & Newell, K. M. (2007). Walking speed influences on gait cycle variability. Gait & posture, 26(1), 128-134.

Karageorghis, C. I., & Priest, D. L. (2012). Music in the exercise domain: a review and synthesis (Part II). International review of sport and exercise psychology, 5(1), 67-84.

Karageorghis, C. I., & Terry, P. C. (1997). The psychophysical effects of music in sport and exercise: A review. Journal of Sport Behavior, 20(1), 54.

Leow, L. A., Rinchon, C., & Grahn, J. (2015). Familiarity with music increases walking speed in rhythmic auditory cuing. Annals of the New York Academy of Sciences, 1337(1), 53-61.

Li, Z., Xiang, Q., Hockman, J., Yang, J., Yi, Y., Fujinaga, I., & Wang, Y. (2010, October). A music search engine for therapeutic gait training. In Proceedings of the 18th ACM international conference on Multimedia (pp. 627-630). ACM.

Lim, I., van Wegen, E., de Goede, C., Deutekom, M., Nieuwboer, A., Willems, A., ... & Kwakkel, G. (2005). Effects of external rhythmical cueing on gait in patients with Parkinson's disease: a systematic review. Clinical rehabilitation, 19(7), 695-713.

McDonough, A. L., Batavia, M., Chen, F. C., Kwon, S., & Ziai, J. (2001). The validity and reliability of the GAITRite system's measurements: A preliminary evaluation. Archives of physical medicine and rehabilitation, 82(3), 419-425.

McIntosh, G. C., Brown, S. H., Rice, R. R., & Thaut, M. H. (1997). Rhythmic auditory-motor facilitation of gait patterns in patients with Parkinson's disease. Journal of Neurology, Neurosurgery & Psychiatry, 62(1), 22-26.

Miyake, Y. (2009). Interpersonal synchronization of body motion and the Walk-Mate walking support robot. IEEE Transactions on Robotics, 25(3), 638-644.

Moens, B., & Leman, M. (2015). Alignment strategies for the entrainment of music and movement rhythms. Annals of the New York Academy of Sciences, 1337(1), 86-93.

Moens, B., Muller, C., van Noorden, L., Franěk, M., Celie, B., Boone, J., ... & Leman, M. (2014). Encouraging spontaneous synchronisation with D-Jogger, an adaptive music player that aligns movement and music. PloS one, 9(12), e114234.

Nieuwboer, A. (2008). Cueing for freezing of gait in patients with Parkinson's disease: a rehabilitation perspective. Movement Disorders, 23(S2), S475-S481.

Nieuwboer, A., Rochester, L., Herman, T., Vandenberghe, W., Emil, G. E., Thomaes, T., & Giladi, N. (2009). Reliability of the new freezing of gait questionnaire: agreement between patients with Parkinson's disease and their carers. Gait & posture, 30(4), 459-463.

O'Boyle, D. J., Freeman, J. S., & Cody, F. W. (1996). The accuracy and precision of timing of self-paced, repetitive movements in subjects with Parkinson's disease. Brain, 119(1), 51-70.

Peng, C. K., Havlin, S., Stanley, H. E., & Goldberger, A. L. (1995). Quantification of scaling exponents and crossover phenomena in nonstationary heartbeat time series. Chaos: An Interdisciplinary Journal of Nonlinear Science, 5(1), 82-87.

Repp, B. H., & Su, Y. H. (2013). Sensorimotor synchronization: a review of recent research (2006–2012). Psychonomic bulletin & review, 20(3), 403-452.

Rochester, L., Hetherington, V., Jones, D., Nieuwboer, A., Willems, A. M., Kwakkel, G., & Van Wegen, E. (2004). Attending to the task: interference effects of functional tasks on walking in Parkinson’s disease and the roles of cognition, depression, fatigue, and balance. Archives of physical medicine and rehabilitation, 85(10), 1578-1585.

Rubinstein, T. C., Giladi, N., & Hausdorff, J. M. (2002). The power of cueing to circumvent dopamine deficits: a review of physical therapy treatment of gait disturbances in Parkinson's disease. Movement Disorders, 17(6), 1148-1160.

Schwartze, M., Keller, P. E., Patel, A. D., & Kotz, S. A. (2011). The impact of basal ganglia lesions on sensorimotor synchronization, spontaneous motor tempo, and the detection of tempo changes. Behavioural brain research, 216(2), 685-691.

Styns, F., van Noorden, L., Moelants, D., & Leman, M. (2007). Walking on music. Human movement science, 26(5), 769-785.

Thaut, M. H. (2005). Rhythm, music, and the brain: Scientific foundations and clinical applications (Vol. 7). Routledge.

Thaut, M. H., & Abiru, M. (2010). Rhythmic auditory stimulation in rehabilitation of movement disorders: a review of current research. Music Perception: An Interdisciplinary Journal, 27(4), 263-269.

Uchitomi, H., Miyake, Y., Orimo, S., Suzuki, K., & Hove, M. J. (2011, September). Co-creative rehabilitation: Effect of rhythmic auditory stimulus on gait cycle fluctuation in Parkinson's disease patients. In SICE Annual Conference (SICE), 2011 Proceedings of (pp. 2575-2580). IEEE.
Van Dyck, E., Moens, B., Buhmann, J., Demey, M., Coorevits, E., Dalla Bella, S., & Leman, M. (2015). Spontaneous entrainment of running cadence to music tempo. Sports medicine-open, 1(1), 15.
Willems, A. M., Nieuwboer, A., Chavret, F., Desloovere, K., Dom, R., Rochester, L., ... & Van Wegen, E. (2006). The use of rhythmic auditory cues to influence gait in patients with Parkinson's disease, the differential effect for freezers and non-freezers, an explorative study. Disability and rehabilitation, 28(11), 721-728.

APPENDIX A: SONG AND BPM VALUES

- 083.78 - The Pixies - Where Is My Mind
- 087.89 - Inner Circle - Bad Boys
- 088.02 - Manu Chao - Me Gustats Tu
- 093.61 - Manau - La Tribu De Dana
- 094.73 - Joan Jett & Blackhearts - I Love Rock & Roll
- 095.00 - Roxette - The Look
- 096.57 - Bob Marley - I Shot The Sheriff
- 096.66 - Kool And The Gang - Lets Go Dancin
- 099.64 - Barry White - Let The Music Play
- 101.96 - Carl Douglas - Kung Fu Fighting
- 103.73 - Pink Floyd - Another Brick In The Wall
- 106.02 - Arno - Oh La La La
- 106.10 - Dolly Parton - 9 To 5
- 108.02 - Scissor Sisters - I Dont Feel Like Dancin
- 109.25 - Kc And The Sunshine Band - Thats The Way (I Like It)
- 109.38 - Jimmy Cliff - Reggae Night
- 109.81 - Queen - Another One Bites The Dust
- 111.71 - Prince - Kiss
- 111.89 - Madonna - Like A Prayer
- 114.89 - Boney M - Rivers Of Babylon
- 116.38 - Gloria Gaynor - I Will Survive
- 117.69 - Arno - Pas Heureux Ni Malheureux
- 119.18 - Prince - 1999
- 119.55 - Abba - Gimme Gimme Gimme
- 122.00 - Mika - Relax (Take It Easy)
- 122.59 - Status Quo - Whatever You Want
- 123.16 - Arabesque - In The Heat Of A Disco Night
- 124.24 - Bob Marley - Jamming
- 124.70 - Boney M - Daddy Cool
- 126.01 - Eurythmics - Sweet Dreams
- 126.37 - Edwyn Collins - A Girl Like You
- 130.55 - Barry White - The First The Last
- 131.60 - Golden Earring - When The Lady Smiles