Perceptual Differences in Sequential Stimuli Across Patients With Musician’s and Writer’s Cramp

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Abstract: Previous research has demonstrated a relationship between the regularity of motor production and the ability to make accurate perceptual judgments. The current study investigated the temporal abilities of two groups of patients with known movement problems (musicians’ and writers’ cramp), some of whom have had many years of training in temporal discrimination. Patients and controls (musician and nonmusician, respectively) judged whether the last of six sequential auditory or tactile stimuli occurred earlier or later in comparison to five previously and regularly presented stimuli. In both sensory domains, patients with musicians’ cramp detected the early stimulus better than controls. When detecting the onset of late stimuli, only in the auditory domain were patients worse than controls. Patients with writers’ cramp, however, did not show any significant group differences in either auditory or tactile domains, suggesting that such patients are not deficient in processing sequential stimuli. In conclusion, compared to controls, patients with musician’s cramp demonstrated generalized timing anomalies, occurring in the symptomatic (tactile) and the asymptomatic (auditory) sensory domains. This timing problem is likely to be a consequence of the dystonic symptoms rather than the cause. © 2003 Movement Disorder Society

To play a musical instrument, musicians must perform highly complex movements with great temporal and spatial accuracy and precision. In some individuals, a task-specific (and usually painless) cramping or incoordination of the fingers (or mouth) may occur, referred to as focal dystonia. The term dystonia is used to describe a syndrome characterized by sustained muscle contractions, frequently causing twisting and repetitive movements, or abnormal postures.1–3

In a recent review,4 it was suggested that the temporal abilities of musicians with a highly specific movement disorder should be examined because the acuity of perceptual judgments correlates with the regularity of motor production.5,6 Indeed, using functional magnetic resonance imaging (fMRI), capacities such as time perception, temporal planning, and the coordination of movement have been shown to have a common cerebral basis.7,8

The neural systems associated with temporal behavior are traditionally linked to the cerebellum,9–12 the basal ganglia,13 and the cortex.14 The cerebellum has a long association for specializing in timing in both the perceptual and motor domains. Patients with cerebellar lesions are impaired on perceptual tasks that require judgments on auditory stimuli,15 and patients show inappropriate timing during rapid limb movements.16,17

The nuclei of the basal ganglia, especially the globus pallidus (internal, GPi)13 may be involved with time keeping and integration. This nucleus is also implicated in the genesis of dystonia and Parkinson’s disease.18 Both clinical groups demonstrate higher simultaneity–discrimination thresholds for paired sensory stimuli.19–22

Patients with Parkinson’s disease also demonstrate a greater temporal variability during repetitive finger-tap-
ping tasks in the off period of their medication\textsuperscript{23,24} and also have greater errors in reproduction and estimation of time intervals.\textsuperscript{25} Thus, damage to any part of a network of timing involving the cerebellum, basal ganglia, and associated cortical structures, may result in deficits in temporal perception and/or reproduction.

**STUDY RATIONALE**

Investigations of temporal processing in patients with writers’ cramp have been limited to paired stimuli.\textsuperscript{19–22} Arguably, sequential stimuli provide more temporal structure than paired stimuli and, therefore, may be even more important for movement sequences.\textsuperscript{26,27} To the best of our knowledge, sequential stimuli have not been used to investigate temporal judgements in patients with focal dystonia. Therefore, the current study extends previous research by investigating a similar group of patients (i.e., with focal dystonia), with the use of sequential rather than paired stimuli in the temporal judgement task. Moreover, as suggested by Tinazzi and colleagues,\textsuperscript{22} two modalities (auditory and tactile) were investigated to examine whether any timing problems were general or localized to the symptomatic (tactile) domain.

Patients with musicians’ cramp were also examined with respect to whether temporal training had an additional benefit for perception and movement. In addition, a smaller group of patients with writers’ cramp was investigated. Given the association between motor production and perceptual abilities, and previous research on paired stimuli in patients with writers’ cramp, it was expected that both patient groups would show differences in perceiving sequentially organised stimuli.

Additionally, two groups of nonmusician controls were used. The first group of nonmusicians acted as a control for patients with writers’ cramp, and the second group of nonmusicians ensured that any possible group differences in the perceptual domain were due to the disorder and not musicianship. That is, there is a substantial amount of research demonstrating differences in the processing of melodic and rhythmic stimuli between musicians and nonmusicians.\textsuperscript{28–33} Nonmusicians might not be as accurate in discriminating sequential stimuli as musician controls because of the amount of training musicians have in temporal tasks.\textsuperscript{34,35}

**PATIENTS AND METHODS**

**Participants**

There were two groups of patients: (1) 8 professional musicians that played either the guitar or piano (average age, 41 ± 7 years; Table 1), and (2) 5 patients with writers’ cramp (average age, 44 ± 6 years; Table 2). For the controls, the first two groups included 8 musicians (32 ± 5 years), and 8 nonmusicians (35 ± 4 years). These were controls for the patients with musicians’ cramp and were matched for handedness and as closely as possible for age; musicians were also matched for length of playing the instrument. The third group of controls was used for comparisons with patients with writers’ cramp, and individuals were also matched for handedness and as closely as possible for age (mean age, 39 ± 8 years).

All musicians were right-handed.\textsuperscript{36} Of the 8 patients with musicians’ cramp, 7 had dystonia in the right hand; only 1 had dystonic symptoms in the left hand. Of the patients with writers’ cramp, 4 had focal dystonia in their right hands; 1 who was left-handed had symptoms in the same hand. The average duration of disability over the 8

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**TABLE 1. Clinical profiles of the patients with musicians’ cramp**

<table>
<thead>
<tr>
<th>Patient no.</th>
<th>Age (yr)</th>
<th>Years playing</th>
<th>Entrance into music academy (age)</th>
<th>Problem duration (yr)</th>
<th>Sx side</th>
<th>Symptom localised*</th>
<th>Task-specific?</th>
<th>Severity (%)**</th>
<th>Previous medication</th>
<th>Type of music played***</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>50</td>
<td>44</td>
<td>3</td>
<td>R</td>
<td>3, F</td>
<td>N*</td>
<td></td>
<td>81</td>
<td>Lidocain 3</td>
<td>1</td>
</tr>
<tr>
<td>2</td>
<td>47</td>
<td>35</td>
<td>33</td>
<td>R</td>
<td>3, F, 2, 5 E</td>
<td>Y</td>
<td>72</td>
<td>12.5\textsuperscript{b}</td>
<td>2</td>
<td></td>
</tr>
<tr>
<td>3</td>
<td>45</td>
<td>35</td>
<td>20</td>
<td>L</td>
<td>2, F</td>
<td>Y</td>
<td>81</td>
<td>No</td>
<td></td>
<td>2</td>
</tr>
<tr>
<td>4</td>
<td>28</td>
<td>22</td>
<td>19</td>
<td>R</td>
<td>3, 4, 5 F</td>
<td>N*</td>
<td>81</td>
<td>0.5% Lidocain</td>
<td>3</td>
<td></td>
</tr>
<tr>
<td>5</td>
<td>38</td>
<td>29</td>
<td>19</td>
<td>R</td>
<td>3.2</td>
<td>Y</td>
<td>86</td>
<td>150\textsuperscript{b}</td>
<td>3</td>
<td></td>
</tr>
<tr>
<td>6</td>
<td>38</td>
<td>29</td>
<td>23</td>
<td>R</td>
<td>2 close to 3</td>
<td>Y</td>
<td>86</td>
<td>No</td>
<td></td>
<td>3</td>
</tr>
<tr>
<td>7</td>
<td>47</td>
<td>30</td>
<td>19</td>
<td>R</td>
<td>2, 4 F</td>
<td>N*</td>
<td>81</td>
<td>Artane</td>
<td>2</td>
<td></td>
</tr>
<tr>
<td>8</td>
<td>36</td>
<td>16</td>
<td>27</td>
<td>R</td>
<td>2 incordination</td>
<td>Y</td>
<td>86</td>
<td>100\textsuperscript{b}</td>
<td>1</td>
<td></td>
</tr>
</tbody>
</table>

*Symptomatic fingers: 3, middle; 4, ring; 5, small.
**Severity from Fahn.\textsuperscript{37}
***1, Classical; 2, Classical and Rock/Pop; 3, Classical, Jazz, and Rock/Pop.
\textsuperscript{a}Writing.
\textsuperscript{b}Units of Botulinum toxin A (Dysport).
Sx, symptom; F, flexion; E, extension.
musician patients was $9 \pm 5$ years; for the patients with writers’ cramp, the average length was $8 \pm 4$ years. The patients with musicians’ cramp had relatively homogeneous symptoms and were classified as having mild dystonic symptoms; the average severity was $82 \pm 4\%$. The patients with writers’ cramp had greater severity in symptoms ($71 \pm 20\%$).

A total of 3 musicians and 4 of the 5 patients with writers’ cramp received treatment with injections of botulinum toxin A (Dysport); the experiment was conducted approximately 3 months after the last injection. The patient who had Artane had his last prescription in 1997, and 1 patient with Lidocaine had his injection after the experiment.

### Stimulation

Two modalities (tactile and auditory) were investigated in this experiment. Sides (left and right) and modalities were blocked and counterbalanced with 12 blocks of 75 trials for each modality. For both the auditory and tactile task, the stimuli were 7 msec in duration. In the auditory task, each stimulus consisted of a single note (261.6 Hz, middle C, $49 \pm 3$ dB); a computer sound card generated the auditory stimuli, the loudness of which was measured with a sound level meter (SL-4001; Lutron). The auditory stimuli were presented monaurally. For the tactile task, the average force of each stimulus was $8 \pm 1$ Newtons (N). A PC computer with Science Workshop Data Logging 500 Interface software and sensor (Pasco scientific sensor CI-6537) measured the force of the mechanical apparatus with a sampling rate of 10 kHz. The stimulating apparatus was an acrylic rod that was 3 mm in diameter except the end, which had a contact surface of 1 mm. This rod was stabilized inside another acrylic tube (10 mm diameter) with support guides; the rods were connected to solenoids and were under computer (parallel port) control. Two separate solenoids were located in shielded boxes and powered by a 12 V DC regulated power supply (GW Laboratory DC, GR 3030). The position of the fingertip from the tactile stimuli was maintained at 2 mm, and stimuli were presented to either the index or ring fingernails. The fingernail stimulated depended on the symptoms the patients displayed; controls were subsequently matched. To mask the sound of the mechanical apparatus, participants listened to white noise played through stereo EEG earphones (EAR Tone).

### Procedure

Participants judged whether a train of six brief pulses delivered to either the left or right side appeared to be regular or not. The first five pulses within a train were delivered at a constant period of 4 Hz (every 250 msec), whereas the sixth pulse appeared at some variable interval after the fifth. This method follows that of previous research. The duration between the fifth and sixth pulse varied randomly between 200, 225, 250, 275, or 300 msec. Thus, two stimulus epochs were shorter or longer by either 25 msec or 50 msec compared to the standard 250-msec interstimulus interval. The fifth time interval was the same as the rest of the train and served as the comparison; participants were not told that some stimuli were the same as the regular stimuli (Fig. 1). Participants used a keyboard to rate how confidently they thought the last stimulus was different to the previous five. There were six options: 1 = definitely early, 2 = probably early, 3 = possibly early, 4 = possibly late, 5 = probably late, 6 = definitely late. Feedback was given after each trial.

### Data Analysis

A well-known bias-free measure of sensitivity from Signal Detection Theory is $d’$, which assumes equal variance. The current data violated the assumption of homogeneity of variance, therefore, $d_a$ was calculated as the measure of sensitivity. Higher values for $d_a$ indicate higher sensitivity and, hence, better discrimination. For

### Table 2: Clinical profiles of the patients with writers’ cramp

<table>
<thead>
<tr>
<th>Patient no.</th>
<th>Age (yr)</th>
<th>Problem duration (yr)</th>
<th>Handedness and sx side</th>
<th>Task-specific?</th>
<th>Severity (%)</th>
<th>Previous medication</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
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<td>All</td>
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<td>50</td>
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<td>R</td>
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<td>85</td>
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<tr>
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<td>40</td>
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<td>R</td>
<td>Y</td>
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<td>No</td>
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<tr>
<td>4</td>
<td>47</td>
<td>15</td>
<td>L</td>
<td>All</td>
<td>85</td>
<td>50</td>
</tr>
<tr>
<td>5</td>
<td>44</td>
<td>6</td>
<td>R</td>
<td>Y</td>
<td>85</td>
<td>150</td>
</tr>
</tbody>
</table>

In all cases, writer’ cramp affected the whole hand.
*Severity from Fahn.37

Units of Botulinum toxin A (Dysport).
Sx, symptom; All, all tasks.
each individual, $d_a$ was calculated for four temporal conditions (200, 225, 275, and 300 msec), modalities (auditory and tactile), and side of stimulation (left or right). Each modality was tested separately between groups comparing the magnitude of change (large vs. small; 50-msec vs. 25-msec change) with time (early vs. late; 200 and 225 msec vs. 275 and 300 msec).

RESULTS

The results of the auditory and tactile domains for the patients with writers’ cramp and their nonmusician controls are described first, followed by the results of the auditory and tactile conditions for the patients with musicians’ cramp and their controls.

There were no significant differences between sides in either the auditory or tactile domains (all $F$ values were less than 2.46, not significant [n.s.]). Therefore, the factor of sides (left and right) were combined and were no longer considered a factor in the remaining analyses.

Writers’ Cramp: Auditory and Tactile Domains

For the patients with writers’ cramp and their nonmusician controls, in both modalities, there were two significant main effects: magnitude of change (large changes were more detectable than small), and time (early changes were more easily detected than late changes; Table 3). There were, however, no significant group effects or group interactions in either sensory domains.

Musicians’ Cramp: Auditory and Tactile Domains

For both auditory ($F_{(1,14)} = 2.49; \text{n.s.}$) and tactile domains ($F_{(1,14)} = 1.14; \text{n.s.}$) there were no significant group differences between musicians without dystonia and nonmusicians; therefore, the two control groups were combined to increase statistical power. All subsequent analyses compared musicians’ cramp patients and controls, irrespective of musical training.

Patients with musicians’ cramp were also investigated to ensure that the type of instrument these patients played did not have an influence. There were no significant differences within the musicians’ cramp patients: guitarists and pianists with focal dystonia were not different in either the auditory ($F_{(1,6)} = 0.69; \text{n.s.}$) or tactile domains ($F_{(1,6)} = 0.68; \text{n.s.}$). Thus, the type of instrument played by these patients did not significantly affect their perceptual abilities.

<p>| TABLE 3. Significant main effects for patients with writers’ cramp and non-musician controls |
|-----------------------------------------------|-----------------------------------------------|</p>
<table>
<thead>
<tr>
<th></th>
<th>Auditory</th>
<th>Tactile</th>
</tr>
</thead>
<tbody>
<tr>
<td>Main effects</td>
<td>$F_{(1,8)}$</td>
<td>$P$</td>
</tr>
<tr>
<td>Magnitude</td>
<td>45.71</td>
<td>&lt;0.01</td>
</tr>
<tr>
<td>Large</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Small</td>
<td>0.88</td>
<td></td>
</tr>
<tr>
<td>Time</td>
<td>49.85</td>
<td>&lt;0.01</td>
</tr>
<tr>
<td>Early</td>
<td>1.64</td>
<td></td>
</tr>
<tr>
<td>Late</td>
<td>1.10</td>
<td></td>
</tr>
</tbody>
</table>
Auditory Domain

There were significant main effects for magnitude of change and for time (Table 4). Large and early changes were more detectable than small and late changes, respectively. There were also two group interactions: an interaction between time and group (F(1,22) = 6.62; P < 0.05) and a significant three-way interaction between magnitude of change, time, and group (F(1,22) = 9.65; P < 0.01). These findings are described below, with the groups examined separately.

First, the time by group interaction was investigated. For patients with musicians’ cramp, there was a significant main effect of time (F(1,7) = 20.65; P < 0.01). That is, when the target stimulus arrived early (d = 2.33), it was discriminated better than when the stimulus came late (d = 1.30). The controls showed no significant effect of time (F(1,15) = 0.37; n.s.; Fig. 2).

The second interaction investigated was the time by magnitude of change by group. The interaction was investigated by analyzing the groups separately. Patients with musicians’ cramp showed a significant time by magnitude of change interaction (F(1,7) = 14.96; P < 0.01). For large temporal differences, patients had a large deficit in discriminating late stimuli compared to early stimuli (t(1,7) = 3.66; P < 0.01; mean difference = 1.13; Fig. 3). Patients also had a smaller early/late difference in the small changes (t(1,7) = 4.27; P < 0.01; mean difference = 0.76). In contrast, there was no magnitude of change interaction (F(1,15) = 0.20; n.s.) for the controls. This significant pattern of results was the same when only comparing the musicians with and without dystonia.

Tactile Domain

In the tactile domain, there were also two significant main effects: magnitude of change and time (Table 4). There was also a significant two-way interaction between time and group (F(1,22) = 4.51; P < 0.05). The interaction was investigated by separate analyses for patients and controls. As shown in Figure 4, for patients with musicians’ cramp, there was a significant main effect of time (F(1,7) = 12.94; P < 0.01) such that when the target stimulus arrived early (d = 1.61), it was discriminated better than when the stimulus came late (d = 1.15). There was no time effect for the controls (F(1,15) = 0.37; n.s.).

TABLE 4. Significant main effects for patients with musicians’ cramp and controls (musicians and non-musicians)

<table>
<thead>
<tr>
<th></th>
<th>Auditory</th>
<th>Tactile</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>F(1,22)</td>
<td>P</td>
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<tr>
<td>Main effects</td>
<td>69.31</td>
<td>&lt;0.01</td>
</tr>
<tr>
<td>Magnitude</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Large</td>
<td>2.32</td>
<td>0.93</td>
</tr>
<tr>
<td>Small</td>
<td>1.31</td>
<td>0.72</td>
</tr>
<tr>
<td>Time</td>
<td>11.11</td>
<td>&lt;0.01</td>
</tr>
<tr>
<td>Early</td>
<td>2.11</td>
<td>1.40</td>
</tr>
<tr>
<td>Late</td>
<td>1.52</td>
<td>1.13</td>
</tr>
</tbody>
</table>

DISCUSSION

There were no group interactions between musician controls and nonmusicians, only a general finding that
occurred in both sensory domains, with larger changes being better discriminated than smaller changes. Whereas it may have been expected that musicians would be significantly better than nonmusicians in a sequential timing task, this was not the case.\textsuperscript{34,35} It is possible there is a general timing mechanism common to all, irrespective of musicianship.\textsuperscript{39} Alternatively, any advantage that musicians have may be related to production of music rather than perception (although Billon and Semjen\textsuperscript{40} did not show any relationship for musical training and production).

For the patients with writers’ cramp, large changes were more easily discriminated than small changes. Furthermore, changes that came early were also easier to discriminate than late changes; these effects are consistent with previous research.\textsuperscript{41,42} Compared to controls, in this sequential timing task, we found no evidence to suggest that patients with writers’ cramp were in any way different. The sequential task in the current study involved richer temporal cues than paired stimuli.\textsuperscript{20,22} In the context of a more structured time frame, patients with writers’ cramp may have benefited from the enhanced cues. This is, however, unlikely because musicians who were highly trained for musical/temporal structures were unable to make use of such enhancement. Therefore, patients with writers’ cramp may have temporal timing deficiencies only for paired but not for sequential stimuli. It should also be noted, however, that in a post hoc analysis, combining all nonmusicians (n = 13) and comparing them with patients with writers’ cramp (n = 5), there was a nonsignificant trend in the same direction as shown by the patients with musicians’ cramp.

In contrast to the patients with writers’ cramp, patients with musicians’ cramp showed significant differences compared to controls in discriminating stimuli that occurred very early (200 msec after the fifth stimulus) and very late (300 msec after the fifth stimulus; Figs. 3 and 4). For the musicians with dystonia, the early stimuli were more easily discriminated compared to the late stimuli. The late stimuli were also not as easily discriminated compared to the controls. The overall timing differences in patients with musicians’ cramp occurred in both sensory domains and the results are consistent with the thesis of a general timing problem that is not confined to the symptomatic domain.

We offer two speculative explanations that are based on anatomical evidence of possible timing mechanisms and on a cognitive model of time processing (pacemaker model \textsuperscript{13,43}). The basal ganglia have been implicated in both perceiving time and producing movements; dysfunction of these nuclei has also been associated with dystonia.\textsuperscript{18,44–49} Any functional damage to the nuclei of the basal ganglia may alter the perceptual abilities of patients with focal dystonia. In the case of patients with writers’ cramp, timing differences appeared only in a limited context (paired stimuli, compared to patients with musicians’ cramp, sequential stimuli).

Within the basal ganglia, a likely place for the relevant functional changes is the striatum. The putamen appears to be active in learned skilled activity, whereas the neurons of the anterior striatum are more active in the acquisition of new activities.\textsuperscript{50} Although normally operating in parallel with the cerebellum,\textsuperscript{51} damage to the putamen may alter the firing rate and synchrony of these pathways such that the putamen fires earlier than expected or opens a timing “gate” too early (see the cognitive pacemaker model of time processing\textsuperscript{13,43}). Either eventuality will result in an advantage in detecting early stimuli, but the mismatch between the timing networks of the basal ganglia and the cerebellum may result in a reduced ability to perceive stimuli that occur later than expected as demonstrated by the results of the musicians with dystonia.

Alternatively, the differential effects of the early and late stimuli for the patients with musicians’ cramp may be a result of a deficiency in time estimation. That is, if the estimation of time in patients with dystonia is somehow extended, the temporal epochs for early and late stimuli will no longer be equal. Stimuli that occur early have a larger temporal difference and, hence, generate a larger signal than stimuli that occur late and, therefore, are easier to detect. The same applies for the late stimuli,
only the signal and pattern are in the opposite direction. In the basal ganglia, damage to the GPi may account for this time estimation error. The GPi is thought to be the “integrand” of time according to the pacemaker model, and dysfunction of the GPi has been suggested as a possible cause of focal dystonia. Therefore, if there is an imbalance (overactivity or lack of inhibition) of the GPi, the ability to integrate time and, thus, estimate time is impaired.

In conclusion, differences in patients with writers’ cramp have been demonstrated with previous studies using paired stimuli; however, there was no evidence for deficiencies with the sequential stimuli used in this study. In contrast, the deficient time estimation or time differences found with the patients with musicians’ cramp have been demonstrated with previous studies using paired stimuli; however, there was no evidence for the prefrontal and neocerebellar cortex to time perception. Cogn Brain Res 1998;7:15–39.

REFERENCES