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Faculteit Geneeskunde en Levenswetenschappen

master in de revalidatiewetenschappen en de kinesitherapie

Masterthesis

An overview of neural networks involved in learning auditory sequences and/or musical sequences during a motor performance

Inneke Huion
Marit Putzeys

Eerste deel van het scriptie ingediend tot het behalen van de graad van master in de revalidatiewetenschappen en de kinesitherapie

PROMOTOR :
Prof. dr. Peter FEYS

COPROMOTOR :
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An overview of neural networks involved in learning auditory sequences and/or musical sequences during a motor performance

‘Which neural networks are involved in learning auditory sequences and/ or musical sequences during a motor performance (such as playing an instrument, finger tapping)?’

Highlights:

- Common involved areas during auditory-motor learning involve the premotor area, cerebellum, superior temporal gyrus, parietal area, frontal gyrus and cingulate area.
- The activated brain regions are task-specific.
- Musicians and non-musicians have structural brain differences that must be considered during future research.
- Learning rates can be predicted and are dependent of the task.

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Marit Putzeys

Promotor: Prof. dr. Peter Feys

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Context

This master thesis situates in the broader topic of neurological rehabilitation. The importance of this thesis is the determination of alternative or improved rehabilitation methods in neurological populations, more precise people with Multiple Sclerosis (PwMS). MS is a progressive autoimmune disease that affects the myelin of the central nervous system. Balance disorders and cognitive impairment are common symptoms of MS and can have a high impact on the daily life. PwMS require a lifelong rehabilitation, therefore patient compliance is an important target factor. Music can be motivating while exercising.

The master thesis is part of a PhD study of Lousin Moumdjian named “Effect of musical biofeedback system on cognitive and motor functions in multiple sclerosis”. The PhD project (2016-2020) is funded and conducted in University of Ghent and by the University of Hasselt (BOF). This project aims to investigate the effect of systematic musicology on motor functions, perceived fatigue, and cognitive functions in PwMS. In this review, we investigated auditory and/or musical sequence, thereby fitting in the PhD project.

This thesis is a duo-master thesis under supervision of promotor prof. dr. Peter Feys and copromotor Lousin Moumdjian at the research centre REVAL of the University of Hasselt in Diepenbeek.

A central format was applied for this literature review. The literature search and writing of the review was done by the two students together. The students defined the research question together with copromotor Lousin Moumdjian and promotor Peter Feys.

Part two of the master thesis will take place at REVAL Diepenbeek. An existing protocol will be used provided by Lousin Moumdjian. This protocol was supplemented and refined by the students. This trial will take place next year. The aim will be to investigate the effects of learning motor sequences with auditory feedback on in PwMS. This thesis was possible due to a good cooperation of both students and with Lousin Moumdjian.

Part 1: Overview of the literature

1. Abstract

1.1 Objective

The aim of this review was to investigate the neural networks that are involved in learning auditory sequences and/ or musical sequences during a motor performance such as playing an instrument and finger tapping.

1.2 Background

There is evidence that brain plasticity can be obtained by music making activities and help overcome neurological impairments.

1.3 Methods

We carried out a systematic search using Web Of Science (WOS) and PubMed. This resulted in 332 articles after removing duplicates. 308 articles were excluded based on abstract. Finally, 17 articles were included in this review according to inclusion criteria. We divided them according to measurement method i.e. (f)MRI, EEG and MEG.

1.4 Results

The literature search resulted in 355 articles, with 16 meeting inclusion criteria for the review. A total of 275 participants were included of which 125 were male (mean 8.38 ± 1.79) and 132 females (mean 8.31 ±1.1). Mostly, fMRI was used as imaging method. MEG and EEG were other imaging methods used in the included studies. Learning tasks included learning to play/reproduce sequences on the piano/keyboard, learning to play a stringed instrument, finger tapping and a finger flexion task. Results from the included studies indicate that most involved areas were found in the frontal and parietal lobule. More precisely, depending on the task the frontal gyri/cortex, the premotor area, the temporal gyri etc. were commonly involved.

1.5 Discussion and conclusion

While learning auditory sequences during motor performance, a variety of brain areas are involved. Activity in certain brain areas are task-specific and dependent on the musical experience of the subjects. There seems to be a clear difference between musicians and non-musicians in terms of structural properties and activation patterns of the brain. Furthermore, learning rates can be predicted and are also task-specific.

1. Introduction

Neuroplasticity is an important mechanism in learning; it is the ability of neurons to change their function, chemical profile (quantities and types of neurotransmitters produced), or structure (Lundy-Ekman, 2013). This process comprises long-lasting changes in the strength of synapses between neurons and within neural networks (Lundy-Ekman, 2013). There is a strong link between obtaining motor skills and neural plasticity[1]. Large and diffuse regions of the brain are active during the initial phases of motor learning, as demonstrated by fMRI studies. Normally, by practicing or repeating a task many times, less brain regions become active during execution of this task. In the course of time, when the motor task is learned, only small, apparent regions of the brain show increased activity during execution of the task (Lundy-Ekman, 2013). This results in improved neural efficiency, for example reduced activation for pianists relative to non-pianists was attributed to pianists' greater efficiency of movements within their expanded motor networks [2]. The primary motor cortex plays a crucial role in motor learning as it stores the engram for the learned motor act [3]. Furthermore, individuals strongly differ in their abilities to learn specific skills [4].

Playing a musical instrument is an example of sensorimotor learning, i.e. adjusting motor performance based on auditory feedback. Music performance is characterized by its sequential nature. According to Ruiz[5] this means that "the events (chords, notes or vowels) have to be accurately produced in a specific temporal (serial) order in which the related actions follow each other" [5].
Generally, there is evidence for activation of the primary sensorimotor cortex, the supplementary and presupplementary motor areas and lateral premotor areas in the frontal lobe, the superior temporal gyrus including cortex around the temporo-parietal junction and, subcortically, the basal ganglia and the cerebellum during rhythm production[6]. The temporal structure of the produced rhythm and how rhythm performance is initiated are parameters of importance while looking into brain activity[6].

While studying the plasticity of the human brain, neuroimaging studies confirmed that music making placed unique demands on the nervous system. Consequently, experienced musicians' brain foresees an excellent model for studying neuroplasticity. This is because of the sensory, motor and multimodal integration regions which provide a strong coupling of perception and action [7].
Therefore, there are many differences between musicians and non-musicians, both anatomical and physiological, most of them neurobiological in nature. The primary factor in most of these differences rely on early musical training, continued intensely into adulthood [8]. For example, in professional musicians with absolute pitch, the left planum temporale is relative larger than the right planum temporale. The left planum temporale plays an important role in the processing of complex sounds. Besides that, when comparing keyboard players and non-musicians, differences of gray matter volume in motor, auditory, and visual brain regions were found [9]. In contrast, there is evidence that the rhythmic element of music may activate the sensorimotor network irrespective of musical training experience or listening task differences [10].

There are several methods to investigate the brain activation patterns such as EEG, MEG, or fMRI. These non-invasive imaging methods are widely used to investigate functional connectivity and to

locate brain areas. In fMRI, Blood-Oxygen-Level Dependent (BOLD) contrast measurements are used to determine changes in brain activity. Measurements of electrical current in the brain are used in both EEG and MEG. EEG uses measurements of extracranial electric fields, while MEG uses magnetic fields [11]. The spatial resolutions of EEG and MEG are about the same [12].

Recent studies provide evidence that music making activities induce brain plasticity to help overcome neurological impairments, i.e. neurodevelopmental disorders and acquired brain injuries [7]. For example, cognitive clinical effects have been observed in the domains of attention, memory, concentration, and learning in stroke patients. These effects are seen after training both passive (listening) and active (producing) music activities as these tasks require cognitive effort[13].

Little is known about the neural mechanisms for serial-order coding during learning of auditory-motor associations in the context of music performance [5]. Also, to this date there is no systematic review on the neural networks involved when learning auditory sequences and/or musical sequences during a motor performance.
The present review focusses on the activated brain regions during movement to learned auditory sequences. We aim to provide an overview of the involved brain regions when musical/auditory sequence learning during a motor performance.

2. Methodology

3.1 Research question

In this review the research question is as followed 'Which neural networks are involved in learning auditory sequences and/or musical sequences during a motor performance?'.
The following PICO summarizes this research question:

P - Adults
I - Learning musical and/or auditory sequences during a motor performance
C - Not applicable
O - Brain imaging

3.2 Literature search

PubMed and Web of Science (Core collection) were used for the literature search.
Relevant articles were identified using the following terms:
(Music OR metronome OR auditory stimuli) AND (learning) AND (movement OR motor function) AND (brain mapping OR brain imaging OR neural pathways OR neuroimaging). This resulted in 289 hits on PubMed and 66 hits on WOS. 332 articles were screened after removal of duplicates. An overview of the used search terms and screened articles can be found in table 1 and figure 1 in the appendix.

3.3 Selection criteria

Studies about adults who underwent brain imagery while/ after/ before learning musical and/or auditory sequences during a motor performance were included (n=16).
Non-English studies, reviews and studies about animals were excluded (n=316). Table 2 further demonstrates an overview of the excluded articles and their reasons. Moreover, figure 1 shows the results of our search method.

3.4 Quality assessment

Because of the inclusion of experimental as well as observational study designs the PEDro scale and STROBE checklist were used for the quality assessment. The checklists are attached in the appendix, figures 2 and 3.

3.5 Data extraction

Data extraction included mainly the experimental procedure, brain imaging protocol and results.
Important data included:

- aim of the study
- design of the study

- number of participants
- age of participants
- characteristics of participants
- musical performance
- experimental instrument
- number of sessions
- imaging techniques
- timepoints of measuring
- imaging protocol/ task in the scanner
- application of the scanner
- brain areas
- behavioural measures
- way of data acquisition

3. Results

4.1 Results study selection

The literature search resulted in 355 articles using WOS and PubMed as databases. Table 1 shows an overview of the used search terms and number of hits within each database. After removal of duplicates 332 articles were left. Screening of the abstracts resulted in exclusion of 308 articles. Finally, 24 articles were screened based on full text. Ultimately, 16 studies were included in this review. Articles were excluded based on predetermined exclusion criteria (Table 2). A detailed flowchart is added in the appendix (Figure 1).

4.2 Results quality assessment

A summary of results of the quality assessment is added in the appendix, tables 3.1 and 3.2 and figures 4 and 5. Both observational (n=9) and experimental (n=7) studies were included.

4.2.1 Observational studies

All included observational studies (n=9) explained the scientific background and rationale for the investigation and specific objectives. For each variable of interest, they gave sources of data and details of methods of assessment and described comparability of assessment methods if there was more than one group. When applicable, all observational studies (n=9) reported numbers of outcome events or summary measures over time or numbers in each exposure category, or summary measures of exposure or numbers of outcome events. In the discussion they also summarised key results with reference to study objectives and gave a cautious overall interpretation of results considering objectives, limitations, etc. All studies (n=9) provided an informative and balanced summary of what was done and what was found in the abstract. Except for one[14], all studies (n=8) clearly defined all outcomes, exposures, etc. and described methods for examining subgroups and interactions. An explanation of how quantitative variables were handled in the analyses and a description of which groupings were chosen and why were given in all studies but one[15]. Additionally, in the same eight studies category boundaries were reported of continuous variables. Only one out of nine studies mentioned a commonly used term in the title or abstract or elsewhere early in the paper to indicate the study's design[16]; explained how missing data were addressed[17]; when applicable, explained how loss to follow-up/ matching of cases and controls was addressed or described analytical methods taking account of sampling strategy[5] and gave reasons for non-participation at each stage[17]. Two studies didn't describe the eligibility criteria, the sources, and methods of selection of participants, case ascertainment and control selection[16, 18]. Four studies reported numbers of individuals at each stage of study[6, 17-19] and discussed limitations of the study[5, 16, 18, 19]. Moreover, four cohort studies summarised follow-up time[5, 17-19]. Seven studies described all statistical methods used [2, 6, 14, 17-20]. Six studies gave unadjusted estimates and, if applicable, confounder-adjusted estimates and their precision (e.g., 95% confidence interval)[2, 5, 6, 14, 16, 19, 20]. Furthermore, five out of nine studies reported other analyses done[2, 6, 16, 17, 20] and gave the source of funding and the role of the funders[5, 6,

[16-18]. Only two out of nine studies gave characteristics of study participants (e.g. demographic, clinical, social) and information on exposures and potential confounders[5, 18]; indicated number of participants with missing data for each variable of interest in the results[17, 18]; gave matching criteria and number of exposed and unexposed or gave matching criteria and the number of controls per case[5, 17]. None of the studies described the setting, locations, and relevant dates, including periods of recruitment, exposure, follow-up, and data collection. Nor did they describe any efforts to address potential sources of bias. They didn't explain how the study size was arrived at and neither used a flow diagram of the participants. Lastly, not one study did a sensitivity analysis and discussed the generalisability (external validity) of the study results.

4.2.2 Experimental studies

When applicable, in all included experimental studies (n=7)[4, 9, 10, 21-24] the groups were similar at baseline regarding the most important prognostic indicators[9, 10, 21-24]. All seven studies provided measures of at least one key outcome from more than 85% of the subjects initially allocated to groups and provided both point measures and measures of variability for at least one key outcome.
Three out of seven studies specified the eligibility criteria[4, 10, 24] and reported the results of between-group statistical comparisons when applicable[9, 21, 22]. Only one study randomly allocated subjects to groups when applicable and/or mentioned[9]. In four studies all subjects for whom outcome measures were available received the treatment or control condition as allocated[9, 10, 22, 24].
When mentioned and applicable none of the studies concealed the allocation and didn't blind all subjects, therapists, and assessors.

4.3 Results data extraction

4.3.1 Participants

A total of 275 participants were included (mean 15.41±1.65) of which 125 were male (mean 8.38±1.79) and 132 females (mean 8.31±1.1). In one study the gender of the participants was unclear [2]. Age ranged from eighteen to forty-six years and all but two [20, 24] participants were right-handed. Fourteen out of sixteen articles used non-musicians or participants with minimal piano/keyboard experience [2-5, 9, 10, 16-19, 21-23]. Five out of sixteen articles included pianists or participants with experience in piano/keyboard performances [2, 17, 19-21]. One article used musicians but without piano experience [24] and in two other articles the musical background was not clear [6, 14]. We assume all participants were healthy although not always explicitly mentioned. However, no pathologies were reported.

4.3.2 Brain imaging

Nine out of sixteen articles used (f)MRI as imaging method[2, 4, 6, 14, 17-19, 22, 23], five out of sixteen used EEG[10, 16, 20, 21, 24] and only two used MEG[5, 9]. Table 5.3 represents an overview of the brain imaging methods used in the included articles, timepoints of measurement, application, brain and behavioral measures, and data acquisition.

4.3.3 Learning task

In twelve out of sixteen studies, the participants learned to play/reproduce sequences on a piano or keyboard[2, 4, 5, 9, 10, 17, 18, 20-24]. In addition, in one study the subjects learned to play a stringed instrument[19]. Finger tapping was also a learning task in two other studies[6, 16]. Lastly, one study used flexion of the right index finger and thumb on the beat of a metronome[14]. Learning was acquired by someone playing the sequence for them, by figuring out the melody line by ear, by visually presented finger sequences, by just listening or by imitating. Auditory feedback was used sometimes compared by visual feedback. Table 5.1 gives an insight on goals of the studies, the learning tasks and duration, participants and their characteristics and the learning. Table 5.2 shows the study aims in detail.
The following section will demonstrate the results for each different task used in the included studies, including learning sequences on the piano, learning to play a stringed instrument, tapping tasks and a finger flexion task. We will present the results per area of activation to get a structured overview. A structured overview can be found in table 6 of the appendices.

4.3.3.1 Learning sequences on the piano

4.3.3.1.1 Frontal lobe

When considering articles that took scans **before** the training sessions began, passively listening to 3 second monophonic piano sequences in Bangert's study[21] lead to increased activation of the frontal area. This area also activated during imagining a familiar song, but the activity was seen more inferior[4]. While imagining this familiar song, the left precentral gyrus also activated, as while only listening to it[4]. The left primary motor area (right hand was used) activated when pressing keys on a soundless piano keyboard in both the map group and no-map group[21]. The map group in this study was the group that was allowed to learn the standard piano key-to-pitch map and in the no-map group

random assignment of keys to tones prevented such a map. Finally, the ventral and dorsal premotor cortex showed increased activation when listening to two 5-note melodies. This was seen bilaterally[18].

Scanning **during** the training period exhibited increased activity of the left frontal area when learning to play random sequences[18].This task also resulted in decreased activity of the right superior frontal sulcus[18]. The right precentral gyrus, the right superior frontal gyrus, the premotor area and the right primary motor cortex showed more activity in musicians compared to non-musicians during sequence trials[2]. The right middle frontal gyrus and the right primary motor cortex also activated when non-pianists played random sequences[2]. When pianists played sequences, the right precentral gyrus, the left middle frontal gyrus and the primary motor cortex activated[2]. The premotor area showed increased activity during both random and sequence trials and the left middle frontal gyrus activated during sequence trials[2]. In the random trials, random keypresses were executed and in the sequence trials sequenced keypresses were executed [2]. When looking into the differences in late compared to early training, the left dorsal cortex of the premotor area and the bilateral ventral cortex of the premotor area showed decreased activation during melody and random playback[18]. Less activity of the right supplementary motor area and the right motor cortex was also seen when playing random sequences. Further, playing a melody resulted in increased orbitofrontal cortex activity[18]. In the study of Bangert et al.[21] the map group showed increased activity of the bilateral lateral frontal cortex while pressing keys on a soundless piano keyboard[21]. This group also showed increased activity of the central sulcus during passively listening to a 3 second monophonic piano sequences and activation lateralized to the left[21]. After five sessions, activity in the right frontotemporal electrodes was also observed for both the auditory and motor task[21]. However, for the motor task, this area activated only on the right[21]. Lastly, increased beta band spectral power was seen in the middle frontoparietal area when comparing alterations of auditory feedback in serial order (ASO) with normal auditory feedback (NAF). Positive clusters were found in theta band right frontoparietal scalp when unrelated auditory feedback (UAF) was given compared to NAF and in beta band left frontal scalp when comparing ASO with UAF[5].

Scanning **after** the training process resulted in decreased activity of the right ventral premotor cortex and increased activity in the dorsal premotor cortex, the right inferior pars opercularis, the dorsolateral prefrontal area and the premotor cortex in general while listening to trained compared to untrained melodies[4, 18]. Listening to trained compared to untrained melodies but the same notes as trained resulted in increased activity of the left posterior premotor cortex, the inferior posterior frontal gyrus (Broca) and the right inferior pars opercularis[23]. Listening to the trained compared to untrained but different notes lead to increased activation of the posterior middle premotor cortex, the posterior inferior frontal gyrus, and the right inferior frontal gyrus[23]. The left pars opercularis activated while listening to trained melodies[23] and the left dorsal premotor cortex activated while listening to trained and untrained melodies[4]. During retrieval of sequences, the dorsolateral prefrontal cortex activated more in musicians than in non-musicians and the primary motor cortex only in musicians[17]. Also, when encoding and replaying visually presented finger sequences the dorsal and medial premotor cortex, bilateral primary motor area and inferior frontal area activated significantly more in musicians[17]. Furthermore, retrieval with auditory feedback resulted in an activated bilateral inferior frontal gyrus and dorsolateral prefrontal cortex for non-musicians but not in musicians or to a lesser degree[17]. However,

in musicians, the premotor cortex activated more compared to non-musicians in this task[17]. Passively listening to 3 second monophonic piano sequences resulted in increased activity of the right frontal area in the map group and in the professional pianists[21]. Lastly, pressing keys on a soundless piano keyboard activated the frontotemporal area, as did passively listening[21].

4.3.3.1.2 Parietal lobe

Scanning the participants **before** the training showed increased activity of the parietal area and the inferior bilateral parietal area while passively listening[18, 21]. The superior parietal area also activated while imagining familiar songs[4].

During training scanning revealed increased activation in the inferior parietal area, right superior parietal cortex and left inferior parietal area in musicians compared to non-musicians when making bimanual keypresses in response to X's presented on a screen[2]. The parietal area also showed increased activation while passively listening in the no-map group, which did not change over the weeks of training[21]. Its activity increased until week three and then decreased when listening passively and while pressing keys on a soundless piano keyboard in the map group[21]. The left primary sensorimotor area activated after five and after ten sessions while passively listening in the map group[21]. However, activity in this area decreased ipsilateral after the first twenty minutes of training in the map group playing the silent piano[21].

Scanning **post-training** showed increased activity in the right inferior parietal area, posterior bilateral intraparietal cortex while listening to trained compared to untrained melodies[4, 18]. Listening to trained compared to untrained different notes activated the bilateral inferior parietal area[23]. The supramarginal and postcentral gyrus also showed increased activation while imagining familiar melodies[4]. When comparing musicians with non-musicians, the primary somatosensory cortex, the bilateral sensorimotor cortex, the bilateral somatosensory cortex, superior and inferior parietal areas showed increased activity while retrieving[17]. The last two also showed increased activity while encoding visually presented finger sequences as did the superior and inferior parietal area in musicians compared to non-musicians[17]. When auditory feedback was combined with the retrieving task, the bilateral primary sensorimotor cortex and the superior and left inferior parietal gyrus were active in musicians but not, or to a lesser degree, in non-musicians[17]. In the map group, activity of the parietal area decreased while passive listening whereas in the no-map group activity in this area increased[21]. In the study of Wu et al.[10], a greater coherence of the left sensorimotor electrode with the right posterior and frontoparietal electrodes was seen after training when listening to tone sequences generated using the same notes as heard in the training paradigm and tone sequences generated using notes of lower pitch[10]. An increase in cortico-cortical task-related coherence between electrodes that cover the sensorimotor network was seen when passively listening to piano tones when comparing pre- to post-training[10]. However, this was not seen when listening to a rhythmic sequence (not piano), which suggested that the training effect was specific for the type of sounds that were associated with action during training[10]. Increased coherence between an electrode over the left sensorimotor cortex with a frontocentral electrode was seen post training for any piano notes heard[10].

The left sensorimotor cortex showed greater activity in the sound-action map group compared to the no-map group when listening to sequences[10]. During the perception of simple rhythm sequences, sound action mapping training did not have an effect on functional connectivity in sensorimotor regions[10]. Schalles et al.[24], showed that listening to a learned song increased suppression of the beta band power over the sensorimotor electrodes. A moderate level of suppression was found for the transposed song and no suppression for the control song was found[24]. The right sensorimotor cortex, contralateral to piano trained hand, exhibited greater beta suppression for musically experienced subjects[24]. Lower levels of mu and beta suppression over the left sensorimotor cortex was seen for subjects who had previous music experience[24].

4.3.3.1.3 Temporal lobe

Listening to two 5-note melodies activated the left Heschl's gyrus and the superior bilateral temporal gyrus in the scanner **before** training proceeded[18]. Further, activity in the primary and secondary auditory cortices increased bilaterally while listening to familiar songs and only the secondary auditory cortex activated while imagining the familiar songs[4].

The scanning **during** training showed increased activity in the inferior temporal gyrus in musicians playing random sequences compared to non-musicians[2]. This area also showed increased activity together with the temporal cortex after five sessions in the map group touching silent piano keys[21]. Theta band activity increased in the inferior temporal gyrus in the UAF condition compared to NAF and in the middle temporal gyrus in the ASO condition compared to NAF. This was seen bilaterally[5].

After the training process, listening to trained melodies compared to not-trained melodies resulted in an activity decrease in the superior temporal gyrus[18]. When listening to short passages from the newly acquired piece and to similar passages from pieces not learned the primary and secondary auditory cortices activated bilaterally[23]. The primary auditory cortex also showed increased activation when comparing musicians with non-musicians while retrieving[17]. The temporal lobe activated bilateral in non-musicians and the temporal area in both musicians and non-musicians while retrieving with auditory feedback. Also, the left Heschl's gyrus activated in musicians while retrieving with auditory feedback[17]. This gyrus also activated in musicians and non-musicians when retrieving but without auditory feedback[17]. Lastly, passively listening activated the temporal area bilateral in professional pianists[21].

Kamiyama[20] and Lappe[9] used mismatch negativity (MMN) to assess cortical plasticity. MMN arises from the primary and secondary auditory cortices so that's why these results will be discussed here. In the study of Kamiyama et al., participants learned to play unfamiliar songs and after training they listened to those melodies during scanning, but ten percent of the tones deviated[20]. The results showed that learning a piece of music by pressing keys induced larger MMN amplitudes compared to training without key pressing during listening to a passage of music[20]. The MMN was also induced in the no-key-press condition but this amplitude was smaller compared to the key-press training[20]. According to Kamiyama et al., this might indicate that the key-press training was more effective than the no-press training[20]. They also conclude that enhancement of auditory memory for learned music

might be caused by the enhanced representation of auditory feedback induced by pressing keys[20]. In the high AP (high score on the absolute pitch test) group, the MMN was most prominent in the middle central and right hemisphere for the key-press condition[20]. The amplitudes were also significantly different between left and right hemispheres but not under the no-key-press condition[20]. In the low AP group, no significant differences in the MMN amplitudes were found for the deviant stimuli between the key-press and no-key press conditions[20]. Laterality was also not significant in both conditions[20]. In the study of Lappe et al., two groups were formed: the sensory-auditory(SA) group learned to play a musical sequence on the piano and the auditory (A) group listened to and made judgements about the music that had been played by the SA group[9]. When listening to a three tone and six tone sequence, the SA group showed a distinct increase in MMN amplitude from pretraining to post-training[9]. On contrary, the A group showed almost no increase in the three-tone condition and only a small increase in the six-tone condition[9]. Enlargement of MMN after training was seen in the SA group when compared to the A group[9]. This reflected greater improvements of musical representations in the auditory cortex after sensorimotor-auditory training[9]. Larger enhancement of MMN occurred also in the SA group after training compared to before[9]. For the SA group, increased MMN was more pronounced in the right hemisphere compared to the left hemisphere for all conditions[9]. It appeared that training was associated with an increase of MMN in the right hemisphere for the three-tone sequence, but almost no effect was seen in the left hemisphere or for the six-tone sequences in either hemisphere[9]. When the sensorimotor system was involved in training, the musical representations in the auditory cortex changed more than when only the auditory system was involved in training[9]. Greater plasticity was seen in the right hemisphere, so they concluded that the plasticity in the auditory cortex was independent of the hand used to learn the motor task[9]. They also showed that greater plastic changes occur when using multimodal sensorimotor-auditory training in non-musicians compared to auditory only training[9].

4.3.3.1.4 Cerebellum

The scanning **before** training revealed increased activity in lobule VI and crus I while listening to familiar songs and imagining familiar songs[4].

During training increased theta band activity was seen in the cerebellum for the ASO and UAF condition compared to the NAF condition. Beta band activity increased in the ASO condition compared to the UAF condition[5].

After training, the left cerebellar area activated more strongly while listening to trained notes compared to untrained different notes[23]. Furthermore, the cerebellum showed increased activation in musicians compared to non-musicians while retrieval happened with auditory feedback. Non-musicians and musicians also showed increased bilateral activity while encoding the finger sequences[17].

4.3.3.1.5 Occipital lobe

When scans were taken **during** training, the right lateral occipital complex showed decreased activation when playing random melodies[18]. Further, the extrastriate region showed increased activity when non-pianists played random sequences[2]. In the **post**-scanning sessions, an increase of activity in the left lobule could also be seen for musicians compared to non-musicians while retrieving with auditory feedback[17]. On the other hand, non-musicians showed increased activity in the occipital area to a greater extent compared to the musicians while carrying out the same task[17].

4.3.3.1.6 Limbic lobe

During training the anterior cingulate cortex's activity increased bilaterally when non-pianists played random sequences[2]. However, in Chen's[18] study, the right anterior and right posterior cingulate gyrus showed decreased activation during random playback when comparing late compared to early training[18]. Also, non-pianists who played sequences showed increased activity of the hippocampus[2]. When comparing musicians with non-musicians, playing sequences activated the left cingulate gyrus more[2]. Increased theta band activity in the ASO condition compared to the NAF condition and beta band activity for the ASO condition compared to the UAF condition was seen in the cingulate gyrus[17].

4.3.3.1.7 Other brain areas

The caudate was seen to be more active during listening to familiar songs before training started[4]. During training this area also activated more strongly in musicians compared to non-musicians[2]. The basal ganglia activated during making bimanual keypresses in response to visual presented Xs[2]. Furthermore, listening to familiar songs resulted in increased activity of the bilateral thalamus[4]. The central area showed increased activation in response to passively listening before training[21]. Also seen during training was an increase in activity of the right retrosplenial cortex in late compared to early training when listening to a melody. Activity in this region decreased over time as a function of learning[18]. Engel et al.[22] found that higher FA (fractional anisotropy) values were related with faster learning of piano melodies. This was observed in the bilateral corticospinal tracts, which is important for execution of voluntary movements, and in the right superior longitudinal fasciculus which is related to audio-motor transformations[22]. The significant cluster had a greater extent in the left hemisphere (contralateral to the right hand which was used in the motor task)[22]. The clusters showing higher FA values in a fast learner were located close to the primary motor and somatosensory cortex[22]. Lastly, retrieving sequences with auditory feedback resulted in greater activity of the insula and putamen when comparing musicians with non-musicians[17]. Schalles et al[24]. showed that beta power is associated with attention and motor processing, so it supported the motor system's activity during covert perception of music one can play and similar musical sequences. A suppression of the beta band relative to baseline and relative to a scrambled melody control was seen while subjects listened to a melody they learned to play and a transposed version of that melody[24]. The engagement of the motor system, indexed by beta suppression, was greater in response to listening to the learned melodies when compared to the transposed version[24]. Mu enhancement was observed in all

conditions[24]. The transposed song lead to a significantly greater mu enhancement compared to the other two conditions[24].

4.3.3.2 Tapping task

4.3.3.2.1 Frontal lobe

Scanning **after** the training process showed increased activation of the left dorsolateral, ventral and mesial premotor cortex during rhythm production[6] .

4.3.3.2.2 Parietal lobe

The intraparietal sulcus, sensorimotor area and pre-sensorimotor area showed increased activity during rhythm production. While tapping to a visual metronome the left angular supramarginal gyrus activated[6]. A higher task-related coherence between the posterior parietal cortex (PPC) and the primary motor cortex (M1) was seen during early compared to late phase sensorimotor training[16]. Facilitation in the PCC-M1 pathway at rest was abolished immediately following sensorimotor training, but returned toward baseline at 30, 60 and 180 minutes after training[16]. However, PPC-M1 interactions became less important and stayed downregulated for a short period beyond training when the new learned sequence was encoded, and the movement became automated[16].

4.3.3.2.3 Temporal lobe

Rhythm production resulted in an increased activation of the temporal-parietal junction and tapping to a visual metronome activated the middle temporal gyrus[6].

4.3.3.2.4 Other brain areas

Rhythm production also resulted in increased activity of the cerebellum, the insular cortex, the motor cingulate area, the globus pallidus and the putamen[6].

4.3.3.3 Learning to play a stringed instrument

4.3.3.3.1 Frontal lobe

After six months of training, the right medial prefrontal cortex and the right inferior frontal gyrus showed decreased activation for the left little finger. Increased activity was seen in the right ventral premotor cortex and the left medial frontal gyrus in the left little finger[19].

4.3.3.3.1 Parietal lobe

Scanning before training showed larger contralateral activation in the sensorimotor cortex in the right little finger than the left little finger movement during repetitive lift-abduction/fall-adduction (LAFA) movement of the little finger[19]. After 6 months of training, increased activation of the inferior Brodmann area and left precuneus was seen for the left little finger[19].

4.3.3.3.1 Temporal lobe

The right anterior superior temporal gyrus and the right posterior middle temporal gyrus showed increased activation for the left little finger and decreased activity was seen in the left middle temporal gyrus. Increased activity was also seen in the middle temporal gyrus for the right little finger[19].

4.3.3.3.1 Other brain areas

The right vermis, middle cingulate gyrus, posterior cingulate gyrus, and substantia nigra showed decreased activation for the left little finger after 6 months of training[19]. For the right little finger, increased activity in the inferior occipital gyrus was observed[19].

4.3.3.4 Finger flexion task

4.3.3.4.1 Frontal lobe

Flexion movements of the right index finger and thumb (by squeezing an air-filled pillow) to an auditory stimulus activated the contralateral precentral gyrus when synchronizing to the beat before and after training[14]. Syncopation (moving off the beat) before training resulted in an increase of activation in the inferior frontal gyrus and the middle frontal gyrus[14]. This was both seen bilaterally. When looking to the scanning after training, the results showed increased activity of the contralateral precentral gyrus during synchronization and of the middle frontal gyrus and the contralateral primary motor cortex during syncopation[14].

4.3.3.4.2 Parietal lobe

Increased activity of the contralateral postcentral gyrus was seen when syncopating to an auditory stimulus[14]. Scanning after training showed increased activation of the right pre-sensorimotor area during syncopation and in the right sensorimotor area during synchronization[14].

4.3.3.4.3 Temporal lobe

During syncopation, the right temporal gyrus showed increased activation[14]. After training, the superior temporal gyrus showed increased activation during synchronization. This was seen bilaterally[14].

4.3.3.4.4 Other brain areas

The cerebellar vermis, the left posterior insula and the bilateral putamen showed increased activity during syncopation[14]. On the other hand, synchronization increased activation in the left insula and the left ventrolateral nucleus[14]. Scanning after training revealed increased activity of the bilateral putamen during both synchronization and syncopation and in the left thalamus during syncopation[14].

5. Discussion

5.1 Reflection on the quality of the studies

More detailed information about strengths and limitations of each study is given in table 4.

Except for one[17], none of the studies report more than 60% of items in the checklists. The 'not-applicable' items must be considered. For example, six studies[4, 10, 14, 19, 20, 24] had only one group, so the items of the STROBE and the PEDro scale about allocation to groups and matching criteria are not applicable. However, these items are important for the quality of the studies.

The sources of data and details of the methods of assessment were reported in all observational studies. 77% described all statistical methods and 88% described methods used to examine subgroups and interactions. Only one[17] observational study addressed missing data.

None of the observational studies addressed potential biases, explained how the study size was arrived at and described the setting, locations, and relevant dates. The studies didn't mention descriptive data of the participants. Only 33% reported limitations of the study. Only 1 study[6] clearly defined the study design and key terms of the design, the other studies often didn't mention the allocation method, blinding method, etc. Translating estimates of relative risk into absolute risk wasn't applicable in these studies.

When applicable the groups of all the experimental studies were similar at baseline regarding the most important prognostic indicators. Measures of at least one key outcome were obtained from more than 85% of the subjects initially allocated to groups and all the experimental studies provided both point measures and measures of variability for at least one key outcome. Eligibility criteria were specified in 43% of the studies.

There wasn't a study where the subjects and therapists were blinded. In such experimental designs blinding of the subjects and therapists isn't possible. Blinding of the assessors would be possible, but it wasn't applied.

5.2 Reflection on the findings in terms of the research question

5.2.1 Task-specific brain regions

Listening, imagining, little finger movements, squeezing movements, key pressing, and rhythmic tapping are divergent tasks. Consequently, not all tasks resulted in the same active brain areas. Learning auditory sequences during movements resulted in activation of the motor areas (i.e. premotor area and primary motor area). Interestingly, after learning an auditory sequence the premotor area activated during imagining the learned sequence[4]. In the study of Lahav et al.[23] the premotor area also activated while listening to the learned sequence. Kim et al.[19], Karabanov et al.[6] and Jantzen et al.[14] used rhythmic auditory stimuli without a melody. Only the temporal gyrus was activated in all three studies[6, 14, 19]. The cerebellum activity decreased in the study of Kim et al.[19] and increased during syncopation in the study of Jantzen et al.[14] During rhythm production of the learned sequence the cerebellum activation also increased[6]. We expected that learning a stringed instrument and learning piano sequences both resulted in greater performance efficiency, so less neurons would be recruited for the given movements. Kim et al.[19] however, used the "maximal efforts without pacing" paradigm. This resulted in new recruitment areas after practicing the stringed instrument[19]. Unfortunately, Kim et al.[19] didn't measure brain activity while playing a stringed instrument. However, we would expect a difference in active brain areas while playing piano versus playing a stringed instrument, because of the specific demands of the different instruments[7].

5.2.2 Training effects

Listening to the trained sequences resulted in training effects of following regions: premotor cortex (i.e. ventral and dorsal), the parietal area (i.e. intraparietal sulcus, right inferior), the superior temporal gyrus, pars opercularis (i.e. right inferior), posterior inferior frontal gyrus (Broca's area), primary and secondary auditory cortex, the left cerebellar area and the lateral prefrontal cortex[4, 18, 23]. These brain regions showed increased activity in contrast to the superior temporal gyrus, which showed decreased activity[18]. It seems that these regions are important for learning auditory sequences. The decreased activity in the superior temporal gyrus suggests that the perceptual representation of a learned auditory-motor melody was developed[18]. The dorsal and ventral premotor cortex form part of the dorsal auditory stream of action processing[18]. To learn a melody on the piano the adequate pitch-to-key pairings need to be selected by activation of the dorsal premotor cortex[18]. Furthermore, the processing of a learned auditory-motor program activates the left ventral premotor cortex[18]. Broca's area also seemed to be of importance because of its mirror neurons and multifunctional role in action listening[23].

Training effects were also reported while playing the trained piano sequences in the study of Chen et al.[18] by a decrease in activation of the right superior frontal sulcus, the right supplementary motor area, the right motor cortex, the lateral occipital complex, the right anterior cingulate cortex, the right posterior cingulate cortex, bilateral ventral premotor cortex and the left dorsal premotor cortex. This decreased activation might imply increased efficiency of neural processing[18]. In contrast, the right retrosplenial cortex and the orbitofrontal cortex showed increased activation when playing the learned

piano sequence[18]. This indicated that neural activity in these regions became progressively less de-activated as a function of learning[18].

Training of synchronization to the beat lead to an increased activation of the contralateral precentral gyrus, middle frontal gyrus, ipsilateral sensorimotor area, bilateral superior temporal gyri and bilateral putamen[14]. On the other hand, syncopation lead to greater activity in the bilateral inferior frontal gyri, bilateral middle frontal gyri, contralateral postcentral parietal gyrus, ipsilateral temporal gyrus, the vermis, the contralateral posterior insular cortex, bilateral caudate, the contralateral premotor cortex, ipsilateral pre-sensorimotor area and the contralateral thalamus[14]. These results suggest that the thalamus, the basal ganglia and the supplementary motor area form a network responsible for precise timing of motor behaviour[14]. This network only activated during syncopation before training[14]. Accordingly, syncopation includes the additional requirement of making movements based on determination of the time between successive stimuli, whilst during synchronization timing information is provided by the external stimulus[14]. In contrast, when looking to post-training effects, no changes were observed in the previously mentioned network during syncopation[14]. The primary auditory area and the anterior insula showed decreased activation following continued exposure to the syncopation task[14]. This may indicate a decrease in attention to auditory stimulation. However, during syncopation the primary auditory cortex and vermis showed increased activation compared to during synchronisation[14]. This might imply an increased awareness of or need for sensory feedback. Practicing syncopation reduces the need to continually monitor behavior in order to maintain a specific performance level and helps to automize behaviour[14].

After six months of practicing a stringed instrument, new activation areas were seen for the left little finger when repetitive ad- and adduction movements were carried out[19]. The precuneus and left inferior parietal lobule are known for multimodal interactions related to praxis, generation of motor plans and spatial attention[19]. They also contain spatiotemporal representations of learned skilled movements[19]. Kim et al.[19] suggests that the motor programs are translated into the appropriate motor output through the premotor cortex. Furthermore, the posterior parietal cortices are strongly connected with both the cingulate gyrus and premotor cortex. This implies their role in mediating the type of sensorimotor and cognitive integration that would be needed for spatial attention. Activity in the posterior sensorimotor area indicates its role for the initiating or executive activity of motor tasks[19]. Another interesting finding is the higher activation of the anterior cingulate gyrus after practice, which is involved in regulation of attention and monitoring of performance[19]. Regions such as the middle and posterior cingulate, right inferior frontal gyrus, prefrontal cortex and basal ganglia are considered to be responsible for inhibition of responses[19].

Bangert et al.[21] used both a passive listening task and a pure motoric task which were components of the original audio-motor task during piano practice. The pure motor task existed of key pressing on a silent piano[21]. Before training, this task resulted in increased activity in the primary motor area in the map group and no-map group[21]. After only twenty minutes of training, the ipsilateral sensorimotor area showed decreased activation and after five training sessions, the bilateral frontolateral cortex, temporal area, the frontotemporal area, and inferior temporal gyrus showed increased activity for the

map group[21]. After training, this motor task still resulted in an increase of frontotemporal activity in the map group[21]. In this study, it seemed that the degree to which a cortex area engages in a certain task was decreased by practice[21]. They suggested that the right anterior network was mainly to process the sequential order of pitch patterns[21]. The right anterior networks are of major importance for perceptual processing, memory, and imagery of pitch sequences[21].

In the study of Karabanov et al.[6] participants learned finger tapping in two rhythms, where one rhythm was presented visually and the other auditory. This activated the left dorsolateral, ventral and mesial premotor cortex, the intraparietal sulcus, sensorimotor area, the pre-sensorimotor area, the temporoparietal junction, the cerebellum, the insula, the motor cingulate area, the putamen and the globus pallidus[6]. In this study, four different conditions were used: AA, auditory training, auditory metronome; VV, visual training, visual metronome; VA, visual training, auditory metronome; AV, auditory training, visual metronome[6]. The significant main effect was due to a deactivation in the conditions with an auditory metronome (AA and VA), rather than an activation in the conditions with visual metronome[6]. Frontal motor and premotor areas, superior temporal and parietal regions, the basal ganglia and the cerebellum were active during performance, regardless of training modality and metronome modality[6]. There was no evidence that auditory and visual training of rhythms resulted in anatomically separated modality-specific long-term representations[6]. There was one region found active during all conditions, namely the posterior part of the left temporal gyrus and the inferior parietal cortex around the temporo-parietal region[6]. This region seems to be active in tasks involving auditory-motor integration, e.g. reproduction of melodic stimuli [25], and musical improvisation[26]. They showed that the temporoparietal junction activated in all conditions, including the one where both pacing and training was visual[6].

5.2.3 Auditory feedback

In the study of Ruiz et al.[5], different kinds of auditory feedback were used: alterations of serial order (ASO), normal auditory feedback (NAF) and unrelated auditory feedback (UAF). They showed that the underlying oscillatory sources of processing different kinds of alterations in auditory feedback during sensorimotor learning can be differentiated in both their spatial and spectral content[5]. Respectively, processing UAF or ASO feedback compared to normal feedback generated theta band oscillations in the cerebellum and superior temporal gyrus[5]. The cerebellum seems to play an important role in implicit learning of spectrotemporal information which is essential for sound and speech recognition[27]. Once learned, this information automatically recognizes incoming auditory signals and predicts consecutive information based on previous experience[27]. So, it is plausible that the cerebellum showed increased activation. Furthermore, the superior temporal gyrus comprises the primary auditory cortex which is important for the sensation of sound.

In addition, processing ASO feedback compared to normal feedback activated the cingulate gyrus[5]. Also, beta band oscillatory activity was enhanced in the cingulate cortex and cerebellum by processing ASO[5]. This kind of feedback lead to larger pitch error rates when compared with normal auditory feedback[5]. It seemed to be expected that the posterior cingulate cortex would be active because of its

action- and error-monitoring role. The findings in this study indicated that in the initial phase of sequence learning, dedicated neural mechanisms check the correspondence between sources of auditory and motor information on the serial order of the produced actions[5]. Hence, they contributed to updating of the sensorimotor representations[5]. It seemed that beta oscillations play a role in tracking serial order during initial sensorimotor learning and in updating the sensorimotor mapping of sequential elements[5]. The enhanced frontal theta oscillations following processing of ASO feedback found in Ruiz et al.[5] is in keeping with the interpretation that increased midfrontal theta oscillations play a role in detecting a mismatch between the predicted and actual sensory consequences of the action. There's an association between oscillatory activity in the theta frequency range across medial frontal or cingulate regions and the processing if correct or incorrect feedback signaling an error in the performance[5].

5.2.4 Musicians versus non-musicians

Two[2, 17] out of sixteen studies compared musicians with non-musicians. Mostly, musicians showed greater activity in the investigated brain areas. In contrast, one would expect that musicians recruit neurons with greater efficiency thus exhibiting less activity. The review of Dawson[8] demonstrated comparable conclusions i.e. fewer neurons need to be excited to perform a given motor task. In addition, it is known that musicians have volumetric structural differences opposed to non-musicians in several brain areas[8]. These structural differences are likely the result of adaptations to long-term training and to the specific demands of the learned musical instrument[7].

The differences were mostly seen in activity of the premotor cortex (i.e. dorsal area), parietal cortex (i.e. superior area, inferior area, primary somatosensory cortex, sensorimotor cortex), temporal cortex (i.e. Heschl's gyri), the primary motor cortex (i.e. right area) and dorsolateral prefrontal cortex (see table 6).

The dorsal premotor cortex was more activated in non-musicians[17], because they had to learn associations between sensory stimuli and specific movements[28], i.e. piano tones association with the correct finger movements. Musicians, on the other hand, know already lots of combinations of finger movements and piano tones, they only don't know the exact ones of this study protocol so little activation is possible in the premotor cortex.

Musicians showed greater activity in different regions of the parietal area than non-musicians[2, 17]. The parietal area is also stated to be bigger in musicians[7], so this region is structurally adapted to the learning of piano sequences. Learning piano sequences involves encoding the sequence and retrieving of the learned sequence. Retrieving is a process that relies on different memory functions, i.e. spatial working memory has been associated with parietal areas[29]. Furthermore, it has been suggested that the anterior superior parietal area has an integrating function of multimodal sensory information and a guiding role for motor operations through reciprocal connections with the premotor cortex[8].

The temporal area is also an area that is often structurally adapted to the specific instrument, in this case to playing the piano. Especially the Heschl's gyri were more activated in musicians[2, 17]. The Heschl's gyrus is located in the temporal lobe, specifically in the superior temporal gyrus, and it forms

on the right side the primary auditory cortex[8]. Schneider et al.[30] found in musicians the volume of the Heschl's gyrus to be 130% larger than in non-musicians, with the size being dependent of the musical expertise. This area is important in this topic because of its part in a language- and music-processing network that includes Broca's area, Wernicke's area, the superior temporal sulcus, planum polare, planum temporale, and anterior superior insular cortices[8]. The lateral Heschl's gyrus areas are known to be pitch-sensitive areas, they are sensitive to slower temporal and spectral processing[30]. Interestingly, Pau et al.[17] and Landau et al.[2] found an increased activity of the right primary motor cortex in musicians while bimanually pressing piano keys. The more pronounced right hemisphere activation is possibly due to years of manual motor practice of the nondominant hand, while the dominant hand undergoes some form of fine-motor training since childhood in other daily activities, like writing and other skilled sensorimotor tasks[7]. In the studies of Pau et al.[17] and Landau et al.[2] the participants were right handed.

5.2.5 Predictors of learning rate

Interestingly, there seems to be differences in brain activity that indicate if you will learn something faster or slower than others. More activity in the right auditory cortex and right hippocampus predicted higher learning rates in the listening to familiar melodies condition[4]. In the imagine condition, where they had to listen to a melody with gaps and fill these gaps by imagining, more activity in the lateral caudate, left mid-premotor cortex and right hippocampus predicted higher learning rates[4]. Higher learning rates were also present if participants showed decreased activity in the medial frontal areas and frontal pole for both the listen and imagine condition and in the occipital and precuneus cortex during the imagine condition[4]. Less neural activity in the left dorsal and ventral premotor cortex was associated with better task performance[18]. In the study of Engel et al.[22], where subjects learned to play three short piano melodies, higher fractional anisotropy (FA) values were related to faster learning of piano melodies. This was observed in the bilateral corticospinal tract, which is important for execution of voluntary movements, and in the right superior longitudinal fasciculus which is related to audio-motor transformations[22]. The right corticospinal tract was ipsilateral to the hand used to perform the task[22]. This might have been because of the complexity of the task whereby the ipsilateral motor cortex appears to play an important role[22]. Parts of the superior longitudinal fasciculus are relevant to pitch discrimination and individual differences in pitch learning[22]. It connects premotor areas and the inferior parietal lobe, which area involved in perception-action matching mechanisms and in transforming sounds into actions[22]. Furthermore, this frontoparietal network seems to be involved in auditory piano learning [23] and piano expertise[31]. Certain properties of white matter fiber tract organization may facilitate obtaining audio-motor associations that are necessary for mastering a musical instrument and may reflect a predisposition to instrumental musical ability[22]. Clusters that showed higher FA values were located close to the primary and somatosensory cortex in faster learners[22]. This could be related to the finer control of body movements in subjects that learned the task more easily[22].

5.3 Reflection on the strengths and limitations

Because of the heterogeneity of the protocols in the studies, we couldn't calculate effect sizes or conduct a meta-analysis. For example, the included studies didn’t use the same training period. The length of the training period can result in higher/ lower performance scores and strengthen/ weaken the activation responses in the brain regions. Unfortunately, we have little knowledge of brain imaging and the imaging methods, therefore we experienced some difficulty to write this review. However, we provided a very detailed overview of the activation patterns in the brain. Another strength is our systematic search strategy and clear overview tables. Additionally, we provided a very detailed overview of all included studies with an explanation of the used brain imaging methods, the learning tasks, the investigated brain areas, etc.

5.4 Recommendations for future research

Based on these results, it would be interesting to investigate the effect of auditory-motor learning in populations with brain damage. In the context of this study, we recommend using more delineated inclusion criteria of the tasks and imaging methods used in the studies so effect sizes can be calculated, and a meta-analysis can be conducted. All included studies contained learning tasks that involve the upper extremity, for future research it would be interesting to investigate learning tasks that involve the lower extremity, like walking sequences. To clearly see which neural networks are active, it is most interesting that brain imaging happens before the training, during all training sessions and after training. Lastly, the behavioral measures in the studies are also very interesting to investigate.

6. Conclusion

We conclude that various brain areas are active while learning auditory sequences during a motor performance. Most commonly the premotor area (i.e. ventral and dorsal) seemed to be active or showed decreased activity. This was seen during imagining a trained melody, listening to a trained melody and while playing trained piano sequences. The cerebellum, superior temporal gyrus, the parietal area, frontal gyrus, and cingulate area were also common involved areas. The activation of certain brain areas is dependent of characteristics of the task and the amount of musical experience, so this must be taken into account. Also, of importance is the differences between musicians and non-musicians. Musicians have volumetric structural differences adapted to their specific instrument such as an increased volume of the parietal area and the Heschl's gyrus. Learning rates are dependent of the task and can be predicted for example by more activity of the auditory cortex, hippocampus, etc. Finally, we recommend further investigation of the use of learning auditory sequences in populations with brain damage.

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8. Appendices part 1 – overview of the literature

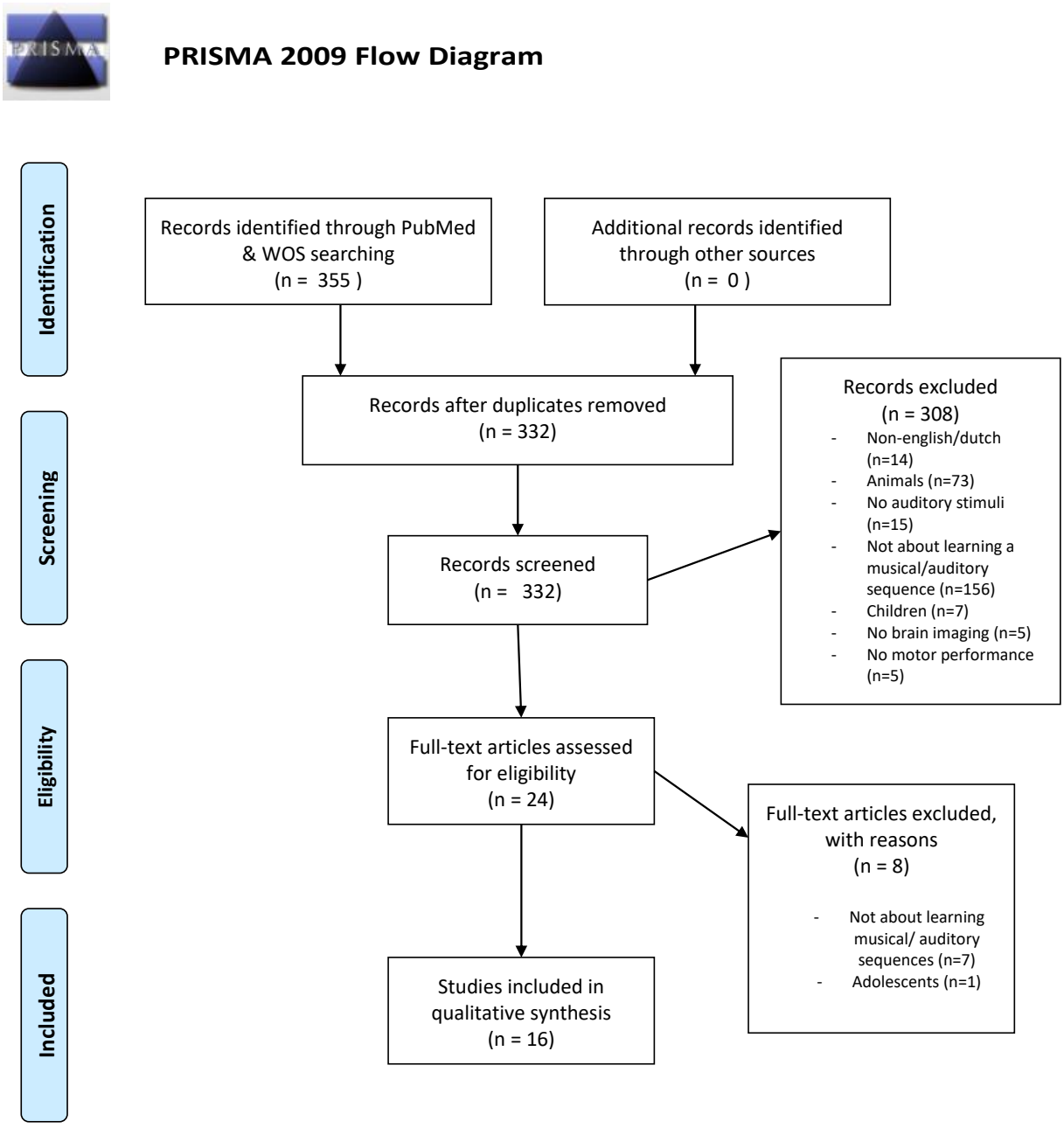

Figure 1: flowchart

From: Moher D, Liberati A, Tetzlaff J, Altman DG, The PRISMA Group (2009). *P*referred *R*eporting *I*tems for *S*ystematic Reviews and *M*eta-*A*nalyses: The PRISMA Statement. PLoS Med 6(7): e1000097. doi:10.1371/journal.pmed1000097

For more information, visit www.prisma-statement.org.

STROBE Statement—checklist of items that should be included in reports of observational studies

	Item No	Recommendation
Title and abstract	1	(*a*) Indicate the study's design with a commonly used term in the title or the abstract
		(*b*) Provide in the abstract an informative and balanced summary of what was done and what was found
Introduction		
Background/rationale	2	Explain the scientific background and rationale for the investigation being reported
Objectives	3	State specific objectives, including any prespecified hypotheses
Methods		
Study design	4	Present key elements of study design early in the paper
Setting	5	Describe the setting, locations, and relevant dates, including periods of recruitment, exposure, follow-up, and data collection
Participants	6	(*a*) *Cohort study*—Give the eligibility criteria, and the sources and methods of selection of participants. Describe methods of follow-up *Case-control study*—Give the eligibility criteria, and the sources and methods of case ascertainment and control selection. Give the rationale for the choice of cases and controls *Cross-sectional study*—Give the eligibility criteria, and the sources and methods of selection of participants
		(*b*) *Cohort study*—For matched studies, give matching criteria and number of exposed and unexposed *Case-control study*—For matched studies, give matching criteria and the number of controls per case
Variables	7	Clearly define all outcomes, exposures, predictors, potential confounders, and effect modifiers. Give diagnostic criteria, if applicable
Data sources/ measurement	8*	For each variable of interest, give sources of data and details of methods of assessment (measurement). Describe comparability of assessment methods if there is more than one group
Bias	9	Describe any efforts to address potential sources of bias
Study size	10	Explain how the study size was arrived at
Quantitative variables	11	Explain how quantitative variables were handled in the analyses. If applicable, describe which groupings were chosen and why
Statistical methods	12	(*a*) Describe all statistical methods, including those used to control for confounding
		(*b*) Describe any methods used to examine subgroups and interactions
		(*c*) Explain how missing data were addressed
		(*d*) *Cohort study*—If applicable, explain how loss to follow-up was addressed *Case-control study*—If applicable, explain how matching of cases and controls was addressed *Cross-sectional study*—If applicable, describe analytical methods taking account of sampling strategy
		(*e*) Describe any sensitivity analyses

Continued on next page

Figure 2: SROBE-checklist

Results		
Participants	13*	(a) Report numbers of individuals at each stage of study—eg numbers potentially eligible, examined for eligibility, confirmed eligible, included in the study, completing follow-up, and analysed
		(b) Give reasons for non-participation at each stage
		(c) Consider use of a flow diagram
Descriptive data	14*	(a) Give characteristics of study participants (eg demographic, clinical, social) and information on exposures and potential confounders
		(b) Indicate number of participants with missing data for each variable of interest
		(c) *Cohort study*—Summarise follow-up time (eg, average and total amount)
Outcome data	15*	*Cohort study*—Report numbers of outcome events or summary measures over time
		Case-control study—Report numbers in each exposure category, or summary measures of exposure
		Cross-sectional study—Report numbers of outcome events or summary measures
Main results	16	(*a*) Give unadjusted estimates and, if applicable, confounder-adjusted estimates and their precision (eg, 95% confidence interval). Make clear which confounders were adjusted for and why they were included
		(*b*) Report category boundaries when continuous variables were categorized
		(*c*) If relevant, consider translating estimates of relative risk into absolute risk for a meaningful time period
Other analyses	17	Report other analyses done—eg analyses of subgroups and interactions, and sensitivity analyses
Discussion		
Key results	18	Summarise key results with reference to study objectives
Limitations	19	Discuss limitations of the study, taking into account sources of potential bias or imprecision. Discuss both direction and magnitude of any potential bias
Interpretation	20	Give a cautious overall interpretation of results considering objectives, limitations, multiplicity of analyses, results from similar studies, and other relevant evidence
Generalisability	21	Discuss the generalisability (external validity) of the study results
Other information		
Funding	22	Give the source of funding and the role of the funders for the present study and, if applicable, for the original study on which the present article is based

*Give information separately for cases and controls in case-control studies and, if applicable, for exposed and unexposed groups in cohort and cross-sectional studies.

Note: An Explanation and Elaboration article discusses each checklist item and gives methodological background and published examples of transparent reporting. The STROBE checklist is best used in conjunction with this article (freely available on the Web sites of PLoS Medicine at http://www.plosmedicine.org/, Annals of Internal Medicine at http://www.annals.org/, and Epidemiology at http://www.epidem.com/). Information on the STROBE Initiative is available at www.strobe-statement.org.

Figure 2: STROBE-checklist

PEDro scale

1.	eligibility criteria were specified	no ❑ yes ❑ where:
2.	subjects were randomly allocated to groups (in a crossover study, subjects were randomly allocated an order in which treatments were received)	no ❑ yes ❑ where:
3.	allocation was concealed	no ❑ yes ❑ where:
4.	the groups were similar at baseline regarding the most important prognostic indicators	no ❑ yes ❑ where:
5.	there was blinding of all subjects	no ❑ yes ❑ where:
6.	there was blinding of all therapists who administered the therapy	no ❑ yes ❑ where:
7.	there was blinding of all assessors who measured at least one key outcome	no ❑ yes ❑ where:
8.	measures of at least one key outcome were obtained from more than 85% of the subjects initially allocated to groups	no ❑ yes ❑ where:
9.	all subjects for whom outcome measures were available received the treatment or control condition as allocated or, where this was not the case, data for at least one key outcome was analysed by "intention to treat"	no ❑ yes ❑ where:
10.	the results of between-group statistical comparisons are reported for at least one key outcome	no ❑ yes ❑ where:
11.	the study provides both point measures and measures of variability for at least one key outcome	no ❑ yes ❑ where:

The PEDro scale is based on the Delphi list developed by Verhagen and colleagues at the Department of Epidemiology, University of Maastricht (*Verhagen AP et al (1998). The Delphi list: a criteria list for quality assessment of randomised clinical trials for conducting systematic reviews developed by Delphi consensus. Journal of Clinical Epidemiology, 51(12):1235-41*). The list is based on "expert consensus" not, for the most part, on empirical data. Two additional items not on the Delphi list (PEDro scale items 8 and 10) have been included in the PEDro scale. As more empirical data comes to hand it may become possible to "weight" scale items so that the PEDro score reflects the importance of individual scale items.

The purpose of the PEDro scale is to help the users of the PEDro database rapidly identify which of the known or suspected randomised clinical trials (ie RCTs or CCTs) archived on the PEDro database are likely to be internally valid (criteria 2-9), and could have sufficient statistical information to make their results interpretable (criteria 10-11). An additional criterion (criterion 1) that relates to the external validity (or "generalisability" or "applicability" of the trial) has been retained so that the Delphi list is complete, but this criterion will not be used to calculate the PEDro score reported on the PEDro web site.

The PEDro scale should not be used as a measure of the "validity" of a study's conclusions. In particular, we caution users of the PEDro scale that studies which show significant treatment effects and which score highly on the PEDro scale do not necessarily provide evidence that the treatment is clinically useful. Additional considerations include whether the treatment effect was big enough to be clinically worthwhile, whether the positive effects of the treatment outweigh its negative effects, and the cost-effectiveness of the treatment. The scale should not be used to compare the "quality" of trials performed in different areas of therapy, primarily because it is not possible to satisfy all scale items in some areas of physiotherapy practice.

Figure 3: PEDro scale

Notes on administration of the PEDro scale:

All criteria	**Points are only awarded when a criterion is clearly satisfied**. If on a literal reading of the trial report it is possible that a criterion was not satisfied, a point should not be awarded for that criterion.
Criterion 1	This criterion is satisfied if the report describes the source of subjects and a list of criteria used to determine who was eligible to participate in the study.
Criterion 2	A study is considered to have used random allocation if the report states that allocation was random. The precise method of randomisation need not be specified. Procedures such as coin-tossing and dice-rolling should be considered random. Quasi-randomisation allocation procedures such as allocation by hospital record number or birth date, or alternation, do not satisfy this criterion.
Criterion 3	*Concealed allocation* means that the person who determined if a subject was eligible for inclusion in the trial was unaware, when this decision was made, of which group the subject would be allocated to. A point is awarded for this criteria, even if it is not stated that allocation was concealed, when the report states that allocation was by sealed opaque envelopes or that allocation involved contacting the holder of the allocation schedule who was "off-site".
Criterion 4	At a minimum, in studies of therapeutic interventions, the report must describe at least one measure of the severity of the condition being treated and at least one (different) key outcome measure at baseline. The rater must be satisfied that the groups' outcomes would not be expected to differ, on the basis of baseline differences in prognostic variables alone, by a clinically significant amount. This criterion is satisfied even if only baseline data of study completers are presented.
Criteria 4, 7-11	*Key outcomes* are those outcomes which provide the primary measure of the effectiveness (or lack of effectiveness) of the therapy. In most studies, more than one variable is used as an outcome measure.
Criterion 5-7	*Blinding* means the person in question (subject, therapist or assessor) did not know which group the subject had been allocated to. In addition, subjects and therapists are only considered to be "blind" if it could be expected that they would have been unable to distinguish between the treatments applied to different groups. In trials in which key outcomes are self-reported (eg, visual analogue scale, pain diary), the assessor is considered to be blind if the subject was blind.
Criterion 8	This criterion is only satisfied if the report explicitly states *both* the number of subjects initially allocated to groups *and* the number of subjects from whom key outcome measures were obtained. In trials in which outcomes are measured at several points in time, a key outcome must have been measured in more than 85% of subjects at one of those points in time.
Criterion 9	An *intention to treat* analysis means that, where subjects did not receive treatment (or the control condition) as allocated, and where measures of outcomes were available, the analysis was performed as if subjects received the treatment (or control condition) they were allocated to. This criterion is satisfied, even if there is no mention of analysis by intention to treat, if the report explicitly states that all subjects received treatment or control conditions as allocated.
Criterion 10	A *between-group* statistical comparison involves statistical comparison of one group with another. Depending on the design of the study, this may involve comparison of two or more treatments, or comparison of treatment with a control condition. The analysis may be a simple comparison of outcomes measured after the treatment was administered, or a comparison of the change in one group with the change in another (when a factorial analysis of variance has been used to analyse the data, the latter is often reported as a group × time interaction). The comparison may be in the form hypothesis testing (which provides a "p" value, describing the probability that the groups differed only by chance) or in the form of an estimate (for example, the mean or median difference, or a difference in proportions, or number needed to treat, or a relative risk or hazard ratio) and its confidence interval.
Criterion 11	A *point measure* is a measure of the size of the treatment effect. The treatment effect may be described as a difference in group outcomes, or as the outcome in (each of) all groups. *Measures of variability* include standard deviations, standard errors, confidence intervals, interquartile ranges (or other quantile ranges), and ranges. Point measures and/or measures of variability may be provided graphically (for example, SDs may be given as error bars in a Figure) as long as it is clear what is being graphed (for example, as long as it is clear whether error bars represent SDs or SEs). Where outcomes are categorical, this criterion is considered to have been met if the number of subjects in each category is given for each group.

Figure 3: PEDro scale

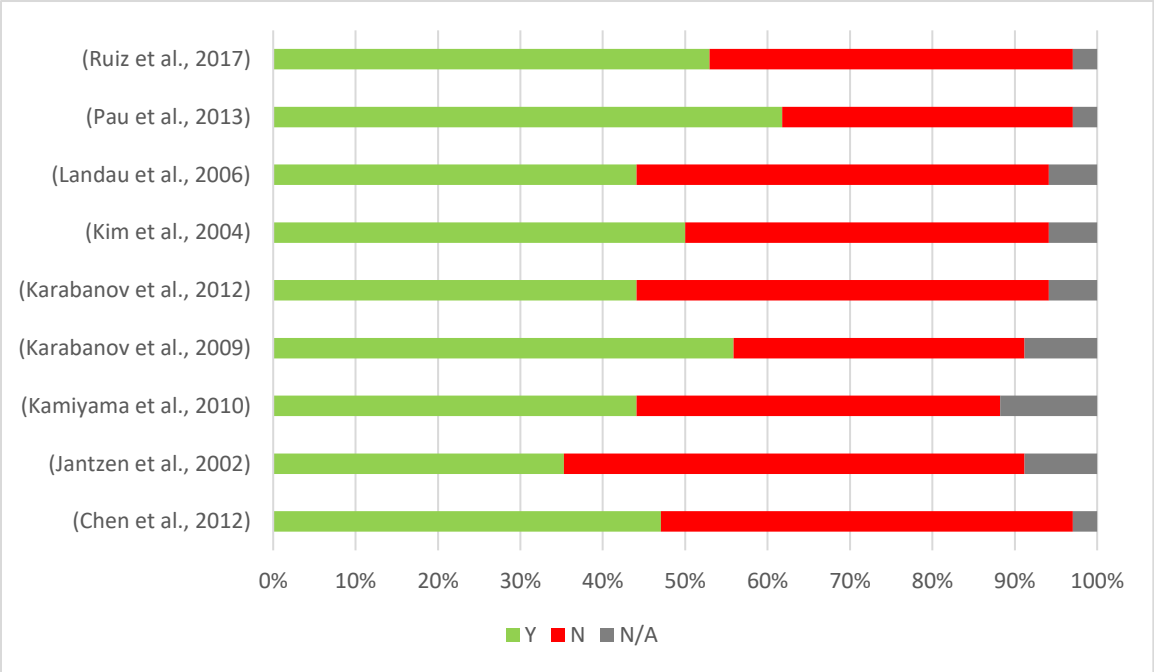

Figure 4: results quality assessment STROBE checklist

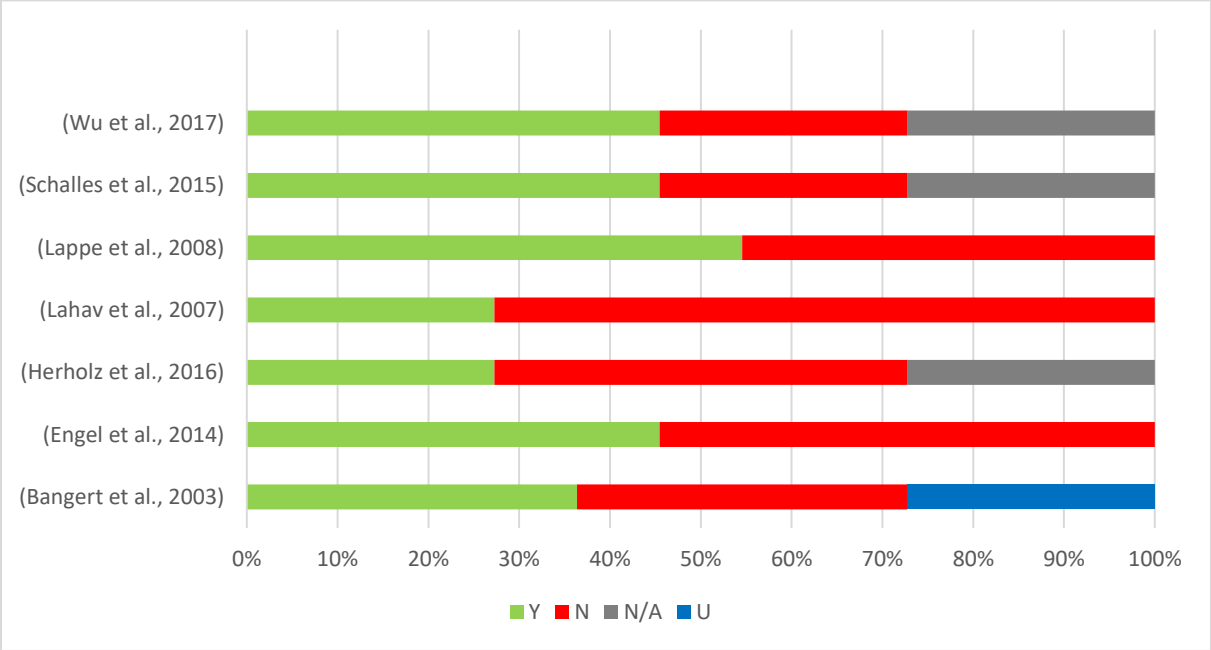

Figure 5: results quality assessment PEDro scale

Table 1 Search terms		
Search terms	**# hits PubMed**	**# hits WOS**
music AND Multiple sclerosis	40	39
music AND neurological patients	39	95
(("Music"[Mesh]) AND "Brain Mapping"[Mesh]) AND "Multiple Sclerosis"[Mesh]	1	2
((healthy[Title/Abstract]) AND nervous system diseases [MeSH Terms]) AND music[MeSH Terms]	129	10
((audiomotor integration[Title/Abstract]) AND brain mapping[MeSH Terms]) AND music[MeSH Terms]	1	1
(("Sensorimotor Cortex"[Mesh]) AND "Music"[Mesh]) AND "Brain Mapping"[Mesh]	129	13
(music or metronome or auditory stimuli) and (analysing or listening) and (movement or motor imagery) and (brain mapping or brain imagery)	158	50
(music or metronome or auditory stimuli) and (producing or listening) and (movement or motor imagery) and (brain mapping or brain imagery)	157	52
(music or metronome or auditory stimuli) and (movement or motor imagery) and (brain mapping or brain imagery)	297	195
((brain activation) AND moving to music) AND motor imagery	2	2
(music or auditory stimuli) and (learning) and (moving) and (brain mapping or brain imagery)	8	2
(music or auditory stimuli) and (learning) and (movement) and (brain mapping or brain imagery)	75	21
(music) and (performance) and (movement) and (neuronal substrate)	2	1
(music) and (performance) and (movement) and (brain imaging or brain mapping)	49	31
(music) and (listening) and (neural substrates) and (brain imaging or brain mapping)	23	7
(music OR pitch OR melody OR rhythm OR timbre) and (listening) and (neural substrates)	62	17

(music or pitch or melody or rhythm or timbre) and (listening) and (brain imaging or brain mapping)	1693	236
(music) and (learning) and (playing) and (neural basis)	2	6
(music instrument) and (learning) and (playing) and (brain)	31	41
(music instrument) and (learning) and (playing) and (brain imaging)	12	4
(musicians) and (playing music) and (brain imaging)	39	25
("Neuroimaging"[Mesh]) AND "Music"[Mesh] AND musicians)	199	43
brain imagery AND listening AND music AND musicians AND non-musicians	3	3
("Neuroimaging"[Mesh]) AND "Music"[Mesh] AND listening AND non-musicians AND musicians)	48	4
neuroimaging AND learning AND melody	59	4
learning AND melody AND brain activity	30	21
neuroimaging AND learning AND melody AND music	44	4
Brain Mapping"[Mesh] AND learning AND melody	42	9
brain plasticity AND music AND non-musicians	36	69
brain plasticity AND music instrument AND non-musicians	10	13
brain imaging AND music instrument AND non-musicians	19	8
brain imaging AND non-musicians AND music AND learning	37	3
neuronal recruitment AND musicians AND music	2	2
Imagery AND music AND Brain Mapping	27	7
(Music OR metronome OR auditory stimuli) AND (learning) AND (movement OR motor function) AND (brain mapping OR brain imaging OR neural pathways OR neuroimaging)	289	66

Table 2 Exclusion		
Reason for exclusion	**Number of studies**	**Author, year**
Language	14	Bykova et al., 1974
		Kratin et al., 1975
		Kratin et al. 1975
		Shcherbakov et al., 1975
		Dolbakian et al. 1976
		Papoian et al., 1976
		Grigor'eva et al., 1981
		Shapovalova et al., 1983
		Storozhuk et al., 1983
		Storozhuk et al., 1984
		Ziniuk et al., 1984
		Dumenko et al., 1985
		Tal'nov et al., 1985
		Borchgrevink et al., 1993
Animals	73	Hui et al., 2009
		Lemus et al., 2009
		Liberman et al., 2009
		Mooney et al., 2009
		Venkatraman et al., 2011
		Alliende et al., 2013
		Graber et al., 2013
		Maseko et al., 2013
		Canopoli et al., 2014
		Lelos et al., 2014
		Lee et al., 2016
		Slater et al., 2016
		Vallentin et al., 2016
		Li et al., 2017

Tiao et al., 1976

Crowne et al., 1982

Perrett et al., 1982

Woody et al., 1982

Levine at al., 1983

Rudell et al., 1983

Chapman et al., 1986

Markowitsch et al., 1987

Okuhata et al., 1987

Suvorov et al., 1988

Barone et al., 1989

Robbins et al., 1990

Sakurai et al., 1990

Wilson et al., 1990

Apicella et al., 1991

Kimura et al., 1992

Tamura et al., 1992

Beitel et al., 1993

Lingenhohl et al., 1994

Rolls et al., 1994

Vicario et al., 1994

Xi et al., 1994

Cohen et al., 1995

Knudsen et al., 1996

Wallace et al., 1996

Young et al., 1996

Kimpo et al., 1997

Margoliash et al., 1997

Riehle et al., 1997

Cooper et al., 1998

		Carretta et al., 1999
		Guzik et al., 1999
		Woody et al., 1999
		Payne. Et al., 2000
		Plummer et al., 2000
		Solis et al., 2000
		Cohen et al., 2002
		Mello et al., 2002
		Halladay et al., 2015
		Tokarev et al., 2011
		Nodal et al., 2010
		Clark et al., 2009
		Plakke et al., 2008
		Coleman et al., 2004
		Doupe et al., 2004
		Doupe et al., 2004
		Sevelinges et al., 2004
		Zhou et al., 2004
		Mullette et al., 2005
		Holschneieder et al., 2006
		Song et al., 2006
		Muller et al., 2007
		Wagner et al., 1993
		Benedetti et al., 1995
		Woody et al., 1998
		Witte et al., 2001
		Evarts et al., 1976
No auditory stimuli	15	Ullen et al., 2007
		Vogt et al., 2007
		Slobounov et al., 2007

		Habib et al., 2004
		Schmithorst et al., 2004
		Moessnang et al., 2013
		Buchel et al., 1998
		Proverbio et al., 2013
		Otto et al., 2006
		Carson et al., 2005
		Klein et al., 2016
		Hund-Georgiadis et al., 1999
		Kirsch et al., 2015
		Metzler-Baddeley et al., 2014
		Leaver et al., 2009
No musical/auditory sequence	162	Zhang et al., 2011
		Ricciardi et al., 2009
		Wallace et al., 2009
		Holper et al., 2012
		Spilka et al., 2010
		Strubing et al., 2012
		Trumpp et al., 2013
		Hasegawa et al., 2004
		Zatorre et al., 2015
		Verrel et al., 2015
		Ridding et al., 2000
		Toni et al., 1999
		Levita et al., 2009
		Louchart-de la Chapelle et al., 2005
		Lewis et al., 2000
		Hughes et al., 2011
		Den Ouden et al., 2010
		Bueti et al., 2010

Nordstrom et al., 2002

Lavigne et al., 2016

Buick et al., 2016

Kopp et al., 2006

Bares et al., 2001

Petsche et al., 1997

Schwartz et al., 2012

LeDoux et al., 1993

Pinho et al., 2016

Oshiro et al., 2007

Bach et al., 2008

Knyazev et al., 2008

Ledoux et al., 1993

Tanabe et al., 2009

Buckner et al., 1996

Alonso et al., 2016

Cacace et al., 1992

Mathias et al., 2015

Jacobsen et al., 2015

Burunat et al., 2014

Buchsbaum et al., 2011

Bender et al., 2010

Shannon et al., 2004

Ohara et al., 2006

Hsieh et al., 2008

Stephan et al., 2016

Proctor et al., 2010

Valls-Sole et al., 1997

Nombre et al., 2003

Melynyte et al., 2017

	Yoshida et al., 2013
	Spinelli et al., 2011
	Manuel et al., 2010
	Sohn et al., 2003
	Verleger et al., 2006
	Martin et al., 2006
	Reivich et al., 1983
	Parker et al., 2015
	Leslie et al., 2013
	Ewald et al., 2014
	Calautti et al., 2001
	Vaquero et al., 2016
	Bailey et al., 2010
	Penhune et al., 2005/Watanabe et al., 2007
	Malmo et al., 2003
	Weinstein et al., 2017
	Schonberg et al., 2014
	Kokal et al., 2011
	Anzak et al., 2011
	Kleber et al., 2013
	Dittinger et al., 2018
	Schlaffke et al., 2015
	McNamara et al., 2008
	Tian et al., 2016
	Rauschecker et al., 2008
	Matteau et al., 2010
	Lametti et al., 2014
	Treille et al., 2017
	Ylinen et al., 2015

Toyomura et al., 2015

Sato et al., 2015

Francois et al., 2014

Agnew et al., 2011

Shiller et al., 2009

Brown et al., 2004

Callan et al., 2006

Saito et al., 2006

Callan et al., 2007

Giraud et al., 2001

Hickok et al., 2003

Nagasawa et al., 2010

Kaiser et al., 2005

Poikonen et al., 2016

Ono et al., 2014

Himberg et al., 2011

Giacosa et al., 2016

Mifsud et al., 2016

Joiner et al., 2007

Martino et al., 2016

Grube et al., 2016

Harris et al., 2016

Adhikari et al., 2016

Harris et al., 2015

De Manzano et al., 2012

Berkowitz et al., 2008

Olshansky et al., 2015

Virji-Babul et al., 2013

Pereire et al., 2011

Peretz et al., 2009

Margulis et al., 2009

Michalka et al., 2016

Yordanova et al., 2013

Thorpe et al., 2012

Pomper et al., 2015

Kida et al., 2013

Van der Burg et al., 2011

Santangeo et al., 2009

Knyazev et al., 2008

Ciaramitaro et al., 2007

Petit et al., 2007

Scheef et al., 2009

Aliu et al., 2009

Griffiths et al., 1998

Salminen et al., 2015

Zimmer et al., 2009

Schulze et al., 2009

Bernasconi et al., 2010

Konoike et al., 2012

Pablos Martin et al., 2007

Hennevin et al., 2007

Hinton et al., 2004

Klaes et al., 2015

Riecker et al., 2003

Jantzen et al., 2005

Meister et al., 2005

Parsons et al., 2005

Ullen et al., 2005

Bengtsson et al., 2006

Byblow et al., 2006

		Bengtsson et al., 2007
		Mutschler et al., 2007
		Chen et al., 2008
		Jancke et al., 2000
		Albani et al., 2001
		Lotze et al., 2003
		Van de Ruit et al., 2017
		Lee et al., 2011
		Butler et al., 2011
		Kleber et al., 2010
		Herdener et al., 2010
		Moore et al., 2017
		Bar et al., 2016
		Groussard et al., 2014
		Bailey et al., 2014
		Han et al., 2009
		Gaser et al., 2003
		Hutchinson et al., 2003
		Riecker et al., 2003
		Lega et al., 2016
		Herrojo Ruiz et al., 2014
		Tsai et al., 2012
		D'Ausilio et al., 2006
		Stewart et al., 2003
		Brunia et al., 2000
		Zhuang et al., 1998
< 18 years	8	Schlaug et al., 2005
		Badian et al., 1977
		Goldsberry et al., 2011
		Haslbecket al., 2017

		Schlaug et al., 2009
		Hyde et al., 2009
		Norton et al., 2005
		Amad et al., 2017
No brain imaging	5	Chen et al., 2016
		Scholz et al., 2015
		Park et al., 2015
		Cappe et al., 2009
		Rosenkranz et al., 2007
No motor performance	5	Cross et al., 2009
		Hasliner et al., 2005
		Halpern et al., 2004
		Herholz et al., 2008
		Gaab et al., 2004
Review	33	Burton et al., 2000
		Kinsbourne et al., 1980
		Schlaug et al., 2001
		Altenmuller et al., 2003
		Janata et al., 2003
		Klim-Klimaszewska et al., 2016
		Vuilleumier et al.? 2015
		Schneider et al., 2015
		Schlaug et al., 2015
		Beaty et al., 2015
		Schaefer et al., 2014
		Francois et al., 2014
		Chang et al., 2014
		Carlile et al., 2014
		Zatorre et al., 2013
		Grahn et al., 2012

	Worthen-Chaudhari et al., 2011
	Penhune et al., 2011
	Lefort et al., 2011
	Garagnani et al., 2011
	Dawson et al., 2011
	Yalachkov et al., 2010
	Wan et al., 2010
	Harley et al., 2004
	Hessl et al., 2004
	Tillmann et al., 2005
	Gordon et al., 2007
	Israel et al., 2008
	Thomposon et al., 1998
	Das et al., 2001
	Pascual-Leone et al., 2001
	Koelsch et al., 2005
	Neumann et al., 2016

Table 3.1 PEDro scale											
	1. Eligibility criteria	**2. Randomisation**	**3. Allocation**	**4. Baseline data**	**5. Blinding patients**	**6. Blinding therapists**	**7. Blinding assessors**	**8. Measures**	**9. Receiving treatment**	**10. Between-group comparison**	**11. Point measures and variability measures**
(Bangert et al., 2003)	N	U	U	Y	N	N	U	Y	N	Y	Y
(Engel et al., 2014)	N	N	N	Y	N	N	N	Y	Y	Y	Y
(Herholz et al., 2016)	Y	N/A	N/A	N/A	N	N	N	Y	N	N	Y
(Lahav et al., 2007)	N	N	N	Y	N	N	N	Y	N	N	Y
(Lappe et al., 2008)	N	Y	N	Y	N	N	N	Y	Y	Y	Y
(Schalles et al., 2015)	Y	N/A	N/A	Y	N	N	N	Y	Y	N/A	Y
(Wu et al., 2017)	Y	N/A	N/A	Y	N	N	N	Y	Y	N/A	Y

Table 3.2 STROBE-checklist

	1. Title and abstract		2. Background/rationale	3. Objectives	4. Study design	5. Setting	6. Participants		7. Variables	8. Data sources/ measurement	9. Bias	10. Study size	11. Quantitative variables	12. Statistical methods					13. Participants			14. Descriptive data			15. Outcome data	16. Main results			17. Other analyses	18. Key results	19. Limitations	20. Interpretation	21. Generalisability	22. Funding
(Chen et al., 2012)	N	Y	Y	Y	N	N	N	N	Y	Y	N	N	N	Y	Y	N	N	N	Y	N	N	Y	Y	Y	Y	N	N	N/A	N	Y	Y	Y	N	Y
(Jantzen et al., 2002)	N	Y	Y	Y	N	N	Y	N/A	N	Y	N	N	Y	Y	N	N	N	N	N	N	N	N	N	N/A	Y	N	Y	N/A	N	Y	N	Y	N	N
(Kamiyama et al., 2010)	N	Y	Y	Y	N	N	Y	N/A	Y	Y	N	N	Y	Y	Y	N	N/A	N	N	N	N	N	N	N/A	Y	Y	Y	N/A	Y	Y	N	Y	N	N
(Karabanov et al., 2009)	Y	Y	Y	Y	Y	N	Y	N	Y	Y	N	N	Y	Y	Y	N	N/A	N	Y	N	N	N	N	N/A	Y	Y	Y	N/A	Y	Y	N	Y	N	Y
(Karabanov et al., 2012)	N	Y	Y	Y	N	N	N	N	Y	Y	N	N	Y	N	Y	N	N	N	N	N	N	N	N	N/A	Y	Y	Y	N/A	Y	Y	Y	Y	N	Y
(Kim et al., 2004)	N	Y	Y	Y	N	N	Y	N/A	Y	Y	N	N	Y	Y	Y	N	N	N	Y	N	N	N	N	Y	Y	Y	Y	N/A	N	Y	Y	Y	N	N
(Landau et al., 2006)	N	Y	Y	Y	N	N	Y	N	Y	Y	N	N	Y	Y	Y	N	N	N	N	N	N	N	N	N/A	Y	Y	Y	N/A	Y	Y	N	Y	N	N
(Pau et al., 2013)	N	Y	Y	Y	N	N	Y	Y	Y	Y	N	N	Y	Y	Y	Y	N	N	Y	Y	N	N	Y	Y	Y	N	Y	N/A	Y	Y	N	Y	N	Y
(Ruiz et al., 2017)	N	Y	Y	Y	N	N	Y	Y	Y	Y	N	N	Y	N	Y	N	Y	N	N	N	N	Y	N	Y	Y	N	Y	N/A	N	Y	Y	Y	N	Y

Table 4 Strengths and limitations		
	Strengths	**Limitations**
(Bangert et al., 2003)	- Groups were similar at baseline - Measures of key outcomes were obtained from more than 85% of the subjects - Reporting between-group statistical comparisons, point measures and measures of variability	- No eligibility criteria - No blinding of subjects and therapists - Unknown if randomisation, concealment, and blinding of assessors
(Chen et al., 2012)	- Balanced summary in abstract and introduction - Specific objectives - Clearly defined outcomes - Sources of data were given - Statistical methods for confounding variables - Limitations of the study are discussed	- Study design is not indicated - No description of setting, locations, and relevant dates - No eligibility criteria - No potential sources of biases mentioned - No missing data reported - No sensitivity analyses, unadjusted estimates, and other analyses
(Engel et al., 2014)	- Similar group baseline characteristics - Between-group statistical comparisons - Point measures and measures of variability were mentioned	- No eligibility criteria - No randomisation - No blinding of the subjects, therapists, assessors
(Herholz et al., 2016)	- Eligibility criteria were specified - Measures of key outcomes were obtained from more than 85% of the subjects - Point measures and measures of variability	- Only one group - No blinding of subjects, therapists, and assessors - No analyses by intention to treat
(Jantzen et al., 2002)	- Informative summary of scientific background - Specific objectives, prespecified hypotheses	- Little structure in the article - No limitations reported - No descriptive information of the participants
(Kamiyama et al., 2010)	- Informative summary of scientific background - Specific objectives, prespecified hypotheses - Clear explanation of the procedure - Clear summary of the key results with reference to study objectives	- Limited descriptive information of the participants - Source of funding is not mentioned - No limitations reported - No missing data reported - not explained how the study size was arrived at
(Karabanov et al., 2009)	- Study design is mentioned - Confounders were considered (e.g. scanner noise)	- No descriptive data - No limitations reported
(Karabanov et al., 2012)	- Limitations are extensively mentioned - Source of funding is reported - Comparison of two learning modalities (visual vs auditory)	- Not mentioned how the allocation happened - Not explained how the study size arrived at
(Kim et al., 2004)	- Informative summary of scientific background - Limitations are reported - Report numbers of individuals at each stage of the study	- No missing data reported - No descriptive data - No source of funding reported
(Lahav et al., 2007)	- Similar group baseline characteristics - Measures of key outcomes were obtained from more than 85% of the subjects - Point measures and measures of variability were mentioned	- No eligibility criteria - No randomisation - No blinding of subjects, therapists, assessors - No intention to treat analyses - No between-group comparison
(Landau et al., 2006)	- Pianists vs non-pianists - Informative summary of scientific background	- Age is the only descriptive data for matching the groups - No limitations reported
(Lappe et al., 2008)	- Randomisation - Similar group baseline characteristics - Between-group statistical comparisons - Point measures and measures of variability are mentioned	- No eligibility criteria - Allocation was not concealed - No blinding of subjects, therapists, assessors

(Pau et al., 2013)	- Eligibility criteria were mentioned - Clearly defined outcomes - Report numbers of individuals and reasons of non-participation at each stage of study - Summary of key results and overall interpretation of results in discussion	- No study design mentioned - No description of potential biases - No explanation of study size - No discussion of limitations
(Ruiz et al., 2017)	- Balanced informative summary in abstract and introduction - Specific objectives and prespecified hypotheses - Eligibility criteria were given - Clearly defined outcomes - Summary of key results and overall interpretation of results in discussion	- Study design is not indicated - No description of setting, locations, and relevant dates - No description of potential biases and limitations of the study - No missing data mentioned
(Schalles et al., 2015)	- Descriptive information is mentioned - Informative summary of scientific background - Eligibility criteria were specified	- No control group - No blinding of subjects, therapists, and assessors - No limitations reported
(Wu et al., 2017)	- Eligibility criteria were specified - Limitations are reported	- No control group - Only 65% of the initial subjects finished the training

Table 5.1 Short summary									
Study	**Aim**	**Study design**	**Nr. of partici-pants**	**Age**	**Participant characteristics**	**Musical perfor-mance**	**Experimental instrument**	**Experimental/learning task**	**Nr. Of sessions**
(Bangert et al., 2003)	Plasticity of motor representations, auditory-sensorimotor integration	Longitudinal experimental case-control study design	26	26.2 ± 5.3	-right handed -non-musicians: 8♀, 9♂ -Professional pianists: 4♀, 5♂	Yes	Piano	Replay acoustically presented melodies with their right hand.	5 weeks, 2 sessions a week, 20min
(Chen et al., 2012)	Auditory-motor associations	Observational not controlled	16	27.13, range 20–34	- right-handed - non-musicians - 8♀, 8♂	Yes	Keyboard	Listening to musical melodies and playing them using the right hand	1 day, 1 session, 20min
(Engel et al., 2014)	Structural properties of white matter fiber tracts, inter-individual differences	Experimental cross-over design	18	21.8 ± 2.4, range 18–26 years	- righthanded - non-musicians - normal vision or vision was corrected to normal - 11♀, 7♂	Yes	Keyboard	Audiomotor training procedure: learning to perform three short melodies on a piano keyboard with their right hand Visuomotor training procedure: learning to perform sequences on a mute piano-keyboard by observing videos	3 consecutive days, 2h per day, audio-motor training: 60 ± 32min visuomotor training: 62 ± 29min
(Herholz et al., 2016)	Piano training, perception and imagery, predictors of learning	Experimental: longitudinal within-subject repeated-measures design	15	25.6, range 20–34	-right handed -Non-musicians -8♀, 7♂	Yes	Electronic keyboard	A 6-week piano training (home- and lab-based): 1st 4 weeks: learn to play simple tone sequences week 5 & 6:	6 weeks, 5 times a week, 30 sessions, 30 min

								Learn to play 6 familiar melodies	
(Jantzen et al., 2002)	Short-term behavioral practice, synchronization, and syncopation	Observational not controlled	8	Range 23–46	-right-handed -Neurologically normal -1♀, 7♂	No	/	'On' block: coordinate flexion movements of the right index finger and thumb (by squeezing an air-filled pillow) to an auditory stimulus 'Off' block: subjects rested Pre-practice phase: performing one session of syncopation and one session of synchronization	8 sessions
(Kamiyama et al., 2010)	Motor practice and auditory memory for sound sequences	Experimental prospective	20	♂: 22.05, range 20–29 years ♀: 22.33, range 20–29	- righthanded (except 1 male) -non-musician - normal hearing - no neurological Disease - 6♀, 14♂	Yes	Keyboard	Learning two unfamiliar pieces of music. 2 conditions: the key-press condition: imitating the piano music presented. No-key-press condition: listening to the musical sequence without pressing any keys.	8-11 sessions
(Karabanov et al., 2009)	Neural control of temporal sequence performance, auditory-motor circuits, auditory pacing	Observational cross-sectional study 2 X 2 factorial design	16	28.8, range 23 - 44	-righthanded - 9♀, 7♂	Yes	Musical key pad	Reproducing temporal sequences by rhythmic tapping with the right index finger. Group 1: learning the visual rhythm (n = 8) Group 2: learning the auditory rhythm (n = 8)	1 day of training, 1 day for scanning

(Karabanov et al., 2012)	PPC–M1 connectivity, functional connectivity	Observational case control study	19	32.1 ±8.3	- right handed - non-musicians - 11♀, 8♂	No	Not applicable	Group 1 (n = 8): learned the rhythmic sequence by visual stimuli Group 2: (n = 9) learned the identical sequence by an auditory stimulus Perform a short dual task to test automaticity	1 day, 5 TMS sessions, 1 EEG session
(Kim et al., 2004)	Learning a stringed instrument, motor memory consolidation	Observational study not controlled	8	Range: 20–22	- righthanded - non-musicians (n = 5) -Some musical experience (n =3) -3♀, 5♂	Yes	Stringed instrument	Learning to play a stringed instrument	6 months of training, 2 scanning sessions
(Lahav et al., 2007)	Action-recognition system, the mirror neuron	Experimental not-controlled	9	22.4 ±2.2	-righthanded -non-musicians -no neurological, psychiatric, or auditory problems - 6♀, 3♂	Yes	Piano	Training to play the piano part of a novel musical piece.	5 days, 5 sessions, ~12-30min
(Landau et al., 2006)	Long term motor expertise, the regional specificity, and the time course of functional plasticity	Observational case control study	17	Pianists: 21.8 Non-pianists: 20.6	- right-handed -musicians: pianists -non-musicians	Yes	Piano keys	Did not practice the task in order to maximize the detection of fast-learning-related activation during the scanning session. Learning sequences while in scanner.	1 day, 1 session, ~30min

(Lappe et al., 2008)	Short-term unimodal and multimodal musical training, sensorimotor training	Experimental: RCT	23	range 24-38	- righthanded -non-musicians -no otological or neurological disorders -normal audiological status - 13♀, 10♂	Yes	Piano	SA group: learned to play a musical sequence on the piano A group: listened to the music that was played by the SA group and made judgments as to whether the sequences were correct or not.	2 weeks, 8 sessions, 25min
(Pau et al., 2013)	Pre-knowledge on audio-motor associations	Observational case-control study	29	Piano players: 24.00 ±3.11 years Controls: 25.40 ±1.18	-righthanded - piano players (n = 14): 6♀, 8♂ - non-musicians :6♀, 9♂ - no neurological impairments	Yes	Keyboard	Replayed visually presented finger sequences with or without acoustic feedback	1 day, 1 training session and an immediately following scanning session, duration unknown
(Ruiz et al., 2017)	Serial order during sensorimotor sequence	Observational not controlled	21	Median 27, range 22 to 34	-right handed -non-musicians -no neurological/ psychiatric disease -10♀, 11♂	Yes	Keyboard	Explicitly learn short movement sequences on a digital piano while listening to the corresponding auditory feedback.	1 day, 1 training session (< 1min per sequence type) & 1 performance session (~5–6 min per sequence type)

(Schalles et al., 2015)	Sequential ordering of information	Experimental study not-controlled	16	19.9	-righthanded (except 1) - musicians but inexperienced with keyboard (n = 8) - non-musicians (n = 8) -7♀, 9♂	Yes	Keyboard	Playing a melody line on a MIDI piano controller, figuring out the melody line by ear, listening to the transposed and control melodies before and after working through the piano sequence	5 consecutive days, duration as long as it took to play the song with no mistakes
(Wu et al., 2017)	Short term musical training, connectivity changes and action representation	Experimental study not controlled	13	24.3 ± 5.74	-right-handed -non-musicians -normal auditory acuity -5♀, 8♂	Yes	Keyboard	Tone sequences were played to the participant, who was then to attempt to reproduce the sequence on a keyboard	5–8 weeks, 2–3 times a week, 15 sessions, 10 to 22 min

*Age is presented as X±SD or X + Range or Median dependent of available information from the study.

Table 5.2 Study aims	
Study	**Aim**
(Bangert et al., 2003)	1) This study deals not only with the plasticity of motor representations but also with the issue of auditory- sensorimotor integration in piano practice. 2) To clarify the temporal dynamics of plasticity arising from this highly specialized sensorimotor training
(Chen et al., 2012)	1) They used fMRI to investigate the formation of auditory-motor associations while participants with no musical training learned to play a melody. 2) To examine the brain areas directly involved in learning auditory-motor associations during the training as well as changes in their response to sounds for which a motor association has been learned.
(Engel et al., 2014)	1) Identifying relations to structural properties of white matter fiber tracts relevant to audio-motor learning. 2) Whether underlying structural differences in white matter fiber tracts explain inter-individual differences in progress during sensorimotor learning.
(Herholz et al., 2016)	They investigated the effects of piano training using a longitudinal design that enabled them: 1) to observe the causal influence of training on brain activity under naturalistic but controlled conditions and 2) to determine individual predictors of learning, within the same individuals. To test whether auditory-motor training would affect neural activity not only during perception but also during imagery, and to what extent changes for perceptual and more abstract cognitive tasks overlap.
(Jantzen et al., 2002)	Use fMRI to investigate how short-term behavioral practice alone affects intrinsic differences in neural activity between synchronized and syncopated coordination modes. How exposure to a quite difficult timing task (syncopation) affects the neural structures supporting an easier but unpracticed task (synchronization).
(Kamiyama et al., 2010)	Investigate the relationship between motor practice and auditory memory for sound sequences.
(Karabanov et al., 2009)	1) To investigate the effect of two factors on the neural control of temporal sequence performance: the modality in which the rhythms had been trained, and the modality of the pacing stimuli preceding performance. 2) To further investigate the role of auditory-motor circuits in this type of tasks. 3) To investigate whether activity in auditory cortex was related specifically to auditory pacing.
(Karabanov et al., 2012)	1) Whether functional PPC–M1 connectivity in humans can be modulated by sensorimotor training. 2) To determine whether changes in functional connectivity would be dependent on the sensory modality used during motor training.
(Kim et al., 2004)	Tried to observe changes in adult brains induced by learning and practice of stringed musical instruments. They set out to answer if: (1) the fMRI activation areas for the LAFA movement or sensory stimuli of the little finger would change after the practice; (2) if TMS motor output maps would correspond with fMRI data; and (3) if the newly activated areas would include neural structures, related to more skillful fingering or possible musical processing, such as parietal cortex, premotor cortex, and temporal association cortex. They tried to locate the areas showing reduced neural activation after practice, considering the decreased prefrontal activation associated with the motor memory consolidation
(Lahav et al., 2007)	1) Whether the human action-recognition system responds to sounds found in a more complex sequence of newly acquired actions.

	2) How the mirror neuron system will respond to actions and sounds that do not have verbal meaning and, most importantly, are well controlled and newly acquired.
(Landau et al., 2006)	Examining the influence of long term motor expertise (slow learning) while pianists and non-pianists performed alternating epochs of sequenced and random keypresses in response to visual cues (fast learning) during functional neuroimaging. To examine the regional specificity and the time course of functional plasticity.
(Lappe et al., 2008)	1) The impact of short-term unimodal and multimodal musical training on brain plasticity. 2) The impact of sensorimotor training comprising auditory, somatosensory, and motor activity has not been compared with auditory training alone in a laboratory environment.
(Pau et al., 2013)	Whether increased pre-knowledge on audio-motor associations in other tasks is transferred in increased primary auditory cortex activation even when playing a newly designed audio-motor task.
(Ruiz et al., 2017)	To investigate the neural mechanisms underlying the monitoring of serial order during sensorimotor sequence learning as revealed by alterations of auditory feedback (AAF).
(Schalles et al., 2015)	1) Whether the audiomotor system might be sensitive to sequential ordering of information in a musical passage, such that it could help generate topdown predictions for incoming auditory stimuli. 2) Whether the motor system is sensitive to preservation of the sequential ordering of musical information, even when the pitch information is altered.
(Wu et al., 2017)	1.to determine if short term musical training results in an attenuation of mu rhythm over sensorimotor cortex while listening to musical sequences. 2.adressing functional connectivity changes that may occur due to musical training. 3.to address additional specificity information of the nature of action representation effects.

Table 5.3 Brain imaging							
Article	**imaging technique**	**Time points**	**Imaging protocol/ task in scanner**	**Application**	**Brain areas**	**Behavioral measures**	**Data acquisition**
(Bangert et al., 2003)	EEG	Pre During Post	The volunteers were placed in an optically and acoustically insulated chamber in front of a sight-shaded piano keyboard. Only a fixation dot and some instructional icons/prompts were presented on a black screen. The subjects' event-related slow DCEEG-potentials were measured either while - passively listening to 3-second monophonic piano sequences (Auditory Probe Task, 60 recordings) or while - arbitrarily pressing keys on a soundless piano keyboard (Motor Probe Task, 60 recordings). The participants were instructed to do either kind of task without any demands being specified. For the mute motor task, the five digits of the right hand were placed on the five white keys c'-g', corresponding to the ambitus of the melodies in the auditory tasks.	The electrodes were mounted on an EasyCap™ and distributed across the whole scalp according to a modified 10–20 system. DC potentials were amplified by a 32-channel SynAmps™ and recorded by means of NeuroScan™.	Fronto-temporal area, Parietal area, Temporal area, M1, Central area, SMA, GTI	Proper timing and fine adjustment of finger forces for the reproduction of rhythm and loudness. Error parameters (pitches, keystroke times, and keystroke force/loudness)	The subjects' event-related slow EEG-potentials were recorded from the scalp by non-polarizable Ag/AgCl-electrodes with an electrode impedance of less than 1 kΩ at 30 electrode sites with linked mastoid electrodes as a reference. The electrodes were mounted on an EasyCap™ and distributed across the whole scalp according to a modified 10–20 system including additional subtemporal electrodes.
(Chen et al., 2012)	fMRI	Pre During Post	The keyboard was embedded in a foamcushion for support and placed over the abdominal area of the participants so that the right hand could comfortably rest on it. A fixed fingering position was used during	Data were acquired on a 3-tesla Varian Inova MRI scanner.	PMv, retrosplenial cortex, OFC, L frontal pole, L PMd, R SMA, R ACC,	Pitch-to-key-press matching ability: Participants heard one of the eight pitches previously used in melody 1 or melody 2 during the Perception run and were	Three functional runs were acquired using a T2*-weighted gradient-echo EPI sequence: 1) Perception pre-training, 2) Training, and3) Perception post-training. For the Perception pre- and post-training runs, 63 volumes were

			scanning to minimize wrist and hand movements. 1) Perception pre-training, 2)Training ,and 3)Perception post- training: During the first Perception run, participants lay motionless and listened to two 5-note melodies. Next, participants remained inside the scanner but were not scanned while performing a behavioral test of pitch-to-key-press matching ability. During Training, participants were scanned while they learned to play Melody 1. During the second Perception run (i.e. post-training), participants underwent the procedure identical to that at pre-training		R motor cortex, R SFS, R PCC, R LOC	asked to press the corresponding key on the keyboard. Percent correct responses were recorded.	acquired; 203 volumes were acquired during the Training run.
(Engel et al., 2014)	DWI	Post	DWI images were acquired about (mean 6 SD) 24, 6, 5 h after the final motor training session of the first motor training condition. During DWI data acquisition, participants lay in supine position on the scanner bed. No task was performed during imaging.	3T Philips Achieva scanner eight-channel synergy SENSE head coil FMRIB Diffusion toolbox FDT of FSL 4.1 for imaging processing	A) Analysis for ROI: Corticospinal tract, Superior longitudinal fasciculus B) Analysis for the whole brain: Cluster I, Corticospinal tract, Superior Corona radiata, Posterior Corana radiata, Superior longitudinal fasciculus, Cluster II, Corpus callosum	Time required to master the task: Learning to play simple piano melodies with the right hand via audiomotor training procedure	DW images were acquired using a single-shot pulsed gradient spin echo echo-planar imaging (EPI) sequence (repetition time (TR) 5 8981 ms, echo time (TE) 5 60 ms, sensitivity encoding (SENSE) factor 5 2.8) on a 3T Philips Achieva scanner, equipped with an eight-channel synergy SENSE head coil for excitation and signal collection. Each volume consisted of 50 transverse slices, recorded with a 96 3 96 matrix (field of view (FOV) 224 3 224 mm, voxel size 2.5 3 2.5 mm, slice thickness 2.5 mm, no gap). DW images were acquired along 60 directions optimized using an electrostatic repulsion model [Jones et al., 1999], using a maximum gradient strength of 40 mT/m and a b-value 5 1000 s/mm2. Six non-DW images (b 5 0 s/mm2, i.e., referred to as b0 image) were also obtained for each dataset.

(Herholz et al., 2016)	fMRI	Pre Post	Scans were collected at each of the 3 measurement timepoints in the study. Duration of each session: ~2 h. Musical cognition tasks were performed, with 4 conditions that involved judging the correctness of the last tone of a familiar melody (Listening), imagining part of the melody and judging if a final tone correctly completed the imagined tune (Imagining), listening to the random tone sequences and pressing a response key but without an auditory cognition task (Random), or resting in silence (Baseline). The order of the stimuli within the blocks was pseudo-randomizedfor each block. In total, 48 trials of each condition were presented.	a 3 Tesla MR scanner with a 32-channel head coil.	bilateral primary and secondary auditory cortices, bilateral thalamus, caudate, cerebellum lobule VI and crus I, superior parietal and inferior frontal cortices, left precentral gyrus, SMA, putamen, premotor cortex, dorsolateral prefrontal cortex, bilateral posterior parietal cortex, incl. intraparietal sulcus, hippocampus	Successfully learning to play 6 melodies	We recorded EPI images covering the whole head (voxel size 3.4 mm3, 42 slices, TE 30 ms, TR 15 000 ms) immediately after the last tonewas presented (Listen, Imagery, and Random conditions) or after an equivalent lapse of time (Baseline condition) (See Fig. 2). Between the first and second functional imaging run, we recorded anatomical T1-weighted images (MPRAGE, voxel size 1mm3).
(Jantzen et al., 2002)	fMRI	Pre During Post	Data were acquired using a block design with ten images in the ‘off’ block followed by ten images in the ‘on’ block. A single session consisted of four consecutive off/on blocks. During the ‘on’ block subjects were required to coordinate flexion movements of the right index finger and thumb (by squeezing an airfilled pillow) to an auditory metronome. During the ‘off’ block subjects rested. The subject’s eyes remained closed during all sessions. During the pre-practice phase subjects performed one session of syncopation and one session of synchronization.	1.5 Tesla Signa Scanner (General Electric Medical Systems, Milwaukee, WI) equipped with real time fMRI capabilities	Precentral gyrus, Medial frontal gyrus, Superior temporal gyrus, Inferior frontal gyrus Insula,Putamen, Thalamus (VLN), Vermis	Behavioral performance during syncopation and synchronization sessions	Echo-planar images were collected using a single shot, gradient-echo, echo planar pulse sequence (echo time (TE) = 60 ms, flip angle (FA) = 908, field of view (FOV) = 24 cm, in plane resolution = 64 X 64). Twenty axial 5 mm thick slices spaced 2.5 mm apart were selected so as to provide coverage of the entire brain (voxel size = 3.75 X 3.75 X 7.5 mm). Prior to functional imaging, high resolution anatomical spoiled gradient-recalled at steady state (SPGR) images (TE = in phase, TR = 325ms, FA = 908, FOV = 24 cm, 5 mm thickness, 2.5 mm spacing, number of excitations = 2) were collected at the same slice locations as the functional images. These images served as the background onto which the functional

							information was displayed and were also used to co-register the functional scans onto anatomical 3D SPGR axial images (TE = 5ms; TR = 34ms; FA = 458, FOV = 24 or 26 cm; resolution = 256 X 256; thickness = 2 mm) which were collected at the end of each experimental session.
(Kamiyama et al., 2010)	EEG	Post	After training, Melody A and Melody B were presented during EEG recording. The melodies alternated 18 times in every session. Within each melody, 10% of the tones were shifted up or down to the neighboring tones within the C-major scale using a Musical Instrument Digital Interface program. Participants were asked simply to listen to the melodies during the three sessions.	EEGs were recorded by a 64-channel Ag–Cl electrode cap using the Scan 4.3 acquisition system (SynAmps; NeuroScan), with a 0.15–30Hz band-pass filter and a sampling rate of 500Hz.	middle anterior (Fp1, Fz, Fp2); middle central (FCz, Cz, CPz); middle posterior (P3, Pz, P4); left anterior (F3, FC3, F7); right anterior (F4, FC4, F8); left posterior (CP3, TP7, P7); and right posterior (CP4, TP8, P8).	Absolute pitch test: 3 octave tones (36 pure tones) were presented randomly. Following each tone, participants identified which notes they heard by pressing the appropriate piano keys (without auditory feedback) Training performance: training stopped when the participants were >95% correct and when they pressed the piano keys within 100ms of the presentation of stimuli in each of the four blocks.	/
(Karabanov et al., 2009)	fMRI	During	Participants were lying in supine position with the arms and hands fixated so that the key presses could be executed by using index finger movements only, i.e. rhythmic tapping on the index finger key of a response glove. The tasks were performed in epochs lasting 40 s. During the first 4.5 s of each epoch, a signal word was presented visually to instruct the participant which task to perform: Auditory Rhythm, Visual Rhythm or Rest. In each	1.5-T scanner (Signa Horizon Echospeed, General Electrics Medical Systems, Milwaukee, WI, USA) using a Birdcage Volume Quatrum head-only coil.	Angular gyrus, Middle temporal gyrus, SMG Central sulcus (M1/S1), Superior frontal gyrus (SMA), Inferior parietal gyrus, preSMA/SMA, Precentral gyrus (PMV), Insula, Temporo-parietal junction, Rolandic	Performance via the E-prime script (online)	At the beginning of each scanning session a high-resolution, three-dimensional gradient-echo T1weighted anatomical image volume of the whole brain (voxel size 1×1×1 mm) was collected. Functional image data were collected as gradient-echo, echo-planar (EPI) T2$*$-weighted images with blood oxygenation level-dependent (BOLD) contrasts (Kwong et al., 1992; Ogawa et al., 1992). Image volumes from the whole brain were built up from contiguous axial slices (n=32). The following parameters were used for the fMRI scanning: echo time, 50 ms; field

			session all four conditions of the 2×2 design (visual or auditory Metronome Modality; visually or auditorily Training Modality) and Rest were presented twice. Four different task-orders were used in different sessions to reduce possible time and order confounds. Four sessions were recorded from each participant.		operculum, Cingulate sulcus /gyrus (CMA/preSMA), Globus pallidus, Intraparietal sulcus, Cerebellum: lobule VI, lobule V, lobule VI/crus I, lobule VIIIA/VIIIB, lobule VIIIA Frontal operculum, Putamen, Cuneus, Internal capsule, STG		of view, 22 cm; matrix size, 64×64 (after ramp sampling); pixel size, 3.4×3.4 mm; flip angle, 90°; slice thickness, 4 mm; repetition time (TR), 2.5 s; number of volumes per session, 164. The image volumes were collected continuously during separate sessions and each volume consisted of 32 evenly spaced out slices. Time between slice echo centers was always 78 ms. We started each session by collecting four 'dummy' image volumes that were not stored, to allow for T1 equilibration effects.
(Karabanov et al., 2012)	EEG	Pre: TMS During Post: TMS	Directly after the initial TMS session the participants were prepared for the EEG recording. EEG was recorded first during a 1-min resting period and after that continuously throughout the 10-min sensorimotor training task. Resting-state EEG was recorded for 1 min while the participants were looking at a fixation cross on a computer monitor. Resting-state EEG was followed by the 10-min sensorimotor training session during which EEG was constantly recorded. (The first and last minutes of this recording were used for EEG analyses.) Sensorimotor training: tapping the right index finger in synchrony to a rhythmic sequence. One group learned the rhythmic sequence by visual	EEG signals were recorded from 32 surface electrodes mounted on a cap (Electro-Cap International, Eaton, OH) Signals were amplified (Neuroscan, El Paso, TX)	Posterior parietal cortex , Primary motor cortex connectivity	Calculating correctly pressed intervals within each sequence repetition Dual task to test automaticity: interresponse intervals between button presses	At the beginning of each scanning session a high-resolution, three-dimensional gradient-echo T1weighted anatomical image volume of the whole brain (voxel size 1×1×1 mm) was collected. Functional image data were collected as gradient-echo, echo-planar (EPI) T2$*$-weighted images with blood oxygenation level-dependent (BOLD) contrasts (Kwong et al., 1992; Ogawa et al., 1992). Image volumes from the whole brain were built up from contiguous axial slices (n=32). The following parameters were used for the fMRI scanning: echo time, 50 ms; field of view, 22 cm; matrix size, 64×64 (after ramp sampling); pixel size, 3.4×3.4 mm; flip angle, 90°; slice thickness, 4 mm; repetition time (TR), 2.5 s; number of volumes per session, 164. The image volumes were collected continuously during separate sessions and each volume consisted of 32 evenly spaced out slices. Time between slice echo

			stimuli (blinking square on a computer screen); the second group learned the identical sequence by an auditory stimulus.				centers was always 78 ms. We started each session by collecting four 'dummy' image volumes that were not stored, to allow for T1 equilibration effects.
(Kim et al., 2004)	fMRI	During Post	In the first fMRI session, subjects carried out repetitive LAFA movement of the little finger with maximal efforts. In the second task, stimulation of the little finger was carried out by two of the authors. A slightly rough string was rubbed back and forth at 12 cm/sec. After 6 months of practice subjects were asked to carry out the LAFA movement at a slower speed, approximately half their maximum effort. Each block paradigm consisted of 16 blocks (21 sec/block) alternating between rest and activation (rest-right-rest-left, repeated for four cycles).	Blood oxygen level-dependent (BOLD) imaging was carried out on a 1.5-T MR scanner (GE Signa whole-body and standard RF coil) equipped with echo-planar imaging (EPI).	middle temporal gyrus, inferior occipital gyrus, superior temporal gyrus, R postcentral gyrus, L precuneus, L inferior parietal lobule, R ventral premotor cortex, Anterior cingulate, cingulate gyrus, R postcentral gyrus, medial frontal gyrus,, R inferior frontal gyrus, R midbrain, (substantia nigra) , R basal ganglia, L posterior cingulate, L middle cingulate, R superior frontal gyrus, postcentral gyrus, Cerebellum, precentral gyrus, R hippocampal gyrus, R/L dorsal frontal gyrus, R inferior occipital gyrus	Fingering frequency Consistent performance was monitored visually	Twenty axial slices of 5 mm thickness, parallel to the line through the anterior and posterior commissure, were collected using a gradient echo EPI sequence (repetition time [TR] = 3s; echo time [TE] = 60ms; flip angle = 90 degrees; field of view [FOV] = 240 mm). For subsequent anatomic coregistration, T1-weighted images (TR = 500ms, TE = 12ms, flip angle = 90 degrees) were acquired in axial planes using the same slice selection parameters as that used in the BOLD imaging.

(Laha v et al., 2007)	fMRI	Post	A total of 32 fully orchestrated short passages extracted from three musical pieces were presented in a counterbalanced block design, with a total of 108 sets of axial images acquired during nine functional runs. After listening to each musical passage, subjects heard a three-tone sequence and had to press a button with their left hand if these notes had appeared as a subsequence in the preceding musical passage they had heard.	A 3T GE whole-body system (GE Medical Systems, Milwaukee, WI)	frontoparietal motor-related brain regions, premotor region, Broca's area and its right hemispheric homolog, posterior inferior frontal gyrus, primary and secondary auditory cortices	Learning time Pitch-recognition-production test: Subjects heard 30 single piano notes and had to press the corresponding piano key with the matching right-hand finger for each note at a time.	During each run, we acquired 12 sets of 28 axial slices (eight listening scans and four rest scans; total run time, 234 s). functional magnetic resonance images using a gradient echo-planar T2* sequence sensitive to the blood oxygenation level-dependent contrast (voxel size, 2 /// 2 /// 4 mm). T1-weighted anatomical images (voxel size, 0.93 /// 0.93 /// 1.5 mm)
(Landau et al., 2006)	fMRI	During	Each participant viewed a backlit projection screen at his or her waist from within the magnet bore through a mirror mounted on the head coil. The participants responded to stimuli presented on the screen by making keypresses on two nonmagnetic bimanual response keyboards (each containing five keys, corresponding to the right and left hands) designed for use in the scanner. They were instructed to respond as quickly and accurately as possible, making bimanual keypresses in response to Xs presented in eight possible locations on the screen that mapped spatially onto response boxes. There were two types of trials: probabilistic sequence trials (S) and random stimuli (R).	Functional and structural images were acquired with a Varian INOVA 4.0T scanner and a TEM send-and receive RF head coil.	Inferior frontal gyrus, Putamen, Middle temporal gyrus, Caudate, Thalamus, Primary motor cortex, Presupplementary motor area, Supplementary motor area, Ventral premotor cortex, Dorsal premotor cortex, Supplementary motor area, Superior temporal gyrus, Ventral premotor cortex, Putamen, Dorsal premotor cortex, Superior parietal lobule	During the scanning session: reaction time Following the scanning session: the participants were questioned about their awareness of sequences in the stimuli.	Functional images were acquired using a two-shot gradient echo EPI sequence (TR = 2.18 sec, TE = .028 sec, matrix size = 64 X 64, FOV = 22.4 cm) to acquire data sensitive to the blood oxygen level dependent (BOLD) signal. Eighteen axial slices of 3.5-mm voxels (with 1.0-mm interslice gap) were acquired. Each slice was acquired with a 22.4 cm2 field of view with a 64 X 64 matrix size resulting in an in-plane resolution of 3.5 X 3.5 mm. This slice prescription allowed for whole-brain coverage. Twenty seconds of dummy gradient and RF pulses preceded each scanning run to approach steady-state tissue magnetization. Two high-resolution structural T1-weighted scans were also acquired for anatomical localization. The first collected 18 axial slices in the same plane as the EPI images (TR = .200 sec, TE = .050 sec, matrix size= 256 X 256, FOV = 22.4 cm). The second was a 3-D MP-FLASH scan (TR = .090 sec, TE = .048 msec, T1 = 300 msec)

(Lappe et al., 2008)	MEG	Pre Post	They used a three- and a six-tone piano sequence. In the three-tone sequence, the duration of a recording epoch was 1.8 s, and in the six-tone sequence, 3.6 s, including 0.2 s prestimulus intervals, respectively. The data recording was synchronized to the stimulus presentation in each trial. The total recording time was 60 min. The recordings were performed in a magnetically and acoustically shielded room. The subjects were in an upright position, seated as comfortably as possible while ensuring that they did not move during the measurement.	Magnetic field responses were recorded with a 275-channel whole-cortex magnetometer system (OMEGA 275; CTF Systems) with interchannel spacing of 2.2 cm. The MEG pickup coils use a 2 cm diameter configured as first-order axial SQUID gradiometers with 5 cm baseline (Vrba and Robinson, 2001).	Cortex Left and right hemisphere	Auditory discrimination test: Thirty-five sequences of the I–IV–V–I chord progression in C-major that were used for training were played after being recorded from a trained musician with built-in mistakes in 13 sequences. The participants listened to these recorded sequences and responded by pressing the right-foot pedal of the piano whenever they heard a wrong note.	/
(Pau et al., 2013)	fMRI	Post	Participants were positioned supine in the MRI scanner and were given four-finger-key pads (LUMItouch, Harvard, USA) adapted for each hand. During the scanning session, immediately following the training, encoding and replaying sequences was performed first with auditory feedback as during training and in a second run without auditory feedback. Sequence encoding was required in each trial and consisted of studying the finger sequences as described in the	A 3 T Siemens Magnetom Verio (Siemens, Erlangen, Germany) a 12-channel head coil was used to acquire both a T1-weighted structural volume of the whole head	Primary somato-sensory cortex (S1), Brodmann area, Primary motor cortex (M1), Supplementary motor area (SMA), Dorsal premotor cortex (dPMC), SPL, Ventral premotor cortex (vPMC), Inferior parietal lobe (IPL), Inferior	Performance: proportion of errors	A 3 T Siemens Magnetom Verio (Siemens, Erlangen, Germany) equipped with a 12-channel head coil was used to acquire both a T1-weighted structural volume of the whole head (MP-Rage; 176 sagittal slices, voxel size: 1 mm×1 mm×1 mm) and T2*-weighted echo-planar images (EPI; TR=2000 ms, TE=30 ms, flip angle 90°, 34 axial slices, voxel size of 3 mm×3 mm×3 mm, field of view (FOV) 192 mm). For each participant 965 3-D echo planar images were obtained, the first 5 dummy volumes in each session being

			training session. In the first run, encoding was immediately followed by sequence retrieval with auditory feedback.		frontal gyrus (IFG), Cerebellar hemispheres, Dorsolateral pre-frontal cortex (DLPFC), Fusiform gyrus Occipital lobe, MT, Insula, Temporal lobe (TL), superior gyrus, middle gyrus, gyrus of Heschl, Putamen		discarded to allow for T1 equilibration effect. The
(Ruiz et al., 2017)	MEG	During	Participants were comfortably seated and were instructed to focus their eyes at a central fixation point on the screen during playing and, in between-trials, to focus on the visual cues. Rate of the signals: 1000 Hz with a bandwidth ranging from direct current (DC) to 330 Hz. Participants listened to the auditory feedback associated to the key presses and were instructed to play the sequence several times during the trial without pause.	Neuromag Vectorview MEG (Elekta, Helsinki, Finland) with 204 orthogonal planar gradiometers and 102 magnetometer s at 102 locations.	Cortical surface of each hemisphere, cingulate gyrus, temporal gyrus, cerebellum,SMA, functional area of the dorsolateral prefrontal cortex	Assess their estimation of rates of self-produced errors in the control condition as well as their awareness of the different types of feedback. General performance: average timing (IOI), temporal variability, pitch error rate, and average keystroke velocity Behavioral adaptations to AAF were evaluated in terms of postfeedback slowing (putative larger IOI at keystrokes following AAF), pitch error rate, and distance of pitch errors from AAF (number of keystrokes away from current AAF).	Individual T1-weighted MRI images (3 T Magnetom Trio, Siemens AG, Germany) were used to construct topographical representations of the cortical surface of each hemisphere with Freesurfer (http://surfer.nmr.mgh.harvard.edu/).
(Schal les et	EEG	Post	Listening to: six-second-long clips (two measures) from the	EEG and ocular EMG	Electrode placement: F3,	Length of time to complete training was recorded each	/

al., 2015)			three songs: the song they learned to play, a transposed version of that song, and a control song with different notes and sequence from the learned song. A pair of probe tones followed each song clip and subjects were asked to respond if the two tones were present in the previous song clip. Ten clips were created from each song, totaling 30 trials across the three conditions. A resting period of two seconds preceded the onset of song stimuli. (A moving baseline for mu ratio calculations was collected from this prestimulus window, across all three conditions.)	were recorded using a Neuroscan Synamps system, according to the 10–20 standards for electrode placement.	Fz, F4, F7, F8, Fp1, Fp2, C3, Cz, C4, P3, Pz, P4, T5, T6, O1, O2, T3, T4, VEOG Frequency band analysis on: theta, mu, beta and gamma bands	day, and a training slope variable was calculated by a linear fit of the difference between the first and the second days of training. Pitch-Recognition-Production Task	
(Wu et al., 2017)	EEG	Pre During Post	EEG was recorded during two timepoints in an electrically shielded, sound-attenuated room: 1 before training and one after training In audio trials: Listening to 3000ms sequences and keep still. In audiomotor block: Listening to a tone sequence and play back the sequence (keyboard) Rest block: sit still and fixating on the centre of the screen	128-channel Electrical Geodesics amplifiers and Ag/AgCl nets	sensorimotor cortex of the left (C3) and right (C4) hemispheres Electrodes of interest: C3, FC3, CP3, Fz, FCz, Cz, C4, FC4 and CP4	Training performance: three-second-long tone sequences consisting of notes between C5 and G5 were generated online using values for the parameters (a) number of notes; b) range of notes; c) note length range) that met the criteria for a particular level (smaller values for lower levels)	/

Table 6 Results brain imaging

Article	Task	Time-point	Frontal							Parietal			Temporal			Occipital	Limbic system	Basal Ganglia	Cerebellum	Retro-splenial cortex	Thalamus	Insula
			Area	Prefrontal cortex	Motor area	Premotor area	Supple-mentary motor area	Frontal gyrus	Primary motor area	Area	Somato-sensory cortex	Sensori-motor cortex	Area	Heschl's gyri	Temporal gyrus	Auditory cortex	Area	Cingulate cortex					
(Bangert et al., 2003)	Passively listening and pressing soundless piano keys	Before	xii,xiv,xv						xiii,xiv,xv: L	xii, xv													
		During	xvi, xii, xiv: B-Lt xii, xiv: central sulcus xvi, xii, xiii, xiv: FT							xii,xv xii,xiii until week 3 xiv xii,xiii after week 3 xiv		xvi,xvii: 1-L xii,xiv xiii,xiv after 20 min: IL	xvi, xii, xiv		xvi,xiii: I xiv								
		After	xii,xiii,xiv: FT xii,xiv: R xii,xviii							xii,xiv xii, xv			xii, xvii: B									
(Chen et al., 2012)	Listening	Before				B-V-D				B-I				L	S-B								
		During	i,ii: R-S sulcus	i,iii: OFC ii: L-OFC	i,ii: R iii: V-B	i,ii,iii: L-D	i,ii: R										i,ii: LOC R	i,ii: R-A & R-P			i,ii: R		
		After			iv: D iv: R-V			iv: I-R PO		iv: I-R					iv								
(Herholz et al., 2016)	Listening, judging, imagining, pressing respons key	Before	v: I						v,vi: L	v: S						vi: 1 & 2 b v:2			vi: caudate	v,vi		vi: B	
		After		iv: DL	iv: L-M	all melodies v: L-D				iv: infraparietal sulcus P-B							vii: LOC			vii			
(Jantzen et al., 2002)	Squeezing to an auditory stimulus	Before						xi: B-I	x: CL, B-M	xi: CL-GPC					xi:R x:R-S				xi: B-putamen	xi		x: L-V-lateral nucleus	x: L xi: L-P
		After						x: M	x&xi: CL			x & xi: R-pre			x: B				xi & x: B-putamen			xi: L	
(Karabanov et al., 2009)	Rhythmic tapping	After				xxxiv: L-DL-V-mesial				xxxiv: Infra-parietal sulcus xxxv: L-SMG		xxxiv: pre	xxxiv: TPJ		xxxv: M			xxxiv: MCA	xxxiv: putamen & Globus Pallidus	xxxiv			xxxiv
(Kim et al., 2004)	Repetitive lift-abduction/fall-adduction little finger	Before										viii > ix											
		After		ix: R-M		ix: R-V		ix: R-I & L-M		ix: I, L-precuneus					ix: R-A-S & R-P-M viii: R-M ix: L		viii: I-gyrus	ix: M-P		ix		ix	

Article	Task	Time-point	Frontal							Parietal				Temporal				Occipital	Limbic system	Basal Ganglia	Cerebellum	Retro-splenial cortex	Thalamus	Insula
			Area	Prefrontal cortex	Motor area	Premotor area	Supple-mentary motor area	Frontal gyrus	Primary motor area	Area	Somato-sensory cortex	Sensori-motor cortex	Area	Heschl's gyri	Temporal gyrus	Auditory cortex	Area	Cingulate cortex						
(Lahav et al., 2007)	Listening	After				xxviii: P-M xxix: L-P		xxx: L-PO xxviii & xxix: I-P (Broca) all: R-PO		xxviii: B-I						xxviii: 1-2-B					xxviii: L			
(Landau et al., 2006)	Bimanual keypresses on visual stimuli	During	xxiii,xix,xxi: R-PCG			xix, xxi		xxi,xxiii: L-M xxi: R-S xix,xx: I xxii: R-M	xxi,xix,xxii: R xxiii	xix,xx,xxi: L-GPC xix,xxi: I-R-S xxiii: L-I xxii: B-precuneus					xix,xx: R-I xix,xx: I		xxii: B-EXR xxiv: L	xxii: B-A xix, xxi: L xxiv: L-Hip xxii: L	xix: B & R-caudate				
(Pau et al., 2003)	Encoding and replaying	After	xix, xxxii: I xxxiii, xxxi + FB: DL	xix,xxxi: DL	xix, xxxii: M +FB	xxxii: D xxxi, xix		xxxiii, xxxi +FB: I-B	xix, xxxi xix,xxxii: B	xix,xxxii: S-Lt xix,xxxii: S-I xix,xxxi+ FB: S-L-I	xix: 1 xix,xxxi: B	xix: B xxvii xix,xxxi+ FB: 1-B	xix,xxxi+ FB: B xxxiii,xxxi+FB	xix,xxxi+ FB: L (m&nm) xxxi- FB		xix,xxxi: 1	xix,xxxi+ FB: L xxxiii,xxxi+FB		xix,xxxi+ FB	(m&nm) xxxii: B xix,xxxi+ FB: B		xix,xxxi+ FB
(Ruiz et al., 2017)	Listening, playing a sequence on the keyboard, sit still	During	xxv: M-FP-theta & R-FP-theta xxvii: L-beta											xxv: M-B-beta xxvi: I-B-theta				xxv& xxvii: theta		xxv: B-theta xxvi: theta xxvii: beta			

L= left, R= right, B= bilateral, I= inferior, S= superior, P= posterior, D= dorsal, V= ventral, CL= contralateral, IL= ipsilateral, DL= dorsolateral, Lt= lateral, M= medial

i= Late compared to early training, ii= during random playback, iii= during melody playback, iv= listening to trained compared to untrained melodies, v= Imagining condition*, vi= listening to familiar songs, vii= imagining trained compared to untrained music, viii= right little finger, ix= left little finger, x= during synchronization, xi= during syncopation, xii= passively listening, xiii= pressing on soundless piano keys, xiv= map group**, xv= no-map group***, xvi= after 5 sessions, xvii= after 10 sessions, xviii= professional pianists, xix= musicians compared to non-musicians, xx= during random trials, xxi= during sequence trials, xxii= non-pianists playing random sequences, xxiii= pianists playing sequences, xxiv= non-pianists playing sequences, xxv= ASO – NAF****, xxvi= UAF – NAF*****, xxvii= ASO-UAF******, xxvii= listening to trained compared to untrained different notes, xxix= listening to trained compared to untrained same notes, xxx= listening to trained music, xxxi= retrieval, xxxii= encoding, xxxiii= non-musicians compared to musicians, xxxiv= during rhythm production, xxxv= visual metronome modality

Timepoints= timepoints when the imagening took place, Pre= pre-sensorimotor cortex, GPC= gyrus postcentralis, FT= frontotemporal area, PCG= precentral gyrus, EXR= extrastriate region, Hip= hippocampus, FP= frontoparietal, theta= theta band spectral power, beta= beta band spectral power, PO= pars opercularis, all= all conditions, FB= feedback, m= musicians, nm= non-musicians, Infra-PS= infra-parietal sulcus, SMG= supramarginal gyrus, TPJ= temporoparietal junction, MCA= motor cingulate area, OFC= orbitofrontal cortex

* instead of the full melody, only an initial segment of melody was presented, followed by a silent gap. Participants had to imagine the continuation of the melody during the silent gap and judge the correctness of the last tone.

** allowed to learn a key-to-pitch map

*** a key-to-pitch map was prevented by random assignment of keys to tones during training

**** Alterations of serial order compared to normal auditory feedback

***** Unrelated auditory feedback compared to normal auditory feedback

****** Alterations of serial order compared to unrelated auditory feedback

Part 2: research protocol

1. Introduction

Multiple sclerosis (MS) is a chronic progressive auto-immune disease which is characterized by random, multifocal demyelination in the central nervous system (Lundy-Ekman, 2013). Most commonly, the disease's age of onset is seen between twenty and thirty years old, with women being affected twice as frequently as men (Grossman, Porth, 2014). Symptoms are highly variable because the demyelination can appear in a wide range of locations and the extent of lesions varies (Lundy-Ekman, 2013). Many people with MS (PwMS) exhibit abnormal balance and gait control, increasing fall risk[32]. Frequently, imbalance is one of the first visible symptoms[32]. This altered postural control is seen in several contexts, including stance under challenging sensory conditions, leaning, or reaching to the limits of stability, postural responses to a loss of balance, continuous gait, and anticipatory postural adjustments (APAs)[33]. Positive results on motor and cognitive functions have been found in patients with neurological diseases after music-based interventions[13]. Growing evidence exists that music might directly promote neuroplasticity through increased activation of auditory-motor, cortico-spinal pathways, and mesolimbic dopaminergic pathways[13]. Previous research showed that auditory cueing has a positive effect on postural balance in quiet standing tasks[34] and verbal memory and focused attention can improve after listening-based music interventions in stroke patients[13]. However, this has not yet been investigated in PwMS. Furthermore, using auditory feedback cues can improve the walking ability in PwMS[34] and be effective in decreasing double-support time during walking[35]. However, there are still no definite conclusions on the rehabilitative effect of music[35]. Another advantage of music-based interventions is the positive effect on mood (e.g. depressive and anxiety disorders), emotional expression, communication, interpersonal skills, self-esteem, and quality of life[36]. Until now, the effects of auditory-motor learning on balance in PwMS is not yet investigated. Theories of embodied association assume that a sequence can be more easily learned when spatial body movement is involved (i.e. a choreography or sequence of steps that execute the sequence)[37, 38]. Embodied associations can be understood as processes that facilitates the recall and execution of sequences due to neural connections between the motor system and the auditory system. Therefore, the aim of this study is to investigate the effects of learning motor sequences with auditory feedback on balance in PwMS.

2. Aim of the study

2.1 Research question

The aim of this study is to investigate the effect of auditory-motor training using embodied associations on motor performance (i.e. postural balance) with the use of a sonified sensor platform. This is translated in following research question:

‘Does auditory-motor learning induce faster learning rates and greater improvements in balance compared to visual-motor learning in PwMS?’

2.2 Hypothesis

Based on our previous research that showed involvement of multiple brain networks during the producing of auditory/musical sequences and the embodied associations theory, we expect an improvement of balance after learning motor sequences with auditory feedback. For the same reasons, we hypothesize that auditory-motor training is superior to visual-motor training concerning learning rates.

3. Methods

3.1 Research design

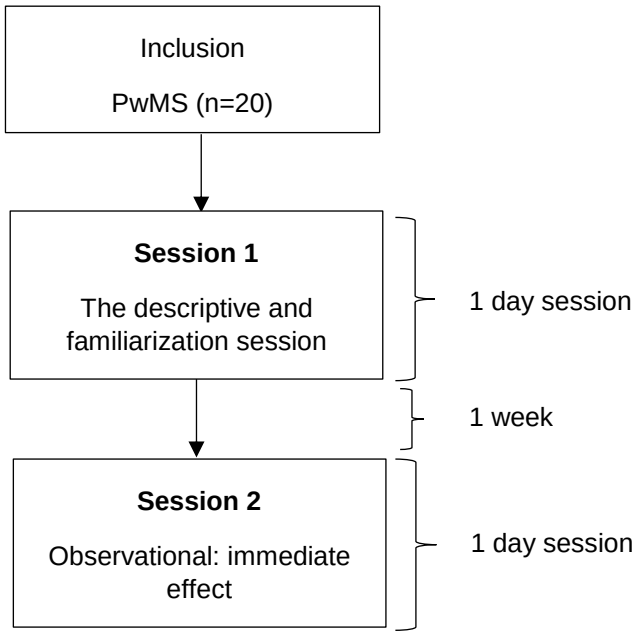

Figure 1 Research design

We will apply an observational study with one group consisting out of 20 PwMS. Once participants are included, they will undergo a descriptive session where an anamnesis and clinical descriptive data will be collected. See table 1 for the descriptive outcome measures that will be collected. Clinical descriptive measures will be assessed in order to be informed of the clinical picture of the participant, and otherwise to perform a responder's analysis once the experiment is completed, in order to interpret the results in depth. See table 2 for a detailed overview. Participants will then be familiarized with the platform. In the observational immediate effects session, two blocks will be tested i.e. one auditory block consisting of musical sequences, and one visual block. Because fatigue is common in PwMS, there will be twenty minutes rest time in between the blocks. The blocks will be administered randomly. Figure 2 illustrates the experimental condition per block. Figure 3 shows an example of the visual condition and figure 4 of the auditory condition. When the pads are triggered by pressure, real-time auditory feedback will be heard because the sensor pads are sonified. The pressure will be created by the steps/movements of the participants on the pads. In block one, the feedback will be auditory with a wrong part of the melody going off when the participant makes an incorrect movement, or a correct part of the melody will occur when the movement is correct. In block two, feedback will be visual with pads lighting up green when the participant's movement is correct and red when the movement is incorrect. All the outcome measures will be tested after block one and after block two of the second session. Only balance will also be measured next to the descriptive tests in the first session.

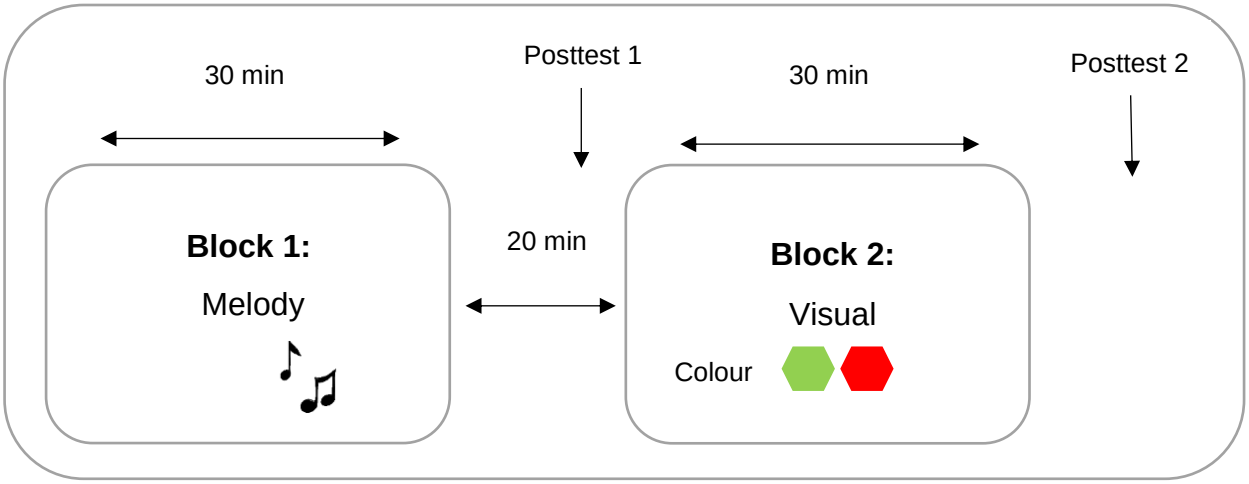

Figure 2 Experimental condition per block

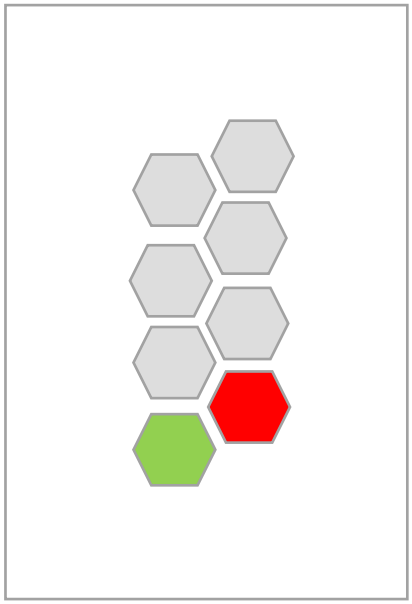

Figure 3 Example of the visual condition

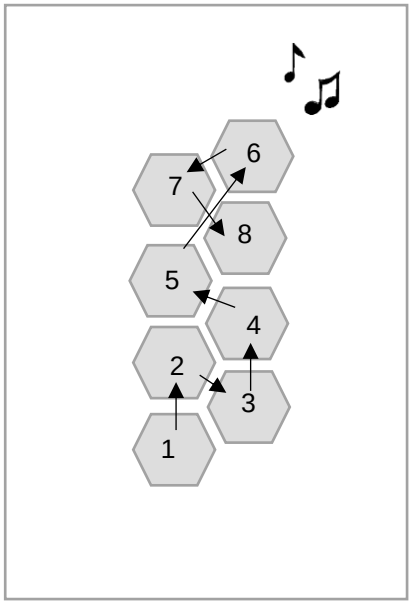

Figure 4 Example of an auditory sequence (the numbers represent the sequence and will not be seen on the pads)

3.2 Participants

3.2.1 Inclusion criteria

Ambulatory PwMS with motor disability of balance, using the outcome measures of dynamic gait index (cut off scores: ≤ 19)[39] .

3.2.2 Exclusion criteria

Exclusion criteria involve cognitive impairment hindering the understanding and execution of the experimental procedures, pregnancy, hearing impairment, amusia and beat deafness. Patients will also be excluded if they have a relapse or acute exacerbation.

3.2.3 Patient recruitment

20 PwMS will be recruited. We will contact the MS-centrum Overpelt and Melsbroek for the recruiting of the participants. The centers have the capacity to accommodate approximately 150 inpatients and more than 400 out-patients. If needed, we will also contact other hospitals, like Virga Jesse and UZ Leuven, and private practices around Hasselt. We will contact them by phone and place flyers in the hospitals.

3.3 Medical ethics

An ethical application will be submitted in August to:

- The central ethical committee in University Hospital of Ghent University
- The local ethical committee of University of Hasselt,
- The local ethical committees of the MS centers, the national MS center and Rehabilitation and MS center Overpelt.

3.4 Intervention

3.4.1 Descriptive and familiarization session

Once participants are included, they will undergo the descriptive session. In this session, we collect an anamnesis and clinical descriptive data. See table 1 and 2 in the appendices. Participants will then be familiarized with the platform. The following Instructions will be given: “each sensor pad corresponds to a specific auditory stimulus, and that stimulus will be triggered by stepping on the respective sensor pad”. Explanation of the task will than follow: sequences will be learnt and reproduced by stepping on the sensor pads. Participants will be clearly told that there will be one melody block and one visual block. In the melody block, musical sequences will be used. Lastly, a demonstration will follow; a melodic sequence will be presented on the platform by the sensor pads lighting in the pattern of the sequence.

3.4.2 The observational immediate effects session

In this session, two blocks will be tested: a melody block and a visual block, with twenty-minute rest time in between. The order of administration will be randomized using concealed envelopes.

3.4.2.1 Block one

The experiment will start by the demonstration of the melodic sequence which will have a constant rhythm. The participant will then be asked to produce the sequence by stepping on the correct sensor pad. When stepping on the right sensor pads, a musical sequence will be heard. However, when stepping on a wrong sensor pad, an incorrect part of the melody will be heard. If the participant fails to reproduce the sequence five times in a row, the sequence will be demonstrated again. Once the participants produce the sequence correctly three times in a row, a new melodic sequence will be given. This sequence will serve as a distractor sequence. Participants will be asked to re-produce this sequence, and then follow it by immediately recalling the first melodic sequence, however the recall will have no feedback. A twenty-minute rest period will be allocated, and then the participants will be asked to recall the first melodic sequence once more.

3.4.2.2 Block two

Block two is the same as block one, but the stimuli will be presented visual instead of auditory. When stepping on the wrong sensor pad, the pad will light up in red. When stepping on the right sensor pad, the pad will light up in green. The sequence will be considered as learned when the participant is able to reproduce the sequence three times in a row. If he fails to reproduce the sequence five times in a row, the sequence will be demonstrated again. A distractor sequence will also be used in this block after executing the sequence correct for three times in a row.

3.5 Outcome measures

3.5.1 Primary outcome measures

Our primary outcome measure will be balance, measured by the FSST and DGI, learning and learning rates, measured by the amount of trials per block required until the correct sequence is produced, and by the recall of the sequence after the distractor sequence. The FSST and DGI can be found in the appendices, document 1 and 2.

3.5.2 Secondary outcome measures

Our secondary outcome measures will be fatigue and motivation, measured by a VAS-scale, so feasibility of the intervention can be assessed. See document 3 in the appendices.

3.6 Data analysis

SAS JMP statistical software will be used for analysis of the clinical data. Pre- and post-measurements are used in the study design, this implies the use of mixed models ANOVA for the statistical analysis.

4. Time planning

The ethical committee will be contacted in September 2018. The recruiting flyers will also be made in this period. The patient recruitment and testing are expected to run from October 2018 until March 2019. Digitizing and processing of the data will start in February/March 2019.

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6. Appendices part 2 – research protocol

- Table 1: Descriptive data
- Table 2: Collection of descriptive data

- Document 1: Dynamic gait index
- Document 2: Four Step Square Test
- Document 3: VAS scale
- Document 4: Descriptive information

Table 1	
Descriptive outcome measure	
Participant information	Name and Surname
	Gender
	D.O.B
	Height
	Weight
	Address- Street name and number, zipcode, town, country
	Email address
	Mobile number
Education level	Highschool
	Practical/skill studies
	Bachelor
	Master
	Doctorate
	Total years of education
MS related information	Date of Diagnosis
	Date of first MS symptom
	Type of MS (RR, PP, SP)
	Date of last relapse
	MS medication
	Last date of MS medication change (and name of previous medication)
	Medication for spasticity, muscle weakness, fatigue
EDSS*	Date of assessment
	From medical record? (yes/no)
	By neurologist? (yes/no)
	If not, please specify
	EDSS score
Music related questions	Experience (actively performing one or more of the following activities once a week: dancing, singing (vocal lessons), playing an instrument).

*The EDSS is scored by the neurologist assisting in screening participants for inclusion, or if available (within 6 months of inclusion) collected from existing patient files.

Abbreviations: D.O.B.- date of birth; RR- relapsing remitting, PP- primary progressive, SP- secondary progressive; EDSS- expanded disability statues scale; FS- functional systems

Table 2			
Domain	**Tests and Outcomes *(unit of measurement)***	**Equipment time needed**	**Estimated time required**
Muscle weakness	Motricity Index: - Dorsi flexors - Knee extensors - Hip flexors	▪ Therapist	10-15 minutes
Spasticity	Modified Ashworth scale for: - Hamstrings - Tricepts surae - Quadricepts		
Ataxia	- Dysdiadochokinesia test - Heel-to- shin test	▪ Instructions ▪ Timer	5 minutes
Balance	TUG with the APDM sensors	▪ Chair ▪ APDM sensors ▪ 3 m walkway ▪ Timer ▪	5 minutes
Ambulatory performance	T25FW	▪ 25m walkway ▪ Timer	5 minutes
Gait pattern and endurance	6MWT *(minute by minute data of distance covered, velocity, cadence and stride length).*	▪ Accelerometers ▪ 30m walkway	10 minutes
Cognitive function	The Brief international cognitive assessment for MS (BICAMS).	▪ Workbook with printed versions of tests (and gadgets, e.g. for 7/24 test). ▪ Stop Watch. ▪ Quiet Office	20 minutes
Cognitive-Motor Interference: Dual Task Protocol	Simultaneous performance of the following tasks: - Cognitive tasks: world list generation phonemic And - Motor task- walking for one minute while carrying a mug filled with water with the dominant hand. *(Distance covered in one minute. Number of correct words uttered for cognitive task*	▪ Laptop ▪ DT protocol software (download) ▪ 8m walkway ▪ Mug	15 minutes
MS walking scale	Is a self-reported measure of the impact of MS on the individual's walking ability.	▪ Quiet room ▪ The questionnaire (12 items)	45 minutes
Activities-specific balance confidence scale	Is a self-reported measure that asks people to rate their balance confidence in performing everyday activities on a numeric rating scale.	▪ Quiet room ▪ The questionnaire (16 items)	

Modified Fatigue Impact Scale	This instrument provides an assessment of the effects of fatigue in terms of physical, cognitive, and psychosocial functioning.	▪ Quiet room ▪ The questionnaire (21 items)
Hospital Anxiety and Depression Scale	Is a self-reported outcome measure to determine the levels of anxiety and depression that a patient is experiencing.	▪ Quiet room ▪ The questionnaire (14 items)
Barcelona Music Reward Questionnaire	Questionnaire regarding musical training, current musical activities/hobbies and the reward value of music.	▪ Quiet room ▪ The questionnaire (10 items)
Dual Task questionnaire	The following questions describes the troubles a person has when performing a dual task during daily activity.	▪ Quiet room ▪ The questionnaire (10 items)

Document 1: DGI

Dynamic Gait Index
Scoring Form

1. Gait Level Surface

Instructions: Walk at your normal pace from here to the next mark (20 feet).
Grading: Mark the lowest category that applies.

____(3) Normal: Walks 20', no assistive devices, good speed, no evidence of imbalance, normal gait pattern.

____(2) Mild Impairment: Walks 20', uses assistive devices, slower speed, mild gait deviations.

____(1) Moderate Impairment: Walks 20', slow speed, abnormal gait pattern, evidence of imbalance.

____(0) Severe Impairment: Walks 20' without assistance, severe gait deviations or imbalance.

2. Change in Gait Speed

Instructions: Begin walking at your normal pace (for 5 feet), when I tell you 'go', walk as fast as you can (for 5 feet). When I tell you 'slow', walk as slowly as you can (for 5 feet).
Grading: Mark the lowest category that applies.

____(3) Normal: Changes walking speed smoothly without loss of balance or gait deviation. Shows a significant difference in walking speeds between normal, fast, and slow.

____(2) Mild Impairment: Changes speed but demonstrates mild gait deviations, or no gait deviations but unable to achieve a significant change in velocity, or uses an assistive device.

____(1) Moderate Impairment: Makes only minor adjustments to walking speed, or accomplishes a change in speed with significant gait deviations, or changes speed but loses significant gait deviations, or changes speed but loses balance but is able to recover and continue walking.

____(0) Severe Impairment: Unable to change speeds, or loses balance and has to reach for wall or be caught.

3. Gait with Horizontal Head Turns

Instructions: Begin walking at your normal pace. When I tell you 'look right', keep walking straight and turn your head to the right. Keep looking to the right until I tell you 'look left', then keep walking straight and turn your head to the left. Keep your head to the left until I tell you 'look straight', then keep walking straight but return your head to the center.
Grading: Mark the lowest category that applies.

____(3) Normal: Turns head smoothly with no change in gait.

____(2) Mild Impairment: Turns head smoothly with slight change in gait, i.e. minor disruption to smooth gait path, or uses walking aid.

____(1) Moderate Impairment: Turns head smoothly with moderate change in gait, i.e. slows down, staggers but recovers, can continue to walk.

____(0) Severe Impairment: Turns head smoothly with severe disruption of gait, i.e. staggers outside 15" path, loses balance, stops, reaches for wall.

*Reproducible Master Scoring Form accompanying VHI's "**Administering Functional Assessment Tests**" DVD #2.*

4. Gait with Vertical Head Turns

Instructions: Begin walking at your normal pace. When I tell you 'look up', keep walking straight and tilt your head up. Keep looking up until I tell you 'look down', then keep walking straight and tilt your head down. Keep looking down until I tell you 'look straight', then keep walking straight and return your head to the center.
Grading: Mark the lowest category that applies.

____(3) Normal: Performs head turns with no change in gait.

____(2) Mild Impairment: Performs head turns with slight change in gait, i.e. minor disruption to smooth gait path or uses walking aid.

____(1) Moderate Impairment: Performs head turns with moderate change in gait, i.e. slows down, staggers but recovers, can continue to walk.

____(0) Severe Impairment: Performs head turns with severe disruption of gait, i.e. staggers outside a 15" path, loses balance, reaches for wall.

5. Gait and Pivot Turn

Instructions: Begin walking at your normal pace. When I tell you 'turn and stop', turn as quickly as you can to face the opposite direction and stop.
Grading: Mark the lowest category that applies.

____(3) Normal: Pivot turns safely within 3 seconds and stops quickly with no loss of balance.

____(2) Mild Impairment: Pivot turns safely in over 3 seconds and stops with no loss in balance.

____(1) Moderate Impairment: Pivot turns slowly, requires verbal cueing, requires several small steps to catch balance following turn and stop.

____(0) Severe Impairment: Cannot pivot turn safely, requires assistance to turn and stop.

6. Step Over Obstacle

Instructions: Begin walking at your normal pace. When you come to the obstacle, step over it, not around it, and continue walking.
Grading: Mark the lowest category that applies.

____(3) Normal: Steps over box without changing gait, no evidence of imbalance.

____(2) Mild Impairment: Steps over box, but must slow down and adjust steps to clear box safely.

____(1) Moderate Impairment: Steps over box, but must stop before stepping over. May require verbal cueing.

____(0) Severe Impairment: Cannot step over box without assistance.

*Reproducible Master Scoring Form accompanying VHI's **"Administering Functional Assessment Tests"** DVD #2.*

7. Step Around Obstacles

Instructions: Begin walking at a normal speed. When you come to the first cone (about 6 feet away), walk around it on the right side. When you come to the second cone (6 feet past first one), walk around it on the left.
Grading: Mark the lowest category that applies.

_____(3) Normal: Walks around cones safely without changing gait, no evidence of imbalance.

_____(2) Mild Impairment: Walks around both cones, but must slow down and adjust gait to clear cones.

_____(1) Moderate Impairment: Walks around both cones, but must significantly slow gait or requires verbal cueing.

_____(0) Severe Impairment: Unable to clear cones, walks into one or both, or requires physical assistance.

8. Steps

Instructions: Walk up these stairs as you would at home (i.e. using the rail if necessary). At the top, turn around and come down.
Grading: Mark the lowest category that applies:

_____(3) Normal: Alternates feet, no rail.

_____(2) Mild Impairment: Alternates feet, must use rail.

_____(1) Moderate Impairment: Two feet to a stair, must use rail.

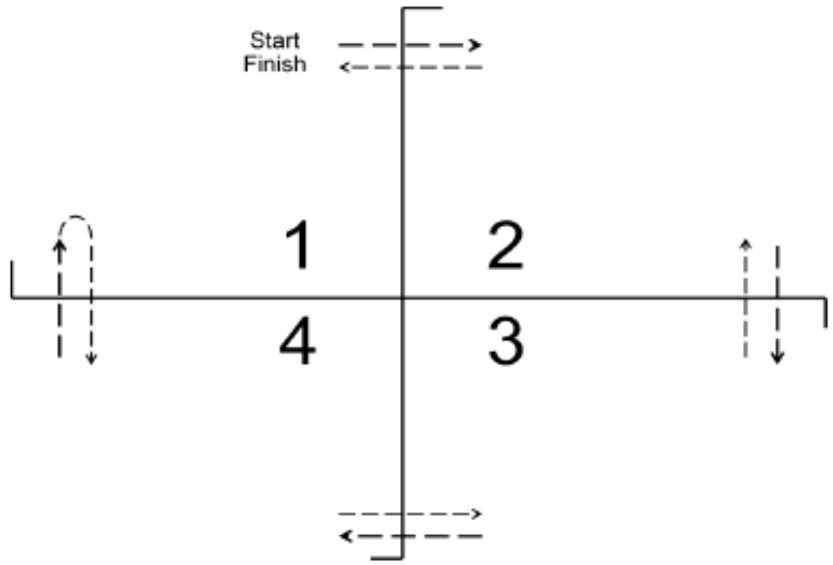
_____(0) Severe Impairment: Cannot do safely.

Four Step Square Test Instructions

General Information:

- The patient is instructed to stand in square 1 facing square number 2 (see figure below)
- The patient is required to step as fast as possible into each square in the following sequence: 2, 3, 4, 1, 4, 3, 2, and 1
  - requires the patient to step forward, backward, and sideway to the right and left
- Equipment required for the FSST includes a stopwatch and 4 canes.

Set-up (derived from Dite and Temple 2002): A square is formed with the 4 canes by resting them flat on the floor.



Patient Instructions (derived from Dite and Temple 2002):

- "Try to complete the sequence as fast as possible without touching the sticks. Both feet must make contact with the floor in each square. If possible, face forward during the entire sequence."
- Demonstrate the sequence to the patient.
- Ask the patient to complete one practice trial to ensure the patient knows the sequence. Repeat the trial if the patient is unsuccessful

at completing the sequence, loses balance, or contacts a cane during the trial.
- Two FSST are completed with the best time taken as the score.
- A score is still provided if the patient is unable to face forward during the entire sequence.

Scoring:
- the best time of two FSST is the score
- stopwatch starts when the first foot contacts the floor in square 2
- stopwatch finishes when the last foot comes back to touch the floor in square 1

Four Step Square Test (FSST)

Name:_____

Assistive Device and/or Bracing Used:_____

Date:_____

Trial 1_____sec.___ Trial 1_____sec.___

FSST Score (best timed trial):_____sec.___

Date:_____

Trial 1_____sec.___ Trial 1_____sec.___

FSST Score (best timed trial):_____sec.___

Date:_____

Trial 1_____sec.___ Trial 1_____sec.___

FSST Score (best timed trial):_____sec.___

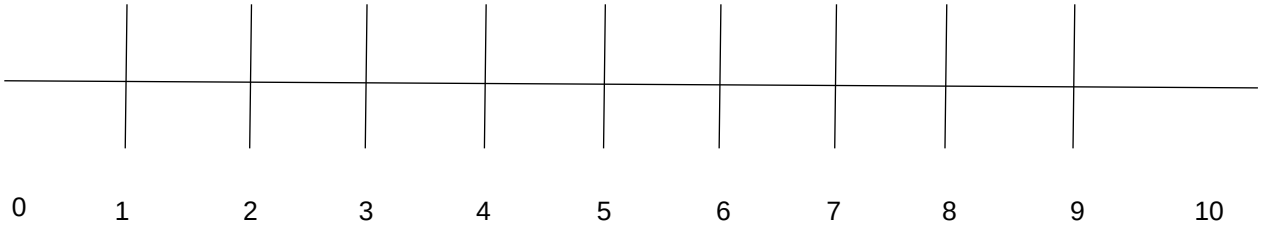
Date:_____

Trial 1_____sec.___ Trial 1_____sec.___

FSST Score (best timed trial):_____sec.___

References:
Dite, W. and Temple, V. A. (2002). "A clinical test of stepping and change of direction to identify multiple falling older adults." Arch Phys Med Rehabil 83(11): 1566-1571.

Document 3: VAS scale



Document 4: Descriptive information

Naam: Geb.datum: Datum:

Motricity Index

De Motricity Index (MI) is gericht op het evalueren van de willekeurige bewegingsactiviteit, dan wel het meten van de maximale isometrische spierkracht, aan de hand van een ordinale 6-puntschaal (0, 11, 19, 22, 26 en 33 punten). Betrouwbaarheid en validiteit bij patiënten met een CVA zijn aangetoond.

Testprotocol Motricity Index

Voor het uitvoeren van de test zijn een stoel of oefenbank en een kubusblokje van 2,5 cm nodig. De Motricity Index wordt afgenomen wanneer de patiënt zonder steun zit. Wanneer er (nog) geen rompbalans is mag de patiënt in de rug en zij worden gesteund. De gewenste beweging van een testitem mag zo nodig worden voorgedaan. Bij een volledige score van de arm (99 punten) en/of het been (99 punten) mag 1 punt worden opgeteld. De ernst van hemiplegie wordt berekend door (arm + been) te delen door 2,6.

A: Arm **1** ..... **punten** **2** ..... **punten** **3** ..... **punten** _____ (subtotaal) ..... **punten**	**Activiteit** **1** pincetgreep: vasthouden van een blokje van 2,5 x 2,5 cm tussen duim en wijsvinger **2** willekeurige elleboogflexie tot volledige flexie (± 160°)a **3** abductie van de schouder van 0° tot 90° b a de elleboog van de patiënt bij het isometrisch testen van de weerstand (25 punten of meer), in 90° flexie houden b de schouder van de patiënt bij het isometrisch testen van de weerstand (25 punten of meer) in 90° abductie houden	**Beoordeling** **Test 1:** 0 = geen beweging 11 = elke willekeurige beweging van vinger en/of duim 19 = patiënt pakt het blokje, maar kan het niet optillen (tegen de zwaartekracht in) 22 = patiënt pakt het blokje, maar kan het niet stevig vasthouden 26 = patiënt pakt het blokje, maar kan het minder stevig vasthouden dan aan de niet-paretische zijde 33 = normale knijpkracht (in vergelijking met de niet-paretische zijde
B: Been	**Activiteit** uitgangshouding patiënt: zit, knie 90° flexie, voeten plat op de grond (0° flexie)	**Beoordeling** **Test 2 t/m 6** 0 = geen willekeurige beweging
Beoordeling **4** ..... **punten** **5** ..... **punten** **6** ..... **punten** _____ (subtotaal) ..... **punten**	**4** willekeurige dorsale flexie van de enkel vanuit 0° flexie c **5** willekeurige extensie van de knie vanuit 90°d **6** willekeurige flexie van de heup vanuit 90° flexie e c de enkel van de patiënt bij het isometrisch testen van de weerstand (25 punten of meer) in ± 20° dorsale flexie houden. d de knie van de patiënt bij het isometrisch testen van de weerstand (25 punten of meer) in 0° extensie houden e de heup van de patiënt bij het isometrisch testen van de weerstand (25 punten of meer) in 90° flexie houden	9 = willekeurige activiteit is palpabel, maar geen beweging is zichtbaar 14 = willekeurige beweging is zichtbaar, maar niet over de hele bewegingsrange 19 = willekeurige beweging is over de hele range mogelijk, maar niet tegen een weerstand in 25 = willekeurige beweging is tegen een weerstand in over de hele range mogelijk, maar is zwakker dan aan de niet-paretische zijde 33 = normale kracht

Naam: Geb.datum: Datum:

Totaal (1 t/m 6)	Opmerkingen:
..... punten	

Scoreformulier Motricity Index

		Datum			
A	**Bovenste extremiteit**				
Arm	pincetgreep				
	elleboog: flexie				
	schouder: abductie				
B	**Onderste extremiteit**				
Been	enkel: dorsale flexie				
	knie: extensie				
	heup: flexie				

Bij een score van 99 punten mag er één punt opgeteld worden.

Subtotaal	Arm:				
	Been:				
Totaal	Arm + Been:				

Opmerkingen (bijvoorbeeld de reden dat de test niet kon worden afgenomen)

.....

.....

.....

.....

Scoreformulier Modified Ashworth Scale

Datum				

A	Bovenste extremiteit	R	L	R	L	R	L	R	L
Elleboog	flexoren								
	extensoren								
Uitgangshouding									
B	Onderste extremiteit								
Knie	flexoren								
	extensoren								

Opmerkingen (bijvoorbeeld de reden dat de test niet kon worden afgenomen)

.....
.....
.....

Naam: Geb.datum: Datum:

Timed Get-Up-and-Go-Test (TGUGT)

De **TGUGT** gradeert de mogelijkheid van een individu om op te staan van een stoel (met armleuningen), drie meter naar een muur te lopen, om te draaien zonder de muur te raken, terug te lopen naar de stoel en terug te keren naar een zittende houding.
De **TGUGT** is een betrouwbare en valide maat van balans bij ouderen, zowel zelfstandig wonenden als patiënten die in een ziekenhuis zijn opgenomen.

Instructies en procedure
Tegelijk met het startsein "start" wordt door de onderzoeker de stopwatch ingedrukt. Het opmeten van de tijd wordt beëindigd als de patiënt niet meer beweegt, nadat hij is neergezeten in de stoel. De test wordt uitgevoerd met het normale schoeisel van de patiënt. Twee oefensessies zijn verplicht. Daarna wordt de test 3x herhaald, waarbij het gemiddelde van de laatste 3 testen wordt berekend. De therapeut loopt zo nodig met de patiënt mee. De therapeut beperkt zich tot de opdracht en vermijdt verdere aanmoediging.

	Test 1	Test 2	Test 3
TGUGT			

Normaal: < 10 seconden
Kwetsbare ouderen (frail): 11 – 20 seconden
Vereist verdere evaluatie: > 20 seconden

Score-formulier Zes Minuten Wandeltest

	Datum			
Afstand*				
Tijd, indien patiënt eerder stopt				

*Afstand in meters

Opmerkingen 6MW:

bv test niet afneembaar, reden: _____

Multiple Sclerosis Walking Scale (MSWS-12)

Code: ..... **Testdatum: .....**

- De volgende vragen hebben betrekking op **uw beperkingen in het lopen als gevolg van MS gedurende de afgelopen 2 weken.**
- Omcirkel bij elke vraag **het ene nummer dat uw mate van beperking het beste beschrijft.**
- S.V.P. **alle** vragen beantwoorden, **ook al lijken sommige vragen op elkaar of lijken ze niet op u van toepassing.**
- ***Als u helemaal niet kunt lopen*, kruis dan dit vakje aan:** ☐

Gedurende de afgelopen twee weken, in welke mate heeft de MS …..	Helemaal niet	Een beetje	Matig	Tamelijk veel	Heel erg
1. U beperkt in uw mogelijkheid te lopen?	1	2	3	4	5
2. U beperkt in uw mogelijkheden te rennen?	1	2	3	4	5
3. U beperkt in uw mogelijkheden de trap op en af te gaan?	1	2	3	4	5
4. Het u moeilijker gemaakt om te staan terwijl u dingen deed?	1	2	3	4	5
5. U beperkt in uw balans als u stond of liep?	1	2	3	4	5
6. U beperkt in hoe ver u kon lopen?	1	2	3	4	5
7. Ervoor gezorgd dat lopen u meer moeite kostte?	1	2	3	4	5
8. Het noodzakelijk gemaakt dat u steun gebruikte bij het lopen in huis (b.v. vastpakken van meubels of gebruik van een stok, etc)?	1	2	3	4	5
9. Het noodzakelijk gemaakt dat u steun gebruikte bij het lopen buitenshuis (b.v. gebruik van een stok of looprekje, etc)?	1	2	3	4	5
10. Ervoor gezorgd dat u langzamer ging lopen?	1	2	3	4	5
11. Invloed gehad op hoe soepel u liep?	1	2	3	4	5
12. Ervoor gezorgd dat u zich moest concentreren op het lopen?	1	2	3	4	5

Controleert u alstublieft of u bij **ALLE** vragen **ÉÉN** cijfer heeft omcirkeld.

Patient Name: _____ Date: _____

The Activities-specific Balance Confidence (ABC) Scale*

Instructions to Participants: For each of the following activities, please indicate your level of confidence in doing the activity without losing your balance or becoming unsteady from choosing one of the percentage points on the scale from 0% to 100% If you do not currently do the activity in question, try and imagine how confident you would be if you had to do the activity. If you normally use a walking aid to do the activity or hold onto someone, rate your confidence as if you were using these supports.

0%	10	20	30	40	50	60	70	80	90	100%
No Confidence										Completely Confident

How confident are you that you will not lose your balance or become unsteady when you…

1. …walk around the house? _____%
2. …walk up or down stairs? _____%
3. …bend over and pick up a slipper from the front of a closet floor? _____%
4. …reach for a small can off a shelf at eye level? _____%
5. …stand on your tip toes and reach for something above your head? _____%
6. …stand on a chair and reach for something? _____%
7. …sweep the floor? _____%
8. …walk outside the house to a car parked in the driveway? _____%
9. …get into or out of a car? _____%
10. …walk across a parking lot to the mall? _____%
11. …walk up or down a ramp? _____%
12. …walk in a crowded mall where people rapidly walk past you? _____%
13. …are bumped into by people as you walk through the mall? _____%
14. …step onto or off of an escalator while you are holding onto a railing? _____%
15. …step onto or off an escalator while holding onto parcels such that you cannot hold onto the railing? _____%
16. …walk outside on icy sidewalks? _____%

*Powell LE & Myers AM. The Activities-specific Balance Confidence (ABC) Scale. Journal of Gerontology Med Sci 1995; 50(1):M28-34.

Total ABC Score: _____

Scoring: _____ / 16 = _____% of self confidence
Total ABC Score

MEDICARE PATIENTS ONLY
100% - _____% Function = _____% Impairment

Patient Signature: _____ Date: _____

Therapist Signature: _____ Date: _____

Modified Fatigue Impact Scale

De scores gaan van 0 ("nooit") tot 4 ("bijna altijd"). Totale score: som van alle scores (range 0-84), Fysieke subschaal: som van alle "F" items (9) (range 0-36)
Cognitieve subschaal: som van alle "C" items (10) (range 0-40), Psychosociale subschaal: som van alle "P" items (2) (range 0-8)
Vermoeidheid is een gevoel van fysiek moe-zijn en een tekort aan energie dat door veel mensen wordt ervaren. Maar personen met een ziekte zoals MS ervaren deze vermoeidheid vaker en met een grotere invloed dan anderen. Hier volgt een lijst met vaststellingen die de effecten van vermoeidheid beschrijven. Gelieve elk van deze vaststellingen zorgvuldig te lezen en aan te duiden welk antwoord het best aangeeft hoe vaak vermoeidheid hierop een invloed gehad heeft gedurende de laatste vier weken. Beantwoord elke vraag (zet een kruisje onder het geschikte antwoord). Als u niet zeker bent van een antwoord, kies dan het antwoord dat het best uw eigen situatie beschrijft.

Omwille van mijn vermoeidheid (gedurende de laatste 4 weken)...		Nooit	Zelden	Soms	Vaak	Bijna altijd
C 1	ben ik minder aandachtig geweest					
C 2	heb ik moeite gehad om me lange tijd te concentreren					
C 3	ben ik niet in staat geweest om helder te denken					
F 4	ben ik onhandig geweest en had ik coördinatieproblemen					
C 5	ben ik vergeetachtig geweest					
F 6	heb ik mijn fysieke activiteiten trager moeten uitvoeren					
F 7	ben ik minder gemotiveerd geweest om fysieke activiteiten uit te voeren					
P 8	ben ik minder gemotiveerd geweest om aan sociale activiteiten deel te nemen					
P 9	ben ik beperkt geweest in de mogelijkheid om dingen buitenshuis te doen					
F 10	heb ik moeite gehad om fysieke inspanningen voor langere tijd vol te houden					
C 11	heb ik moeite gehad om beslissingen te nemen					
C 12	ben ik minder gemotiveerd geweest om iets te doen waarbij ik moest nadenken					
F 13	voelden mijn spieren zwak aan					
F 14	voelde ik mij fysiek niet goed					
C 15	heb ik moeite gehad om taken af te werken waarbij ik moest nadenken					
C 16	heb ik moeite gehad om mijn gedachten te ordenen bij taken thuis of op het werk					
F 17	ben ik minder in staat geweest om taken af te werken die fysieke inspanning vragen					
C 18	is mijn gedachtegang vertraagd geweest					
C 19	heb ik moeite gehad me te concentreren					
F 20	heb ik mijn fysieke activiteiten beperkt					
F 21	heb ik vaker of langer moeten rusten					

Hospital Anxiety and Depression Scale (HADS)

Naam: Leeftijd:

Geslacht: Datum:

Het is bekend dat emoties bij de meeste ziektes een belangrijke rol kunnen spelen.

Deze vragenlijst dient als hulpmiddel om te weten te komen hoe u zich voelt. Lees iedere vraag en onderstreep het antwoord dat het beste weergeeft hoe u zich **gedurende de laatste week** gevoeld heeft.

Denk niet te lang na over uw antwoord. Uw eerste reactie op elke vraag is waarschijnlijk betrouwbaarder dan een lang doordacht antwoord.

---

1. **Ik voel me gespannen:**

   Meestal
   Vaak
   Af en toe, soms
   Helemaal niet

2. **Ik geniet nog steeds van de dingen waar ik vroeger van genoot:**

   Zeker zo veel
   Niet zo veel als vroeger
   Weinig
   Haast helemaal niet

3. **Ik krijg een soort angstgevoel alsof er elk moment iets vreselijks zal gebeuren:**

   Heel zeker en vrij erg
   Ja, maar niet zo erg
   Een beetje, maar ik maak me er geen zorgen over
   Helemaal niet

4. **Ik kan lachen en de dingen van de vrolijke kant zien:**

   Net zoveel als vroeger
   Niet zo goed als vroeger
   Beslist niet zoveel als vroeger
   Helemaal niet

5. **Ik maak me vaak ongerust:**

   Heel erg vaak
   Vaak
   Af en toe maar niet te vaak
   Alleen soms

6. **Ik voel me opgewekt:**

   Helemaal niet
   Niet vaak
   Soms
   Meestal

7. **Ik kan rustig zitten en me ontspannen:**

   Zeker
   Meestal
   Niet vaak
   Helemaal niet

8. **Ik voel me alsof alles moeizamer gaat:**

   Bijna altijd
   Heel vaak
   Soms
   Helemaal niet

9. **Ik krijg een soort benauwd, gespannen gevoel in mijn maag:**

   Helemaal niet
   Soms
   Vrij vaak
   Heel vaak

10. **Ik heb geen interesse meer in mijn uiterlijk:**

    Zeker
    Niet meer zoveel als ik zou moeten
    Waarschijnlijk niet zoveel
    Evenveel interesse als vroeger

11. Ik voel me rusteloos en voel dat ik iets te doen moet hebben:

Heel erg
Tamelijk veel
Niet erg veel
Helemaal niet

12. Ik verheug me van tevoren al op dingen:

Net zoveel als vroeger
Een beetje minder dan vroeger
Zeker minder dan vroeger
Bijna nooit

13. Ik krijg plotseling gevoelens van panische angst:

Zeer vaak
Tamelijk vaak
Niet erg vaak
Helemaal niet

14. Ik kan van een goed boek genieten, of van een radio- of televisieprogramma:

Vaak
Soms
Niet vaak
Heel zelden

Wilt u controleren of u alle vragen beantwoord heeft?
BEDANKT.

Hospital Anxiety and Depression Scale (HADS)
Ontwikkeld door Snaith & Zigmond (1994)

De hier afgedrukte HADS is een experimentele Nederlandstalige versie en mag alleen ten behoeve van wetenschappelijk onderzoek worden gebruikt:
Spinhoven, Ph., Ormel, J., Sloekers, P.P.A., Kempen, G.J.M., Speckens, A.E.M & Van Hemert, A.M. (1997). A validation study of the Hospital Anxiety and Depression Scale (HADS) in different groups of Dutch subjects. Psychological Medicine, 27, 363-370.

De officiële Engelstalige versie (en vertalingen) kunnen worden besteld via:
nferNelson, Unit 28, Bramble Road, Techno Trading Centre, Swindon, Wiltshire, SN2 8EZ, U.K.
(http:/www.nfer-nelson.co.uk).

Barcelona Music Reward Questionnaire

Elk onderdeel van deze vragenlijst bevat een standpunt waarmee iemand al dan niet akkoord kan gaan. Duidt, voor elk onderdeel, aan in welke mate jij al dan niet akkoord gaat. Wij vragen u om op elk standpunt te antwoorden en geen enkel blanco te laten. Kies voor elk standpunt slechts één antwoord. Wees zo correct en eerlijk mogelijk. Antwoord bij elk standpunt alsof dit het enige standpunt is waarvoor je al dan niet akkoord moet gaan. Dit wil ook zeggen dat je je niet moet afvragen of je antwoorden wel consistent zijn. Kies voor elk standpunt één van de vijf mogelijkheden in de reeks van « absoluut niet akkoord »(links) tot « volledig akkoord » (rechts) :

{1}-absoluut niet akkoord {2}-niet akkoord {3}-geen standpunt {4}-akkoord {5}-volledig akkoord

1. Als ik samen met iemand naar muziek luister, dan voel ik een speciale band met die persoon
2. Ik luister amper naar muziek in mijn vrije tijd
3. Ik luister graag naar emotionele muziek
4. Muziek houdt mij gezelschap wanneer ik alleen ben
5. Ik dans niet graag, zelfs niet op muziek waar ik van hou
6. Muziek geeft mij een band met andere mensen
7. Ik informeer mezelf over de muziek waar ik van hou
8. Ik wordt emotioneel als ik naar bepaalde muziekstukken luister
9. Ik wordt rustig en ontspannen door muziek
10. Muziek brengt mij dikwijls aan het dansen
11. Ik ben altijd op zoek naar nieuwe muziek
12. Bij het beluisteren van een melodie waar ik erg van hou, krijg ik soms de tranen in de ogen of begin te wenen
13. Ik hou ervan om samen met anderen te zingen of een instrument te bespelen
14. Muziek helpt mij om te ontspannen
15. Ik kan het niet helpen dat ik begin te neuriën of mee te zingen bij muziek waar ik van hou
16. Bij een concert voel ik mij verbonden met de uitvoerders en met het publiek
17. Ik geef vrij veel geld uit aan muziek en alles wat ermee te maken heeft
18. Soms voel ik mij volledig ontspannen als ik een melodie hoor waar ik van hou
19. Muziek troost mij
20. Bij het horen van een liedje dat ik zeer graag hoor, kan ik het niet vermijden om de maat te slaan of op de maat te bewegen

Deelnemer nr. Datum:

VRAGENLIJST DUBBEL TAKEN (ZELF)

De volgende vragen gaan over problemen die iedereen van tijd tot tijd ervaart, maar waarvan sommige vaker gebeuren dan andere. We willen weten hoe vaak deze dingen bij u zijn gebeurd in de afgelopen weken. Er zijn 5 opties, gaande van 'zeer vaak' tot 'nooit, of 'niet van toepassing'. Gelieve het gepaste vakje aan te vinken.

	Heeft u één van deze moeilijkheden….	Zeer vaak	Eerder vaak	occasioneel	Zeer zelden	nooit	Niet van toepassing
1	Aandacht geven aan meer dan één ding tegelijk?						
2	Nood hebben aan een activiteit te stoppen om te praten?						
3	Onbewust zijn dat anderen tegen u praten wanneer je een andere activiteit aan het doen bent?						
4	Volgen of deelnemen in een gesprek waar verscheidene personen tegelijk aan het spreken zijn?						
5	Verslechteren van het stappen wanneer je aan het spreken of luisteren bent naar iemand?						
6	Verdiept zijn in je eigen gedachten, dus zonder op te merken wat er rondom u gebeurd?						
7	Een drankje morsen tijdens het dragen ervan.						
8	Meer morsen indien je op hetzelfde moment spreekt.						
9.	Tegen mensen aanbotsen of dingen laten vallen indien je tevens iets anders doet?						
10.	Moeilijkheden om te eten en televisie te kijken of te luisteren naar de radio tegelijkertijd.						

Questionnaire reported in: Evans, J.J., Greenfield, E., Wilson, B.A. and Bateman, A. (2009) Walking and talking therapy: Improving cognitive–motor dual-tasking in neurological illness *Journal of the International Neuropsychological Society*, **15** , 112 – 120 .

	Totaal in iedere categorie	x4	x3	x2	x1	x0	-
	subtotalen						

som van 4 subtotalen = ;
gedeeld door aantal antwoorden =
gemiddelde per beantwoorde vraag =

www.uhasselt.be
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Campus Diepenbeek | Agoralaan gebouw D | BE-3590 Diepenbeek
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UHASSELT

VOORTGANGSFORMULIER WETENSCHAPPELIJKE STAGE DEEL 1

DATUM	INHOUD OVERLEG	HANDTEKENINGEN
20/11/2017	• Zoektermen • Mri verschil • Pico • Onderzoeksvraag • Sleutelwoorden • Prisma checklist • Inclusie/exclusie	Promotor: Copromotor: Student(e): Student(e):
27/11/2017	• Verfijnen van de strategie • Verfijnen van de vraag: pico • Scooping • Ideeën doorsturen	Promotor: Copromotor: Student(e): Student(e):
08/01/2018	• Deadline onderzoeksstrategie • Wat verder te doen: keuzes maken • Pico en onderzoeksvraag definitief	Promotor: Copromotor: Student(e): Student(e):
22/01/2018	• Endnote installeren • Duplicates filteren • Inclusie en exclusie • Populatie • Tabel date extractie	Promotor: Copromotor: Student(e): Student(e):
15/02/2018	• Alignement tussen artikels endnote Marit en Inneke • Prisma flowchart • Verschillende documenten voor inclusie en exclusie artikels • Inclusie artikels tabellen apart voor brain imaging	Promotor: Copromotor: Student(e): Student(e):
27/03/2018	• Verfijnen van de tabellen zodat een duidelijk overzicht mogelijk is • Hoe opdelen van tabellen/ classificeren • Nog wachten met methodologie • Updaten flowchart	Promotor: Copromotor: Student(e): Student(e):
3/04/2018	• Tabellen bekijken • Volgende stappen overlopen • checklists	Promotor: Copromotor: Student(e): Student(e):
9/04/2018	• Tabellen bekijken • Volgende stappen overlopen • Updaten flowchart • Bespreken schrijven van de tekst	Promotor: Copromotor: Student(e): Student(e):
16/04/2018	• Tabellen • Quality assessment • Verdere stappen overlopen	Promotor: Copromotor: Student(e):

		Student(e):
7/05/2018	• Bespreken voorlopige thesis • Tabellen bespreken • Verdere stappen overlopen	Promotor: Copromotor: Student(e): Student(e):
5/06/2018	• Bespreken voorlopige thesis • Bespreken protocol	Promotor: Copromotor: Student(e): Student(e):

Masterproefcoördinatie Revalidatiewetenschappen en Kinesitherapie Prof. M. Vanvuchelen Agoralaan Gebouw A Room 0.01 Campus Diepenbeek
marleen.vanvuchelen@uhasselt.be

Naam & Voornaam STUDENT: Putzeys Marit

Naam & Voornaam (CO)PROMOTOR & PROMOTOR: Moumdjian Lousin, Prof. Dr. Feys Peter

TITEL masterproef (Nederlandstalig of Engels): An overview of neural networks involved in learning auditory sequences and/or musical sequences during a motor performance

LITERATUURSTUDIE	**Gestelde deadline**	**Behaald op**	**Reflectie**
De belangrijkste concepten en conceptuele kaders van het onderzoekdomein uitdiepen en verwerken	November	November	
De belangrijkste informatie opzoeken als inleiding op de onderzoeksvraag van de literatuurstudie	November	November	
De opzoekbare onderzoeksvraag identificeren en helder formuleren in functie van de literatuurstudie	20/11/2017	20/11/2017	Werd nog verder verfijnd tot 08/01/2018
De zoekstrategie op systematische wijze uitvoeren in relevante databanken	06/11/2017-22/01/2018	06/11/2017-22/01/2018	
De kwaliteitsbeoordeling van de artikels diepgaand uitvoeren	28/05/2018	28/05/2018	
De data-extractie grondig uitvoeren	3/04/2018	3/04/2018	
De bevindingen ïntegreren tot een synthese	Juni	Juni	

ONDERZOEKSPROTOCOL	**Gestelde deadline**	**Behaald op**	**Reflectie**
De onderzoeksvraag in functie van het onderzoeksprotocol identificeren	Juni	Juni	
Het onderzoeksdesign bepalen en/of kritisch reflecteren over bestaande onderzoeksdesign	Juni	Juni	
De methodesectie (participanten, interventie, uitkomstmaten, data-analyse) uitwerken	Juni	Juni	

ACADEMISCHE SCHRIJVEN	**Gestelde deadline**	**Behaald op**	**Reflectie**
Het abstract tot he point schrijven	11/06/2018	1/06/2018	

De inleiding van de literatuurstudie logisch opbouwen	28/05/2018	28/05/2018	
De methodesectie van de literatuurstudie transparant weergegeven	April	April	
De resultatensectie afstemmen op de onderzoeksvragen	1/06/2018	1/06/2018	
In de discussiesectie de bekomen resultaten in een wetenschappelijke tekst integreren en synthetiseren	12/06/2018	12/06/2018	
Het onderzoeksprotocol deskundig technisch uitschrijven	Juni	Juni	
Referenties correct en volledig weergeven	05/06/2018	05/06/2018	

ZELFSTUREND EN WETENSCHAPPELIJK DENLEN EN HANDELEN	**Aanvangsfase**	**Tussentijdse fase**	**Eindfase**
Een realistische planning opmaken, deadlines stellen en opvolgen	G	G	G
Initiatief en verantwoordelijkheid opnemen ten aanzien van de realisatie van de wetenschappelijke stage	G	ZG	U
Kritisch wetenschappelijk denken	V	G	ZG
De contacten met de promotor voorbereiden en efficiënt benutten	G	G	G
De richtlijnen van de wetenschappelijke stage autonoom opvolgen en toepassen	V	G	G
De communicatie met de medestudent helder en transparant voeren	G	G	G
De communicatie met de promotor/copromotor helder en transparant voeren	G	G	G
Andere verdiensten:			

Naam & Voornaam STUDENT: Huion Inneke

Naam & Voornaam (CO)PROMOTOR & PROMOTOR: Moumdjian Lousin & Feys Peter

TITEL masterproef (Nederlandstalig of Engels): An overview of neural networks involved in learning auditory sequences and/or musical sequences during a motor performance

LITERATUURSTUDIE	**Gestelde deadline**	**Behaald op**	**Reflectie**
De belangrijkste concepten en conceptuele kaders van het onderzoekdomein uitdiepen en verwerken	November	November	
De belangrijkste informatie opzoeken als inleiding op de onderzoeksvraag van de literatuurstudie	November	November	
De opzoekbare onderzoeksvraag identificeren en helder formuleren in functie van de literatuurstudie	20/11/2017	20/11/2017	Werd nog verder verfijnd tot 06/01/2018
De zoekstrategie op systematische wijze uitvoeren in relevante databanken	06/11/2017 – 22/01/2018	06/11/2017 – 22/01/2018	
De kwaliteitsbeoordeling van de artikels diepgaand uitvoeren	28/05/2018	28/05/2018	
De data-extractie grondig uitvoeren	3/04/2018	3/04/2018	
De bevindingen ïntegreren tot een synthese	Juni	Juni	

ONDERZOEKSPROTOCOL	**Gestelde deadline**	**Behaald op**	**Reflectie**
De onderzoeksvraag in functie van het onderzoeksprotocol identificeren	Juni	Juni	
Het onderzoeksdesign bepalen en/of kritisch reflecteren over bestaande onderzoeksdesign	Juni	Juni	
De methodesectie (participanten, interventie, uitkomstmaten, data-analyse) uitwerken	Juni	Juni	

ACADEMISCHE SCHRIJVEN	**Gestelde deadline**	**Behaald op**	**Reflectie**
Het abstract to the point schrijven	11/06/2018	11/06/2018	

De inleiding van de literatuurstudie logisch opbouwen	28/05/2018	28/05/2018	
De methodesectie van de literatuurstudie transparant weergegeven	April	April	
De resultatensectie afstemmen op de onderzoeksvragen	01/06/2018	01/06/2018	
In de discussiesectie de bekomen resultaten in een wetenschappelijke tekst integreren en synthetiseren	12/06/2018	12/06/2018	
Het onderzoeksprotocol deskundig technisch uitschrijven	Juni	Juni	
Referenties correct en volledig weergeven	05/06/2018	05/06/2018	

ZELFSTUREND EN WETENSCHAPPELIJK DENLEN EN HANDELEN	**Aanvangsfase**	**Tussentijdse fase**	**Eindfase**
Een realistische planning opmaken, deadlines stellen en opvolgen	G	G	G
Initiatief en verantwoordelijkheid opnemen ten aanzien van de realisatie van de wetenschappelijke stage	G	ZG	U
Kritisch wetenschappelijk denken	V	G	ZG
De contacten met de promotor voorbereiden en efficiënt benutten	G	G	G
De richtlijnen van de wetenschappelijke stage autonoom opvolgen en toepassen	V	G	G
De communicatie met de medestudent helder en transparant voeren	G	G	G
De communicatie met de promotor/copromotor helder en transparant voeren	G	G	G
Andere verdiensten:			