Chapter 7

Rhythm perturbations in acoustically paced treadmill walking after stroke

Submitted as:
Roerdink, M., Lamoth, C. J. C., van Kordelaar, J., Elich, P., Konijnenbelt, M., Kwakkel, G., & Beek, P. J. (revision submitted). Rhythm perturbations in acoustically paced treadmill walking after stroke
Abstract

In rehabilitation acoustic rhythms are often used to improve gait after stroke. Acoustic cueing may enhance gait coordination by creating a stable coupling between heel strikes and metronome beats, and provide a means to train the adaptability of gait coordination to environmental changes, as required in everyday-life ambulation. The aim of the present study was to examine the stability and adaptability of auditory-motor synchronization in acoustically paced treadmill walking in stroke patients. Eleven stroke patients and ten healthy controls walked on a treadmill at preferred speed and cadence under no metronome, single metronome (pacing only paretic or non-paretic steps), and double metronome (pacing both footfalls) conditions. The stability of auditory-motor synchronization was quantified by the variability of the phase relation between footfalls and beats. In a separate session, the acoustic rhythms were perturbed and adaptations to restore auditory-motor synchronization were quantified. For both groups, auditory-motor synchronization was more stable for double than single metronome conditions, with stroke patients exhibiting an overall weaker coupling of footfalls to metronome beats than controls. The recovery characteristics following rhythm perturbations corroborated the stability findings and further revealed that stroke patients had difficulty in accelerating their steps and instead preferred a slower-step response to restore synchronization. In gait rehabilitation practice, the use of acoustic rhythms may be more effective when both footfalls are paced. In addition, rhythm perturbations during acoustically paced treadmill walking may not only be employed to evaluate the stability of auditory-motor synchronization but have promising implications for evaluation and training of gait adaptations in neurorehabilitation practice.
Chapter 7

Introduction

Humans easily move in time with acoustic rhythms (e.g., dancing to music), and effortlessly adjust their movements to rhythmic acoustic elements such as beat and tempo. In neurorehabilitation practice, acoustic rhythms are often used to improve stroke-related gait deficits: physical therapists provide acoustic cues by clapping their hands, counting out loud, or by verbally emphasizing particular events in the gait cycle, such as footsteps of the paretic leg. Rhythmic acoustic stimuli prove to be beneficial for gait after stroke, with facilitating effects on cadence, step length, and walking speed (Prassas et al., 1997; Thaut, 2008; Thaut et al., 1993, 1997, 2007). Also improvements in gait coordination have been observed with acoustic pacing, such as reduced gait asymmetry and increased fluency of walking (Chapter 6; Ford et al., 2007; Prassas et al., 1997). These favorable effects of acoustic cues on the execution of rhythmic movements have motivated a number of – generally beneficial – intervention strategies in neuro-rehabilitation (Thaut, 2008; Thaut et al., 2007). However, the precise coordination between gait events and acoustic pacing, so-called auditory-motor coordination, has received little attention, even though understanding the manner in which gait is adjusted to acoustic pacing stimuli may lead to more effective applications of acoustic cueing in neurorehabilitation.

In the study on acoustically paced walking presented in Chapter 6, both stroke patients and healthy controls were found to be well able to adjust their step frequency to metronome rhythms corresponding to individuals' preferred step frequency as well as rhythms 10% faster or slower than preferred. It was therefore concluded that acoustic pacing provides an effective means for modifying step frequency in stroke patients, which is important in view of the fact that they typically have difficulty changing pace with variations in walking speed (Bayat et al., 2005; Nakamura et al., 1988).

During acoustically paced walking the footfalls are often synchronized with the metronome beats. If synchronized, the stability of the resultant auditory-motor coordination pattern can be quantified by the variability of the phase relation between motor events and metronome beats, with lower variability representing more stable coordination (Beek et al., 1995; Kelso, 1995; Kudo et al., 2006; Post et al., 2000; Richardson et al., 2007).

Alternatively, pattern stability can also be probed by rhythm perturbations (e.g.,

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metronome beats are presented earlier than expected, requiring an adjustment of the movement to restore the initial phase relation between motor events and metronome beats. An inverse relation is usually observed between response time and pattern stability (Chen et al., 2006; de Poel et al., 2007; Post et al., 2000; Repp, 2005; Richardson et al., 2007). Thus, a stronger auditory-motor coupling is represented by a less variable phase relation between motor events and metronome beats and a faster restoration of the phase relation with beats of the ongoing metronome following rhythm perturbations. A detailed evaluation of auditory-motor coupling strength of acoustically paced walking after stroke is relevant for gait rehabilitation because a stronger coupling of gait to the beat may enhance the efficacy of acoustic pacing for improving gait after stroke.

In the present study the stability of auditory-motor coordination was examined in acoustically paced walking at preferred speed and cadence in stroke patients with a hemiplegic gait pattern and healthy controls via pattern variability and response characteristics following rhythm perturbations. A stronger coupling of gait to the metronome was expected for healthy controls than for stroke patients. While studies of acoustically paced walking generally used metronomes pacing both footfalls, the stability of auditory-motor coordination of acoustically paced walking in time with a double metronome (pacing steps, PBI) was compared with that of a single metronome, pacing either paretic (PP) or non-paretic (PNP) footfalls. For both groups more stable auditory-motor coordination was expected for double than for single metronome conditions, because of the stronger environmental coupling induced by pacing two versus one event in a movement cycle (cf., Fink et al., 2000; Kudo et al., 2006). In view of the lateralized nature of the impairment following stroke, which is often accompanied by lateralized control (Roerdink et al., in press), a stronger coupling of the non-paretic leg to corresponding metronome beats was expected in the PBI condition (Chapter 6). For the same reason, also a more stable auditory-motor coordination was expected for PNP than for PP conditions. Although the emphasis of the present study was on auditory-motor coordination, the effect of the three acoustically paced walking conditions (PBI, PNP, PP) on spatial and temporal gait asymmetries and step width was examined and compared with unpaced walking to cover all aspects associated with acoustically paced walking.

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Methods

Participants

Eleven adults with a first-ever cerebrovascular accident (four women, seven men) and ten healthy controls (four women, six men) participated in the experiment. All participants reported to have no hearing deficits. Stroke patients with a lower extremity hemiparesis (paretic side: eight right, three left) being able to walk for at least 3 minutes without walking aid were selected by local MDs from the outpatient community of the Rehabilitation Centre Amsterdam. Potential candidates must be able to understand and act in accordance with simple spoken instructions. The stroke group was on average 60 years old (range 42 to 71 years), 1.72 m tall (range 1.59 to 1.86 m), and 75 kg in weight (range 50 to 100 kg). The control group was on average 60 years old (range 46 to 74 years), 1.74 m tall (range 1.59 to 1.91 m), and 73 kg in weight (range 60 to 102 kg). Independent t-tests indicated that stroke and control groups did not differ from each other in age, height, and weight (all t(19) < 0.55, p > 0.59). Stroke patients were all able to walk independently (Functional Ambulation Category 5) but most of them used a walking aid for ambulation during normal everyday activities (Table 7.1). The study was approved by the ethics committee of VU University Medical Centre before it was conducted. Prior to participation each participant signed an informed consent after having been informed about the protocol.

Apparatus

A 3D passive-marker motion registration system (SIMI Motion), positioned around a treadmill 11 (ForceLink, Culemborg, The Netherlands), was used to record light reflecting markers attached to the heel of the shoes within a calibrated area at a sampling rate of 50 Hz. In addition, accelerometers mounted on the heel of participants’ shoes recorded vertical accelerations (i.e., with respect to a local reference frame) at a sampling rate of 1000 Hz. Computer-produced rhythmic acoustic pacing stimuli (50 ms beats programmed in LabVIEW) were administered through an earphone; the corresponding beat 11 Because acoustic pacing affects walking velocity (Prassas et al., 1997; Thaut et al., 1997) measurements were performed on a treadmill with a stationary velocity to exclude possible speed-dependent contaminations in the effect of acoustic pacing on gait coordination (see also Chapter 6). It further allows for the detailed examination of auditory-motor coordination over multiple consecutive steps, which would be hard to achieve during overground walking (Chapter 6).

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Onsets and offsets were also sampled at 1000 Hz. Video, accelerometer, and acoustic data registration were synchronized. Participants wore a safety harness and were accompanied alongside the treadmill by two persons.

**Procedure**

For stroke patients, the experiment involved three sessions performed on separate days to avoid fatigue. Each session lasted approximately 2 hours including rest. In Session 1, an experienced physical therapist conducted a number of standard functional assessments (Fugl-Meyer motor assessment of the legs, Berg balance scale, Motricity Index, mini mental state examination, 10-m timed walking test at comfortable [CWS] and maximal [MWS] walking speed, see Table 7.1). Furthermore, patients were acquainted with treadmill walking on various speeds and were encouraged to walk without external support. Once this was achieved, comfortable walking speed on the treadmill and the corresponding step frequency was determined, serving as the belt velocity and acoustic pacing frequency in the actual experiment. These individual adjustments were deemed essential in view of the large inter-individual differences in CWS and MWS (Table 7.1).

In Session 2, a warm-up and familiarization period of treadmill walking preceded four experimental conditions performed twice each: 1) unpaced treadmill walking (UP), acoustically paced treadmill walking with beats prescribing 2) non-paretic footfalls only (PNP), 3) paretic footfalls only (PP), and 4) both non-paretic and paretic footfalls (PBI). The order of the eight trials was randomized within two blocks of four (i.e., one trial per condition per block). Between trials participants were seated to rest for as long as they wished (generally about 5 minutes). In these rest periods, participants became acquainted with the acoustic rhythm of the following trial and practiced synchronization of self-selected bodily movements (e.g., head, hands, trunk, feet) in a seated position to ensure that the instructions were fully understood (Thaut et al., 1993). In the PBI condition the metronome rate corresponded to the step frequency (i.e., so-called double metronome condition with beats pacing both footfalls), while in PNP and PP conditions, metronome beats prescribed footfalls of only one step per stride (i.e., so-called single metronome conditions). The number of paced stride cycles was kept constant across participants to 70 strides, implying longer trial duration for participants with lower stride frequencies. Before the trial started, participants were instructed which
footfall(s) had to be synchronized with acoustic pacing stimuli. Belt velocity was gradually increased to each individual's experimental speed (Table 7.1) after which the acoustic stimuli started. Data collection started after 10 strides. Video registrations were made for 15 strides because of the large storage capacity required.

Table 7.1. Characteristics of stroke patients

<table>
<thead>
<tr>
<th>Stroke patient</th>
<th>Variable</th>
<th>P1</th>
<th>P2</th>
<th>P3</th>
<th>P4</th>
<th>P5</th>
<th>P6</th>
<th>P7</th>
<th>P8</th>
<th>P9</th>
<th>P10</th>
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<td>71</td>
<td>68</td>
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<td></td>
<td>Sex</td>
<td>F</td>
<td>F</td>
<td>M</td>
<td>M</td>
<td>M</td>
<td>M</td>
<td>M</td>
<td>M</td>
<td>M</td>
<td>M</td>
<td>F</td>
</tr>
<tr>
<td></td>
<td>Months past stroke</td>
<td>10</td>
<td>18</td>
<td>7</td>
<td>65</td>
<td>29</td>
<td>9</td>
<td>28</td>
<td>4</td>
<td>16</td>
<td>12</td>
<td>6</td>
</tr>
<tr>
<td></td>
<td>Type of stroke</td>
<td>INF</td>
<td>H</td>
<td>INF</td>
<td>INF</td>
<td>INF</td>
<td>H</td>
<td>INF</td>
<td>INF</td>
<td>INF</td>
<td>INF</td>
<td>INF</td>
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<td>R</td>
<td>L</td>
<td>R</td>
<td>L</td>
<td>R</td>
<td>R</td>
<td>R</td>
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<td>cane</td>
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<td>MMSE score (0-30)</td>
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<td>29</td>
<td>28</td>
<td>24</td>
<td>16</td>
<td>30</td>
<td>28</td>
<td>26</td>
<td>28</td>
<td>26</td>
<td>26</td>
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<td>MI score (0-100)</td>
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<td>64</td>
<td>64</td>
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<td>BBS score (0-56)</td>
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<td>52</td>
<td>44</td>
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<td>34</td>
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<td>23</td>
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<td>mild</td>
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<td>no</td>
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<tr>
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<td>Cognitive problems</td>
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<td>mild</td>
<td>yes</td>
<td>mild</td>
<td>yes</td>
<td>mild</td>
<td>no</td>
<td>no</td>
<td>mild</td>
<td>no</td>
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<tr>
<td></td>
<td>CWS (km/h)</td>
<td>2.9</td>
<td>1.9</td>
<td>3.6</td>
<td>1.4</td>
<td>2.7</td>
<td>4.3</td>
<td>0.9</td>
<td>2.3</td>
<td>2.8</td>
<td>3.4</td>
<td>2.7</td>
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<tr>
<td></td>
<td>MWS (km/h)</td>
<td>3.6</td>
<td>2.0</td>
<td>4.6</td>
<td>1.8</td>
<td>3.1</td>
<td>4.7</td>
<td>1.0</td>
<td>3.4</td>
<td>3.2</td>
<td>4.4</td>
<td>3.4</td>
</tr>
<tr>
<td></td>
<td>Treadmill speed (km/h)</td>
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<td>1.9</td>
<td>3.4</td>
<td>2.0</td>
<td>2.4</td>
<td>4.3</td>
<td>0.8</td>
<td>1.7</td>
<td>2.4</td>
<td>3.2</td>
<td>1.9</td>
</tr>
<tr>
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<td>fstride (strides/minute)</td>
<td>52.4</td>
<td>33.7</td>
<td>52.5</td>
<td>52.9</td>
<td>46.2</td>
<td>57.5</td>
<td>34.4</td>
<td>44.2</td>
<td>47.3</td>
<td>57.3</td>
<td>55.5</td>
</tr>
<tr>
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<td>% temporal asymmetry</td>
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<td>22.2</td>
<td>0.1</td>
<td>17.5</td>
<td>3.9</td>
<td>9.3</td>
<td>27.0</td>
<td>18.3</td>
<td>16.8</td>
<td>17.5</td>
<td>26.4</td>
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<td></td>
<td>% spatial asymmetry</td>
<td>20.3</td>
<td>3.4</td>
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<td>1.9</td>
<td>9.5</td>
<td>-7.3</td>
<td>6.9</td>
<td>-5.9</td>
</tr>
</tbody>
</table>

Note: M/F = Male/Female, H/INF = hemorrhaged/infarction, R/L = Right/Left, MMSE = Mini Mental State Examination, MI = Motricity Index, BBS = Berg Balance Scale, FMNP/P = Fugl-Meyer Motor Assessment (non-paretic/paretic leg), CWS = comfortable overground walking speed, MWS = maximal overground walking speed

In Session 3, a warm-up and familiarization period of treadmill walking preceded eight experimental trials of acoustically paced treadmill walking, but now with perturbations in the acoustic rhythm (see Figure 7.1 for an example). The same three pacing conditions were used (P NP, PP, and P BI) containing four perturbations per trial (beats came earlier or later than expected) with the purpose to suddenly perturb the phase relation between footfalls and metronome.
beats. Participants were instructed to restore phase synchronization as quickly as possible. In each trial, two positive (later) and two negative (earlier) phase shifts of 60° were administered in random order at random instants that were at least 10 strides apart. Participants performed four P BI trials and two P NP and P P trials to present eight perturbations to each acoustically paced leg. The order of the eight trials was again randomized within two blocks of four and in between trials rest was given as outlined for Session 2. Only accelerometer and acoustic pacing data were registered.

Figure 7.1. Perturbations in a sequence of beats during double metronome pacing. A) perturbation left, B) perturbation right. Shifts in beats are indicated by arrows with thin line segments representing beats if perturbations would not have occurred.

Healthy controls performed the protocol in a single session lasting approximately 2.5 hours including rests. Controls rested shorter and only after every other trial. From the abovementioned functional assessments only 10-m timed walking tests were performed. Furthermore, P NP and P P implied acoustic pacing for right and left footfalls, respectively.

Data analysis

Video registrations were processed using SIMI Motion software to determine 3D coordinate time series of heel marker trajectories (Figure 7.2, upper part), which served to determine spatial gait parameters. Indices of heel strike were...
derived from accelerometer data (Figure 7.2, lower part) to determine temporal gait parameters. Specifically, stride frequency was determined by taking the inverse of the averaged stride time intervals. Step time on the paretic side was quantified as the time interval between heel strikes of the paretic limb following heel strikes of the non-paretic limb, and vice versa for the step time on the non-paretic side. Step width was quantified as the mean absolute mediolateral difference in the landing position of consecutive contralateral heel strikes. Step length on the paretic (non-paretic) side was derived by multiplying belt speed by the paretic (non-paretic) step time while correcting for positional differences between consecutive contralateral foot placements in the sagittal plane (Chapter 6). Stride length was the sum of the step lengths. Asymmetry in step length and step time (i.e., spatial and temporal asymmetry) was quantified by subtracting non-paretic from paretic step lengths and times, normalized to the maximum value of both (Chen et al., 2005). A corresponding asymmetry index of zero indicates perfect symmetry. The magnitude of the index represents the degree of asymmetry in step time or step length and the sign indicates the direction of asymmetry (i.e., a positive index indicates a larger paretic step length or step time).

Figure 7.2. Vertical heel marker trajectories (upper part, based on video registrations) and heel accelerations (lower part, based on accelerometer data) of stroke patient P1 from Table 7.1 during the double metronome condition. Metronome beats are indicated by vertical shaded patches of 50 ms. Dark gray time series correspond to the paretic side; brighter time series represent the non-paretic leg. Contents under embargo
With regard to auditory-motor coordination, we first evaluated frequency synchronization. Specifically, an error measure \( E \) was calculated for acoustic pacing trials to determine how well participants coupled their stride frequency to the metronome frequency, using 
\[
E = c \cdot (f_{pacing} - f_{stride}) / f_{pacing},
\]
where \( c \) is a constant representing the number of prescribed strides included in the analysis and \( f_{pacing} \) and \( f_{stride} \) are acoustic pacing and observed stride frequencies (both in strides/minute), respectively. An error of zero indicates perfect frequency synchronization, whereas negative values of \( E \) indicate that more strides than prescribed were taken in the course of \( c \) paced stride cycles.

For trials with good frequency synchronization, defined as \( |E| < 0.1 \), phase synchronization was assessed by quantifying the mean phase relation between footfalls and acoustic stimuli (\( \phi \) in °), with positive values indicating that the footfalls are leading the metronome in time while \( \phi \) near zero indicates concurrent footfalls and metronome beats. In addition, the variability of the relative timing between footfalls and metronome beats was determined (\( \phi_{σ} \) in °), with larger \( \phi_{σ} \) reflecting less stable auditory-motor coordination. A paired comparison was made of \( \phi_{σ} \) between both sides in the PBI condition to examine hypothesized lateralized differences in auditory-motor coupling strength. For comparison with single metronome conditions, \( \phi \) and \( \phi_{σ} \) were subsequently averaged over sides for the double metronome condition. Circular statistics was applied in the calculation of \( \phi \) and \( \phi_{σ} \) (Mardia, 1972).

For the perturbation trials, the relative phase \( \phi \) between footfalls and metronome beats was determined. The sudden positive or negative phase shifts of 60° in the metronome rhythm (i.e., beats came later or earlier than expected, respectively; see Figure 7.1) required different responses to restore the initial phase relation. We followed Chen and colleagues (2006) in the analyses of responses to perturbations (Figure 7.3). Specifically, \( \phi \) was determined for a specific interval around the perturbation, where \( T \) is used to represent the response where the phase shift occurred and \( T±n \) for the \( n \)th response preceding or following \( T \). The baseline phase relation \( *\phi \), averaged over \( T-3 \) to \( T-1 \), was subtracted from \( \phi \), so that the phase shift at \( T \) corresponded to the size of the perturbation (i.e., ±60°; Figure 7.3).

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Figure 7.3 schematically depicts the to-be-expected responses following perturbations. When beats come later than expected (phase delay, bright gray traces), the associated footfall at T is timed ahead of the acoustic stimulus, invoking a positive shift of 60°. The initial phase relation can be restored by taking a slower-step response, consisting of a number of steps with a longer duration than prescribed, to undo the 60° shift. In contrast, when beats suddenly come earlier than expected (phase advance, dark gray traces), footfalls at T will be too late, invoking a negative phase shift of 60°. A faster-step response, consisting of a number of steps that are shorter in duration than prescribed, is in place to restore the initial phase relation. In both single and double metronome conditions these are the to-be-expected typical responses. For these typical responses, the percentage correction of the phase error at T+1, T+2, …, T+8 was quantified (Chen et al., 2006) to statistically test response time characteristics between groups, metronome conditions, and direction of perturbation. Besides these typical responses, some adequate yet out of the ordinary responses may be expected, albeit less frequent (Figure 7.3).
Chapter 7

Statistics

Independent t-tests were performed to examine gait differences between stroke patients and controls in unpaced treadmill walking. To examine differential effects of the three acoustic pacing configurations (P NP, P P, P BI) on dependent variables of auditory-motor coordination and gait, a repeated measures analysis of variance (ANOVA) was conducted with acoustic pacing as within-subject factor (3 levels: P NP, P P, P BI) and group as between-subject factor (2 levels: stroke patients and controls). The effect of acoustic pacing on spatial and temporal gait asymmetry and step width was examined by comparing these dependent variables for unpaced walking to those for acoustically paced walking (averaged over P NP, PP, and P BI) using a 2 (stroke patients, controls) by 2 (with and without pacing) repeated measures ANOVA. Effect size was indexed by partial eta squared ($\eta^2_p$). Post hoc testing was performed for significant main and interaction effects using paired-samples t-tests, separate for both groups in case of significant interactions.

Results

Table 7.1 summarizes the individual characteristics of the eleven stroke patients with respect to age, sex, time post-stroke, and type and hemisphere of stroke. Clinically-rated aphasia and cognitive problems are also indicated in Table 7.1. Patients varied in individual functional scores (Table 7.1).

Differences in gait between stroke patients and controls CWS was significantly lower for stroke patients than controls (2.6 vs. 5.0 km/h; $t(19) = 6.75, p < 0.001$). The same was true for MWS (3.2 vs. 6.5 km/h; $t(19) = 7.43, p < 0.001$). CWS was on average slightly lower on the treadmill than for overground walking (2.4 and 4.8 km/h for stroke and control groups, respectively; cf. Bayat et al., 2005). Stroke patients walked with significantly lower stride frequency than controls (48.5 vs. 60.8 strides/minute; $t(19) = 4.02, p < 0.001$) and showed a marked asymmetry in step time (15.3%) that was absent in controls (1.1%; $t(19) = 5.24, p < 0.001$). The sign of step time asymmetry was always positive, implying longer step times on the paretic side (Table 7.1).

Indeed, paretic step time (0.695 s) was significantly larger than non-paretic step time (0.581 s, $t(10) = 4.60, p < 0.001$), whereas for controls, left and right step time (i.e., 0.499 vs. 0.494 s, respectively) did not differ ($t(9) = 1.60, p = 0.144$).

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Stroke patients walked with significantly smaller stride lengths than controls (0.82 vs. 1.33 m; \( t(19) = 5.63, p < 0.001 \)) and showed an asymmetry in step length that varied in direction (Table 7.1; cf. Chapter 6; Chen et al., 2005). Finally, stroke patients showed larger step widths than controls (21.2 vs. 16.4 cm; \( t(19) = 2.54, p < 0.05 \)).

Auditory-motor synchronization

Although the metronome rate was set according to the individual’s comfortable pace observed in UP trials (Table 7.1), stride and metronome frequency often fell out of sync. We therefore searched for the episode of 40 consecutive strides with minimal \( |E| \) (reflecting the part of the trial with the best frequency synchronization) and excluded all trials for which \( |E| > 0.1 \). Two stroke patients (P4 and P5 from Table 7.1) were clearly incapable of synchronizing their footfalls to the beat of the metronome and generally took fewer strides than prescribed (\( E \) was on average 0.5 and 1.3, respectively). For the other 9 stroke patients, 3 trials in each of the single pacing conditions were performed with \( |E| > 0.1 \) while in the double pacing condition footfalls were always perfectly synchronized to the beat of the metronome. The included trials had good frequency synchronization (mean \( |E| = 0.0073, SD = 0.0113 \)). Healthy controls were all able to walk to the beat of the metronome and showed excellent frequency synchronization in all trials (mean \( |E| = 0.0038, SD = 0.0045 \)).

Dependent auditory-motor coordination variables were calculated for frequency synchronization segments of \( c = 40 \) cycles with \( |E| < 0.1 \) only. Hence, P4 and P5 were excluded for further analyses (i.e., unperturbed and perturbed trials).

Effects of acoustic pacing on auditory-motor synchronization

No significant effects of pacing for \( \phi \) were observed (all \( F(2,34) < 0.50, p > 0.547, \eta^2 < 0.03 \)); on average \( \phi \) was 17.1° (±3.9°), indicating that footfalls slightly preceded metronome beats. Significant effects of group (\( F(1,17) = 6.53, p < 0.05, \eta^2 = 0.28 \)) and pacing (\( F(2,34) = 15.22, p < 0.001, \eta^2 = 0.47 \)) were observed for \( \phi_\sigma \). In line with our hypotheses, \( \phi_\sigma \) was larger for stroke patients (12.8°) than controls (7.8°), indicating overall reduced stability of auditory-motor coordination in stroke patients, while, furthermore, auditory-motor coordination was more stable in the double (7.9°) than in both single metronome conditions (P NP: 11.3°, \( t(18) = 5.00, p < 0.001 \); P P: 11.8°, \( t(18) = 4.85, p < 0.001 \)).
0.001), in the absence of a difference between the latter (\( t^{(18)} = 0.54, p = 0.594 \)). Because no significant Group × Pacing interaction was found (\( F^{(2,34)} = 1.44, p = 0.251, \eta^2 = 0.08 \)), this effect of pacing held for stroke patients and controls alike. For stroke patients, the difference in \( \phi \sigma \) between paretic and non-paretic sides (10.3° vs. 8.9°, respectively) in the double metronome condition did not reach significance (\( t^{(8)} = 1.59, p = 0.15 \)).

Effects of acoustic pacing on gait

Because of the good frequency synchronization (|E| < 0.1) and the stationary belt speed, stride frequency and stride length could not differ across pacing conditions. Single and double metronome conditions might thus only affect step width and asymmetries in step length and step time. Steps were again wider for stroke patients (21.6 cm) than controls (17.0 cm), but step width was not affected by the different acoustic pacing conditions (all \( F^{(2,34)} < 0.42, p > 0.658, \eta^2 < 0.02 \)). No significant main or interaction effect of pacing was observed for spatial and temporal gait asymmetry (all \( F^{(2,34)} < 1.29, p > 0.290, \eta^2 < 0.07 \)), indicating that there were no systematic differences in gait asymmetry between single and double metronome conditions.

Step width differed significantly between pacing and no pacing conditions for stroke patients and healthy controls alike, as evidenced by significant main effects of pacing (\( F^{(1,17)} = 7.12, p < 0.05, \eta^2 = 0.30 \)) and group (\( F^{(1,17)} = 4.76, p < 0.05, \eta^2 = 0.22 \)) in the absence of an interaction between them (\( F^{(1,17)} = 0.03, p = 0.867, \eta^2 < 0.01 \): steps were significantly wider with than without acoustic pacing (stroke patients: 21.6 vs. 20.9 cm, controls: 17.0 vs. 16.4 cm). For step time asymmetry, the main effect of pacing tended towards significance (\( F^{(1,17)} = 4.21, p = 0.056, \eta^2 = 0.20 \), suggesting that temporal asymmetry slightly decreased with acoustic pacing (8.7 vs. 7.9%). This tendency was present for both groups in that no significant interaction was observed (\( F^{(1,17)} = 1.07, p = 0.316, \eta^2 = 0.06 \)). Spatial gait asymmetry did not improve with acoustic pacing (all \( F^{(1,17)} < 2.11, p > 0.164, \eta^2 < 0.11 \)).

Responses to phase shifts

One control participant was excluded from further analyses due to an error in data collection while one stroke patient (P10 from Table 7.1) did not perform Session 3. For stroke patients, metronome conditions with perturbations were...
difficult to perform, especially the single metronome conditions. Following perturbations, frequency or phase synchronization was regularly lost, implying that subsequent phase shifts were applied to non-stationary or arbitrary phase relations between beats and footfalls. These perturbations were discarded from further analyses because associated “responses” were meaningless. Congruent with the reported findings for auditory-motor coupling strength (i.e., $\phi_{\sigma}$), the amount of adequate responses was much larger for controls than for stroke patients (90.5% vs. 67.2%; Table 7.2) and, similarly, also a higher percentage of adequate responses was observed for double than single metronome conditions (patients: 73.4% vs. 60.9%; controls: 93.6% vs. 87.5%; Table 7.2).

Unfortunately, due to the relatively large number of excluded responses, leading to missing values for P6, P7, and P11 of Table 7.1, dependent measures of responses to phase perturbations could not be tested statistically (note that P4 and P5 were also excluded from the analyses and that P10 did not perform the third session). Below, the observed characteristics of the remaining adequate responses for stroke patients are therefore described in a qualitative manner.

For stroke patients, in the double metronome condition a clear difference was observed in responses to positive and negative phase shifts. When beats came later than expected (positive phase shifts of 60°), stroke patients always showed a slower-step response (Figure 7.4A and 7.4B, Table 7.2). In contrast, when beats came earlier than expected (negative phase shift), typical faster-step responses were adopted in only 59.3% of the perturbations as footfalls became frequently synchronized with acoustic beats that initially prescribed contralateral footfalls (21.9%, Figures 7.4A and 7.4B, Table 7.2), adopting a slower-step response to compensate the then required phase change of 120°.

### Table 7.2. Response statistics following perturbations, with expected typical responses in italic font.

<table>
<thead>
<tr>
<th></th>
<th>Phase delay (+60°)</th>
<th>Phase advance (-60°)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>False steps</td>
<td>Faster steps</td>
</tr>
<tr>
<td>Single controls</td>
<td>12.5% 87.5%</td>
<td>0% 12.5%</td>
</tr>
<tr>
<td>Double controls</td>
<td>4.3% 82.9%</td>
<td>12.9% 8.6%</td>
</tr>
<tr>
<td></td>
<td>34.4% 65.6%</td>
<td>0% 37.5%</td>
</tr>
<tr>
<td>Pattern</td>
<td>40.6% 59.4%</td>
<td>0% 43.8%</td>
</tr>
<tr>
<td>Stroke patients</td>
<td>32.3% 67.7%</td>
<td>0% 18.2%</td>
</tr>
</tbody>
</table>

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Figure 7.4. Responses for double (A-C) and single (D-F) metronome conditions to phase delay (light gray lines) and phase advance (dark gray lines) perturbations. Following phase delays (advances) usually slower (faster) steps were taken, restoring the phase relation to $\phi-\approx^\circ$, i.e., the initial phase relation between beats and footfalls. In the double pacing conditions, stroke patients (A-B) sometimes took slower-step responses following phase advance perturbations (i.e., $180^\circ-\approx^\circ$), one beat was skipped), whereas controls (C) showed also faster-step responses following phase delays ($180^\circ-\approx^\circ$). Out-of-the-ordinary responses were rare in the single pacing condition; in the PNP condition (D) in one occasion a full cycle was skipped, $360^\circ-\approx^\circ$, restoring auditory-motor synchronization with the instructed non-paretic leg. In the PP condition (E), incorrect transitions from paretic to non-paretic footfall synchronization were occasionally observed ($180^\circ-\approx^\circ$). Contents under embargo
As can be appreciated from Figure 7.4 (panels D and E), stroke patients generally followed expected typical responses in P NP and P P conditions. Responses appeared more variable and slower than in the double pacing condition, especially when faster-step responses were adopted. Also a few atypical responses were observed, again showing slower-step responses instead of the typical faster-step response when beats came earlier than expected. In one occasion in the P NP condition (Figure 7.4D), an auditory-motor synchronization with the non-paretic leg was restored by skipping almost a full gait cycle relative to metronome beats (i.e., phase shift of 300°). Furthermore, three incorrect responses were observed in the P P condition (Figure 7.4E), where, following a slower-step response, non-paretic instead of the instructed paretic footfalls became synchronized with the single metronome.

Controls restored the initial phase relation between beats and footfalls by the anticipated typical responses in 84.4% of the perturbations in the double metronome condition; steps were elongated when beats came later than expected and shortened when beats came earlier than expected (Figure 7.4C, Table 7.2). For the remaining perturbations, controls restored the phase relation by taking slower steps instead of the typical faster steps with phase advance shifts (5.7%) and vice versa for phase delay shifts (12.9%), thereby compensating 120° instead of 60° to obtain phase synchronization (Figure 7.4C). Consequently, footfalls become synchronized to metronome beats initially prescribing contralateral footfalls (Figure 7.3A), implying that one more step is taken than beats are provided following phase delays and vice versa for phase advances. Such reverse responses could be expected because in the double metronome condition phase shifts cause phase relations in which footfalls are almost centered between consecutive metronome beats (see Figure 7.1; as would be the case for phase shifts of precisely 90°). This may be more pronounced for healthy controls for whom acoustic pacing was typically faster due to higher cadence.

In the single metronome conditions, healthy controls always followed the anticipated typical responses (Figure 7.4F; Table 7.2). For controls, the percentage correction of phase error with typical responses following the perturbation T (i.e., the responses T+1 to T+8) was subjected to an 8 (Response) × 2 (Acoustic Pacing: single versus double metronome) × 2 (Direction: phase delay versus phase advance) × 2 (Side: left versus right) repeated measures ANOVA, revealing a significant main effect of response ($F_{(7,56)} = 53.77$, $p < 0.05$).
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intervals for this group due to faster cadence and because phase shifts of 60° are almost mid-way between contralateral footfalls (Figures 7.1 and 7.3). With smaller phase shifts reversed responses become increasingly less likely. For example, Chen and colleagues (2006) applied sudden phase shifts of 36° in stepping on the spot and always observed typical responses. With shifts of 90° both responses would in principle be equally probable when there is no preference for using faster- or slower-step responses. A progressive scaling of the size and direction of the phase shift may identify a preference towards a certain response and thereby signifying potential deficits in the ability to adjust gait. Presumably, the increased prevalence of slower-step responses indicates that stroke patients had difficulty in accelerating their pace and rather preferred to decelerate their pace, supporting the general notion that stroke patients have difficulty in increasing their stride frequency (Chapter 6; Bayat et al., 2005; Nakamura et al., 1988), even at preferred walking speed and cadence. In a study on obstacle avoidance during treadmill walking in stroke patients, den Otter and colleagues (2005) also observed that the preference for step lengthening (i.e., slower-step response) over step shortening (i.e., faster-step response) was more pronounced in stroke patients than in healthy controls, irrespective of the side of obstacle presentation.

It was further expected that for stroke patients the coupling of non-paretic footfalls to the beat of the metronome would be stronger than that of paretic footfalls (Chapter 6) given the lateralized control associated with their impairment (Roerdink et al., in press). Weak evidence was found in support of this expectation: 1) $\phi_{\sigma}$ did not differ between the two single pacing conditions or between paretic and non-paretic sides in the double pacing condition, despite slightly lower $\phi_{\sigma}$ values in expected directions, 2) in the single pacing conditions occasional transitions from paretic to non-paretic auditory-motor synchronization occurred following perturbations and never the other way around, 3) as can be seen in Figure 7.4, typical responses following phase delays were seemingly faster and less variable in the PNP than in the PP condition, although the large number of excluded responses unfortunately omitted a statistical evaluation of this observation. The observation that footfalls were on average slightly leading the metronome beats in time in combination with the observed temporal asymmetry in stroke patients (i.e., longer paretic than non-paretic step duration) implies a greater phase lead for non-paretic than for...
Paretic footfalls. In view of the fact that movements paced by a moderate to fast predictable acoustic rhythm are typically leading the beats in time (e.g., Asschersleben, 2002; Repp, 2005), the greater phase lead of non-paretic footfalls with double pacing apparently suggests that predominantly non-paretic footfalls are actively coordinated or anchored to the metronome beats, while paretic footfalls more or less follow. This interpretation is consistent with observed anchoring phenomena in favor of the non-paretic leg in acoustically paced treadmill walking after stroke (Chapter 6).

An important side observation was that step width increased with acoustic pacing for both healthy controls and stroke patients. Previous studies have taken preferred step width as an inverse marker for the stability of walking (e.g., Donelan et al., 2004), which seems reasonable in view of our finding that stroke patients exhibited significantly wider steps than controls (see also Chapter 6). The increased step width with acoustically paced walking might be related to the fact that paced treadmill walking requires more attention than unpaced treadmill walking (Lamoth et al., 2007). Wider steps might tentatively have increased stability limits allowing for allocating attention to synchronization of steps to the beat.

Stroke patients' gait deviated from that of controls in terms of walking speed (and hence stride frequency and stride length), spatial and temporal asymmetry, and step width. With acoustic pacing minor improvements in gait coordination were observed compared to unpaced walking. Because of the extended familiarization period of treadmill walking (Wass et al., 2005), our sample of stroke patients may have optimally benefited from positive effects of treadmill walking itself on gait coordination (e.g., Bayat et al., 2005; Harris-Love et al., 2001, 2004), leaving little room for further improvements with acoustic pacing. In line with this interpretation is the fact that the stroke patients who participated in this study were in general more severely affected than those reported in Chapter 6 with a much shorter familiarization period, yet showed smaller spatial and temporal gait asymmetries (Table 7.1). Larger beneficial effects of acoustic pacing on gait parameters have typically been observed for higher pacing frequencies than preferred and in situations where stride length is not constrained (Chapter 6; Arias & Cudeiro, 2008; Howe et al., 2003; Prassas et al., 1997; Styns et al., 2007; Thaut et al., 1993, 2007). The use of a treadmill (i.e., dictating mean walking speed) of limited length (i.e., restricting variations...
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in walking speed) may have diminished facilitating effects of rhythmic acoustic stimulation given the general observation that with acoustic pacing gait speed increases. This limitation notwithstanding, future gait training with acoustic pacing is recommended to pace both footfalls in view of the observed superior auditory-motor coordination stability of acoustically paced walking in synchrony with a double rather than a single metronome.

With regard to gait adaptability, it is important to note that differences in gait speed and cadence between stroke and control groups reduced rather than amplified group differences in response characteristics compared to a situation where speed and cadence would be matched over groups. The reason is that the rhythm perturbations were phase perturbations, implying that the time shift induced by the perturbation depended on the adopted cadence. In particular, interbeat intervals increase with slower pacing rhythms rendering it highly unlikely that healthy controls would more often adopt a slower-step response if a beat came earlier than expected (as was the case for stroke patients) because in this situation they would have even more time to respond to the perturbation than with shorter interbeat intervals. Vice versa, if stroke patients would be forced to walk faster with increased cadence, the opposite would occur: more strict time demands would probably invoke more slower-step responses.

A key question for rehabilitation practice is who will and who will not benefit from a particular form of training. For this reason we discuss the two stroke patients who were unable to walk to the beat of a metronome, taking consistently fewer steps than required. The inability to synchronize steps to beats is often observed (see also Chapter 6; Ford et al., 2007) and may tentatively be related to clinically-rated attention deficits (P4 from Table 7.1) as acoustically paced treadmill walking requires more attention than unpaced treadmill walking (Lamoth et al., 2007). Alternatively, it may also be related to expressive aphasia (P5 from Table 7.1) because associated brain areas are also involved in sensorimotor integration (Patel, 2005; see also Chapter 3 of Thaut, 2008) and temporal processing (e.g., Fries & Swihart, 1990; Szelag et al., 1997). It may also have been the case that P4 and P5 were unable to walk to the beat of the metronome due to deficits in cognitive functioning since their MMSE scores were the lowest of all participants (Table 7.1). Future studies are required to identify contraindications in assessing which individuals benefit most from

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acoustic pacing, with attention deficits, expressive aphasia, and cognitive deficits as likely candidates. The present findings illustrate that, next to improving gait (Chapter 6; Ford et al., 2007; Prassas et al., 1997; Thaut, 2008; Thaut et al., 1993, 1997, 2007), acoustically paced treadmill walking may be used to identify deficits in the ability to adjust gait to environmental changes, for example by applying sudden shifts in the sequence of beats (present study) or by changing the frequency of pacing (Chapter 6). Weerdesteyn and colleagues (e.g., Weerdesteyn et al., 2005, 2006, in press) and den Otter and colleagues (2005) recently identified differences in gait adjustment strategies in an obstacle avoidance task during treadmill walking, with healthy elderly and stroke patients preferring stride lengthening to shortening in avoiding obstacles, even in situations in which stride shortening would be highly favorable (den Otter et al., 2005; Weerdesteyn et al., 2005). These findings are akin to the here-observed increased likelihood of a slower-step response in stroke patients, because this also involves stride lengthening. Underlying mechanisms for this preference may thus be related. Patla and colleagues (1999) proposed that stride lengthening (i.e., a slower-step response) is more favorable because it is less destabilizing than stride shortening (see also Chen et al., 1994; Weerdesteyn et al., 2005). In addition, a slower-step response allows more time to adjust gait, which seems important in view of the elevated decision times in the elderly required for choice stepping reaction time tasks (St. George et al., 2007). The ability to adjust gait based on changes in the environment is important for everyday life ambulation, such as increasing speed in crossing the street when the traffic light changes red or adjusting foot placement to avoid clutter. It represents a functional and adaptive way of walking.

The ability to avoid obstacles through successful gait adjustments is trainable in elderly, effectively reducing their fall risk (Weerdesteyn et al., 2006, in press). Five weeks of fall prevention exercise training, including practicing fall techniques, walking exercises, and crossing a functionally oriented obstacle course, were already effective (Weerdesteyn et al., 2006, in press). Alternatively, acoustically paced treadmill walking may also provide an effective method for training gait adjustments to environmental changes (i.e., gait adaptability). It allows for a convenient, task-oriented, and repetitive practice environment for gait training in which factors such as belt speed and...

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The metronome frequency can easily be controlled independently. It further allows for the use of weight-bearing and/or handrail support to start training early in rehabilitation. The observed stronger coupling with double pacing suggests that this type of training would fare best by using metronome beats for both footfalls.

The efficacy of gait training using acoustically paced walking with phase perturbations (present study) and/or shifts in the frequency of pacing (Chapter 6) in stroke patients must be assessed in randomized clinical trials and contrasted with conventional gait training to evaluate their relative merits. In view of established beneficial effects of treadmill training (e.g., Ada et al., 2003; Pohl et al., 2002) and overground rhythmic acoustic stimulation (e.g., Thaut et al., 2007) on various aspects of gait, positive results may be anticipated when used in combination.

Acknowledgements

The authors are grateful to Peter Koppe and Thomas Janssen for insightful discussions, Bert Clairbois for building and testing the apparatus, and Mariëlle Eversdijk and Annieck Ricken for their kind assistance in planning the experiments.

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