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Sonification of arm movements
in stroke rehabilitation:
a novel approach in neurologic music therapy

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1 Summary

Sonification of arm movements in stroke rehabilitation: a novel approach in neurologic music therapy

Daniel S. Scholz

Stroke is one of the leading causes of disabilities worldwide, and the number of affected patients per year and country is increasing due to the societies growing older. Rehabilitation of stroke patients remains a challenge, although currently several new training programs are being investigated, all aiming at an improved efficiency and sustainability of rehabilitation effects. Some traditional rehabilitation programs lack general acceptance by patients, due to high demands on the patients' cooperation, which sometimes may be perceived by patients as frustrating. Yet, even the well established standard physiotherapeutical approaches do not unambiguously provide evidence of efficacy when it comes to improvement of skilled motor behavior. Therefore there is an urgent need for innovative, patient motivating, goal directed and efficient training programs in stroke rehabilitation.

Sonification stands for the usage of non-speech audio conveying otherwise not audible information. The first sonification device was the Geiger-Müller counter which detects electromagnetic radiation and communicates a decay by a click sound. In this thesis, stroke patients arm movements in a predefined three dimensional space were sonified. Sonification was then applied to develop and to incorporate musical retraining for the arm affected by the stroke.

The first experimental study was conducted in order to examine and validate the effectiveness of a certain type of sonification for a later application in stroke rehabilitation. To date, no established sonification-supported rehabilitation protocol strategy exists. Therefore a computer program was developed, the “SonicPointer”, to sonify participants' computer mouse movements in real-time with complex tones. Tone characteristics were derived from a parameter mapping, invisible and unbeknown to the participants, which was overlaid on the computer screen. In each trial, a target tone was presented and subjects were
instructed to indicate its “origin” with respect to the overlaid parameter mappings on the screen as quickly and accurately as possible with a mouse click. Due to the participants' ignorance of the parameter map on the screen, only implicit learning over a series of trials led to an increase in accuracy in this task. One of the aims of the study was to find out how sonification parameters should be mapped in space optimally. Twenty-six elderly healthy participants were tested with this device. Generally, subjects' localizing performance was better on the tone pitch axis as compared to the tone brightness axis. Furthermore, the learning curves were steepest and participants were fastest when pitch was mapped onto the vertical and brightness onto the horizontal axis, suggesting that this is the optimal constellation for this two-dimensional sonification.

In the second experimental study presented herein we applied the previously acquired optimal sonification mapping in a newly developed musical sonification therapy designed to retrain gross-motor functions. Four stroke patients were included in this clinical pre-post feasibility study and were trained with the musical sonification therapy. Patients' upper extremity functions and their psychological states were assessed pre and post training with numerous standardized motor function tests, assessments and neuropsychological questionnaires. The four patients were subdivided into two groups. Both groups received nine days of musical sonification therapy (MG) or a sham sonification movement training (CG). The only difference between the training protocols was that in the CG no sound was played back at the patients. During the training, patients started by exploring the acoustic effects when moving their affected arm in a predefined three-dimensional space. The training proceeded with increasingly complex tone sequences leading to the patients playing simple melodies only by moving their impaired arms in the 3D space. The two MG patients improved in nearly all motor-function tests after the training. Also they reported to be less impaired by the stroke. The two CG patients did not benefit noticeably from the movement training.

Since the second feasibility study yielded promising results, - although with limited statistical power,- a third clinical musical sonification therapy study was run. The setup was basically the same as in experiment two but this time 25 stroke patients were trained and tested. An advanced 3D analysis of the arm movement smoothness was developed and
included into the pre post-test battery. The 15 MG patients showed significantly reduced joint pain in the Fugl Meyer Assessment as compared to the control-group after the musical sonification training. They also reported a trend to have an improved hand function on the Stroke Impact Scale.

Summarizing the results of the experiments presented in this thesis it can be concluded that the mapping of sounds in space is crucial for the outcome and a musical sonification can be applied as a promising stroke rehabilitation tool. Of course the number of patients investigated is limited and further evaluation and research is necessary. Furthermore, different motor tests should be included in future research in order to prevent floor and ceiling effects.
Zusammenfassung

Sonifikation von Armbewegungen in der Schlaganfall Rehabilitation: ein innovativer Ansatz in der neurologischen Musik Therapie

Daniel S. Scholz


2 Introduction

Stroke

Stroke is a major cause of mortality and morbidity in both the developed and developing world. It is a focal neurological deficit resulting from disruption of the cerebral blood supply. There are two main types of stroke, ischemic stroke, which comprises 80 percent of cases, and hemorrhagic stroke that accounts for about 20 percent of cases (Black et al., 2015). In Germany stroke is one of the most common disorders with an estimated 200,000 first events and 66,000 recurrent events in 2008 (Wiedmann et al., 2014).

Cardioembolism is the most frequent etiology of stroke (25.6%). It is particularly common in the elderly (those aged > 70 years) and is associated with an adverse outcome, a low rate of early stroke recurrence, and frequent use of thrombolytic therapy and intravenous anticoagulation. Large-artery atherosclerosis (20.9%), which is the most common cause of stroke in middle-aged patients (those aged 45 to 70 years), shows the highest male prevalence, highest rate of early stroke recurrence, and the highest prevalence of previous transient ischemic attack. Risk factors are amongst others current smoking, and daily alcohol consumption among all subtypes. The highest prevalence of hypertension, diabetes mellitus, hypercholesterolemia, and obesity is found in small-vessel disease (20.5%), which, in turn, is associated with the lowest stroke severity and mortality (Grau et al., 2001).

Neuroinflammation is one of the predominant mechanisms of secondary progression of brain injury following stroke and is far from being well understood (Worthmann et al., 2010).

Clinically, impairments of motor control of the upper limbs are frequent consequences of stroke. Opheim et al., 2014 describe the prevalence and the severity of upper-limb spasticity during the first year after stroke and analyzed sensorimotor function, pain, reduced range of motion, and sensibility in persons with and without spasticity. Spasticity was present in 25 % of the patients at day three and in 46 % after twelve months. In most patients with spasticity, the severity increased during the first year after stroke. Spasticity appeared first in the elbow
flexors and later in the elbow extensors and the wrist flexors. The patients with spasticity had significantly worse sensorimotor function and more pain, reduced joint range of motion, and reduced sensibility. Spasticity developed in almost half of the assessed patients, and the severity of spasticity increased over time. Of course spasticity and impairments related to spasticity, such as pain and limitation in joint range of motion, influence upper extremity function negatively.

Concerning the rehabilitation of deficits following stroke, the World Health Organization stresses the need to collect high quality longitudinal data on rehabilitation and to improve the comparability between studies. This implies using all the information available and transparent reporting. Sauzet et al., 2015 for example investigated the quality of reported or planned randomized controlled trials on rehabilitation post-stroke with a repeated measure of physical functioning. They came to the conclusion that improvements of research methods are still needed. This holds especially for the analysis of longitudinal trials in post stroke rehabilitation. Here, it is important to maximize the use of collected data and improve comparability between studies. Although numerous training approaches have been designed, addressing different aspects of sensory-motor rehabilitation, data on effectiveness derived from prospective randomized trials are still scarce and implementation especially of novel motivating therapies is needed.
In what might be termed conventional physiotherapy, numerous training approaches have been designed, addressing different aspects of sensory-motor rehabilitation. For example, intensive practice of the disabled arm leads to a clear improvement, which is even more pronounced when the unimpaired limb is immobilized. However, this constraint-induced movement therapy (CIMT, Taub et al., 1999), – albeit efficient (Hakkennes and Keating, 2005; Peurala et al., 2012; Stevenson et al., 2012) – is not always very motivating and may even lead to increased stress and thus sometimes fails to improve the mood and the overall quality of life of patients due to the nature of the intervention (Pulman et al., 2013). Veerbeek et al., 2014) conducted a systematic review to provide an update of the evidence for stroke rehabilitation interventions in the domain of Physical Therapy (PT). Therein strong evidence was found for significant positive effects of thirteen interventions related to gait, eleven interventions related to arm-hand activities (see Figure 2.1), one intervention for ADL, and three interventions for physical fitness. Summary Effect Sizes (SESs) ranged from 0.17 (95% CI = [0.03-0.70]; I(2)= 0%) for therapeutic positioning of the paretic arm to 2.47 (95% CI = [0.84-4.11]; I(2)= 77%) for training of sitting balance. They found strong evidence that a higher dose of practice is better, with SESs ranging from 0.21 (95% CI = [0.02-0.39]; I(2)= 6%) for motor function of the paretic arm to 0.61 (95% CI = [0.41-0.82]; I(2)= 41%) and for muscle strength of the paretic leg. Neurological treatment approaches to training of body functions and activities showed equal or unfavourable effects when compared to other training interventions. They concluded that there is strong evidence for physical therapy interventions favoring intensive high repetitive task-oriented and task-specific training in all phases poststroke. But the effects of these trainings are mostly restricted to the actually trained functions and activities.
Figure 2.1. Summary effect sizes for physical therapy interventions – arm-hand activities. Legend: A green colored diamond indicates that the summary effect size is significant, while a blue colored diamond indicates that the summary effect size is nonsignificant; CI, Confidence Interval; CIMT, Constraint-induced movement therapy; EMG-BF, Electromyographic biofeedback; EMG-NMS, Electromyography-triggered neuromuscular stimulation; GHS, Glenohumeral subluxation; HSP, Hemiplegic shoulder pain; mCIMT, modified Constraint-induced movement therapy; NA, Not applicable; NMS, Neuromuscular stimulation; TENS, Transcutaneous electrical nerve stimulation. (From Veerbeek et al., 2014; doi:10.1371/journal.pone.0087987.g003)

<table>
<thead>
<tr>
<th>Intervention</th>
<th>Comparisons (n) / Patients (N)</th>
<th>$i^2$ (%)</th>
<th>Hedges’ g (95%CI)</th>
<th>Power</th>
</tr>
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<tbody>
<tr>
<td><strong>Outcomes: arm-hand activities</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Therapeutic positioning arm</td>
<td>NA</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Reflex-inhibiting/immobilization</td>
<td>NA</td>
<td></td>
<td></td>
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<tr>
<td>All-splints</td>
<td>3 / 180</td>
<td>0</td>
<td>0.050</td>
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<tr>
<td>Techniques and devices GHS</td>
<td>NA</td>
<td></td>
<td></td>
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<td>Bilateral arm training</td>
<td>10 / 417</td>
<td>40</td>
<td>0.061</td>
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<td>Original CIMT</td>
<td>1 / 222</td>
<td>0</td>
<td>0.927</td>
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<tr>
<td>High-intensity mCIMT</td>
<td>16 / 348</td>
<td>11</td>
<td>0.676</td>
<td></td>
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<tr>
<td>Low-intensity mCIMT</td>
<td>16 / 337</td>
<td>41</td>
<td>0.697</td>
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<td>Robotics—unilateral shoulder-elbow</td>
<td>10 / 261</td>
<td>0</td>
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<td>Robotics—bilateral elbow-wrist</td>
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<tr>
<td>Robotics—shoulder-elbow-wrist-hand</td>
<td>NA</td>
<td></td>
<td></td>
<td></td>
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<td>Mental practice with motor imagery</td>
<td>15 / 246</td>
<td>63</td>
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<td>Mirror therapy</td>
<td>4 / 104</td>
<td>0</td>
<td>0.252</td>
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<td>Virtual reality training</td>
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<td>0</td>
<td>0.098</td>
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<td>NMS wrist/finger extenders</td>
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<td>70</td>
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<td>2 / 41</td>
<td>13</td>
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<td>NMS shoulder</td>
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<td>0.971</td>
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<td>EMG-NMS wrist/finger flexors/extensions</td>
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<td>22</td>
<td>0.284</td>
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<td>TENS</td>
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<td>EMG-BF</td>
<td>5 / 102</td>
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<td>Trunk restraint</td>
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<td>0</td>
<td>0.056</td>
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<td>Interventions somatosensory functions</td>
<td>12 / 286</td>
<td>0</td>
<td>0.308</td>
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</tbody>
</table>

| **Outcomes: motor function arm** | | | | |
| Therapeutic positioning arm | NA | | | |
| Reflex-inhibiting/immobilization | NA | | | |
| All-splints | 5 / 205 | 68 | 0.066 |
| Techniques and devices GHS | 4 / 140 | 20 | 0.162 |
| Bilateral arm training | 9 / 274 | 80 | 0.281 |
| Original CIMT | NA | | | |
| High-intensity mCIMT | 4 / 50 | 67 | 0.097 |
| Low-intensity mCIMT | 15 / 333 | 39 | 0.087 |
| Robotics—unilateral shoulder-elbow | 17 / 327 | 0 | 0.343 |
| Robotics—bilateral elbow-wrist | 4 / 62 | 0 | 0.341 |
| Robotics—shoulder-elbow-wrist-hand | 2 / 36 | 75 | 0.053 |
| Mental practice with motor imagery | 11 / 149 | 20 | 0.164 |
| Mirror therapy | 3 / 112 | 52 | 0.434 |
| Virtual reality training | 6 / 158 | 0 | 0.183 |
| NMS wrist/finger extends | 2 / 47 | 84 | 0.053 |
| NMS wrist/finger flexors/extensions | 2 / 41 | 0 | 0.527 |
| NMS shoulder | 2 / 32 | 33 | 0.219 |
| EMG-NMS wrist/finger extenders | 3 / 48 | 0 | 0.398 |
| EMG-NMS wrist/finger flexors/extensions | 2 / 31 | 0 | 0.315 |
| TENS | NA | | | |
| EMG-BF | 2 / 65 | 0 | 0.280 |
| Trunk restraint | NA | | | |
| Interventions somatosensory functions | 4 / 170 | 51 | 0.716 |
Alternatively, training programs using playful interactions in video games (Joo et al., 2010; Hijmans et al., 2011; Neil et al., 2013) point at the possibility to utilize multisensory visual-motor-convergence in order to improve motor control. Again, these rehabilitation strategies, although more motivating and sometimes more effective, have not yet gained wide acceptance in rehabilitation units. Lohse et al. (2014) conducted a meta-analysis in which 26 studies were included. For body function outcomes, there was a significant benefit of virtual reality therapy (VR) compared to conventional therapy (CT) controls (G=0.48, 95% CI=[0.27, 0.70]), and no significant difference between virtual environments (VE) and commercial gaming (CG) interventions (P=0.38). For activity outcomes, there was a significant benefit of VR therapy, (G=0.58, 95% CI=[0.32, 0.85]), and no significant difference between VE (see Figure 2.2) and CG interventions (P=0.66). For participation outcomes, the overall effect size was (G=0.56, 95% CI=[0.02, 1.10]).
Figure 2.2. Activity outcomes in virtual environment (VE) studies. The funnel plot (top) for activity outcomes showing effect-sizes (G) as a function of precision (standard error) in each virtual environment study. The forest plot (bottom) shows the effect-sizes and 95% confidence intervals for each study and the summary effect-size from the random-effects model. Positive values show a difference in favour of VE therapy. Negative values show a difference in favour of CT. Abbreviations: RE, random effects.
(From Lohse et al., 2014; doi:10.1371/journal.pone.0093318.g004)
Music therapy

Schneider et al. (2007) demonstrated the efficacy of a music-supported stroke rehabilitation training utilizing a MIDI-drum-set and a MIDI-piano (Altenmüller et al., 2009). Stroke patients with some remaining abilities to move the arm and the fingers were instructed to play simple tunes on either instrument. The researchers could convincingly demonstrate that auditory-sensorimotor circuits, established via such a music supported therapy (MST) promotes beneficial neuroplasticity in stroke patients (Rojo et al., 2011; Amengual et al., 2013). The only constraint of MST was that it was mainly designed to retrain fine-motor skills on MIDI instruments and did not provide continuous real time feedback of the more frequently impaired proximal upper limb muscles.
Sonification

Sonification is the usage of non-speech audio to represent information, which is otherwise not audible (Kramer et al., 1999). The first sonification device was the Geiger-Müller counter which detects electromagnetic radiation and communicates a decay by a click sound. The general idea of the research in this thesis was to use auditory information supplementary to visual feedback in order to inform patients about movements of their impaired arms. The next step was to apply this type of sonification to develop an innovative sonification supported gross-motor music therapy.

In order to find the most effective and intuitive musical sonification therapy, it is important to clarify how movements in different spatial dimensions should best be musically mapped in space. Dubus and Bresin (2013) reviewed 60 sonification research projects and found in most of them verticality to be associated with pitch. However, for example in pianists, pitch is associated with horizontality. Walker (2007) developed an influential framework for sonification. He found that three design decisions are critical when applying sonification. First, it is crucial which sound dimension should represent a given data dimension. Second, an appropriate polarity for the data-to-display mappings needs to be chosen. Third, the scaling of the mapping has to be carefully adjusted to the respective needs. Fine motor movements of the fingers require a different scale of sound mapping as compared, for example, the sonification of gait.

Several preliminary studies used sonification in motor control and investigated the perception of movements (i.e. Scheef et al., 2009). Schmitz et al. (2013) found that sonifying breast stroke swimming movements led to more precise perceptual judgments of movement velocity. They concluded that sonification of movements amplifies the human action observation system including subcortical parts of the motor loop. Thus sonification may be an important method to enhance training and therapy effects in neurological rehabilitation. Chen et al. (2006) developed a real-time, multi-modal feedback system for stroke rehabilitation. This sonification system was tested with stroke patients and showed promising results (Wallis et al., 2007). However, in this sonification design music was only a passive byproduct of the arm movements of the participants. In contrast, we developed a musical
sonification therapy to train the stroke patients to play music with their affected upper extremity. Thus, we hope to be able to use the beneficial effects of music on neuroplasticity to facilitate the recovery after a stroke (Rojo et al., 2011). Since in other studies repetitive exercise was proven to be effective our training is of repetitive nature too (Taub et al., 1999; Stevenson et al., 2012). We hypothesize that the auditory cues provided by the sonification may make multimodal associative learning possible where otherwise mere visual and motor learning would have taken place. After evaluating an optimal two-dimensional sonification mapping in experimental study one (Scholz et al., 2014) the three-dimensional musical sonification therapy is presented herein in study two and three (Scholz et al., 2015). With the musical sonification therapy introduced we broaden the scope to train stroke patients from an earlier stage on, when still suffering from gross motor dysfunction compared to the music supported therapy introduced by Schneider et al. (2007). Musical sonification did contribute to the motivation of the patients also due to its playful and positive emotional character. It also improved parts of motor control, maybe also because potentially lost proprioception might have been substituted by the auditory real-time feedback of the patient’s arm movements.
3 Manuscript I

Sonification as a possible stroke rehabilitation strategy
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Laboratory work:
Liming Wu: 30 %, Jonas Pirzer: 30 %, Johann Schneider: 30%, Daniel S. Scholz: 10 %

Evaluation:
Daniel S. Scholz: 60 %, Michael Großbach: 30 %, Eckart O. Altenmüller: 10 %

Scientific writing:
Daniel S. Scholz: 60 %, Eckart O. Altenmüller: 20 %, Michael Großbach: 10 %, Jens D. Rollnik 10 %
Abstract

Despite cerebral stroke being one of the main causes of acquired impairments of motor skills worldwide, well-established therapies to improve motor functions are sparse. Recently, attempts have been made to improve gross motor rehabilitation by mapping patient movements to sound, termed sonification. Sonification provides additional sensory input, supplementing impaired proprioception. However, to date no established sonification-supported rehabilitation protocol strategy exists.

In order to examine and validate the effectiveness of sonification in stroke rehabilitation, we developed a computer program, termed “SonicPointer”: Participants' computer mouse movements were sonified in real-time with complex tones. Tone characteristics were derived from an invisible parameter mapping, overlaid on the computer screen. The parameters were: tone pitch and tone brightness. One parameter varied along the x, the other along the y-axis. The order of parameter assignment to axes was balanced in two blocks between subjects so that each participant performed under both conditions. Subjects were naive to the overlaid parameter mapping and its change between blocks. In each trial a target tone was presented and subjects were instructed to indicate its origin with respect to the overlaid parameter mappings on the screen as quickly and accurately as possible with a mouse click. Twenty-six elderly healthy participants were tested. Required time and two-dimensional accuracy were recorded. Trial duration times and learning curves were derived. We hypothesized that subjects performed in one of the two parameter-to-axis–mappings better, indicating the most natural sonification.

Generally, subjects' localizing performance was better on the pitch axis as compared to the brightness axis. Furthermore, the learning curves were steepest when pitch was mapped onto the vertical and brightness onto the horizontal axis. This seems to be the optimal constellation for this two-dimensional sonification.
4 Manuscript II

Moving with Music for Stroke Rehabilitation: A sonification feasibility study

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Laboratory work:
Sönke Rohde: 70 %, Daniel S. Scholz: 20 %, Jens D. Rollnik: 10 %

Evaluation:
Daniel S. Scholz: 60 %, Michael Großbach: 30 %, Eckart O. Altenmüller: 10 %

Scientific writing:
Daniel S. Scholz: 60 %, Eckart O. Altenmüller: 20 %, Michael Großbach: 10 %, Jens D. Rollnik: 10 %
**Abstract**

Gross-motor impairments are common after stroke, but efficacious and motivating therapies for these impairments are scarce. We present a novel musical sonification therapy especially designed to retrain gross-motor functions. Four stroke patients were included in a clinical pre-post feasibility study and were trained with our sonification training. Patient's upper-extremity functions and their psychological states were assessed pre and post training. The four patients were subdivided into two groups. Both groups received nine days of musical sonification therapy (music group, MG) or a sham sonification training (control group, CG). The only difference between the training protocols was that in the CG no sound was played back. During the training the patients in the beginning explored the acoustic effects of their arm movements. At the end of the training the patients played simple melodies by moving their arms. The two patients in the MG improved in nearly all motor-function tests after the training. They also reported in the stroke impact scale which assesses well-being, memory, thinking and social participation to be less impaired by the stroke. The two patients in the CG did benefit less from the movement training. Taken together a musical sonification may be a promising therapy for impairments after stroke.
5 Manuscript III

Sonification of arm movements in stroke rehabilitation – a clinical trial

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Laboratory work:
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Daniel S. Scholz: 60 %, Eckart O. Altenmüller: 20 %, Michael Großbach: 10 %, Jens D. Rollnik: 10 %
Abstract

Gross-motor impairments are common after stroke, but efficient and motivating therapies for these impairments are scarce. We present an innovative musical sonification therapy especially designed to retrain patients' gross-motor functions. Sonification should motivate patients and provides additional sensory input informing about relative limb position. Twenty-five stroke patients were included in a clinical pre-post study and took part in the sonification training. The patients' upper extremity functions, their psychological states and their arm movement smoothness were assessed pre and post training. Patients were randomly assigned to either of two groups. Both groups received an average of ten days (M = 9.88; SD = 2.03; 30min/day) of musical sonification therapy (music group, MG) or a sham sonification movement training (control group, CG), respectively. The only difference between the two protocols was that in the CG no sound was played back during training. In the beginning, patients explored the acoustic effects of their arm movements in space. At the end of the training, the patients played simple melodies by coordinated arm movements. The 15 patients in the MG showed significantly reduced joint pain ($F = 19.96, p < 0.001$) in the Fugl Meyer Assessment after training. They also reported a trend to have improved hand function in the Stroke Impact Scale as compared to the control group. Movement smoothness pre and post intervention was compared in MG patients and found to be significantly better (effect size $r = 0.293$) after the therapy. Taken together, musical sonification may be a promising therapy for motor impairments after stroke but further research is required since estimated effect sizes point to moderate treatment outcomes.
5.1 Introduction

Stroke is a major cause of mortality and morbidity in both the developed and developing world (Black et al., 2015). In Germany stroke is one of the most common disorders with an estimated 200,000 first events and 66,000 recurrent events in 2008 (Wiedmann et al., 2014). The World Health Organization stresses the need to collect high quality longitudinal data on rehabilitation and to improve the comparability between studies (Sauzet et al., 2015). The rehabilitation of stroke patients remains a challenge although there are currently several new training programs under development that aim at improved efficiency and sustainability of stroke rehabilitation (Lohse et al., 2014). Some of the traditional rehabilitation programs lack general acceptance by patients, due to the required endurance and high demands on the patients’ cooperation, which sometimes is perceived as a frustrating experience (Pulman et al., 2013). Yet, even the well established standard physiotherapies do not unambiguously provide evidence of efficacy when it comes to improvement of skilled motor behaviour (Hakkennes and Keating, 2005; Peurala et al., 2012; Stevenson et al., 2012). Therefore there is an urgent need for innovative, motivating, and goal-directed training protocols in stroke rehabilitation.

In this article we present an innovative approach to rehabilitation by retraining the gross-motor functions of the affected upper limbs using musical sonification. In an earlier clinical feasibility study (Scholz et al., 2015) we showed how a musical sonification therapy could be applied. The herein presented data where obtained with this method from a larger number of patients. Sonification stands for the usage of non-speech sound representing otherwise not audible information (Kramer et al., 1999). One of the first sonification devices was the Geiger-Müller counter which detects electromagnetic radiation and communicates a decay by a click sound. In the present study, arm movements were translated into sound. In two earlier studies we demonstrated the efficacy of a music-supported stroke rehabilitation training utilizing a MIDI-drum-set and a MIDI-piano (Schneider et al., 2007; Altenmüller et al., 2009). Stroke patients with some residual abilities to move the arm and the fingers were
instructed to play simple tunes (nursery rhymes or folk songs) on either instrument. We could show that auditory sensorimotor circuits, established via this form of music supported therapy (MST) promotes beneficial neuroplasticity in stroke patients (Rojo et al., 2011; Amengual et al., 2013). One of the few constraints of MST was that it was mainly designed to retrain fine-motor skills on MIDI instruments and did not provide continuous real time feedback for the in early rehabilitation stages more frequently impaired gross-motor functions of the arm. A real-time movement feedback may be very beneficial since it informs the patients about the way they move not only whether they hit the goal or not. With the musical sonification therapy presented here, patients repeatedly train movements with their affected arm in a predefined space. They form associations of their relative arm-position in space and the corresponding sound at this specific position. In the end, they play familiar melodies by moving their arm. This musical sonification therapy therefore broadens the scope to train stroke patients from an earlier stage on, when still suffering from gross motor dysfunction. Musical sonification will not only contribute to the motivation of the patients due to its playful and positive emotional character. It also may improve motor control, since potentially lost proprioception might be substituted by auditory real-time feedback of the patient's arm movements. There are several preliminary studies with healthy participants applying non-musical sonification in motor control and the perception of movements (Scheef et al., 2009; Schmitz et al., 2013; Schmitz et al., 2014). Schmitz et al. found that sonifying breast stroke swimming movements led to more precise perceptual judgments of movement velocity. They showed that sonification of movements amplifies the human action observation system indicated by more pronounced fMRI connectivity patterns between the activation peaks of the left superior and medial posterior temporal regions with the basal ganglia, the thalamus and frontal regions for movement congruent sonification stimuli. Thus, sonification may be an important method to enhance training and therapy effects in neurological rehabilitation. Chen et al. developed a real-time, multi-modal feedback system for stroke rehabilitation (Chen et al., 2006). This sonification system was tested with stroke patients and showed promising results (Wallis et al., 2007). However, in that sonification design music was only a passive byproduct of the arm movements. That means participants did not play with the sonification sound intentionally. They moved their arms and harmonic music progressions were then played back to them. In contrast to that, we developed a
musical sonification therapy to train stroke patients to explicitly and consciously play music through intended movements of their affected upper extremity. Thus, we hope to be able to use the beneficial effects of music on neuroplasticity to facilitate the recovery after stroke (Rojo et al., 2011). Since in other studies repetitive exercise has been proven to be effective (Taub et al., 1999; Stevenson et al., 2012), our training is of repetitive nature, too. We hypothesize that the auditory cues provided by the sonification may make multimodal associative learning possible where otherwise mere visual and motor learning would have taken place. We assume that patients will benefit in their rehabilitation process from guided attention, necessary concentration and long-term motivation to play music. After having evaluated an optimal two-dimensional sonification mapping (Scholz et al., 2014), we now present a more detailed analysis of our three-dimensional musical sonification therapy with a larger sample (Scholz et al., 2015).
5.2 Materials and Methods

Patients
Twenty-five inpatients at the BDH neurological rehabilitation hospital in Hessisch-Oldendorf, Germany, participated after giving informed consent. They suffered from a moderate impairment of motor function of the upper extremity after stroke. Inclusion criteria were (a) patients had to have residual function of the affected extremity (i.e. the ability to move the affected arm and the index finger without help from the healthy side). Furthermore, (b) an overall Barthel Index higher than 50. (c) Patients had to be right-handed. (d) Patients with other neurological or psychiatric disorders were excluded.

Patients were pseudo-randomly assigned to the experimental or to the control group by the supervisor of the study who was not the experimenter. The experimental group received conventional physiotherapy plus in average ten days of a musical sonification training (music group, MG henceforth).

The control group (CG) also received conventional physiotherapy plus a sham sonification movement training with exactly the same movements required as in the sonification study, but with no sound being played back. All patients were German native speakers. The study was approved by the Ethics Review Board of the Hannover Medical School (MHH).

Evaluation of Motor Functions, stroke impact, and movement smoothness

Procedure. Patients were tested pre and post training with a battery of clinical motor function tests and a psychological questionnaire. The test battery consisted of (a) the upper extremity part of the Fugl Meyer Assessment (FMA), which is still considered the gold standard in assessing motor recovery after stroke (Crow and van der Wel, 2008; Woodbury et al., 2008). (b) The Action Research Arm Test (ARAT) which assesses upper limb functioning by using observational methods and collecting behavioural data (Platz et al., 2005; Nijland et al., 2010). (c) The Box and Block Test (BBT) to assess unilateral gross manual dexterity (Canny et al., 2009; Chen et al., 2009). (d) The Nine-Hole Pegboard Test (NHPT) which measures finger dexterity (Grice et al., 2003), and (e) the Stroke Impact Scale (SIS) to assess
the health status following a stroke including sub-scales for emotional well-being, memory, thinking and social participation (Duncan et al., 2003; Lin et al., 2010). Movement smoothness data were recorded via inertial sensors (Xsens, X-MB-XB3) and a custom made computer program. It took approximately one hour to complete the test battery.

**Sonification Training**

*Training.* After the pretests the patients received either an average of ten days ($M = 9.88; SD = 2.03$) of musical sonification training (MG), or ten days of sham sonification training (CG), following the same protocol as MG but with loudspeakers switched off. The sessions lasted 30 minutes per day. The whole procedure followed a standardized protocol to train gross-motor functions of the affected right upper extremity in a repetitive manner. To get acquainted with the sonification system and the acoustic effects produced by their own arm movements, patients first had to freely move their arm in a three-dimensional sonification space, a wooden cubic frame of 51 centimetres side length, confined by four vertical beams in the corners of the bottom board (Fig. 5.1). The beams were labelled with the note pitches; the board was subdivided into nine labelled fields for ease of instructions.
Figure 5.1. shows the 3D Space defined by a wooden frame in which the patients moved their arm. Pitch was mapped onto the y-axis ranging from c\textsuperscript{''} (256 Hz) at the bottom to a\textsuperscript{'} (440 Hz) at the top, brightness was mapped onto the x-axis from the left (dull) to the right (bright), and volume onto the z-axis being louder when closer to the patient and less loud further away. Positions in the x-z plane were labelled with numbers 1 through 9 to instruct patients where to carry out the exercises.

Movement sonification was implemented so that upward movements resulted in an ascending C-major scale from c\textsuperscript{''} (256 Hz, in Helmholtz pitch notation) to the sixth interval a\textsuperscript{'} (440 Hz). Horizontal movements in this space resulted in a change in brightness of sound (see legend of Figure 5.1 for details), and movements along the z-axis manipulated the volume level of the sonification output. After a first exploration phase to allow for implicitly learning the rules of the musical sonification, more complex exercises followed, demanding incremental degrees of difficulty: At the beginning of each training session patients had to play four upward and downward legato c major scales at position 1 (Figure 5.1). The same exercise was then repeated at positions 2, 3, 7 and 9. These exercises were followed by playing musical intervals by moving their arm faster but as precisely as possible, from c\textsuperscript{'} to d\textsuperscript{'}, from c\textsuperscript{'} to e\textsuperscript{'}, from c\textsuperscript{'} to f\textsuperscript{'}, from c\textsuperscript{'} to g\textsuperscript{'}, and from c\textsuperscript{'} to a\textsuperscript{'}.

This exercise was repeated four
times at position 1 and then likewise at positions 2, 3, 7 and 9. The final goal of the training was to teach patients to play several simple nursery rhymes or other familiar tunes only by moving their affected right arm in the three-dimensional sonification space.

The experimenter gave verbal instructions for the training procedure. Additionally, the experimenter pointed at the visual cues written at the positions on the wooden frame of the 3D space (Fig. 5.1). When playing the melodies, patients could read the required “coordinates” from a sheet provided. All melodies were played vertically, i.e. along the y-axis, at position 1 (Fig. 5.1). Tones could be repeated by dipping the hand horizontally in one direction while maintaining vertical position. Patients always moved their impaired arms by themselves. Arm movements were never guided nor physically supported by the experimenter.

Patients’ arm movements were sonified in real-time via two small inertial sensors (Xsens, X-MB-XB3) placed at the wrist and the upper arm of the affected limb. These sensors sent a continuous data stream of acceleration, rotation, and gravity via Bluetooth to a Laptop. Data were recorded for later evaluation, and the spatial information of the arm movements in 3D space were mapped and sonified at the same time. The parameters of this mapping were pitch on the y-axis (ranging from c’ = 226.6 Hz at the bottom to a’ = 440 Hz at the top, in Helmholtz pitch notation), timbre on the x-axis (modelled by varying the number and amplification of overtones in the sound synthesis; SynthesisToolKit – STK; Scavone and Cook, 2013; from dull = clarinet sound at the very left, to saxophone in the middle and at the very right a bowed instrument = bright), and volume on the z-axis (sounds increased in loudness from proximal to distal). The only difference in the training procedure for the sham sonification group (CG) were the muted playback system. Otherwise, exactly the same exercises were carried out during the training sessions.
Data analysis

Statistical analysis was conducted using R (http://www.r-project.org, version 3.2.1) in RStudio Server (http://www.rstudio.com, version 0.99.467). Data of the motor function tests and the Stroke Impact Scale were collected. Motor test and questionnaire data were preprocessed and tested whether it fulfilled the assumptions to calculate ANCOVAs. Pretest results of the patients were used as covariate to prevent the potential post treatment group differences being caused by pre existing pre training group differences. We controlled for inhomogeneous regression slopes of the groups by applying the Johnson-Neyman technique (Kowalski et al., 1994) where appropriate.

Arm movement data were collected and transformed into Cartesian coordinates using the inertial sensors and a custom made computer program. Three-dimensional movement trajectories from one task (four upward and downward legato c major scales) at one position on the board (“Position 1”) were manually selected and Butterworth lowpass filtered (cut-off 8 Hz) to eliminate tremor movements. Movement smoothness was calculated (Osu et al., 2011) and compared between pre and post therapy sessions (Signed Rank Test).
5.3 Results

Motor tests

The main results of this study are depicted in Table 5.1. The music group patients showed a significantly higher improvement (see Figure 5.2) compared to the control group in the subscale FM.J of the Fugl-Meyer Assessment ($F = 19.96$, $p < 0.0002$). This means music group patients showed reduced joint pain after the training. The ANCOVA group comparisons for ARAT, BBT, NHPT were non significant.

![Region of significance](image)

**Fig 5.2.** Johnson-Neyman corrected ANCOVA of the Fugl-Meyer Joint Pain subscale results. The regression lines were non-parallel [$F(1,4) = 21.23$, $p < 0.05$], resulting in significant differences between pre and post rehabilitation scores for subjects reaching a score < 20 in the pre test (see confidence interval).
**Stroke Impact Scale**

The Stroke Impact Scale total value was also significantly higher for the music group as compared to the control group after the training ($F = 4.63, p < 0.0445$). But after correcting for the random group difference prior to the training there was no more pretest : group interaction to be found. The subscale SIS.7 showed a trend ($F = 4.278, p < 0.0552$) towards better hand function of the music group patients after the training. All other ANCOVA group comparisons were non significant.
Table 5.1: ANCOVA group comparison results for the motor tests and the stroke impact scale. Abbreviations: ARAT, Action Research Arm Test; BBT, Box And Block Test; NHPT, Nine Hole Pegboard Test; FM, Fugl-Meyer Assessment; SIS, Stroke Impact Scale. Significant group differences are indicated by *p < 0.05 and ** p < 0.001.

<table>
<thead>
<tr>
<th>Test (Pretest : Group Interaction)</th>
<th>Sum Sq</th>
<th>Mean Sq</th>
<th>F value</th>
<th>Pr (&gt;F)</th>
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<tbody>
<tr>
<td>ARAT</td>
<td>6.635</td>
<td>6.635</td>
<td>0.1102</td>
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<td>BBT</td>
<td>0.7481</td>
<td>0.7481</td>
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<td>1694</td>
<td>2.206</td>
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<td>FM.A.D</td>
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<td>0.01179</td>
<td>0.9146</td>
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<td>0.8866</td>
<td>1.641</td>
<td>0.2155</td>
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<tr>
<td>FM.I</td>
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<td>1.775</td>
<td>0.363</td>
<td>0.5536</td>
</tr>
<tr>
<td>FM.J</td>
<td>48.61</td>
<td>48.61</td>
<td>19.96</td>
<td>0.0002**</td>
</tr>
<tr>
<td>SIS (total)</td>
<td>2091</td>
<td>2091</td>
<td>4.63</td>
<td>0.0445*</td>
</tr>
<tr>
<td>SIS.1</td>
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<td>69.03</td>
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<td>159.3</td>
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<td>48.42</td>
<td>0.1189</td>
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<td>0.4477</td>
</tr>
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<td>39.39</td>
<td>39.39</td>
<td>0.1303</td>
<td>0.7229</td>
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<tr>
<td>SIS.7</td>
<td>878</td>
<td>878</td>
<td>4.278</td>
<td>0.0552</td>
</tr>
<tr>
<td>SIS.8</td>
<td>833.5</td>
<td>833.5</td>
<td>0.8634</td>
<td>0.3666</td>
</tr>
<tr>
<td>SIS.9</td>
<td>207.4</td>
<td>207.4</td>
<td>0.8629</td>
<td>0.3667</td>
</tr>
</tbody>
</table>
Arm movement smoothness

Movement data from two MG patients could not be retrieved due to technical failure of the recording system. For the remaining 13 patients, trajectory smoothness was derived and shown to have improved after therapy \( V = 88; \ p < 0.001; \) effect size \( r = 0.293 \), (Kerby, 2014); see Fig. 5.3]


5.4 Discussion

The results of this clinical sonification study show that a musical sonification therapy may be a promising new way of treating motor impairments after stroke. Musical sonification therapy may even improve psychological well-being after stroke. The patients of the musical sonification group improved significantly compared to the movement training group in the Fugl-Meyer subscale assessing joint pain. They also showed a trend to regain a better hand function in the Stroke Impact Scale after the training. And movement smoothness pre and post intervention was found to be significantly better after the therapy in the MG. In addition to the motor domain, the Stroke Impact Scale assesses the emotional state of the patient, memory and social participation. In contrast, the patients of the control group, receiving only a “sham“ movement training without musical feedback improved very little and non-significantly in some of the tests. Thus we assume that the musical aspect plays an important role in the sonification therapy. However, in this study we did not control whether it is the musical aspect of sonification or just any sound information provided by the sonification. Furthermore, different motor tests should be included in future research in order to prevent floor (Nine-Hole Pegboard Test) and ceiling effects (Action Research Arm Test) which were found in some of the tests in this study. Of course, as we only present a small clinical trial with limited statistical power, results need to be verified with a larger group of patients.

The novel aspect of our approach is that we encouraged the patients in the musical sonification group to actively play and create music by moving their arms. This way, music was not only a byproduct of e.g. a grasping motion. Instead, movements resembled more a novel musical instrument patients were starting to play. This musical instrument was sometimes compared to a Teremin by professional musicians. Hence, our sonification training was designed to resemble a music lesson rather than shaping a movement during sound playback. Furthermore, we used musical stimuli such as a musical major scale with discrete intervals and timbre parameters derived from the sound characteristics of acoustical musical instruments, as opposed to the in the sonification community widely used sound
mappings where tone pitch is scaled continuously and rather artificial sounds are applied (Dubus and Bresin, 2013). The main idea underlying our hypothesis was that participants could improve control of arm positions in space via associative learning, leading to associating a given relative arm position with a specific musical sound. This sound-location association may then substitute the frequently declined or even lost proprioception. Additionally, the arm movement trajectories from outset to the target point were audible as well. Thus, multi-modal learning might have taken place because patients received sound as an additional parameter supplying information. One could speculate that this multi-modal learning could help to close the sensorimotor loop, which may be affected by the stroke.

In view of the clinical application, reduced gross motor functions of the arm and reduced proprioception are common disabilities in stroke patients (Sacco et al., 1987). Hence, the advantages of continuous real-time musical feedback are obvious: the therapy therefore aims at retraining gross motor movements of the arm, which are the most disabling challenges in early rehabilitation of stroke. Second, real-time sonification may substitute deficits in proprioception of the arm, which frequently are a consequence of stroke.

Finally, this form of therapy is highly motivating and could thus enhance motor functions and the emotional well-being in some patients. Maybe through the creative, playful character of this musical sonification device (Koelsch, 2005; Eschrich et al., 2008; Koelsch, 2009; Bood et al., 2013).

Taken together, we have developed and tested a novel musical sonification therapy in a group of patients, supporting learning effects in auditory sensory-motor integration. Now, multi-modal learning of spatial, motor, auditory, and proprioceptive information in rehabilitation of arm motor control in stroke patients needs to be evaluated in a larger multi-centred representative randomized controlled clinical trial.
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5.5 References


6 Comprehensive Discussion

For the current thesis the aim was to develop and test a musical sonification therapy. Therefore first a computer program was developed to test basic principals of how to design a specific musical sonification. Dubus and Bresin (2013) reviewed 60 sonification research projects and found that only in a marginal number of them the sonification mappings had been carefully assessed in advance. This review therefore stressed the need for validation of sonification parameter mappings as conducted in the present first experimental study. The results of this “Sonicpointer” study were, first: participants become faster in finding the target when pitch is being mapped onto the vertical movement axis and brightness is being mapped onto the horizontal movement axis. Second, they learn to accurately pinpoint an auditive target on screen best with this mapping. Third, pitch as an auxilliary localization parameter is generally learned better and localisation is more precise than with brightness. Pitch is the more effective mapping in both conditions. Brightness is only learned well when being mapped onto the horizontal movement axis.

The results found in that first “Sonicpointer” study were then transferred and applied in two clinical studies. In those we showed that a musical sonification therapy may be a promising new way of treating motor impairments after stroke. Musical sonification therapy may even improve psychological well-being in stroke patients. The 15 patients in the musical sonification group showed reduced joint pain in the Fugl Meyer Assessment after the training, compared to the control group. And they showed a trend to having improved hand function in the Stroke Impact Scale. They also improved in some of the motor-function tests and in some other parts of the Stroke Impact Scale, which assesses additionally to the motor domains the emotional state of the patient, memory and social participation. And movement smoothness pre and post intervention was found to be significantly better after the therapy in the MG. In contrast the patients of the control-group, the mere movement therapy group, benefited less from their training.
The new and innovative aspect of this approach is that we encouraged the patients in the musical sonification group to actively play and create music by their arm movements. This way, music is not only a passive byproduct of a motion or some physical parameter. Instead, movements resembled more a novel musical instrument, often compared to a teremin by musicians, which the patients were starting to play. Hence, our sonification training was designed to resemble a music lesson rather than shaping a movement during sound playback. Furthermore, we used a new approach by introducing musical stimuli such as a musical major scale with discrete intervals and timbre parameters derived from the sound characteristics of acoustical musical instruments.

One of the key ideas was that participants could improve control of arm positions in space via associative learning, leading to associating a given relative arm position with a specific musical sound. This sound-location association could have substituted the frequently declined or even lost proprioception, which could unfortunately not be properly assessed because the clinical tests applied were not sensitive enough. Additionally, the trajectories while moving their arms to the target point were audible as well. Thus multi-modal learning could have taken place because patients received sound as an additional parameter supplying information.

Currently a clinical sonification trial is run in which a further developed sonificator is used with a new and very promising audio design. We aim to replicate our earlier findings and to also advance the musical sonification therapy aesthetically so as to make the therapeutic experience for the patients as pleasant as possible.
6.1 References


Affidavit

I herewith declare that I autonomously carried out the PhD-thesis entitled “Sonification of arm movements in stroke rehabilitation: a novel approach in neurologic music therapy”. No third party assistance has been used. I did not receive any assistance in return for payment by consulting agencies or any other person. No one received any kind of payment for direct or indirect assistance in correlation to the content of the submitted thesis. I conducted the project at the following institution: Institute of Music Physiology and Musicians' Medicine, Hanover University of Music, Drama and Media. The thesis has not been submitted elsewhere for an exam, as thesis or for evaluation in a similar context.

I hereby affirm the above statement to be complete and true to the best of my knowledge.

(place, date)  (signature)
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