MAX PLANCK INSTITUTE FOR HUMAN COGNITIVE AND BRAIN SCIENCES LEIPZIG

Maria Christine van der Steen: Temporal adaptation and anticipation mechanisms in sensorimotor synchronization. Leipzig: Max Planck Institute for Human Cognitive and Brain Sciences, 2014 (MPI Series in Human Cognitive and Brain Sciences; 162)

CC BY NC

Temporal adaptation and anticipation mechanisms in sensorimotor synchronization

Impressum

Max Planck Institute for Human Cognitive and Brain Sciences, 2014
Diese Arbeit ist unter folgender Creative Commons-Lizenz lizenziert:
http://creativecommons.org/licenses/by-nc/3.0

Druck: Sächsisches Druck- und Verlagshaus Direct World, Dresden
Titelbild: © Maria Christine van der Steen, 2014

ISBN 978-3-941504-46-2

Temporal adaptation and anticipation mechanisms in sensorimotor synchronization

Der Fakultät für Biowissenschaften, Pharmazie und Psychologie

der Universität Leipzig

eingereichte

D I S S E R T A T I O N

zur Erlangung des akademischen Grades

doctor rerum naturalium

Dr. rer. Nat

vorgelegt von

Maria Christine van der Steen, MSc.

geboren am 03.12.1985 in Veghel, die Niederlande

Leipzig, 10.07.2014

Gutachter

Prof. Dr. Sonja A. Kotz

Prof. Dr. Erich Schröger

Univ. Prof. Dr. med. Eckart Altenmüller

Tag der Verteidigung: 18. Dezember 2014

Acknowledgements

These acknowledgements are most likely the first and probably by far the most often read part of this PhD-thesis. I must admit I have been looking forward to writing these words of thank. Without your help, support, and the relax-moments you gave me this thesis would have never been written.

First, I would like to express my gratitude to Peter Keller, my supervisor who accepted me via a Skype-interview into his group at the Max Planck Institute for Human Cognitive and Brain Sciences and the EBRAMUS program. Full of expectations and plans I came to Leipzig in the fall of 2010. Although most of these did not come true, the last 3.5 years did allow me to explore and develop new sides of myself and visit many interesting places. Thank you for your guidance and all the opportunities you gave me!

A big thank you goes out to all the members of the Music Cognition and Action group. I keep good memories of our time at the Seeburgstraße. Especially, I would like to thank Kerstin, Felix and Maria who helped me to collect the data for the projects in Leipzig. A special thank you goes out to Annerose, who welcomed me into her amazing apartment and therefore gave me a great start in Leipzig. Furthermore, a very warm thank you to Merle and Marie, who taught me that girls wear dresses and who were always up for a fairytale ball or a relaxing cup of coffee.

Second, I am in great debt with Eckart Altenmuller and the members of the Institute of Music Physiology and Musicians' Medicine for a great time in Hannover. What started off as 3 month visit, turned into a 16 month stay. The amazing atmosphere made me feel right at home. Dear professor, thank you for your hospitality, interest, and support. I really enjoyed being part of your group. Shinichi, it was an honor being able to work with you. You showed me again that science can be straightforward and fun. Daniel, my roomie, I appreciate your attempts to make me less of a control freak and to enjoy more. Christos, Felicia, Mee-Ling, Britta, and Eva thank you for the coffees, girls-nights, and Dutch-dinners, they were a welcome distraction. André, Mai, and Maic thank you for introducing me to Benedict Cumberbatch and the fun nights that followed. I would like to thank Erwin, Michael, Martin, and Frau Pölkner for our discussions and your help. Additionally, I would like to thank the students at IMMM for their help running the experiments, for correcting my attempts to write in German, and mostly for the sparks in their eyes when they realized how cool science can be.

Furthermore, I would like to thank all the people that have enriched these last 3.5 years in many different ways. Of course I would like to thank the EBRAMUS consortium for the interesting schools, workshops and meetings all over Europe! My fellow ER/ESRs, it was a pleasure and great honor to take this journey together with you. I hope we will manage to somehow stay in contact. Floris, thank you for our fun and successful EBRAMUS-collaboration, which is presented in Chapter 4. Laura, thank you for the wonderful time in Leipzig and for being my personal crisis-intervention person. Without your friendship it would not have been the same. Riccardo, Ellie, Kristina, David, and Charles-Etienne: I still enjoy the memories of our amusing evenings filled with good food and playing games. I would like to thank my fellow conference attendees from all over the world for the fun and inspiring conferences. Nori, thank you for the collaboration that resulted in Chapter 3. Furthermore, I would –once again– like to thank Raoul for introducing me to the world of science and for always having an open door that welcomes me whenever I am seeking for advice or just would like to catch up.

A final and perhaps even most deeply word of thanks goes out to my friends and family, the people who stood always by me. I want to thank Steffie, Evelien, Imke, Sophie, Karin, and Liesbet for the many (Skype-) phone calls, for visiting me in Germany, and for the lovely dinners in the Netherlands. I also enjoyed the visits and remote but continuous support from Mariska & Rob, Loes, and Michelle & Rob; I hope there are many 'leuke-mensen-etentjes' yet to come! Jeroen, Lonneke, Willem, Eva, Ruud, Roel, Joran, Lydia, Wilbert, Hanneke, Rudi, Sylvia, Arthur, Marieke, Kyra, Gijs, Thijs en Willeke: Thank you for your friendship. I would like to thank Tonnie, Ans, Renske, Ron, and Fenne for welcoming me to the family. Thanks to my entire family for accepting that I was not always there and for always being interested in my developments and new plans. Mam, pap, Geerte, Sebas, and Iris thank you for keeping me grounded and for your unconditional love and support. And last but definitely not least my dearest Twan, thank you for always having been there, for all your help and support, for giving me the space and time to find myself, and for bringing me home. Ik vind je de allerliefste!

Marieke van der Steen
's-Hertogenbosch, July 2014

In loving memory of my grandfather, Joan van der Steen

Table of content

Acknowledgements _ _ _ 3

Table of content _ _ _ 5

Chapter 1 _ _ _ 7
Introduction

Chapter 2 _ _ _ 23
The Adaptation and Anticipation Model (ADAM) of sensorimotor synchronization

Chapter 3 _ _ _ 59
Sensorimotor synchronization with tempo changing auditory sequences

Chapter 4 _ _ _ 99
Basic timing abilities stay intact in patients with musician's dystonia

Summary _ _ _ 127
Zusammenfassung _ _ _ 131

List of figures _ _ _ 137
List of tables _ _ _ 141

Curriculum Vitae _ _ _ 143
Publications _ _ _ 144

Confirmation of contribution of co-authors _ _ _ 147
Confirmation of contribution of co-authors _ _ _ 148
Confirmation of contribution of co-authors _ _ _ 149

Selbständigkeitserklärung zum monographischen Kapitel 1 _ _ _ 151
Selbständigkeitserklärung _ _ _ 152

Bibliographic details _ _ _ 153

Chapter 1

INTRODUCTION

1.1 GOAL OF THE DISSERTATION

We live in a constantly changing environment. Many of our activities require interaction with this dynamic environment, not uncommonly also involving other people. Consider yourself dancing during a night out with friends. Seemingly effortlessly you synchronize your dance moves to the music and your friends. How are we able to effectively coordinate our actions without losing flexibility? This flexibility is, for example, necessary to be able to continue to dance also with the next song that might be of a different genre and at a different tempo.

Sensorimotor synchronization (SMS) is the temporal coordination of actions with external events (cf. Repp, 2005[1]). SMS is essential for the successful coordination of movements. Some people, like professional dancers, musicians, and rowers, display extraordinary skills in timing their movement accurately and precisely (e.g. Keller & Appel, 2010; Wing, Endo, Bradbury, & Vorberg, 2014; Wing & Woodburn, 1995), while other people seem to be less skilled. Several patient groups have even shown explicit problems related to SMS. For example, Parkinson's disease patients exhibit problems when reproducing intervals of different lengths (Pastor, Artieda, Jahanshahi, & Obeso, 1992) and Musician's dystonia patients show impairments in detecting late stimuli in a train of auditory onsets (Lim, Bradshaw, Nicholls, & Altenmüller, 2003). Furthermore, patients with lesions in the basal ganglia or cerebellum as a result of a stroke have been found to have compromised synchronization behavior (e.g. Ivry, Spencer, Zelaznik, & Diedrichsen, 2002; Schwartze, Keller, Patel, & Kotz, 2011). Interestingly, despite the timing problems Parkinson's patients might display, the gait of these patients has been shown to benefit from external auditory timing cues (Lim et al., 2005). Furthermore, stroke and traumatic brain injury patients achieve significant improvements after rehabilitation programs involving synchronization with music (e.g. Schneider, Schönle, Altenmüller, & Münte, 2007; Thaut et al., 2009).

Overall, these studies suggest that SMS is an important aspect of successful motor timing and that it might be exploited in motor rehabilitation programs for different patient groups. The goal of this PhD was to get a better understanding of the underlying mechanisms of SMS, in

[1] Citations in this chapter follow the rules and regulations established by the American Psychological Association (APA). In the remaining chapters the citation style of the specific journal were the paper was published/ submitted was applied.

both healthy and patient populations. This goal was motivated by the assumption that, once we have a better understanding of the mechanisms underlying temporal sensorimotor synchronization and related deficits in patient populations, we will be better able to set up targeted rehabilitation programs focusing on the timing of movements.

1.2 SENSORIMOTOR SYNCHRONIZATION

SMS is a fundamental human skill underpinning behaviors that require humans to coordinate their movements (action) with something or someone else (event). Whether one is practicing a forehand with a tennis ball machine, preparing to cross a street full of driving cars, or is making music in a group, to be successful at these tasks one's movements need to be synchronized with the timing of the other, externally controlled events. In many cases, SMS will occur more or less spontaneously, for example, people tend to nod their head in synchrony with music and steps become synchronized when walking together with a friend (van Ulzen, Lamoth, Daffertshofer, Semin, & Beek, 2008). On the other hand, highly accurate and precise SMS can be the goal of extensive practice, as is the case for musical ensembles (Keller & Appel, 2010) and rowing crews (Wing & Woodburn, 1995). Since SMS is part of such a broad range of behavioral coordination it is important that SMS is precise yet flexible. Both temporal adaptation (reactive error correction processes) and anticipation (predictive processes) mechanisms are thought to play an important role in achieving this balance between precision and flexibility (e.g., Keller, 2008; Repp & Su, 2013).

A common paradigm to investigate SMS and its underlying mechanisms involves a finger tapping task (Repp, 2005). During this simple task participants are asked to tap their finger in synchrony with a pacing stimulus, often consisting of an auditory sequence. Measures of interest are typically related the asynchrony, the timing error between the participants tap and the event in the stimulus sequence (Figure 1.1). By convention, taps that precede the even are reflected in negative asynchronies. Frequently the mean asynchrony is used as an inverse measure of SMS accuracy and as an inverse measure of SMS precision the variability (i.e., standard deviation) of the signed asynchrony is used (Repp, 2005). Other measures are often related to the intervals between successive actions (ITI) or onsets of the stimulus sequence (IOI) (Figure 1.1).

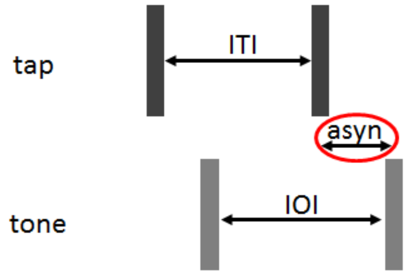


Figure 1.1 Standard variables related to a finger tapping task. asyn, asynchrony; ITI, interval between successive actions; IOI, interval between the onsets of the stimulus sequence.

1.3 TEMPORAL ADAPATION

SMS has been studied extensively in the tradition of information-processing approaches. According to the information-processing theory, the timing of simple movements is assumed to be the result of a timekeeping process that generates pulses that trigger motor responses (Wing & Kristofferson 1973a, 1973b). Timing errors (i.e., asynchronies) between events in the stimulus sequence and the movements are the result of variability in movement timing caused by biological noise. Furthermore, asynchronies occur due to intentional deviations from regularity (e.g. expressive timing in music performance). Error correction processes compensate for timing errors in a reactive fashion (Mates, 1994a, 1994b; Vorberg & Schulze, 2002; Vorberg & Wing, 1996).

Phase and period correction are two types of adaptation mechanism that have been distinguished (Mates, 1994a, 1994b; Semjen, Vorberg, & Schulze, 1998; Vorberg & Wing, 1996). It has been claimed that both error correction processes modify the timing of the next action based on the asynchrony (e.g., Semjen et al., 1998). Phase correction is an automatic and local adjustment of the interval generated by the internal timekeeper. It influences the temporal alignment but leaves the interval setting of the timekeeper unaffected (Repp, 2001a, 2002a). Period correction, on the other hand, changes the interval setting of the timekeeper that drives the motor activity. This change in timekeeper setting persists until period correction is again applied and has an influence on the rate of the motor responses (Repp, 2001b). Successful period correction requires the conscious perception of a tempo change in the stimulus sequence (Repp & Keller, 2004). Without these adaptation mechanisms, variability would accumulate over time. This would lead to increasing asynchronies, phase drift, and eventually even the loss of synchrony between the stimulus event and movement (Vorberg & Wing, 1996).

There are different methods available to estimate the amount of phase correction implemented by the participant during synchronization tasks. For example, the amount of phase correction can be estimated based on lag-1 (AC1) and lag-2 (AC2) autocorrelations via a simple analytic solution; $amount\ of\ phase\ correction\ (\alpha) = 1 - AC2/AC1$ (Pressing, 1998; Schulze & Vorberg, 2002). Unfortunately, this estimate can be problematic because AC1 approaches zero when phase correction is optimal and AC2 values are unreliable of based on short time series (Schulze & Schulze, 2002; Repp & Keller, 2008). Recently, the bounded Generalized Least Squeares (bGLS) method was proposed (Jacoby & Repp, 2012; Repp, Keller, & Jacoby, 2012). This analytic method is related to the numerical optimization method of Vorberg and Schulze (2002) but finds a maximum likelihood approximation to the equation that describes the relation between successive asynchronies governed by phase correction (Repp et al., 2012). The advantage of this latter method is that it can be applied to different types of synchronization paradigm and that also parameter estimates such as period correction can be obtained (Jacoby & Repp, 2012).

1.4 TEMPORAL ANTICIPATION

Although successful SMS depends crucially on adaptation mechanisms, these reactive processes alone cannot account for all aspects of SMS: temporal adaptation is thus necessary but not sufficient. For example, when trained musicians play together in an ensemble, the asynchronies between the tones that should be played simultaneously according to the notated score are usually in the order of 30-50 ms (e.g., Keller & Appel, 2010; Rasch, 1979). Asynchronies of this magnitude are too small to be the result of purely reactive mechanisms (Keller, 2008) and are therefore suggestive of anticipation mechanisms related to SMS. During synchronization with tempo changing sequences that resemble expressively timed music, participants are able to predict the tempo changes (e.g., Pecenka & Keller, 2011; Rankin, Large, & Fink, 2009). The predictive processes allow the anticipation of the precise onset of stimulus events. Based on the anticipated onset, individuals can get their movements under way early enough so that the responses coincide with the events (Schmidt, 1968). Anticipation occurs when actions not only depend on the past and present but also on predictions, expectations, or beliefs about the future (Butz, Sigaud, & Gérard, 2003).

Anticipatory mechanisms have been linked to online action simulations and internal models (Keller, 2008). Internal models generate predictions based on the effects of the intention to perform a specific movement (Wolpert & Kawato, 1998). Two types of internal model have been distinguished: forward and inverse models. Forward models predict the effect a particular motor command will have upon the body and the dynamic environment, given the current state of the action control system. Forward models therefore represent the causal relationship between the input and output of the action control system. Inverse models serve as a controller for intentional movements by providing the motor command that is necessary to change the current state of the body and the environment to the desired end state (Wolpert & Kawato, 1998).

Paired forward and inverse models have been linked to flexible and successful motor control, because the predicted effect can be used to adjust the planned motor command (e.g., Wolpert & Kawato, 1998). Internal models can also be used to predict the outcome of others' actions (e.g., from a stimulus event or another person) (Wolpert, Doya, & Kawato, 2003). The coupling of 'own' and 'other' internal models in facilitates SMS because it allows potential errors in timing to be foreseen and corrected before they occur (Wolpert et al., 2003; Keller, 2008).

Measures pertaining to underlying anticipation mechanisms are related to the dependencies between ITIs and IOIs at lag 0 and lag 1 (Figure 1.1). The lag 0 cross-correlation reflects the tendency to predict the intervals in the stimulus sequence, while the lag 1 cross-correlation mirrors the tendency to track, or copy, the intervals during synchronization with the tempo changes (Repp, 2002b; Rankin et al., 2009). The ratio between the lag 0 and lag 1 cross-correlations can be used as a measure of prediction in SMS with tempo changing tapping tasks, where a ratio larger than 1 indicates that the participant anticipates the tempo changes (Pecenka & Keller, 2011).

In Chapter 2, a more detailed overview of the existing literature on adaptation and anticipation mechanisms in SMS is given. In the following, an overview of the theoretical contribution of this dissertation in terms of the development of a computational model is given, followed by descriptions of key results obtained in studies using model-based computer simulations and related behavioral experiments.

1.5 ADAM: THE **AD**APTATION AND **A**NTICIPATION **M**ODEL

In 1987, George Box pointed out that essentially all models are wrong, but that some might nevertheless be useful. Models are a simplified representation of the reality. The downside of working with models is that one always ignores parts of the reality that might also influence the process that is the main focus of the model. On the other hand, due to the simplification it might be possible to get a better understanding of this aspect of the real state of affairs. One can systematically vary and investigate parts of the model in order to obtain more knowledge and a better understanding of the modeled reality. The latter can then help to improve the model and therefore lead to a better representation of reality.

An important model for the timing of self-paced, repetitive discrete motor responses was proposed by Wing and Kristofferson (1973a, 1973b). This two-level timing model assumes two independent processes that are uncorrelated: (1) a timekeeping process that generates pulses that trigger motor responses and (2) a delay processes that accounts for transmission lags and movement time. Later, this two-level timing model was extended by including error correction mechanisms to account for synchronization with an external sequence (e.g., Mates, 1994a, 1994b; Vorberg & Wing, 1996). But, as mentioned before, not all aspects of SMS can be explained by means of reactive adaptation mechanisms as phase and period correction. Instead anticipation mechanisms seem to also play a role in SMS (e.g., Pecenka & Keller, 2011).

Traditionally, adaptation and anticipation mechanisms are investigated using separate paradigms. Although this has contributed much to our knowledge about SMS, it is likely that both mechanisms interact with each other and influence SMS. For example, a precise prediction will lead to a smaller timing error and with smaller the timing errors better predictions can be made. It is therefore important to investigate both mechanisms within a unified framework. Hence, our work has focused on creating ADAM, the ADaptation and Anticipation Model. ADAM combines phase and period correction based on the asynchrony (adaptation module) (Repp & Keller, 2008) with a predictive temporal extrapolation process based on a series of intervals (anticipation module) (Figure 1.2). ADAM can be used to run simulations to systematically investigate the effect of phase and period correction on SMS, while also taking into account aspects of anticipation, such as the number of intervals used to make the prediction. Furthermore, with ADAM the link between adaptation and anticipation mechanisms can be examined. It has been proposed that 'joint' internal models, pairing both forward and inverse models focusing on 'own' and 'others' action could play a role in linking both mechanisms (e.g., Keller, 2008).

The primary motivation for designing ADAM was to contribute to the theoretical understanding of SMS. However, in the long run we envision ADAM playing a role in the clinical assessment and rehabilitation of patients with motor timing problems. By creating a virtual partner that is based on ADAM, patients could be allowed to interact with ADAM. In such as system, ADAM could adopt different roles (e.g., facilitate SMS or create challenging SMS situations) by means of implementing adaptation and anticipation mechanisms in different manners. This would allow problems with different aspects of SMS to be identified and a customized rehabilitation program involving ADAM could be created to address such specific deficits in the future.

Chapter 2 gives an introduction to ADAM and outlines possible extensions of ADAM.

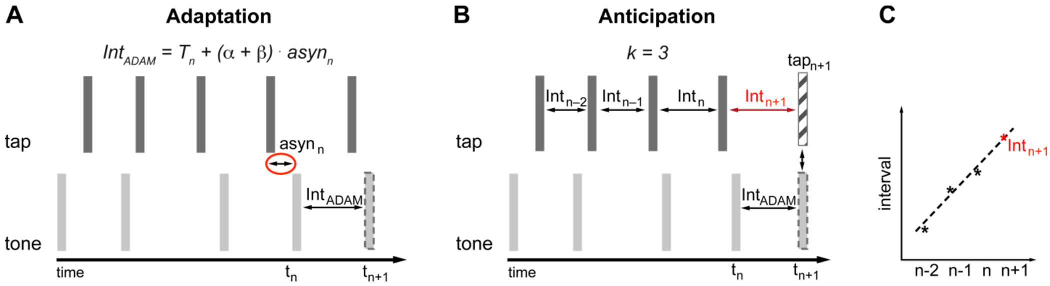


Figure 1.2 Implementation of adaptation (A) and anticipation (B, C) in ADAM. asyn, asynchrony; Int, interval; T, Timekeeper period; α, phase correction parameter; β, period correction parameter; k, number of intervals. **(A)** The time of the occurrence of the next tone is determined based on the asynchrony and the settings of the error correction parameters α and β. **(B, C)** A curve-fitting process, applied to the preceding intervals, predicts the next tap [Reprinted from "The Adaptation and Anticipation Model (ADAM) of sensorimotor synchronization," by M.C. van der Steen and P.E. Keller, *Frontiers in Human Neuroscience*, *7*:253, p. 9]

1.6 SIMULATIONS

Running simulations based on models can be used to systematically investigate the effect of the different parameter settings; with human participants this is not possible. Simulations combined with behavioral data create a powerful method to gain knowledge on the modeled reality, which, in the case of ADAM, refers to knowledge on the effects of adaptation and anticipation mechanisms in SMS.

Initial simulations conducted with ADAM while developing and improving the model included variations of the parameter settings for phase and period correction in the adaptation module of ADAM. The goal of these simulations was to investigate with which parameter settings phase and period correction would lead to synchronization versus loss of synchronization due to drift both in SMS with stable and tempo changing sequences. Examples of simulations related to the anticipation module of ADAM include variations of the order of fitted line and the numbers of intervals used for the extrapolation process. Furthermore, simulations were carried to investigate how different noise settings affect SMS and whether additional assumptions are necessary in order for the model to be able to deal with human input data.

In a second step, simulations with ADAM were run to obtain hypotheses on the relationship between anticipatory and adaptive timing skills (Mills, van der Steen, Schultz, & Keller, *submitted*). Simulations were set up to model the process of synchronizing with tempo changing sequences. The effect of different parameter settings on measures pertaining to the underlying adaptation and anticipation mechanisms were the main focus of the simulations. Based on the results of these simulations, it was hypothesized that temporal anticipation and adaptation mechanisms would show a positive relation and that both mechanisms would contribute to successful SMS. These hypotheses were tested in a behavioral experiment. As hypothesized, results demonstrated a relationship between adaptation and anticipation mechanisms. Furthermore, adaptation mechanisms seemed to contribute more to SMS accuracy, while both adaptation and anticipation mechanisms predicted SMS precision (Mills et al., *submitted*).

In a third line of inquiry, simulations with ADAM were matched to behavioral results directly. The study reported in Chapter 3 of the current dissertation focused on different types of potential links between adaptation and anticipation mechanisms during synchronization with tempo changing sequences. Simulations were run with four versions of ADAM. 1) In the 'Adaptation Model' synchronization is established and maintained by means of phase and period correction. In the other three models both adaptation and anticipation mechanisms were active. 2) In the 'Independent ADAM' model adaption and anticipation mechanisms contribute independent of each other to SMS. Based on anticipation a prediction about the next tone and thus occurrence of the next tap is made. The timing of this tap is subjected to a phase correction process. In the 'Joint ADAM (α | β)' models adaptation and anticipation mechanisms are linked in a joint internal module that implements an anticipatory phase correction process. 3) In the Joint ADAM (α) model adaptation simulates the next tap, which is subjected to phase correction. Anticipation predicts the timing of the next tone. The simulated asynchrony between the simulated next tap and the predicted next tone is minimized by means of an anticipatory phase correction process when determining the timing of the next tap that will be executed. 4) The Joint ADAM (β) model is similar to the Joint ADAM (α) model except that the now period correction is applied as adaptation mechanism. In 'Joint ADAM (α | β)' models potential errors are thus predicted and corrected before they could occur. Using a newly developed bGLS method (Jacoby & Repp, 2012; Repp et al., 2012) parameters relevant for the different models were estimated from a behavioral data set (see below). The bGLS method tries to solve a generalized regression problem. Furthermore, the fit of the models to the behavioral data was determined to compare the models. Simulations showed the advantage of implementing both adaptation and anticipation mechanisms when synchronizing with a tempo changing sequence. Including the anticipation in the model increased the precision of simulated sensorimotor synchronization and improved the fit of model to behavioral data. Joint internal models seem to play a role in linking adaptation and anticipation mechanisms.

Chapter 3 describes the four models in more detail and shows with simulations the effect of different parameter settings on SMS. Furthermore, the models were used to estimate parameter settings from the behavioral data and the fit between simulated and behavioral data was assessed.

1.7 EXPERIMENTS

As mentioned before, it is standard practice to investigate aspects of SMS and the underlying mechanisms by means of finger tapping tasks. Typically, during such tasks, participants are instructed to tap their finger in time with (auditory) stimulus sequences. The nature of the stimulus sequence differs depending on the topic of interest. For example, studies of synchronization with fixed, step change or adaptive sequences have revealed specific information about the operation of adaption mechanisms (cf., Repp, 2005; Repp & Su, 2013). Adaptive sequences can be programmed to implement phase and or period correction in order to boost SMS or to create more challenging SMS tasks, thereby creating scenarios that capture the demands of synchronization with partners displaying different levels of dynamic cooperativity (e.g. Fairhurst, Janata, & Keller, 2012, 2014; Repp & Keller, 2008). Anticipation mechanisms, on the other hand, are usually investigated via tempo changing sequences (e.g., Pecenka & Keller, 2011; Rankin et al., 2009).

The study presented in chapter 3 aimed to investigate participants' ability to synchronize with continuously tempo changing sequences. Seventeen participants tapped in synchrony with three auditory tempo changing stimulus sequences. The pattern of the stimulus sequences differed in the rate with which the tempo changed and the number of turning points. The tempo changes were designed to resemble musical accelerando and ritardando and followed a sigmoidal function (cf. Schulze, Corde, & Vorberg, 2005). Participants were instructed to tap with the tempo changing sequences as accurately and precisely as possible across a series of trials for each pattern. The mean signed asynchrony was calculated as inverse measure of SMS accuracy and the standard deviation of the signed asynchronies was used as inverse measure of precision. To investigate adaptation, the amount of phase and period correction implemented by the participants was estimated by means of the bGLS method (Jacoby and Repp, 2012, Repp et al., 2012). Anticipation during synchronization with tempo changing sequences was quantified based on the lag-1 and lag-0 cross-correlations between the inter-stimulus and inter-tap intervals, the prediction/tracking ratio, as well as by a prediction index based on an autoregressive modeling technique (Pecenka & Keller, 2009; Mills et al., *submitted*). Results showed that participants were capable of synchronizing their finger taps with the tempo changing auditory stimulus sequence in a high level of SMS accuracy and precision. Although synchronization was less accurate and precise in pattern 3, that contained the most turning points and during which the tempo changes from interval to interval were the largest. Phase correction estimates increased across patterns, while period estimates decreased across patterns. Furthermore, participants were found to predict the tempo changes for all three patterns. However, prediction/tracking ratio increased with increasing degree of tempo change between successive intervals, indicating that there was a tendency to engage in more predictive behavior when differences in tempo were more salient. In conclusion both adaptation and anticipation mechanisms were employed by the participants in order to synchronize with continuously tempo changing sequences.

Research from different fields, such as animal, pharmacological, neuropsychological, patient and brain studies, has provided evidence for a widespread timing network in the brain. Brain areas typically implicated in SMS, temporal processing, and evaluation of temporal structures include the cerebellum, basal ganglia, and supplementary motor area (cf., Coull, Cheng, & Meck, 2011). The basal ganglia have been shown to play an important role in timekeeping while the cerebellum seems to have a more important role in generating temporal predictions (Coull et al., 2011).

SMS plays an important role during ensemble music making (Repp, 2005). Disorders that affect basic mechanisms underpinning SMS can therefore have profound implications for a common and cultural universal form of human communicative behavior. Even highly skilled professional musicians may come to experience compromised SMS skills due to acquired neurological conditions. Musician’s dystonia is a neurological movement disorder specific to musicians and is characterized by the loss of voluntary motor control of skilled movements related to instrumental playing (cf. Altenmüller & Jabusch, 2010). This disorder has also been linked to disturbed movement planning, somatosensory functions, and aspects of timing (e.g., Avanizo et al., 2013; Lim et al., 2003; Stamelou, Edwards, Hallett, & Bhatia, 2012). Approximately 1% of professional musicians are affected by this disabling disorder (Altenmüller & Jabusch, 2010). Despite the available therapies, musician’s dystonia often forces professional musicians to change profession (Jabusch, Zschucke, Schmidt, Schuele, & Altenmüller, 2005). The pathophysiology of the disorder is still unclear but both functional and structural abnormalities have been identified in brain areas implicated in timing (e.g., primary motor cortex, supplementary motor areas, basal ganglia and the cerebellum).

The study reported in chapter 4 investigates the timing abilities in musician's dystonia patients [N = 15] and matched controls [N=15] using a battery of auditory-motor tasks focusing on basic perceptual and action aspects of timing relevant for music making. To test SMS abilities and examine underlying anticipation and adaptation mechanisms, participants synchronized their taps with tempo changing and adaptive auditory sequences. In addition, an adjusted version of the Beat Alignment Test (during which participants are asked to judge if a superimposed metronome is aligned with the beat of the musical excerpt [Iversen & Patel, 2008]) was used to examine the precision of beat synchrony perception. Performance on these tasks was compared with elementary perceptual tasks, namely anisochrony detection and auditory-motor delay detection. Machine learning techniques were used to investigate whether musician's dystonia patients were characterized by non-linear combinations of the assessed timing abilities. Results did not show any timing deficits for patients relative to the matched controls. Both groups benefited from a pacing sequence that adapted to their timing in a stable SMS task. Furthermore, in the Beat Alignment Test, both groups were able to detect a misaligned metronome when it was late rather than early relative to the musical beat. Overall, the results suggest that timing abilities are intact in patients with musician's dystonia. This supports the idea that musician's dystonia is a highly task-specific movement disorder in which impairments are most pronounced during instrumental playing. The finding that musician's dystonia patients benefited from synchronizing with adaptive stimulus sequences is promising for the development of rehabilitation programs. Musician's dystonia patients could maintain their timing skills by practicing sensorimotor timing tasks away from their instrument. Challenging synchronization tasks could be developed involving adaptive virtual partners that could be driven by ADAM.

In an ongoing study, we are investigating adaptation and anticipation mechanisms in patients with lesions to the basal ganglia and the cerebellum. SMS abilities were tested in these patient groups and matched controls using synchronization tasks with fixed, adaptive, and tempo changing sequences. Results suggest that only patients with lesions to the basal ganglia display impaired SMS precision (while SMS accuracy was intact). Furthermore, patient groups and control participants alike showed more accurate and precise SMS when synchronizing with an adaptive stimulus sequence. These preliminary results highlight the importance of the basal ganglia for successful SMS and suggest that patients benefit from synchronizing with an adaptive stimulus sequence that implements error correction as a cooperative synchronization partner. The latter finding opens up possibilities for customized rehabilitation programs using virtual synchronization partners to scaffold the patient's behavior.

Chapter 3 describes the study on the synchronization with tempo changing sequences. A behavioral experiment is combined with simulations with ADAM in order to gain insights into adaptation and anticipation mechanisms that support SMS with tempo changing sequences. The study on timing abilities in musician's dystonia patients is presented in chapter 4.

1.8 CONCLUSION

The goal of this dissertation was to get a better understanding of the underlying mechanisms of SMS. To this end ADAM, an ADaptation and Anticipation Model was developed, simulations with ADAM were run and experiments focusing on different aspects of timing with healthy participants and patients were performed. ADAM was found to be a useful framework to investigate adaptation and anticipation mechanisms and possible links between these mechanisms. Hypothesized relationships between adaptation and anticipation were investigated by comparing computer simulations based on ADAM with data from behavioral experiments, leading to novel insights into SMS. Notably, it was shown not only that both adaptation and anticipation mechanisms play a role during SMS with tempo changing sequences, but also that internal models may provide link between the mechanisms. It is proposed that ADAM, with the envisioned extensions into the visual domain, will also be able to contribute to the understanding of the different aspects of SMS that arise in everyday life, where synchronization takes place via multiple domains and time scales. Furthermore, the finding that different patient groups, despite impaired performance in other domains, benefit from synchronizing with adaptive stimulus sequences is a promising outcome for rehabilitation programs. Targeted rehabilitation programs focusing on the facilitation of movement timing could be developed involving adaptive virtual partners driven by ADAM.

1.9 REFERENCES

Altenmüller, E., & Jabusch, H.C. (2010). Focal dystonia in musicians: phenomenology, pathophysiology, triggering factors, and treatment. *Medical Problems of Performing Arts, 25*, 3-9.

Avanizo, L., Martine, D., Martine, I., Pelosin, E., Vicario, C.M., Bove, M., Defazio, G., & Abbruzzese, G. (2013). Temporal expectation in focal hand dystonia. *Brain, 136,* 444-454.

Box, G.E.P., & Draper, N.R. (1987). *Empirical Model-Building and Response Surfaces* (pp. 424). Wiley Series of Probability and Statistics

Butz, M.V., Sigaud, O., & Gérard, P. (2003). Anticipatory behavior: exploiting knowledge about the future to improve current behavior. In M.V. Butz, O. Sigaud, & P. Gérard (Ed.), *Anticipatory behavior in adaptive learning systems. Foundations, theories, and systems* (pp. 1-10). Berlin, Germany: Springer.

Coull, J.T., Cheng, R., & Meck, W.H. (2011). Neuroanatomical and neurochemical substrates of timing. *Neuropsychopharmacology, 36,* 3-25.

Fairhurst, M.T., Janata, P., & Keller, P.E. (2012). Being and feeling in sync with an adaptive virtual partner: Brain mechanisms underlying dynamic cooperativity. *Cerebral Cortex, 67,* 313-321.

Fairhurst, M.T., Janata, P., & Keller, P.E. (2014). Leading the follower: An fMRI investigation of dynamic cooperativity and leader-follower strategies in synchronization with an adaptive virtual partner. *NeuroImage*, *84,* 688-697.

Fleischer, J.G. (2007). Neural correlates of anticipation in cerebellum, basal ganglia, and hippocampus. *Lecture Notes in Computer Sciences, 4520,* 19-34.

Ivry, R.B., Spencer, R.M., Zelaznik, H.N., & Diedrichsen J. (2002). The cerebellum and event timing. *Annuals New York Academy of Science, 978,* 203-317.

Jabusch, H.C., Zschucke, D., Schmidt, A., Schuele, S., & Altenmüller, E. (2005). Focal dystonia in musicians: Treatment strategies and long-term outcome in 144 patients. *Movement Disorders, 20,* 1623-1626.

Jacoby, N., & Repp, B.H. (2012). A general linear framework for the comparison and evaluation of models of sensorimotor synchronization. *Biological Cybernetics, 106,* 135-154.

Keller, P.E., (2008). Joint action in music performance. In F. Morganti, A. Carassa, & G. Riva (Ed.), *Enacting intersubjectivity: a cognitive and social perspective to the study of interactions* (pp. 205-221). Amsterdam, the Netherlands: IOS Press.

Keller, P.E., & Appel, M. (2010). Individual differences, auditory imagery, and the coordination of body movements and sounds in musical ensembles. *Music Perception, 28,* 27-46.

Lim, V.K., Bradshaw, J.L., Nicholls, M.E.R., Altenmüller, E.A. (2003). Perceptual differences in sequential stimuli across patients with musician's and writer's cramp. *Movement Disorders, 18,* 1286–1293.

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

Mates, J. (1994a). A model of synchronization of motor acts to a stimulus sequence: I. Timing and error corrections. *Biological Cybernetics, 70,* 463-473.

Mates, J. (1994b). A model of synchronization of motor acts to a stimulus sequence: II. Stability analysis, error estimation and simulations. *Biological Cybernetics, 70,* 475-484.

Mills, P.F., van der Steen, M.C., Schultz, B.G., & Keller, P.E. (*submitted*). Individual differences in temporal anticipation and adaptation during sensorimotor synchronization.

Pastor, M.A., Artieda, J., Jahanshahi, M., & Obeso, J.A. (1992). Time estimation and reproduction is abnormal in Parkinson's disease. *Brain, 115,* 211–225.

Pecenka, N., & Keller, P.E. (2011). The role of temporal prediction abilities in interpersonal sensorimotor synchronization. *Experimental Brain Research, 211,* 505-515.

Pressing, J. (1999). The referential dynamics of cognition and action. *Psychological Review, 106,* 714-747.

Rankin, S.K., Large, E.W., & Fink, P.W. (2009). Fractal tempo fluctuation and pulse prediction. *Music Perception, 26,* 401-413.

Rasch, R.A. (1979). Synchronization in performed ensemble music. *Acustica, 43,* 121-131.

Repp, B.H. (2001a). Phase correction, phase resetting, and phase shifts after subliminal timing perturbations in sensorimotor synchronization. *Journal of Experimental Psychology: Human Perception and Performance, 27,* 600-621.

Repp, B.H. (2001b). Processes underlying adaptation to tempo changes in sensorimotor synchronization. *Human Movement Sciences, 20,* 277-312.

Repp, B.H. (2002a). Automaticity and voluntary control of phase correction following event onset shifts in sensorimotor synchronization. *Journal of Experimental Psychology: Human Perception and Performance, 28,* 410-430.

Repp, B.H. (2002b). The embodiment of musical structure: effects of musical context on sensorimotor synchronization with complex timing patterns. In W. Prinz, & B.

Hommel (Ed.), *Common mechanisms in perception and action: attention and performance XIX* (pp. 245-265). Oxford, UK: Oxford University Press.

Repp, B.H. (2005). Sensorimotor synchronization: A review of the tapping literature. *Psychononmic Bulletin & Review, 12,* 969-992.

Repp, B.H., & Keller, P.E. (2004). Adaptation to tempo changes in sensorimotor synchronization: Effects of intention, attention, and awareness. *The Quarterly Journal of Experimental Psychology. Section A: Human Experimental Psychology, 57A,* 499-521.

Repp, B.H., Keller, P.E., & Jacoby, N. (2012). Quantifying phase correction in sensorimotor synchronization: empirical comparison of three paradigms. *Acta Psychologica, 139,* 281–290.

Repp, B.H., & Su, Y-H. (2013). Sensorimotor synchronization: A review of recent research (2006–2012). *Psychononmic Bulletin & Review, 20,* 403-452.

Schmidt, R.A. (1968). Anticipation and timing in human motor performance. *Psychological Bulletin, 70,* 631-646.

Schneider, S., Schönle, P.W., Altenmüller, E., & Münte, T.F. (2007). Using musical instruments to improve motor skill recovery following a stroke. *Journal of Neurology, 254,* 1339-1346.

Schulze, H.-H., Cordes, A., & Vorberg, D. (2005). Keeping synchrony while tempo changes: accelerando and ritardando. *Music Perception, 22,* 461-477.

Schulze, H-H., & Vorberg, D. (2002b). Linear phase-correction in syhchronizations: Predictiosn, parameter estimation, and simulations. *Brain and Cognition,* 48, 80-97.

Schwartze, M., Keller, P.E., Patel, A.D., & Kotz, S.A. (2011). The impact of basal ganglia lesions of sensorimotor synchronization, spontaneous motor tempo and the detection of tempo changes. *Behavioural Brain Research, 216,* 685–691.

Semjen, A., Vorberg, D., Schulze, H-H. (1998). Getting synchronized with the metronome: Comparisons between phase and period correction. *Psychological Research, 61,* 44-55.

Stamelou, M., Edwards, M.J., Hallett, M., & Bhatia, K.P. (2012). The non-motor syndrome of primary dystonia: clinical and pathophysiological implications. *Brain, 135,* 1668-1681.

Thaut, M.H., Stephan, K.M., Wunderlich, G., Schicks, W., Tellmann, L., Herzog, H., McIntosh, G.C., Seitz, R.J., & Hömber, V. (2009). Distinct cortico-cerebellar activations in rhythmic auditory motor synchronization. *Cortex, 45,* 44-53.

van Ulzen, N.R., Lamoth, C.J., Daffertshofer, A., Semin, G.R., & Beek, P.J. (2008). Characteristics of instructed and uninstructed interpersonal coordination while walking side-by-side. *Neuroscience Letters, 432,* 88-93.

Vorberg, D., & Schulze, H-H. (2002). A two-level timing model for synchronization. *Journal of Mathematical Psychology, 46,* 56-87.

Vorberg, D., Wing, A., (1996). Modeling variability and dependence in timing. In H-H. Heuer, & S.W. Keele (Ed.), *Handbook of perception and action Vol. 2* (pp. 181-262). London, UK: Academic Press.

Wing, A.M., & Kristofferson, A.B. (1973a). Response delays and the timing of discrete motor responses. *Perception & Psychophysics, 14,* 5-12.

Wing, A.M., & Kristofferson, A.B. (1973b). The timing of interresponse intervals. *Perception & Psychophysics, 13,* 455–460.

Wing, A.M., & Woodburn, C. (1995). The coordination and consistency of rowers in a racing eight. *Journal of Sports Sciences, 13,* 187-197.

Wing, A.M., Endo, S., Bradbury, A., & Vorberg, D. (2014). Optimal feedback correction in string quartet synchronization. *Journal of the Royal Society Interface, 11,* 20131125. http://dx.doi.org/10.1098/rsif.2013.1125

Wolpert, D.M., Doya, K., & Kawato, M. (2003). A unifying computational framework for motor control and social interaction. *Philosophical Transactions of the Royal Society B, 358,* 593-602.

Wolpert, D.M., & Kawato, M. (1998). Multiple paired forward and inverse models for motor control. *Neural Networks, 11,* 1317-1329.

Chapter 2

MANUSCRIPT 1

The ADaptation and Anticipation Model (ADAM) of sensorimotor synchronization

M.C. (Marieke) van der Steen[1], Peter E. Keller[1,2]

[1] Max Planck Institute for Human Cognitive and Brain Sciences, Research Group "Music Cognition & Action", Leipzig, Germany

[2] The MARCS Institute, University of Western Sydney, Sydney, Australia

Published in

***Frontiers in Human Neuroscience*, 7:253**

2.1 ABSTRACT

A constantly changing environment requires precise yet flexible timing of movements. Sensorimotor synchronization (SMS) —the temporal coordination of an action with events in a predictable external rhythm— is a fundamental human skill that contributes to optimal sensory-motor control in daily life. A large body of research related to SMS has focused on adaptive error correction mechanisms that support the synchronization of periodic movements (e.g., finger taps) with events in regular pacing sequences. The results of recent studies additionally highlight the importance of anticipatory mechanisms that support temporal prediction in the context of SMS with sequences that contain tempo changes. To investigate the role of adaptation and anticipatory mechanisms in SMS we introduce ADAM: an ADaptation and Anticipation Model. ADAM combines reactive error correction processes (adaptation) with predictive temporal extrapolation processes (anticipation) inspired by the computational neuroscience concept of internal models. The combination of simulations and experimental manipulations based on ADAM creates a novel and promising approach for exploring adaptation and anticipation in SMS. The current paper describes the conceptual basis and architecture of ADAM.

Keywords: sensorimotor synchronization – computational model –temporal adaptation – error correction – temporal anticipation – predictive internal models

2.2 INTRODUCTION

An intriguing question about motor control in daily life is how people effectively time their coordinated actions during everyday activities. The question is especially interesting when one considers that coordination needs to occur in a constantly changing environment and with other people who are also dynamic in their behavior. Precise but flexible motor timing is an important aspect of successful coordination. Sensorimotor synchronization (SMS) is a fundamental human skill that is the basis of numerous forms of behavioral coordination. Broadly speaking, SMS is the temporal coordination of an action with a predictable external event, an external rhythm (Repp, 2005).

SMS frequently takes place in social contexts in the sense that other humans produce the sequences with which one's movements need to be synchronized. Many examples can be found in musical settings; people tend to nod their head, clap, or dance in synchrony with music performed live by musicians. When listening to music, people generate temporal expectations based on structural regularities related to the musical beat (a periodic pulse), and they are often compelled to produce movements in synchrony with these regularities (Repp, 2005; Large, 2008). The external events with which actions are temporally coordinated can also be actions themselves, such as when the chaotic applause of an enthusiastic audience after a concert morphs into synchronized clapping (Néda et al., 2000). The act of synchronizing movements with sequences that are produced by other humans is not restricted to musical settings. Another classic example of –involuntary– interpersonal coordination is the tendency for two people walking together to synchronize their walking rhythm with each other (van Ulzen et al., 2008). The above mentioned examples are situations from daily life during which SMS occurs more or less spontaneously. But precise synchronization might also be the explicit goal of extensive practice schedules that are intended to achieve artistic or athletic perfection, as in musical ensembles (Keller and Appel, 2010) or rowing crews (Wing and Woodburn, 1995).

Precise yet flexible SMS requires temporal adaptation (reactive error correction) and anticipation (predictive processes) (see Keller, 2008; Repp and Su, 2013). The mechanisms that support these processes are typically studied separately in SMS research. Here we argue that, to get a better understanding of the nature of SMS, it is fruitful to study adaptive and anticipatory mechanisms within a single framework. The goal of the present paper is therefore twofold:

The first aim is to give an overview of the existing literature on the roles of temporal adaptation and anticipation in SMS. To this end, we provide a sketch of what can be considered to be the state-of-the-art in the field of SMS research, covering its main approaches, including those that employ behavioral experimentation, computational modeling, and the study of brain structures and functional processes that support SMS. This brief review serves to illustrate that, although SMS is a basic and fundamental human skill, its workings are far from simple and are not yet fully understood. In our view, an important gap that needs to be bridged is that between research on adaptive and anticipatory processes in SMS. However, it is also the case that research devoted to understanding each class of process alone has taken divergent paths. In an attempt to make steps towards redressing this divergence, we delineate connections between fields of research that are relevant to the investigation of the role of temporal adaptation and anticipation in SMS but that, to our knowledge, have not been linked before (e.g., tau theory and the concept of 'strong anticipation', see section 2.5.2).

The second aim is to introduce ADAM (Figure 2.1), an ADaptation and Anticipation Model that is intended to account for both adaptive and anticipatory aspects of sensorimotor synchronization. After introducing ADAM, we give a brief overview of novel research paradigms that employ the model in the context of computer simulations and behavioral experiments. These simulations and experiments permit different aspect of SMS — specifically, the effects of, and the link between, adaptation and anticipation mechanisms— to be investigated systematically within a unified theoretical framework.

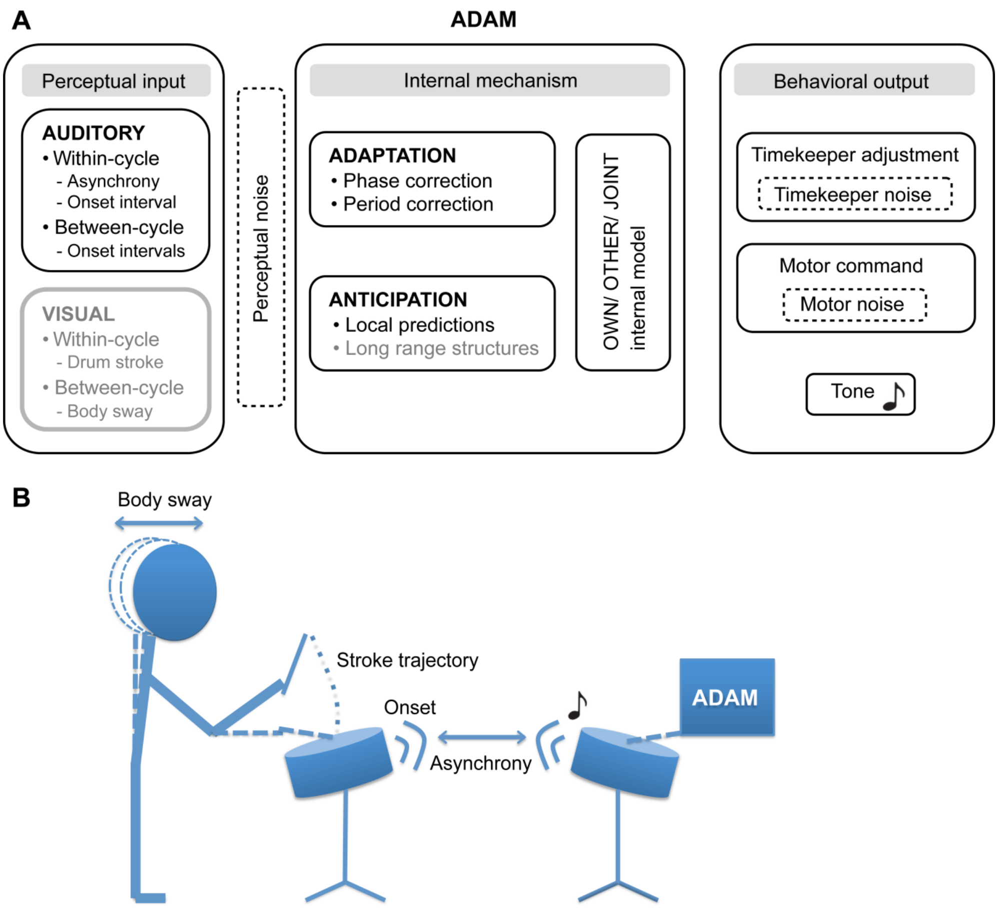


Figure 2.1 (**A**) The proposed architecture of the ADaptation and Anticipation Model, ADAM. The main components that are illustrated include auditory and visual input, internal mechanisms that support adaptation to and anticipation of this input, and —by communing with internal models of one's own actions, others' actions, and collective joint actions— control behavioral output. In addition, three sources of noise (perceptual, timekeeper, and motor) can affect ADAM's SMS accuracy and precision. Components illustrated in grey have not been implemented in the current version of ADAM, though their relevance to SMS is discussed in this article.
(**B**) An example of a bi-directional experimental set up in which the participant and ADAM influence each other in the context of a joint drumming task.

2.3 SENSORIMOTOR SYNCHRONIZATION

SMS is a form of referential behavior in which actions are timed relative to an external event, the referent (Pressing, 1999, Repp, 2005). There is a long tradition of studying sensorimotor synchronization in laboratory tasks that require participants to produce simple movements (such as finger taps) in time with events in computer-controlled pacing sequences (e.g., tones). In such paced finger tapping tasks, participants are asked to tap their finger with a specific phase and/or period relation to the timing of an auditory or visual pacing sequence. It is standard practice for participants to be instructed to tap with their index finger in synchrony with the tones produced by a metronome they hear over headphones, while keeping the beat of their taps as stable as possible. Drum strokes may be substituted for finger taps, as shown in the drumming task illustrated in Figure 2.1B.

A common variable of interest when assessing SMS accuracy is the timing error –the asynchrony– between the occurrence of the action (the drum stick contacting the drum) and the pacing event (see Figure 2.1B). Although asynchronies can vary in magnitude across experimental conditions and cohorts, and large inter-individual differences are usually evident, the action typically precedes the event, resulting in what has been termed a 'negative mean asynchrony' (Aschersleben, 2002). The level of participants' synchronization skill is also reflected in measures of precision, including the variability of asynchronies (i.e., an inverse index of the strength of sensorimotor coupling) and the variability of the intervals between consecutive movements (i.e., an inverse index of stability in tapping tempo) [see Repp, 2005; Repp and Su (2013) for extensive reviews on SMS].

Although SMS is a widespread and fundamental human skill, individual differences in SMS ability can be observed (e.g., Pecenka and Keller, 2009; Repp, 2010; Pecenka and Keller, 2011; Repp and Su, 2013), with certain individuals exhibiting marked impairment in SMS in some contexts (Phillips-Silver et al., 2011). The sources of these individual differences may lie in variations of three broad classes of functional processes that underlie SMS: (1) the perception of timing in rhythmic stimuli, and, specifically a periodic beat, (2) the production of rhythmic movements, and (3) the multisensory integration, or coupling, of perceived rhythms and produced motor rhythms (see Phillips-Silver et al., 2010).

Neuroscientific work on SMS has revealed that these processes are implemented in an extensive network of brain regions, including the primary sensorimotor cortices, premotor cortex, inferior parietal cortex, the supplementary motor area, the cerebellum and the basal ganglia (e.g., Witt et al., 2008; Coull et al., 2011; see Repp and Su (2013) part 4 for a review on the neuroscience of SMS). The cerebellar-premotor network seems to be of particular importance for SMS presumably because this network is involved in sensorimotor coordination (Molinari et al., 2007) and audio-motor coupling (Chen et al., 2009). It follows that damage to regions within this network may impair SMS skills, and thus have detrimental effects on the fulfillment of daily activities. To understand the specific sub-components of SMS skill that may be affected, it is helpful to unpack SMS in terms of the sensory modalities that it may involve, the processes that characterize interactions between mutually responsive agents in naturalistic SMS tasks, and the mechanisms related to temporal error correction and prediction in SMS.

2.3.1 SMS between mutually responsive agents

Studies related to SMS traditionally investigate participants' synchronization with a pacing sequence that is either isochronous or perturbed in more or less systematic ways (see Repp, 2005 for review). The coupling in these cases is unidirectional: the human participant synchronizes with the unresponsive pacing sequence. But in daily life, most of SMS activities involve two mutually responsive agents that are coupled bidirectionally (e.g. interpersonal coordination, musicians playing together). Recently, several paradigms have been introduced to investigate these types of SMS activity.

2.3.1.1 SMS between a human and virtual partner

Following a precedent set by Vorberg (2005), Repp and Keller (2008) examined mutual adaptation during SMS using a paradigm that required interaction with an 'adaptive virtual partner'. Specifically, the task entailed a human participant tapping a finger in time with a computer-controlled auditory pacing signal that simulated the potential behavior of a human partner by adapting to the participant's tap timing to varying degrees. This allowed the bidirectional coupling between two interacting agents to be studied under conditions where the behavior of one agent (the virtual partner) was under experimental control. The advantage of this approach is that the effects of parametric variations in adaptation strategy (programmed into the virtual partner) on the behavior of the human participant can be assessed.

Taking a different approach, Kelso and colleagues (2009) employed a real-time interaction paradigm involving visually mediated coupling between a human and a virtual partner to investigate the dynamics of basic human social coordination. The virtual partner was an avatar of a hand whose movements were driven by a non-linearly coupled component oscillator of the Haken-Kelso-Bunz (HKB) model, a model of basic coordination dynamics. The original HKB model described phase transitions between two hands (Haken et al., 1985). Since then, it has been shown that the HKB equations can be used to describe rhythmic coordination between similar effectors (e.g., fingers) as well as between different effectors (e.g., arm-leg) and even between two individuals (e.g., Kelso, 1995; Schmidt and Richardson, 2008). In the study by Kelso and colleagues (2009) participants were coupled with the virtual partner via the visual modality. The coupling term for the oscillator used the participant's finger position and velocity to adapt to the participant's performance. Having participants interact with the virtual partner based on the HKB model therefore created an opportunity to investigate reciprocal coordination. Results showed that being reciprocally coordinated with the virtual partner led to different levels of stability and novel behavioral strategies employed by the participants. For example, participants transiently switched between in-phase and anti-phase relations or varied the spatial amplitude of their movements relative to the virtual partner in order to maintain synchronization.

Both of the studies described above (Repp & Keller, 2008; Kelso et al., 2009) combined the use of experiments involving a human participant and a virtual partner with the use of simulations in order to arrive at a better understanding of the observed behavior and its underlying mechanisms. In doing so, these paradigms were successful in identifying new characteristics of SMS behavior.

2.3.1.2 SMS between two humans

Related work that investigated interaction between live humans in dyadic sensorimotor synchronization tasks has revealed evidence for mutual temporal adaptation. Konvalinka and colleagues (2010) explored the ongoing dynamics that result from a coordinated joint tapping task under different coupling conditions created by varying the auditory feedback settings. Participants were asked to maintain a given beat while producing or synchronizing with an auditory signal. The auditory signals were produced either by the participant's own taps, the other person's taps, or the computer metronome. In the metronome conditions, both participants heard only the computer sounds. In the uncoupled condition each participant only heard sounds triggered by his or her own taps, in the unidirectional coupling condition both participants heard taps generated by just one of them, while in the bidirectional coupling condition both participants received the taps generated by the other participant. Results showed that participants were able to synchronize equally well with a human partner that was relatively unpredictable but responsive and with a predictable but unresponsive computer metronome. Furthermore, in the bidirectional coupled condition, the lagged cross-correlations of interpersonal inter-tap intervals showed negative lag-0 and positive lag-1 cross-correlations (e.g., if one participant produced a relatively long interval, the next interval produced by the other individual would be relatively long, suggesting assimilation at the level of inter-onset interval timing). The authors concluded that synchronization between two participants was characterized by continuous adaptation on a millisecond timescale by both individuals.

Taking a different approach, Nowicki and colleagues (2013) employed a dyadic finger-tapping task in which paired musicians were required to tap in alternation, in synchrony with an auditory pacing signal. Serial dependencies between successive asynchronies produced by alternating individuals' taps relative to the pacing tones revealed evidence for mutual temporal assimilation –a form of behavioral mimicry– when both individuals' taps generated auditory feedback. This result suggested that mutual adaptive timing is characterized more strongly by temporal assimilation than by a compensation processes whereby individuals correct each other's timing errors.

2.4 ADAPTATION: REACTIVE, ERROR CORRECTION MECHANISMS

SMS, like any human behavior, is characterized by biological noise that leads to variability in movement timing and, therefore, temporal error even when synchronizing with a regular pacing signal. Many instances of SMS, however, involve coordination with signals containing deviations from regularity (e.g., expressive timing in music performance), leading to some degree of uncertainty about event timing and, again, temporal error. Adaptation processes that correct these errors are hence necessary to sustain SMS and to behave with temporal flexibility in the face of this variability. Without these error correction processes, which compensate for timing errors in a reactive fashion, variability would accumulate from movement cycle to movement cycle. This would result in increasingly large asynchronies, phase drift, and the eventual loss of synchronization (Vorberg and Wing, 1996).

2.4.1 Models of error correction

The modeling of error correction in SMS has been done in myriad ways. Two main approaches can be distinguished: dynamic systems theory and information-processing theory. Dynamic systems models of SMS deal with the relative phase of periodic oscillators, while information processing models posit internal clocks, or timekeepers, that measure or generate discrete time intervals.

Dynamic systems theory assumes that an external rhythmic signal evokes intrinsic neural oscillations that entrain to periodicities in the rhythmic sequence (Large, 2008). The focus within this field is on continuous, non-linear, and within-cycle coupling between these oscillations and the pacing signal. SMS behavior can therefore be modeled with non-linearly coupled oscillators that are described formally in terms of differential equations (e.g. Schöner and Kelso, 1988; Fink et al., 2000; Assis et al., 2005; Torre and Balasubramaniam, 2009). According to these models, the accuracy and precision of SMS vary as a function of the strength of the phase entrainment of the oscillation to the stimulus sequence, which is defined by a coupling term. To maintain synchrony when the tempo of the stimulus sequence undergoes change, an additional term reflecting period matching is necessary (Large et al., 2002).

The information-processing theory focuses on cycle-to-cycle correction of timing errors and uses linear timekeeper models to model this error correction process. According to timekeeper models, error correction can be described according to linear autoregressive processes (Wing and Kristofferson, 1973; Vorberg and Wing, 1996). These processes produce local dependencies between successive taps: the deviation of the current tap from the mean inter-tap interval and mean asynchrony is proportionally related to the deviation of the inter-tap interval and asynchrony associated with the previous tap plus random noise (Wing and Kristofferson, 1973; Wing and Beek, 2002). The models assume the existence of a timekeeper and different sources of timing variability. The timekeeper functions as a clock that generates pulses, which initiate motor commands (Wing and Kristofferson, 1973). Two additive sources of random timing variability are noise in the timekeeper (related to variability in neural activity) and in the execution of motor commands (due to variable transmission delays in the peripheral motor system). Timing variability can result in large asynchronies and tempo drift. Error correction mechanisms counteract these effects of variability and therefore contribute to maintenance of synchrony with external stimulus sequences (Mates 1994a; 1994b; Vorberg and Wing, 1996; Vorberg and Schulze, 2002).

It has been argued that the information-processing theory and the dynamic systems theory are closely related, as both can be regarded as variants of a general control equation for referential behavior (Pressing, 1999). However, situations have been documented in which one approach fares better than the other in explaining observed behavioral patterns, as in a recent study that favored a dynamic systems model of synchronized finger tapping with sequences containing gradual tempo changes (Loehr et al., 2011). An alternative to the view that dynamic and information-processing models are essentially equivalent posits that the approaches account for different synchronization processes, and are therefore better suited to explain distinct aspects of SMS (Repp, 2005; Torre and Balasubramaniam, 2009). In the current article, we focus mainly on the information-processing theory because the adaptation module of ADAM is based on work (Repp and Keller, 2008) that took an information-processing approach using autoregressive linear models that account for the behavior in question adequately.

2.4.2 Phase and period correction

In the information-processing theory framework, like in the dynamic systems theory, two separate adaptive processes (namely phase and period correction) have been proposed (Mates, 1994a; 1994b; Vorberg and Wing, 1996; Semjen et al., 1998). Both processes independently modify the timing of the next action based on a percentage (α for phase correction; β for period correction) of the asynchrony (Repp and Keller, 2008) (Figure 2.2) or the difference between the preceding inter-onset interval and the preceding timekeeper interval (Hary and Moore 1985; 1987). Phase correction is a local adjustment to the interval generated by the internal timekeeper, leaving the period of the timekeeper unaffected (Figure 2.2A). Phase correction is automatic and does not require conscious registration of the timing error (Repp, 2001a; 2002a), although the gain of implemented phase correction can be manipulated voluntarily to some extent, for example, by suppressing the tendency to react to perturbations (Repp, 2002a; Repp and Keller, 2004). Furthermore, participants can implement phase correction in advance of an expected perturbation to reduce timing errors (Repp and Moseley, 2012). When systematic tempo fluctuations exceed a certain threshold, depending on several parameters like the base tempo (e.g., Takano and Miyake, 2007), phase correction alone is insufficient for maintaining synchronization and the additional process of period correction is necessary. Period correction adjusts the period of the timekeeper that drives the motor activity, and this change to the timekeeper period persists until period correction is applied again (Repp, 2001b) (Figure 2.2B). Based on simulations, Schulze and colleagues (2005) proposed that additional control mechanisms function to set the gain of period correction and can thereby determine when it is started and stopped. Period correction is largely under cognitive control, requires attentional resources, and relies on the conscious perception of a tempo change in the pacing sequence (Repp and Keller, 2004).

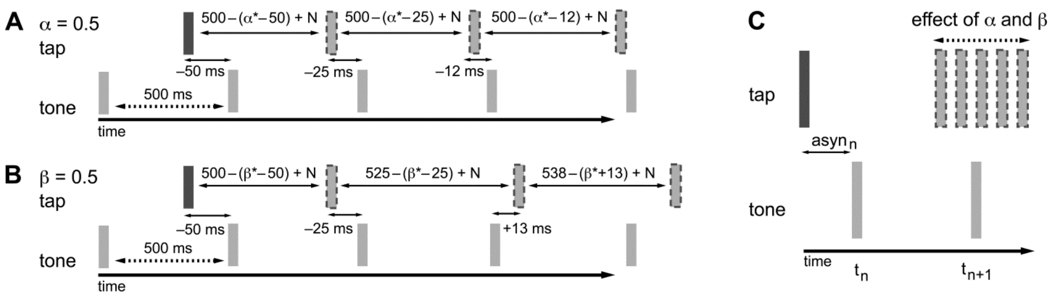


Figure 2.2 Adaptation processes based on the asynchrony following the information-processing theory. In the examples, α and β are both equal to 0.5, which is a value that fits within the typical range of empirical α and β estimates (0.2-0.8). The examples given show how the timing of the next tap is adjusted to compensate for the asynchrony. As a result of the timekeeper setting, the asynchrony (asyn) in combination with error correction mechanisms, and motor and timekeeper noise (N [which is set to zero in the present example]) the next tap is shifted in the opposite direction of the asynchrony.

(**A**) Phase correction (α = 0.5): half of the asynchrony is corrected. Phase correction is a local adjustment; the setting of the timekeeper (in this example 500 ms) is not affected.

(**B**) Period correction (β = 0.5): the correction of the asynchrony has a cumulative effect on the setting of the timekeeper (in this example the base timekeeper is 500 ms), leading to tempo drift.

(**C**) In practice, phase and period correction can be both active during SMS. As a result of the combination of both error correction mechanisms, the timing of the next tap is adjusted based on a percentage of the asynchrony.

A number of techniques can be used to estimate the amount of phase correction implemented by humans (see Repp et al., 2012). One technique that has been employed extensively is a perturbation method that involves introducing an abrupt change to a single pacing inter-onset interval in order to examine the so-called 'phase correction response' in taps that follow this change (e.g., Repp, 2001a). Recently, Repp and colleagues (2012) compared the perturbation method with two different methods for estimating phase correction that are based on data from tasks that require participants to synchronize with a regular metronome or an "adaptively timed" pacing signal. In the latter two methods, the estimation of the amount of phase correction implemented by humans is based on analytical techniques that examine the degree of autocorrelation in the time series of asynchronies between finger taps and pacing events. Repp and colleagues (2012) found that estimates of the amount of phase correction implemented by humans obtained with the regular and "adaptively timed" methods were strongly correlated while estimates obtained with the perturbation method were uncorrelated. According to the authors, these results suggest that keeping in synchrony with a metronome that contains occasional timing perturbations requires different phase correction mechanisms than when synchronizing with a regular metronome or an "adaptively timed" signal (Repp et al., 2012). Estimating the amount of phase and period correction implemented by humans is possible through the use of two-process error correction models that account for short-term phase correction and longer-lasting period correction within a single model (Mates, 1994a, 1994b; Vorberg and Schulze 2002; Schulze et al., 2005). Repp and Keller (2004) estimated error correction by applying a two-process error correction model (Mates, 1994a; 1994b) to tapping data obtained in a task that required synchronization with a metronome that implemented an abrupt tempo change, after which the participant was required to continue tapping at the new tempo (see Repp and Keller, 2004 for a detailed description). Phase and period correction estimates depend on several aspects of the experimental method (e.g., tempo, task, and analytical technique) but typically vary between 0.2 and 0.8 (Repp and Keller, 2004; Fairhurst et al., 2012; Repp et al., 2012).

2.4.3 Adaptation mechanisms in the brain

Further evidence that phase and period correction are distinct processes comes from studies using different procedures to investigate brain function (functional magnetic resonance imaging [fMRI], electroencephalography [EEG], and transcranial magnetic stimulation [TMS]) (see Witt et al., 2008; Repp and Su, 2013). This work has revealed extensive subcortical and cortical networks (spanning the cerebellum, basal ganglia, premotor cortex, [pre-]supplementary motor area, sensorimotor cortex, superior temporal gyrus, and inferior frontal gyrus) that exhibit different patterns of functional connectivity depending on whether error correction is automatic or effortful (Rao et al., 1997; Jänke et al., 2000; Oullier et al., 2005; Chen et al., 2008; Thaut et al., 2009; Bijsterbosch et al., 2011a; Bijsterbosch et al., 2011b). An EEG study that specifically targeted the distinction between phase and period correction using source localization placed the former in auditory and secondary somatosensory cortices and the latter in medial frontal cortex, particularly the supplementary motor area (Praamstra et al., 2003).

The brain-based distinction between automatic and effortful error correction has received further support from a recent fMRI study of SMS with virtual partners (Fairhurst et al., 2012). This study, which required participants to synchronize with an adaptive virtual partner that implemented varying degrees of phase correction, highlighted the importance of the hippocampus, precuneus, posterior cingulate, and cuneus cortex for successful synchronization (Fairhurst et al., 2012). Moreover, when the adaptive partner was easier to synchronize with (i.e., when it implemented moderate degrees of phase correction), cortical midline structures were strongly activated. However, when synchronizing with an overly adaptive virtual partner that made the interaction more cognitively challenging, lateral prefrontal areas were recruited to a greater degree. This shift between brain areas suggests a link between action and social processes related to cooperation in the former case and brain areas associated with cognitive control in the latter case, and might indicate an increase in phase correction or the engagement of period correction by the participants (Fairhurst et al., 2012).

2.5 ANTICIPATION: PREDICTIVE MECHANISMS

Anticipating the precise onset of stimulus events is important for successful SMS because it allows an individual to get his or her response under way early enough so as to coincide with the event (Schmidt, 1968). To achieve this, the brain has evolved the capacity to extract structural regularities rapidly from ongoing events in the environment, and to use this information as a basis for generating online predictions about the immediate future (e.g., Schubotz, 2007; Friston and Kiebel, 2009). These predictions can coevolve via two routes, one characterized by automatic bottom-up expectancies and the other by top-down processes involving mental imagery (Vuust et al., 2009; Keller, 2012).

Evidence for the involvement of anticipatory mechanisms in SMS comes from several sources. One SMS-related phenomenon that has been attributed to predictive processes is the negative mean asynchrony —indicating that participants' finger taps precede pacing signal tones— that is often observed in simple finger tapping tasks. It has been suggested that the negative mean asynchrony provides evidence that participants anticipate the occurrence of the events in the pacing signal, rather than simply reacting to each successive pacing event, to ensure that (relatively slow) somatosensory feedback from finger taps coincides with (faster) auditory feedback from pacing events (Aschersleben, 2002; for a review see Repp, 2005). However, it may also be the case that the negative mean asynchrony reflects the perceptual underestimation of the time interval between the stimulus events (Wohlschläger and Koch, 2000) resulting in a timekeeper setting that is slightly shorter than the pacing interval (Repp and Keller, 2008), which is not necessarily related to anticipation.

Clearer evidence for anticipation mechanisms related to SMS comes from musical activities. When musicians play together, actions need to be coordinated with a high precision but also flexibility to create a coherent piece of ensemble music. Trained ensemble musicians typically show asynchronies in the order of 30-50 ms between tones that, according to the notated score, should be played simultaneously (e.g., Rasch, 1979; Keller and Appel, 2010; Keller, in press). These small asynchronies, indicating a high level of temporal precision, are suggestive of predictive mechanisms related to SMS, as the asynchronies are too small to be the result of purely reactive mechanisms (the fastest reaction times to auditory stimuli are in the order of 100 ms, with average times being around 160 ms [Galton, 1899]) (Keller, 2008).

Furthermore, evidence for anticipation during SMS can be found in studies focusing on the abilities of participants to tap along in synchrony with pacing stimuli (simple tone sequences or musical pieces) that contain gradual tempo changes (Repp, 1999; 2002b; Rankin et al., 2009; Pecenka and Keller, 2011). The relevant dependent variable in these studies is a ratio based on the lag-0 and lag-1 cross-correlation between inter-tap and inter-stimulus intervals. This ratio reflects the degree to which an individual's taps anticipate ('predict') or follow ('track') the tempo changes. If an individual tends towards predicting tempo changes (ratio > 1), then the lag-0 cross-correlation coefficient is high relative to the lag-1 cross-correlation coefficient (i.e., the prediction/tracking ratio is greater than 1), because prediction leads to a close match between the current inter-tap and inter-stimulus interval. A tendency to track (ratio < 1), on the other hand, is reflected in higher lag-1 than lag-0 cross-correlations (prediction/tracking ratios less than one) because the current inter-tap interval will most closely match the previous inter-stimulus interval when tracking (Repp, 2002b; Pecenka and Keller, 2011). Prediction and tracking are not mutually exclusive, as an individual can simultaneously engage in both behaviors to some degree.

The tendency to predict tempo changes has been found to differ between individuals in a manner that is positively correlated with musical experience (Pecenka and Keller, 2009). Prediction/tracking tendencies are, furthermore, stable over time and they are able to account for how accurately and precisely an individual synchronizes with computer controlled pacing sequences, as well as how accurately and precisely two individuals synchronize with one another during dyadic finger tapping (Pecenka and Keller, 2011). Studies on prediction during SMS have revealed that prediction can take place at multiple timescales. Local predictions at short timescales (between-cycles) are evident in the observed over- and undershooting that occurs when the tempo alternates between increasing and decreasing in sequences with smooth tempo changes over multiple intervals. Long-range (fractal) scaling of tap timing suggests that global prediction at longer timescales takes place when synchronizing with musical pieces that contained serial correlation (dependencies between the timing of consecutive events) and fractal scaling (long-range correlations affecting non-consecutive events) (Rankin et al., 2009).

2.5.1 Anticipation and internal models

It has been claimed that anticipatory mechanisms that subserve SMS with tempo changing sequences are grounded in online action simulations and internal models (Keller, 2008; 2012). Action simulation occurs when sensorimotor brain processes that resemble those associated with executing an action are engaged in a manner that does not directly produce overt movement (Decety and Grezes, 2006; Rizzolati and Sinigalia, 2010). The process of action simulation is supported by internal models that represent the sensorimotor transformations that mediate intentions, motor commands, and behavioral effects. Internal models can run independently of action execution, and they can therefore be used to generate predictions about the effects of the intention to perform a particular act, and of a specific movement (Wolpert and Kawato, 1998). Two types of internal model have been distinguished: forward and inverse models. Forward models represent the causal relationship between the input and output of the action control system. They predict the effect that a particular motor command will have upon the body and the dynamic environment, given the current state of the action control system. Inverse models, on the other hand, provide the motor command that is necessary to produce a desired change in state of the body and the environment. By providing motor commands, inverse models serve as controllers for intentional action (Wolpert and Kawato, 1998).

Forward and inverse models are tightly coupled and together facilitate efficient motor control by allowing potential movement errors to be corrected in advance. Internal models can be employed to make predictions about others' actions, including the timing of these actions (e.g., Wolpert et al., 2003; Knoblich and Jordan, 2003; Blakemore and Frith, 2005; Wilson and Knoblich, 2005; Keller, 2008). Utilizing these predictions of future events during the planning of one's own actions is important for successful interpersonal coordination (Knoblich and Jordan, 2003; Konvalinka et al., 2010; Vesper et al., 2011). The predictive abilities of the motor system can extend from actions to external events more generally, which allows for the prediction of spatiotemporal properties even of event sequences that humans are not capable of producing themselves (e.g., when a wave will hit the coast) (Schubotz, 2007). Internal models thus provide an effective mechanism for anticipating future events, and for controlling behavior accordingly, which is a crucial aspect of successful SMS.

2.5.2 Strong and weak anticipation

A relatively recent development related to anticipation is the distinction between 'strong anticipation' and 'weak anticipation'. Weak anticipation refers to anticipation based on a model of the environment (akin to an internal model). Strong anticipation is based on anticipation of the system itself and relies on systemic lawfulness, a dynamic process in which behavior adapts itself to the global statistical structure of the environment (Stepp and Turvey, 2010). Strong anticipation can therefore occur without any reference to an internal model (Dubois, 2003). In the former (weak) case, anticipation involves prediction and expectation, whereas in the latter (strong) case, anticipation arises from lawful regularities between a system and its environment, rather than from a process of action planning that takes future states of the environment into account (Dubois, 2003; Stepp and Turvey, 2010). Strong anticipation is thus not about solving a model of the predicted future but instead about keeping specific relationships between components of the to-be-performed task stable and, by doing so, the future states of the components will emerge without the need for an active process of prediction.

An apt example of strong anticipation in music can be found in work on general tau theory (although strong anticipation is not explicitly mentioned in this work) (Lee, 1998; Lee and Schögler, 2009). The general tau theory assumes that purposeful movements involve closing 'gaps' between the current state of the body and a goal state. For example, successful violin playing entails controlling the closure of the gap between the initial position of the bow and the end position, to produce the desired tone. According to the general tau theory, the only variable necessary to guide the gap closure is the time-to-closure of the gap at the current closure rate (tau). An intrinsic tau, necessary to close the gap, is computed in the brain, and while playing the violinist tries to maintain a constant relation between this intrinsic tau and the actual tau of the gap, which changes during the movement (Lee and Schögler, 2009). By keeping the ratio constant, it is not necessary to use a model to predict the appropriate movement; the movement emerges as the gap closes.

Weak and strong anticipation may play complementary roles in sensorimotor synchronization. Weak anticipation has been linked to event-based timing, as conceptualized by the information processing theory, while strong anticipation is more closely aligned with emergent timing, which is a key feature of the dynamical systems theory (Torre and Balasubramaniam, 2009; Marmelat and Delignières, 2012). Although the exact role of the processes and how the two interact with each other is still unclear, weak anticipation may subserve local timing at short time scales while strong anticipation may be relevant to global timing at long time scales. Thus, weak anticipation may entail local predictions generated via action simulation and internal models, while strong anticipation arises naturally as a consequence of the presence of long-range correlations in environmental event sequences and behavior performed in synchrony with these event sequences (Stephen et al., 2008; Marmelat and Delignières, 2012).

2.5.3 Anticipation in the brain

The distinction between types of anticipation that differ in terms of timescale and whether they are generated in a top-down or bottom-up fashion is reflected in different brain networks, which nevertheless interact with one another. The extent of these networks is large, prompting Bubic and colleagues (2010) to point out that the "predictive brain" is in fact the whole brain. However, it is still possible to paint a picture in broad brushstrokes where higher-level areas (e.g., premotor and lateral, medial and prefrontal regions) formulate expectations that are communicated to sensory, lower-level areas (Bubic et al., 2010). These top-down mechanisms could then interact with predictions that are generated automatically in a bottom-up manner in sensory areas such as the auditory cortex (see Bendixen et al., 2012).

A recent fMRI-study by Pecenka and colleagues (*submitted*), which investigated synchronization with tempo changing sequences, highlights the extent of the brain network that is involved in generating predictions at multiple levels during SMS. This study identified a large-scale network of areas —including superior temporal gyrus, medial orbitofrontal cortex, midcingulate cortex, posterior cingulate gyrus, and cerebellum— in which activation was related to behavioral measures of the degree to which tempo changes were anticipated. This study, taken together with other work on temporal prediction (Schubotz, 2007; Leaver et al., 2009), suggests that the mixture of processes related to action simulation and expectancy generation during SMS is orchestrated by a network of cortical areas (including prefrontal cortex, inferior frontal gyrus, premotor cortex, superior/middle temporal gyrus and sensorimotor cortex) that communes with internal models in cerebellum (see Wolpert et al., 1998; Fleisher, 2007; Ito, 2008; Coull et al., 2011).

2.6 ADAM: THE **AD**APTATION AND **A**NTICIPATION **M**ODEL

The literature reviewed in the foregoing sections of this article suggests that adaptation and anticipation mechanisms are involved when synchronizing actions to external events. To get a more complete idea about what the role of both mechanisms is, how they are linked, and how they influence each other, it is desirable to consider both mechanisms within a unified framework. In the following paragraphs we introduce ADAM (Figure 2.1), an ADaptiation and Anticipation model as an appropriate next step in the process of disentangling the reactive and proactive processes that underpin SMS.

Our goal in creating ADAM was to provide a novel tool that can be employed to explore different sensory modalities (e.g., auditory and visual input) and timescales (within-cycle, between-cycles, and long range structures) in SMS. Furthermore, we propose that ADAM can assist in evaluating the degree of motor impairment and can be used in guiding patients through motor rehabilitation. The current article describes how ADAM handles auditory input, taking within- and between-cycle information into account when computing its behavioral output via timekeeper adjustment and the issuing of 'motor' commands.

ADAM is an adaptation and anticipation model that combines the adaptive model used by Repp and Keller (2008) with an anticipation process instantiated as an internal model. Combining adaptation and anticipation within one framework holds the potential to shed light on the relation between these mechanisms by allowing a direct comparison of the effect of adaptive timing and anticipatory processes on SMS. To provide an intuitive description of ADAM, in the current article, a drumming paradigm in which ADAM produces the stimulus sequence by means of percussion sounds and the human participant strikes a drum is used to describe the model. Obviously these sounds can be substituted by any discrete event and drum strokes are simply a convenient, exemplary action. For the sake of consistency with the large body of research on finger tapping with pacing sequences comprised of tones, we refer here to percussion sounds as 'tones' and drum strikes as 'taps'.

2.6.1 Adaptation with ADAM

The adaptive module is conceived in the spirit of the information processing approach. Therefore the occurrence of the next tone (t_{n+1}) produced by ADAM is based on a timekeeper (T) with additional phase (α) and period (β) correction linked to the asynchrony ($asyn$) between the tone produced by ADAM and the tap produced by the participant (Figure 2.3A). The adaptive module uses a two-process error correction model (Repp and Keller, 2008) that can be described by the following equations[1]:

$$t_{n+1} = t_n + T_n + (\alpha + \beta) \cdot asyn_n \quad (1)$$
$$T_{n+1} = T_n + \beta \cdot asyn_n \quad (2)$$

The most recent asynchrony ($asyn_n$) is multiplied by the sum of the phase (α) and period (β) correction parameters and the result is added to the current timekeeper period (T_n) in order to obtain the current tone inter-onset interval ($T_n + (\alpha + \beta) \cdot asyn_n$). This current tone inter-onset interval is added to the onset time of the current tone (t_n) to calculate the time of occurrence of the next tone (t_{n+1}) (eq. 1). Period correction is a lasting change of the timekeeper setting. To accomplish this, the next timekeeper period (T_{n+1}) is given by the last asynchrony ($asyn_n$) multiplied by the period correction parameter (β) added to the current timekeeper (T_n) (eq.2).

The phase (α) and period (β) correction parameter can be set separately. The settings of α and β cause ADAM to implement phase or period correction, or a combination of both error correction mechanisms (eq. 1 and 2). Repp and Keller (2008) used a similar adaptive virtual partner that varied α between -1 and 1 and β between 0 and 1. Setting both parameters to 0 results in a conventional non-responding metronome, while an α less than 0 leads to negative phase correction (onset of the tone shifts in opposite direction to the asynchrony), which makes SMS difficult for the participant. Optimal phase correction, operationally defined as the α value that minimizes the variability of asynchronies, is achieved with an α between 0.3-0.5, both for the adaptive pacing signal and humans (Repp and Keller, 2008; Fairhurst et al., 2012). A phase correction parameter of 1 would be perfect phase correction, an α of 2 would imply over-correction and settings greater than 2 result in instability (Repp and Keller, 2008).

Repp and Keller (2008) showed that participants are capable of synchronizing with different types of adaptive virtual partners that implement varying degrees of (positive and negative) phase and/or period correction. Strategies used by the participant to maintain synchrony with the virtual partner were determined with the help of computer simulations. The simulations aimed to find error correction settings for the human participants that showed the best fit with empirical data across the parameter settings employed by the virtual partner. Results showed that strategies differed as a function of the settings of the adaptive virtual partner. For example, participants implemented a fixed gain of phase correction as long as the adaptive partner was cooperative (i.e., the partner implemented a small-to-modest amount of positive phase correction), while the error correction strategy of the participants changed when participants were dealing with an uncooperative adaptive partner (i.e., the partner implemented negative phase correction). Furthermore it turned out to be important that participants assumed responsibility for maintaining the correct tempo when the virtual partner implemented period correction and was therefore liable to drift (see Repp and Keller, 2008 for additional findings). With the adaptation module ADAM, we are able to replicate the computer simulations and patterns of effects.

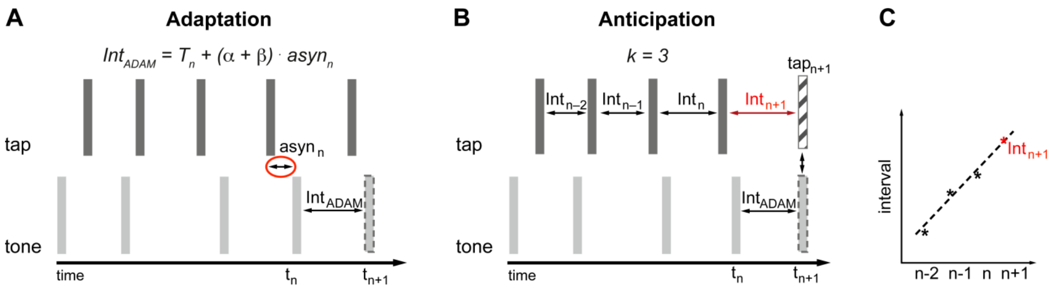


Figure 2.3 Implementation of adaptation (A) and anticipation (B + C) in ADAM. asyn = asynchrony | Int = interval | T = Timekeeper period

(**A**) The time of occurrence of the next tone is determined based on the asynchrony and the settings of error correction parameters α and β (eq. 1). The setting of β affects the current timekeeper period (eq. 2). The interval produced by ADAM between t_n and t_{n+1} is equal to $T_n + (\alpha + \beta) \cdot asyn_n$.

(**B-C**) A curve-fitting process that is applied to the preceding intervals predicts the participant's next tap time (eq. 3 and 4). The timing of upcoming tone or the next interval produced by ADAM can be set to enable ADAM's next tone to coincide with the predicted next tap of the participant.

2.6.2 Anticipation with ADAM

The anticipatory module in ADAM is based on a temporal extrapolation process that generates a prediction about the timing of the participant's next tap based on the most recent series of inter-tap intervals that ADAM receives as input (Figure 2.3B-C). This temporal extrapolation process works by extending systematic patterns of tempo changes in such a way that a decelerating sequence with inter-tap intervals that increase in duration will result in a prediction that the next tap will occur after an even longer interval, and vice versa for tempo accelerations. The timing of the participant's next tap is determined via curve fitting: An over-determined linear system based on at least three inter-tap intervals ($k \geq 3$) is created and solved to find the straight line that fits best to the intervals. The line that fits best is defined as the one that minimizes the sum of the squared errors between the line itself and the interval data[2]. Extrapolating from this best-fitting function, the upcoming inter-tap interval of the participant is predicted (Int_{n+1}) (Figure 2.3C). Equation 3 is used to determine this predicted interval. The predicted time of the next tap (tap_{n+1}) is based on equation 4.

$$Int_{n+1} = a + b \cdot (n + 1) \qquad (3)$$

$$tap_{n+1} = tap_n + Int_{n+1} \qquad (4)$$

In equation 3, a represents the intercept and b stands for the slope of the best fitting line. Both parameters a and b depend on the number of intervals (k) used to determine the best-fitting straight line. Based on this predicted next tap it can be determined when the next tone produced by ADAM should occur or what the next interval of ADAM should be (Int_{ADAM}) in order for ADAM's next tone (t_{n+1}) to coincide with the predicted next tap of the participant (tap_{n+1}) (Figure 2.3B). The anticipatory module of ADAM thus constitutes an over-determined system in which the number of intervals (k) used to create and solve the linear system can vary, but at least three intervals are used (a minimum of two intervals is necessary to find a straight line). An over-determined system is useful when dealing with noisy data — such as those that arise, for example, due to variability in human sensorimotor systems— because the error resulting from the noise is averaged out when fitting the line to multiple intervals.

The above implementation of anticipation in ADAM leads to patterns of inter-onset intervals that are classified as the behavior of a 'predictor' as the lag-0 cross-correlation between the inter-tap and inter-stimulus intervals is higher than the lag-1 cross-correlation, and therefore the prediction/tracking ratio will be bigger than 1 (Repp, 2002b; Pecenka and Keller, 2011). Tracking behavior can be produced by introducing into ADAM the tendency to mimic the previous inter-tap interval (cf. Konvalinka et al., 2010).

2.6.3 Linking adaptation and anticipation mechanisms in ADAM

One of our goals when developing ADAM was to shed light on the link between adaptation and anticipation. We hypothesize that a combination of paired internal models used to simulate one's own and others' actions plays a role in this link. Following seminal work by Wolpert and colleagues (2003), a number of approaches have proposed that such paired forward and inverse models are employed during social interaction (e.g., Pacherie, 2008, 2012). In ADAM, separate classes of forward and inverse models are harnessed to simulate ADAM's own actions and the human participant's actions slightly in advance of their production (Figure 2.4). The coupling of 'own' and 'other' internal models facilitates fluent SMS by allowing potential errors in timing to be anticipated and corrected before they occur (Wolpert et al., 2003; Keller, 2008).

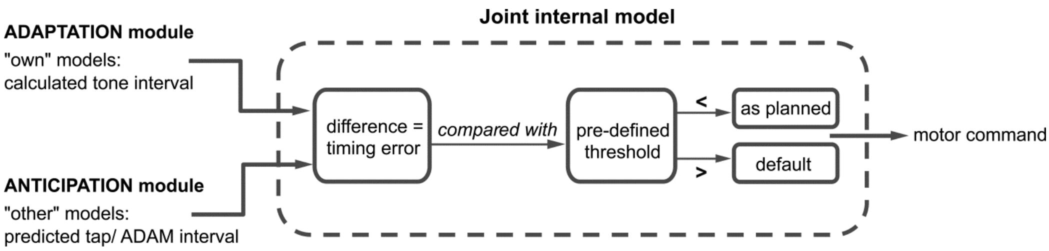


Figure 2.4 A schematic overview of the joint internal model, where the adaptation and anticipation module interact via 'own' and 'other' internal models. The difference between the outputs of the adaptation and anticipation module of ADAM is compared to a predefined threshold. Depending on this comparison, the motor command is either executed as planned or in accordance with a default setting. A detailed description of this process can be found in the text.

ADAM simulates its next action with an 'own' inverse model that receives the output of the adaptive module (i.e., the next planned inter-tone interval) and, based on this, selects an appropriate motor command. An 'own' forward model then generates a prediction of the timing of the next tone that would result if the motor command were to be carried out. Independently of the operation of these 'own' internal models, the anticipatory module of ADAM runs an 'other' forward model, which generates a prediction of the participant's next tap-interval and therefore a predicted tap time. In situations characterized by complex but systematic patterns of tempo change, as in expressively performed music, ADAM can be equipped with a template descripting the tempo changes that functions as an inverse model of the other's actions.

The predicted tap-interval of the participant or planned interval of ADAM (based on the 'other' model) is compared with the predicted tone-interval (from the 'own' model) in a 'joint' internal model (see Figure 2.1). This joint model is where adaptation and anticipation mechanisms interact in ADAM (Figure 2.4). It essentially simulates the timing error that would arise as a result of the current parameter settings related to reactive error correction and predictive temporal extrapolation processes in ADAM's adaptation and anticipation modules. If the error falls within a pre-defined tolerance region (e.g., a threshold that is based on whether the difference is perceivable or not [Repp, 2001b]), then the motor command is issued and ADAM produces a tone. If not, then ADAM refers to the default mechanism, which is either the interval computed via the adaptation or anticipation module, to set the motor command to produce the next tone. ADAM's complete architecture (Figure 2.1) includes multiple, hierarchically nested internal models (cf. Pacherie, 2008) that can simulate processes unfolding at different timescales (within- and between-cycle) in different modalities (auditory and visual, see below). Combining adaptation and anticipation mechanisms at multiple levels in ADAM's action control hierarchy engenders SMS that is accurate, precise, and flexible (in the sense that tempo changes can be negotiated).

2.6.4 Simulations and experiments using ADAM

The purpose of developing ADAM was twofold. The first goal was to provide a platform on which the multiple mechanisms and processes involved in SMS can be systematically explored in computer simulations and behavioral experiments. Under both investigative methods, the parameter settings for the adaptive and anticipatory components of ADAM can be varied in order to test hypotheses about the role of individual components, and the interaction of multiple components, on the accuracy and precision of SMS. Specific questions that we have considered in simulations include (1) the conditions under which adaptive phase correction (α) and period correction (β) processes are necessary and sufficient for stable SMS, (2) the way in which phase correction and period correction are combined (e.g., under-additive, additive, or over-additive), (3) the effects of the type of function (e.g., linear, 2^{nd} order polynomial) and the number of inter-onset intervals used by the anticipation module of ADAM to generate temporal predictions, (4) the relationship between temporal adaption and anticipation (as described in section 5.3), and (5) how varying levels of perceptual, timekeeper, or motor noise affect the optimal settings for parameters governing temporal adaptation and anticipation. The results of simulations addressing these issues have been used to inform the process of designing experiments to test how the effects observed in computer simulations generalize to situations that involve the interaction between ADAM and live human partners. The match between the results of the simulations and the behavior of ADAM with human participants can be used to improve the model in terms of optimizing the goodness of fit.

Several different real-time experimental setups (finger tapping or drumming tasks; see Figure 2.1B) are possible in which participants and ADAM interact with each other through different coupling regimens (unidirectional vs. bidirectional). These setups allow us to explore social aspects of SMS between two responsive agents. In addition to interrogating ADAM's behavior, this approach lends itself to the investigation of how participants respond to pacing signals associated with different types of interaction partner that ADAM can provide. Questions of interest include how human participants respond (in terms of objective behavior and subjective judgments) to ADAM when it is more or less adaptive or anticipatory. During such experiments, ADAM's parameter settings are known, and therefore the controlled variation of these parameters allows causal connections between adaptive and anticipatory processes and behavioral outcomes to be established.

The second goal in developing ADAM relates to the assessment and rehabilitation of disorders that affect rhythmic movement timing (e.g., Parkinson's disease and stroke-related lesions to areas such as the cerebellum and basal ganglia). It is envisaged that assessment can be carried out using a strategy that combines behavioral experiments and computer simulations. This strategy will allow deficits in specific mechanisms (phase correction, period correction, and prediction at short- or long-time scales) and modalities (auditory and visual; see below) to be identified and linked to lesions identified in structural brain images. Information about specific mechanisms that cause impairment to rhythmic movement timing can then be used in targeted interventions during motor rehabilitation.

2.6.5 Extensions of ADAM

We envision three future extensions of ADAM: (1) ADAM could make use of visual information from human participants; (2) ADAM could provide visual information to participants; (3) a version of ADAM based on the principles of dynamic systems theory could be created.

Although it is often reported that movements can be synchronized more accurately based on auditory information than with other stimuli, SMS is possible with a variety of stimuli in different sensory modalities (e.g., auditory, visual, tactile) (Repp and Penel, 2004; Hove and Keller, 2010; Hove et al., 2013). Adding spatial variation to the visual stimuli with which participants are required to synchronize –for example, by means of apparent or biological motion– significantly improves participants' synchronization abilities (Hove et al., 2010; Hove et al., 2013), sometimes even leading to performance that is similar to synchronization with an auditory metronome (Hove et al., 2012). To address this aspect of SMS, it would be useful to provide ADAM with visual information from the movements of the participants.

This new component of ADAM could deal with within-cycle (the movement trajectory of a drum stroke or finger tap) and between-cycle (e.g., body-sway) information (Figure 2.1). SMS studies involving finger movements have demonstrated that features of the produced movement trajectories affect timing accuracy (Balasubramaniam et al., 2004; Balasubramaniam, 2006; Elliott et al., 2009; Hove and Keller, 2010), and this information is presumably available to an individual who intends to synchronize with the observed movements. Furthermore, studies of body movements during music performance have shown that head motion and body sway play a role in regulating performance timing and achieving interpersonal coordination in ensembles (Davidson, 2009; Keller and Appel, 2010).

We propose that combining this visual module with ADAM's auditory module would yield benefits deriving from the fact that information from different modalities play complementary roles during SMS. Consider for example a dyadic drumming task where two individuals synchronize their drum strokes under a regime where they start at a moderate tempo, then gradually accelerate to a fast tempo, and finally decelerate through the initial moderate tempo down to a slow tempo. Each drum stroke –or movement cycle– includes (1) auditory information in the form of a discrete sound with a sharp onset when the drumstick impacts upon the drum, and (2) visual information about the trajectory of the drumstick and the drummer's body movements (Figure 2.1B). Auditory information (i.e., the onset time of the drum sound) is only available at one time point within a movement cycle, and each sound alone is not informative about how the next movement cycle should be timed. However, sounds associated with successive drum strokes provide between-cycle information – sequences of inter-onset intervals– that can be used to guide movement timing from cycle to cycle. Drumstick and body movement trajectories, on the other hand, are potentially informative about within-cycle and between-cycle timing, respectively. Specifically, the velocity and acceleration of a drum stroke during its descent provides information about the time point of the strike, while body movements –such as head motion and body sway– are informative about timing at longer timescales spanning multiple cycles.

The foregoing suggests that auditory and visual information may assist with different aspects of SMS in the context of challenging coordination tasks, such as those that involve systematic tempo changes. Another way in which information from several sensory modalities may assist SMS is through a multisensory integration process that takes into account the sensory and temporal reliability of events (Elliott et al., 2010). Thus, when multiple information streams are available and the temporal discrepancy between them is small, the combination of information streams in different modalities (e.g., auditory, visual, and tactile timing cues) leads to optimal cue integration and hence more accurate synchronization (Elliott et al., 2010; Wing et al., 2010).

The second proposed extension of ADAM involves using the visual module to drive multimodal displays of virtual synchronization partners that comprise dynamic visual representations of human body segments that move in time with music according to biological kinematic principles. The rationale behind using multimodal displays is that they exploit the benefits of auditory-motor coupling (Zatorre et al. 2007) as well as the tendency for visual depictions of biological motion to induce movement tendencies in an observer (Saygin et al., 2004; Press, 2011). Thus, combined auditory information and continuous biological motion in a virtual synchronization partner based on ADAM should provide a more potent means of driving the participant's movements than either modality alone.

In the context of motor rehabilitation, such multimodal virtual synchronization partners could illustrate the movements that should be synchronized with the music, and they could accompany the patient in executing these movements. Importantly, as noted above, the virtual partner would receive input concerning the patient's behavior via auditory and visual modules of ADAM. It is hypothesized that, by anticipating and adapting to the patient's movement timing and kinematics to varying degrees, the virtual partner would be effective at encouraging as accurate and graceful movement as possible given the individual patient's specific impairment. Furthermore, the parameter settings of the virtual synchronization partner could be adjusted incrementally, leading to different levels of responsiveness and variability that affect the predictability and perceived cooperativity of the partner (Vesper et al., 2011; Fairhurst et al., 2012). These different settings could be used to challenge the patient at later stages of rehabilitation, in order to simulate challenges that arise in complex dynamics environments encountered in daily life.

Finally, we believe that it would be fruitful to develop a version of ADAM based on the principles of dynamic systems theory, or a hybrid version in which both the information-processing theory and the dynamic systems theory are combined. This extension of ADAM could potentially inform the ongoing debate about the validity of the information-processing and dynamical systems theory in relation to SMS. Given that the focus of dynamic systems theory is on continuous, non-linear, and within-cycle coupling (Large, 2008), the envisaged visual module of ADAM that deals with continuous within-cycle information, like drum stroke trajectories (Figure 2.1), seems especially amenable to the dynamic approach. A virtual partner paradigm similar to that used by Kelso and colleagues (2009) could serve as a starting point for such an endeavor. Furthermore, the auditory module of ADAM could also be instantiated in a dynamical framework. For instance, work on non-linearly coupled oscillators, described formally in terms of differential equations (e.g. Schöner and Kelso, 1988; Torre and

Balasubramaniam, 2009; Loehr et al., 2011), and period matching (Large et al., 2002) provide clear guidance with regard to the steps that could be taken towards a dynamic version of the adaptive module of ADAM. The anticipatory module presents a greater challenge, and it would be worthwhile to evaluate the degree to which the concept of strong anticipation can deal with predictive processes that characterize SMS in challenging contexts that involve tempo changes.

2.7 CONCLUSION

Adaptation (reactive) and anticipatory (predictive) mechanisms are important for precise yet flexible sensorimotor synchronization with externally controlled sequential events. To investigate the role of temporal adaptation and anticipation in SMS, and the link between both classes of mechanism, we introduced ADAM: an ADaptation and Anticipation Model. ADAM combines adaptive, error correction processes with an anticipatory, predictive temporal extrapolation process inspired by the computational neuroscience concept of internal models. ADAM provides a unified framework in which simulations can be combined with experimental manipulations, and therefore constitutes a promising tool for exploring adaptation and anticipation in SMS. In a next step, ADAM could be extended in several ways (e.g., equipped to deal with between-cycle information in the visual modality) to work towards a better understanding of the different aspects of SMS that arise in everyday life, where coordination takes place via multiple modalities and at multiple time scales. ADAM is expected to prove beneficial in advancing our theoretical understanding of basic mechanisms that allow healthy individuals to coordinate their actions with events in the dynamic environment, as well as in the clinical assessment and rehabilitation of individuals with deficits that cause them to struggle with such coordination.

2.8 CONFLICT OF INTEREST STATEMENT

The authors declare that there is no conflict of interest.

2.9 ACKNOWLEDGMENTS

This work was supported by funding from the European Community's Seventh Framework Programme under the EBRAMUS project - grant agreement n° 238157.

2.10 REFERENCES

Aschersleben, G. (2002). Temporal control of movements in sensorimotor synchronization. *Brain Cogn*. 48, 66-79.

Assisi, C. G., Jirsa, V. K., and Kelso, J. A. S. (2005). Dynamics of multifrequency coordination using parametric driving: theory and experiment. *Biol. Cybern*. 93, 6-21.

Balasubramaniam, R. (2006). "Trajectory formation in timed rhythmic movements." in *Progress in motor control IV*, ed. M.L. Latash, and F. Lestienne (New York, U.S.A.: Springer), 47-54.

Balasubramaniam, R., Wing, A. M., and Daffertshofer, A. (2004). Keeping with the beat: movement trajectories contribute to movement timing. *Exp. Brain Res*. 159, 129-134.

Bendixen, A., SanMiguel, I., and Schröger, E. (2012). Early electrophysiological indicators for predictive processing in audition: A review. *Int. J. Psychophysiol.* 83, 120-131.

Bijsterbosch, J. D., Lee, K.-H., Dyson-Sutton, W., Barker, A. T., and Woodruff, P. W. R. (2011a). Continuous theta burst stimulation over the left pre-motor cortex affects sensorimotor timing accuracy and supraliminal error correction. *Brain Res*. 1410, 101-111.

Bijsterbosch, J. D., Lee, K.-H., Hunter, M. D., Tsoi, D. T., Lankappa, S., Wilkinson, I. D., Barker, A. T., and Woodruff, P. W. R. (2011b). The role of the cerebellum in sub- and supraliminal error correction during sensorimotor synchronization: evidence from fMRI and TMS. *J. Cog. Neurosci*. 23, 1100-1112.

Blakemore, S. J., and Frith, C. (2005). The role of motor contagion in the prediction of action. *Neuropsychologia* 43, 260-267.

Bubic A., Von Cramon, D. Y., and Schubotz, R. I. (2009). Prediction, cognition and the brain. *Front. Hum. Neurosci*. 5:12. doi: 10.3389/fnhum.2010.00025

Chen, J. L., Penhune, V. B., and Zatorre, R. J. (2008). Moving on time: Brain network for auditory–motor synchronization is modulated by rhythm complexity and musical training. *J. Cognitive Neurosci*. 20, 226-239.

Chen, J. L., Penhune, V. B., and Zatorre, R. J. (2009). The role of auditory and premotor cortex in sensorimotor transformations. *Ann. NY Acad. Sci*. 1169, 15-34.

Coull, J. T., Cheng, R., and Meck, W. H. (2011). Neuroanatomical and neurochemical substrates of timing. *Neuropsychopharmacology* 36, 3-25.

Davidson, J. W. (2009). "Movement and collaboration in music performance" in *The Oxford Handbook of Music Psychology,* ed. S. Hallam, I. Cross and M. Thaut. (Oxford, U.K.: Oxford University Press), 364-376.

Decety, J., and Grezes, J. (2006). The power of simulation: Imagining one's own and other's behavior. *Brain Res.* 1079, 4-14.

Dubois, D. M. (2003). Mathematical foundations of discrete and functional systems with strong and weak anticipations. *Lect. Notes Comput. Sc.* 2684, 110-132.

Elliott, M. T., Welchman, A. M., and Wing, A. E. (2009). Being discrete helps keep to the beat. *Exp. Brain Res.* 192, 731-737.

Elliott, M. T., Wing, A. M., and Welchman, A. E. (2010). Multisensory cues improve sensorimotor synchronisation. *Eur. J. Neurosci.* 31, 1828-1835.

Fairhurst, M. T., Janata, P., and Keller, P. E. (2012). Being and feeling in sync with an adaptive virtual partner: Brain mechanisms underlying dynamic cooperativity. *Cerebral Cortex* 67, 313-321.

Fleischer, J. G. (2007). Neural correlates of anticipation in cerebellum, basal ganglia, and hippocampus. *Lect. Notes Artif. Int.* 4520, 19-34.

Fink, P. W., Foo, P., Jirsa, V. K., and Kelso, J. A. S. (2000). Local and global stabilization of coordination by sensory information. *Exp. Brain Res.* 134, 9-20.

Friston, K. J., and Kiebel, S. J. (2009). Predictive coding under the free-energy principle. *Philos. T. Roy. Soc. B.* 364, 1211-1221.

Galton, F. (1899). On instruments for (1) testing perception of differences of tint and for (2) determining reaction time. *J. Royal Anthr. Inst.* 19, 27-29.

Haken, H., Kelso, J. A. S., and Bunz, H. (1985). A theoretical model of phase transitions in human hand movements. *Biol. Cybern.* 51, 347-356.

Hary, D., and Moore, G. P. (1985). Temporal tracking and synchronization strategies. *Hum. Neurobiol* 4, 73-77.

Hary, D., and Moore, G. P. (1987). Synchronizing human movement with an external clock source. *Biol. Cybern.* 56, 305-311.

Hove, M. J., Fairhurst, M. T., Kotz, S. A., and Keller, P. E. (2013). Synchronizing with auditory and visual rhythms: An fMRI assessment of modality differences and modality appropriateness. *NeuroImage* 67, 313-321.

Hove, M. J., Iversen, J. R., Zang, A., and Repp, B. H. (Epub ahead of print). Synchronization with competing visual and auditory rhythms: bouncing ball meets metronome. *Psychol. Res.*

Hove, M. J., and Keller, P. E. (2010). Spatiotemporal relations and movement trajectories in visuomotor synchronization. *Music Percept.* 28, 15-26.

Hove, M. J., Spivey, M. J., and Krumhansl, C. L. (2010). Compatibility of motion facilitates visuomotor synchronization. *J. Exp. Psychol. Hum. Percept. Perform.* 36, 1525-1534.

Ito, M. (2008). Control of mental activities by internal models in the cerebellum. *Nat. Rev. Neurosci.* 9, 304-313.

Jäncke, L., Loose, R., Lutz, K., Specht, K., and Shah, N. J. (2000). Cortical activations during paced finger-tapping applying visual and auditory pacing stimuli. *Brain Res. Cogn. Brain Res.* 10, 51-66.

Keller, P. E. (2008). "Joint action in music performance." in *Enacting intersubjectivity: a cognitive and social perspective to the study of interactions*, ed. F. Morganti, A. Carassa, and G. Riva (Amsterdam, the Netherlands: IOS Press), 205-221.

Keller, P. E. (2012). Mental imagery in music performance: underlying mechanisms and potential benefits. *Ann. NY Acad. Sci.* 1252, 206-213.

Keller, P. E. (in press). "Ensemble performance: Interpersonal alignment of musical expression." In *Expressiveness in music performance: Empirical approaches across styles and cultures*, ed. D. Fabian, R. Timmers, and E. Schubert (Oxford, UK: Oxford University Press).

Keller, P. E., and Appel, M. (2010). Individual differences, auditory imagery, and the coordination of body movements and sounds in musical ensembles. *Music Percept.* 28, 27-46.

Kelso, J. A. S. (1995). *Dynamic Patterns: The Self-Organization of Brain and Behavior.* Cambridge: MIT Press.

Kelso, J. A. S., de Guzman, G. C., Reveley, C., and Tognoli, E. (2009). Virtual Partner Interaction (VPI): exploring novel behaviors via coordination dynamics. *PLoS ONE* 4(6): e5749. doi:10.1371/journal.pone.0005749.

Knoblich, G., and Jordan, J. S. (2003). Action coordination in groups and individuals: Learning anticipatory control. *J. Exp. Psychol. Learn. Mem. Cogn.* 29, 1006-1016.

Konvalinka, I., Vuust, P., Roepstorff, A., and Frith, C. D. (2010). Follow you, follow me: Continuous mutual prediction and adaptation in joint tapping. *Q. J. Exp. Psychol* . 63, 2220-2230.

Large, E. W. (2008). "Resonating to musical rhythm: Theory and experiment." in *Psychology of time*, ed. S. Grondin (Bingley, U.K.: Emerald Group), 189-232.

Large, E. W., Fink, P., and Kelso, J. A. S. (2002). Tracking simple and complex sequences. *Psychol. Res.* 66, 3-17.

Leaver, A. M., Van Lare, J., Zielinski, B., Halpern, A. R., and Rauschecker, J. P. (2009). Brain activation during anticipation of sound sequences. *J. Neurosci*. 29, 2477-2485.

Lee, D. N. (1998). Guiding movement by coupling taus. *Ecol. Psychol*. 10, 221-250.

Lee, D. N., and Schögler, B. (2009). "Tau in musical expression." in *Communicative Musicality: Exploring the basis of human companionship*, ed. S. Malloch and C. Trevarthen (Oxford, U.K.: Oxford University Press.

Loehr, J. D., Large, E. W., and Palmer, C. (2011). Temporal Coordination and Adaptation to Rate Change in Music Performance. *J. Exp. Psychol. Hum. Percept. Perform*. 37, 1292-1309.

Marmelat, V., and Delignières, D. (2012). Strong anticipation: complexity matching in interpersonal coordination. *Exp. Brain Res.* 222, 137-148.

Mates, J. (1994a). A model of synchronization of motor acts to a stimulus sequence: I. Timing and error corrections. *Biol. Cybern*. 70, 463-473.

Mates, J. (1994b). A model of synchronization of motor acts to a stimulus sequence: II. Stability analysis, error estimation and simulations. *Biol. Cybern*. 70, 475-484.

Molinari, M., Leggio, M., and Thaut, M. (2007). The cerebellum and neural networks for rhythmic sensorimotor synchronization in the human brain. *Cerebellum* 6, 18-23.

Néda, Z., Ravasz, E., Brechet, Y., Vicsek, T., and Barabási, A. (2000). The sound of many hands clapping. *Nature* 403, 849-850.

Nowicki, L., Prinz, W., Grosjean, M., Repp, B. H., and Keller, P. E. (Epub ahead of print). Mutual adaptive timing in interpersonal action synchronization. *Psychomusicology: Music, Mind and Brain*.

Oullier, O., Jantzen, K. J., Steinberg, F. L., and Kelso, J. A. S. (2005). Neural substrates of real and imagined sensorimotor coordination. *Cerebral Cortex* 15, 975-985.

Pacherie, E. (2008). The phenomenology of action: a conceptual framework. *Cogn.* 107, 179-217.

Pacherie, E. (2012). "The Phenomenology of Joint Action: Self-Agency vs. Joint-Agency" in *Joint attention: New developments in psychology, philosophy of mind, and social neuroscience,* ed. A. Seemann. (Cambridge, U.S.A.: MIT Press), 343-389.

Pecenka, N., and Keller, P. E. (2009). Auditory pitch imagery and its relationship to musical synchronization. *Ann .NY Acad. Sci*. 1169, 282-286.

Pecenka, N., and Keller, P. E. (2011). The role of temporal prediction abilities in interpersonal sensorimotor synchronization. *Exp. Brain Res*. 211, 505-515.

Pecenka, N., Engel, A., and Keller, P. E. (*submitted*). Neural correlates of auditory temporal predictions during sensorimotor synchronization. *Frontiers in Human Neurosci.*

Phillips-Silver, J., Aktipis, C. A., and Bryant, G. A. (2010). The ecology of entrainment: foundations of coordinated rhythmic movement. *Music Percept*. 28, 3-14.

Phillips-Silver, J., Toiviainen, P., Gosselin, N., Piché, O., Nozaradan, S., Palmer, C., and Peretz., I. (2011). Born to dance but beat deaf: a new form of congenital amusia. *Neuropsychologia* 49, 961-969.

Praamstra, P., Turgeon, M., Hesse, C. W., Wing, A. M., and Perryer, L. (2003). Neurophysiological correlates of error correction in sensorimotor-synchronization. *NeuroImage* 20, 1283-1297.

Press, C. (2011). Action observation and robotic agents: Learning and anthropomorphism. *Neurosci. Biobehav. Rev*. 35, 1410-1418.

Pressing, J. (1999). The referential dynamics of cognition and action. *Psychol. Rev*. 106, 714-747.

Rankin, S. K., Large, E. W., and Fink, P. W. (2009). Fractal tempo fluctuation and pulse prediction. *Music Percept*. 26, 401-413.

Rao, S. M., Harrington, D. L., Haaland, K. Y., Bobholz, J. A., Cox, R. W., and Binder, J. R. (1997). Distributed neural systems underlying the timing of movements. *J. Neurosci.* 17, 5528-5535.

Rasch, R. A. (1979). Synchronization in performed ensemble music. *Acustica* 43, 121-131.

Repp, B. H. (1999). Control of expressive and metronomic timing in pianists. *J. Motor Behav*. 31, 145-164.

Repp, B. H. (2001a). Phase correction, phase resetting, and phase shifts after subliminal timing perturbations in sensorimotor synchronization. *J. Exp. Psychol. Hum. Percept. Perform*. 27, 600-621.

Repp, B. H. (2001b). Processes underlying adaptation to tempo changes in sensorimotor synchronization. *Hum. Movement Sci*. 20, 277-312.

Repp, B. H. (2002a). Automaticity and voluntary control of phase correction following event onset shifts in sensorimotor synchronization. *J. Exp. Psychol. Hum. Percept. Perform*. 28, 410-430.

Repp, B. H. (2002b). "The embodiment of musical structure: Effects of musical context on sensorimotor synchronization with complex timing patterns." in *Common mechanisms in perception and action: Attention and Performance XIX*, ed. W. Prinz and B. Hommel (Oxford, U.K.: Oxford University Press), 245-265.

Repp, B. H. (2005). Sensorimotor synchronization: A review of the tapping literature. *Psychon. B. Rev*. 12, 969-992.

Repp, B. H. (2010). Sensorimotor synchronization and perception of timing: Effects of music training and task experience. *Hum. Movement Sci*. 29, 200-213.

Repp, B. H., and Keller, P. E. (2004). Adaptation to tempo changes in sensorimotor synchronization: Effects of intention, attention, and awareness. *Q. J. Exp. Psychol*. 57A, 499-521.

Repp, B. H., and Keller, P. E. (2008). Sensorimotor synchronization with adaptively timed sequences. *Hum. Movement Sci*. 27, 423-456.

Repp, B. H., Keller, P. E., and Jacoby, N. (2012). Quantifying phase correction in sensorimotor synchronization: empirical comparison of three paradigms. *Acta Psychol*. 139, 281-329.

Repp, B. H., and Moseley, G. P. (2012). Anticipatory phase correction in sensorimotor synchronization. *Hum. Movement Sci*. 3, 1118-1136.

Repp, B. H., and Penel, A. (2004). Rhythmic movement is attracted more strongly to auditory than to visual rhythms. *Psychol. Res*. 68, 252-270.

Repp, B. H., and Su, Y-H. (Epub ahead of print). Sensorimotor synchronization: A review of recent research. (2006–2012) *Psychon. B. Rev.*

Rizzolatti, G., and Sinigaglia C. (2010). The functional role of the parieto-frontal mirror circuit: Interpretations and misinterpretations. *Nat. Rev. Neurosci*. 11, 264-274.

Saygin A. P., Wilson S. M., Hagler D. J., Bates E., and Sereno M. I. (2004). Point-light biological motion perception activates human premotor cortex. *J. Neurosci*. 24, 6181–88.

Semjen, A., Vorberg, D., and Schulze, H.-H. (1998). Getting synchronized with the metronome: Comparisons between phase and period correction. *Psychol. Res*. 61, 44-55.

Schmidt, R. A. (1986). Anticipation and timing in human motor performance. *Psychol. Bull*. 70, 631-646.

Schmidt, R. C., and Richardson, M. J. (2008). "Dynamics of interpersonal coordination." In *Coordination: Neural, behavioural and social dynamics,* ed. A. Fuchs and V. Jirsa (Heidelberg, Germany: Springer-Verlag), 281-308

Schöner, G., and Kelso, J. A. S. (1988). A synergetic theory of environmentally-specified and learned patterns of movement coordination: II. Component oscillator dynamics. *Biol. Cybern*. 58, 81-89.

Schubotz, R. I. (2007). Prediction of external events with our motor system: towards a new framework. *Trends Cogn. Sci.* 11, 211-218.

Schulze, H.-H., Cordes, A., and Vorberg, D. (2005). Keeping synchrony while tempo changes: accelerando and ritardando. *Music Percept.* 22, 461-477.

Stephen, D. G., Stepp, N., Dixon, J., and Turvey, M. T. (2008). Strong anticipation: sensitivity to long-range correlations in synchronization behavior. *Physica A.* 387, 5271-5278.

Stepp, N., and Turvey, M. T. (2010). On strong anticipation. *Cogn. Syst. Res.* 11, 148-164.

Takano, K., and Miyake, Y. (2007). Two types of phase correction mechanism involved in synchronized tapping. *Neurosci. Lett.* 417, 196-200.

Thaut, M. H., Stephan, K. M., Wunderlich, G., Schicks, W., Tellmann, L., Herzog, H., McIntosh, G. C., Seitz, R. J., and Hömber, V. (2009). Distinct cortico-cerebellar activations in rhythmic auditory motor synchronization. *Cortex* 45, 44-53.

Torre, K., and Balasubramaniam, R. (2009). Two different processes for sensorimotor synchronization in continuous and discontinuous rhythmic movements. *Exp. Brain Res.* 199, 157-166.

van Ulzen, N. R., Lamoth, C. J., Daffertshofer, A., Semin, G. R., and Beek, P. J. (2008). Characteristics of instructed and uninstructed interpersonal coordination while walking side-by-side. *Neurosci. Lett.* 432, 88-93.

Vesper, C., van der Wel, P. R. D., Knoblich, G., and Sebanz, N. (2011). Making oneself predictable: reduced temporal variability facilitates joint action coordination. *Exp. Brain Res.* 211, 517-530.

Vorberg, D. (2005). *Synchronization in duet performance: Testing the two-person phase error correction model.* Paper presented at the Tenth Rhythm Perception and Production Workshop, Alden Biesen, Belgium, July 2005.
(Slides at http://www.rppw.org/rppw10/vorberg/presentation.pdf.)

Vorberg, D., and Schulze, H.-H. (2002). A two-level timing model for synchronization. *J. Math. Psychol.* 46, 56-87.

Vorberg, D., and Wing, A. (1996). "Modeling variability and dependence in timing." in *Handbook of perception and action Vol. 2*, ed. H. Heuer and S. W. Keele (London, UK: Academic Press), 181-262.

Vuust, P., Ostergaard, L, Pallesen, K. J., Bailey, C., and Roepstorff A. (2009). Predictive coding of music: brain responses to rhythmic incongruity. *Cortex* 45, 80-92.

Wilson, M., and Knoblich, G. (2005). The case for motor involvement in perceiving conspecifics. *Psychol. Bull.* 131, 460-473.

Wing, A. M., and Beek, P. J. (2002). "Movement timing: a tutorial", in *Attention and Performance 19*, ed. W. Prinz and B. Hommel (Oxford, U.K.: Oxford University Press), 202-226.

Wing, A. M., Doumas, M., and Welchman, A. E. (2010). Combining multisensory temporal information for movement synchronisation. *Exp. Brain Res.* 200, 277-282.

Wing, A. M., and Kristofferson, A. B. (1973). Response delays and the timing of discrete motor responses. *Percept. Psychophys.* 14, 5-12.

Wing, A. M., and Woodburn, C. (1995). The coordination and consistency of rowers in a racing eight. *J. Sport. Sci.* 13, 187-197.

Witt, S. T., Laird, A. R., and Meyerand, M. E. (2008). Functional neuroimaging correlates of finger-tapping task variations: an ALE metaanalysis. *NeuroImage* 42, 343-356.

Wohlschläger, A., and Koch, R. (2000). "Synchronization error: An error in time perception." in *Rhythm perception and production*, ed. P. Desain and L. Windsor (Lisse, The Netherlands: Swets and Zeitlinger), 115-127.

Wolpert, D. M., Doya, K., and Kawato, M. (2003). A unifying computational framework for motor control and social interaction. *Philos. T. Roy. Soc. B* 358, 593-602.

Wolpert, D. M., and Kawato, M. (1998). Multiple paired forward and inverse models for motor control. *Neural Networks* 11, 1317-1329.

Wolpert, D. M., Miall, R. C., and Kawato, M. (1998). Internal models in the cerebellum. *Trends Cogn. Sci.* 2, 338-347.

Zatorre, R. J., Chen, J. L., and Penhune, V. B. (2007). When the brain plays music: auditory-motor interactions in music perception and production. *Nat. Rev. Neurosci.* 8, 547-558.

Chapter 3

MANUSCRIPT 3

Sensorimotor synchronization with tempo changing auditory sequences

M.C. (Marieke) van der Steen[1], Nori Jacoby[2], Merle T. Fairhurst[1], Peter E. Keller[1,3]

[1] Max Planck Institute for Human Cognitive and Brain Sciences, Research Group "Music Cognition & Action", Leipzig, Germany

[2] The Edmond and Lily Safra Center for Brain Sciences, Hebrew University, Jerusalem, Israel and Music Department, Bar Ilan University, Ramat Gan, Israel.

[3] The MARCS Institute, University of Western Sydney, Australia

Submitted to Brain Research

3.1 ABSTRACT

The current study investigated the human ability to synchronize movements with event sequences containing continuous tempo changes. This capacity is evident, for example, in ensemble musicians who maintain precise interpersonal coordination while modulating the performance tempo for expressive purposes. Here we tested an ADaptation and Anticipation Model (ADAM) that was developed to account for such behavior by combining error correction processes (adaptation) with a predictive temporal extrapolation process (anticipation). The fit between behavioral data and computer simulations based on four versions of ADAM was assessed. These versions included a model with adaptation only, one with independent contributions of adaptation and anticipation, and two models in which adaptation and anticipation were linked in a joint internal model. The behavioral experiment required participants to tap their finger in time with three auditory pacing sequences containing tempo changes that differed in the rate of change and the number of turning points. Behavioral results indicated that sensorimotor synchronization accuracy and precision, while generally high, decreased with increases in the rate of tempo change and number of turning points. Simulations and model-based parameter estimates showed that adaptation mechanisms alone could not fully explain the observed sensorimotor synchronization behavior. Including anticipation in the model increased the precision of simulated sensorimotor synchronization and improved the fit of model to behavioral data, especially when adaptation and anticipation mechanisms were linked via a joint internal model. Overall results suggest that adaptation and anticipation mechanisms both play an important role during sensorimotor synchronization with tempo changing sequences.

Abbreviations: SMS = sensorimotor synchronization; IOI = inter-onset interval; ITI = inter-tap interval; ADAM = ADaptation and Anticipation Model; ANOVA = analysis of variance; bGLS = bounded Generalized Least Squares

Keywords: sensorimotor synchronization – temporal adaptation – error correction – temporal anticipation – predictive internal models – computation model

3.2 INTRODUCTION

Music making often involves multiple performers collectively producing actions that vary in tempo. This purposeful non-stationarity in tempo, which plays a role in communicating musical expression to an audience, places challenges upon interpersonal coordination. Sometimes the composer specifies the manner in which the tempo should change by using terms such as 'ritardando' (slowing down gradually) and 'accelerando' (speeding up) in the musical notation. However, performers typically introduce additional planned or spontaneous tempo changes to convey their interpretation of a piece (e.g., Keller, 2014; Wing et al., 2014). Furthermore, tempo changes might arise unintentionally as a result of the relation between musical structure and patterns of performance expression (e.g., Repp, 1998; Repp, 2008; Repp and Bruttomesso, 2009) and as a result of the dynamic interplay between musicians (Palmer, 1997; Madison and Merker, 2005).

One of the underlying factors that contribute to successful interpersonal coordination is the timing of one's actions with an external stimulus (e.g., the tones produced by a fellow musician) (Repp, 2005). Humans have the ability to synchronize their movements successfully even with complex timing sequences that contain tempo changes (Repp, 2002a, Rankin et al., 2009, Pecenka and Keller, 2011). Synchronizing actions with tempo changing sequences is not only important in the music domain. In sports and daily life, people are required to synchronize their movements with sequential events at different rates, and to negotiate rate changes, in order to fulfill task requirements successfully. An example is the Olympic rowing team that in the heat of the moment is instructed by the coxswain to speed up the pace in order to overtake a competing team. A daily life example would occur if you change pace while walking through the city together with a friend who suddenly speeds up in order to be able to cross the street before the light at the pedestrian crossing turns red. The current study focuses on how people synchronize their movements with different types of ongoing tempo changes, and identifying the underlying mechanisms of this extraordinary sensorimotor synchronization skill.

Individuals' sensorimotor synchronization (SMS) abilities and the underlying mechanisms are often investigated by means of a paced finger-tapping task (Michon, 1967; Repp, 2005). During such a task, participants are asked to tap with their finger in time with the events (e.g. tones) of computer-controlled pacing sequences. The instruction is typically to synchronize finger taps as accurately and precisely as possible with the stimulus sequence. The mean asynchrony can be used as an inverse measure of SMS accuracy, and the variability (i.e., standard deviation) of the asynchronies can serve an inverse measure of SMS precision. The pacing sequences are often isochronous series of tones, but sometimes timing perturbations (inter-onset interval lengthening or shortening) are added. These perturbations can be predictable or unpredictable and local (i.e., affecting one single event or interval) or global (i.e., affecting every event).

It has been hypothesized that in order to successfully time movements relative to external events, humans employ mechanisms that enable adaptation (reactive error correction) and anticipation (predictive processes) (e.g., Keller 2008; van der Steen and Keller, 2013). Temporal adaptation processes have been studied extensively in the tradition of information-processing approaches to SMS. According to the information-processing theory, the timing of simple movements is the determined by a timekeeping process that generates pulses that in turn trigger motor responses (Wing and Kristofferson 1973). Variability in movement timing arises due to variance in this central timekeeper but also as a result of variable transmission delays in the peripheral motor system (e.g., Vorberg and Wing, 1996). In SMS tasks, these two sources of unintentional timing variability (or 'noise') can lead to large asynchronies and even tempo drift.

Adaptation mechanisms reduce the effects of timing variability and therefore contribute to successful SMS (e.g., Mates, 1994a, b; Vorberg and Wing, 1996). Two types of adaptation mechanism —phase and period correction— have been distinguished (Mates, 1994a, b; Vorberg and Wing, 1996; Semjen et al., 1998). Both error correction processes modify the timing of the next tap based on a proportion of the asynchrony, the timing error between a tap and stimulus event (Figure 3.1). Phase correction is an automatic and local adjustment of the interval generated by the internal timekeeper, leaving the interval setting of this timekeeper unaffected (Repp, 2001a; 2002b) (Figure 3.1A). Period correction on the other hand changes the interval setting of the timekeeper that drives the motor activity (Figure 3.1B). This change in timekeeper setting persists until period correction is applied again (Repp, 2001b). Successful period correction requires the conscious perception of a tempo change in the stimulus sequence (Repp and Keller, 2004). Without these adaptation mechanisms, movement timing variability would accumulate from movement cycle to movement cycle. This would lead to increasingly large asynchronies, phase drift and eventually the loss of synchronization (Vorberg and Wing, 1996).

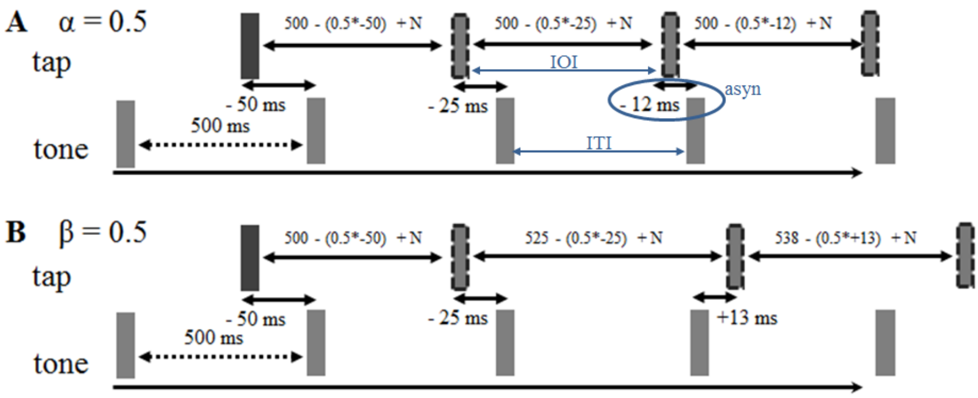


Figure 3.1 Schematic representation of phase and period correction. Equations governing phase and period correction are: $t_{n+1} = t_n + T_n - (\alpha + \beta) * asyn_n + noise$ and $T_{n+1} = T_n - \beta * asyn_n$. Where α reflects the phase correction parameter and β the period correction parameter, t_n is the timing of the next tap, and T_n the current timekeeper setting (see Experimental procedure). The timekeeper originally has an interval setting of 500ms. In blue standard variable related to a finger tapping task are presented; asyn, asynchrony; ITI, interval between successive actions; IOI, interval between the onsets of the stimulus sequence. Adapted from van der Steen and Keller (2013).

Insights into how individuals implement phase and period correction during SMS have been gained mostly from studies employing local perturbations, in which the timing of a single event is altered or the stimulus sequence suddenly changes tempo. One type of perturbation is the step-change perturbation, during which the length of all inter-onset intervals (IOIs) changes at a certain point (Repp, 2005). These perturbations are designed to engage both phase and period correction (Large et al., 2002). Previous results have shown that different responses occur depending on the size of the step change (Thaut et al., 1998a). With large step changes, which are easy to detect, the subsequent inter-tap intervals (ITIs) initially exceed the new sequence IOI, i.e. ITIs display overshoot (Michon, 1967). Small, subliminal step changes do not elicit this overshoot (Hary and Moore, 1985). The overshoot in ITIs is thought to be the result of a combination of phase and period correction (Repp, 2005). Theoretically, implementing only phase correction can lead to adjusted ITIs but the mean asynchrony after the step change would converge to a mean asynchrony that is bigger than the size of the step change (Repp, 2005). Period correction is sensitive to the attentional requirements of a task and can be suppressed, while for automatic phase correction this is not the case (Repp and Keller, 2004), although the gain of phase correction can be controlled voluntarily to some extent (Repp, 2002b).

In addition to the adaptation mechanisms, SMS has been found to benefit from anticipation mechanisms (Keller, 2008; van der Steen & Keller, 2013). These predictive processes allow the anticipation of the precise time of onset of upcoming stimulus events. Based on the anticipated onsets, individuals can initiate their movements early enough to ensure that responses coincide with the events (Schmidt, 1968). It has been claimed that anticipatory movement control is underpinned by internal models that represent bi-directional ('forward' and 'inverse') transformations between movements and their sensory effects (Wolpert and Kawato, 1998). Forward models represent the causal relationship between the input and output of the action control system and are thereby able to predict the effect of a given motor command on the body and the environment. Inverse models serve as a controller for intentional movements by providing motor commands that are potentially able to change the current state of the body and the environment to the desired end state. Paired inverse and forward models facilitate online motor control by allowing potential movement errors to be corrected for they occur. In the social domain, it has been claimed that internal models of one's 'own' actions operate in tandem with models that simulate the actions of 'others' (e.g., a stimulus event or another person) (Wolpert et al., 2003) to support joint action (Keller, 2008). It has been proposed that the coupling of 'own' and 'other' internal models in a 'joint' model facilitates sensorimotor synchronization by allowing the action control system to foresee potential errors in timing (asynchronies) and to correct these errors before they occur (van der Steen and Keller, 2013).

Insights into anticipation mechanisms during SMS tasks have mostly been obtained in studies employing global perturbations, in which the tempo changes for every event in the stimulus sequence. This work has demonstrated that individuals are able to reduce their asynchronies when global perturbations are detectable and regular by predicting upcoming fluctuations (Michon, 1967; Repp 2005; Pecenka and Keller, 2011). Furthermore, individuals can anticipate tempo variations of familiar musical pieces and synchronization performance improves as a result of learning (Repp, 2002a; Rankin et al., 2009). Behavioral evidence for the prediction of global perturbations can be found in positive dependencies (lag-0 cross-correlations) between the ITIs and IOIs. Often the lag-0 cross-correlation is compared to the lag-1 cross-correlation between ITIs and IOIs, which reflects the tendency to track, or copy, rather than to predict the IOIs during synchronization with the tempo changes (Repp, 2002a; Rankin et al., 2009). Tracking behavior has been mainly observed during synchronization tasks in which the stimulus sequence contains random or barely detectable timing perturbations (e.g., Thaut et al., 1998a; Thaut et al., 1998b; Madison and Merker, 2005; Thaut et al., 2009). Furthermore, tracking behavior is often observed when participants are unaware that the pacing sequence is mirroring the expressive timing profile of a musical performance (e.g. ritardando or accelerando) (Repp, 2002a, 2005). Pecenka and Keller (2011) used the ratio between the lag-0 and lag-1 cross-correlations of ITIs and IOIs (PT-ratio) as a measure of prediction in SMS with tempo-changing tapping tasks. A PT-ratio larger than 1 reflects the individual's tendency to predict the tempo change, while a ratio smaller than 1 indicates that the individual tends to copy (track) the tempo changes. The PT-ratio has been found to correlate positively with musical experience, tapping abilities, and neural activation in brain networks comprising cortico-cerebellar motor-related areas and medial cortical areas (Pecenka and Keller, 2009; 2011; Pecenka et al., 2013).

Traditionally, adaptation and anticipation mechanisms have been investigated using separate paradigms. The ADaptation and Anticipation Model -ADAM- (van der Steen and Keller, 2013) was proposed as unified framework to investigate the relationship between adaptation and anticipation mechanisms. The adaptation module of ADAM combines phase and period correction, which compensate for a proportion of each asynchrony, while the anticipation module controls a predictive temporal extrapolation process based on a series of intervals. One of the envisioned goals of the development of ADAM was to provide a unified platform upon which adaptation and anticipation mechanisms, and possible links between these mechanisms, can be systematically explored by means of computer simulations and their relation to behavioral data.

The current study aims to understand how individuals synchronize their movements with continuously tempo-changing sequences. Participants tapped their finger in synchrony with three auditory sequences that differed in the rate of tempo change and the number of turning points (Figure 3.2). After a section in which the tempo was stable (to allow synchronization to be easily established), the tempo of the stimulus sequences varied between 600 and 400 ms IOI. The difference between two successive IOIs ranged between 1 and 14 ms for pattern 1, between 4 and 28 ms for pattern 2, and between 10 and 44 ms for pattern 3, the rate of tempo change thus increased from pattern 1 to 3. The tempo changes followed sigmoidal patterns that resembled musical accelerando and ritardando (Schulze et al., 2005). Standard synchronization measures related to the asynchrony between the participants' taps and the tones were employed as indices of SMS accuracy and precision. Two approaches were used to measure tempo-change prediction, the lagged cross-correlation method (cf., Pecenka & Keller, 2009; 2011) and a newer method that deals with autocorrelation in the time series by implementing pre-whitening and auto-regressive modeling (Mills et al., *submitted*). Measures of anticipation therefore included cross-correlations at lag-1, lag-0, PT-ratios, and PT-indices. Phase and period correction estimates, as indicators of adaption, were obtained by means of the bGLS method, an analytical technique for solving a generalized regression problem (cf., Jacoby and Repp, 2012, Jacoby et al. *submitted*). In addition, simulations with ADAM were run to investigate the effect of the different mechanisms on SMS precision in a tempo changing synchronization task. We employed four versions of ADAM: a model that only included adaptation, one with independent contributions of the adaptation and anticipation mechanisms, and two models in which adaptation and anticipation were linked in a joint internal model. In order to ascertain the optimal usage of adaptation and anticipation mechanisms for successfully fulfilling the task instructions, different parameter settings (such as the amount of phase/period correction, amount of anticipation) were varied in the simulations (see Experimental procedure). Across the four versions of ADAM, parameter estimates were obtained by means of the bGLS-method, and the fit of the model to the behavioral data was calculated.

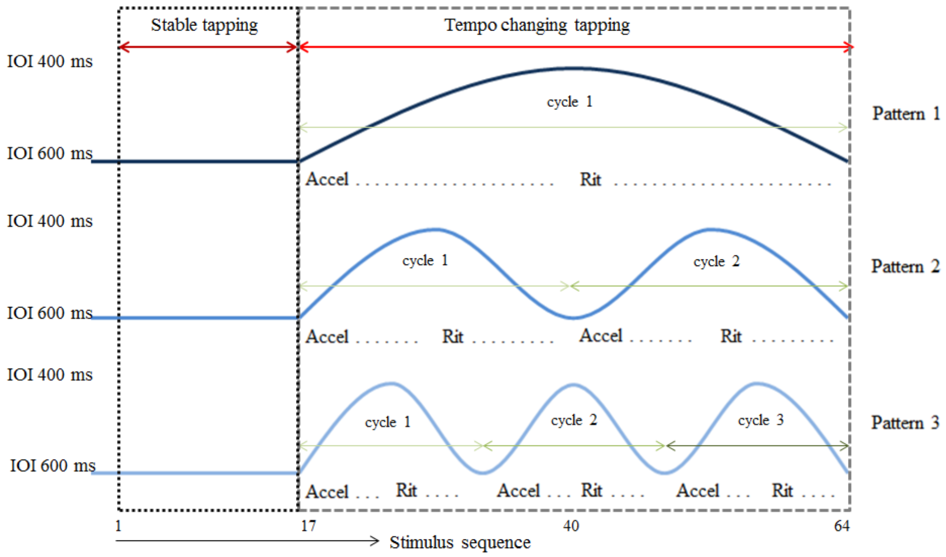


Figure 3.2 The three tempo changing patterns. Each trial started with four initiation tones with an IOI of 600 ms. The stimulus sequences consisted of 64 tones. The tempo of the first 16 tones was stable (IOI 600 ms) [black dotted box], allowing synchrony to be established. The tempo during the following 48 tones varied between 600 and 400 ms IOI, following three sigmoidal patterns that resembled musical accelerando and ritardando. Data analyses focus on the tempo changing part of the trials [grey dashed box] (see Experimental procedure).

Our hypotheses address how the underlying adaptation and anticipation mechanisms are employed to achieve successful SMS with the three tempo-changing patterns. Based on previous studies that investigated the mechanisms separately, we hypothesize participants will generally show evidence for active adaptation and anticipation mechanisms when synchronizing with the tempo changing sequences (e.g., Repp, 2005; Pecenka & Keller, 2009;

2011). Accordingly, simulations and the fit of the different versions of ADAM should favor a synchronization model that includes both adaptation and anticipation mechanisms. Furthermore, we expect that adaptation and anticipation will be affected by the rate of tempo change and frequency of turning points. Specifically, we hypothesize that period correction will increase with the step size of the continuous tempo changes and that due to the automatic nature of phase correction these estimates remain constant. Alternatively, as period correction only occurs if the tempo change is perceived, participants might adapt their ITIs in a stepwise fashion (Michon, 1967). Since the difference between sequential IOIs is small in continuous tempo change, it might take several tones before the perceptual threshold of tempo change is passed and period correction can be applied. Between the period adjustments, phase correction could be applied to maintain synchronization (Repp, 2005). Stepwise adaptation might be an economical approach especially when dealing with frequent tempo changes. This follows from the assumption that period correction is effortful and, due to the longer-lasting effects of adjusting the timekeeper period, costly to implement, as an incorrect period setting would cause continuous impairment to SMS. Finally, we assume that the prediction of the tempo changes is more beneficial during the acceleration or deceleration phases of the tempo changes than at the transition between these phases, which are difficult to predict. We therefore hypothesize that an increasing number of transitions in the tempo changing stimulus sequence will decrease SMS accuracy and precision.

3.3 RESULTS

3.3.1 Experiment

3.3.1.1 Synchronization measures

The mean asynchrony and the standard deviation of asynchronies between participants' taps and pacing sequence tones were examined to investigate differences in synchronization accuracy and precision across the three tempo-changing patterns. The repeated measures ANOVAs on each of these measures included pattern (1-2-3) as within subject variables.

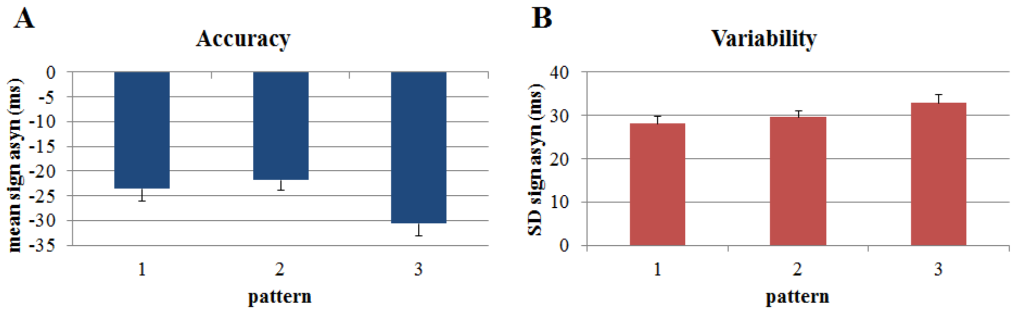


Figure 3.3 The mean signed asynchrony as a measure of SMS accuracy (A) en the standard deviation of the signed asynchrony as a measure of SMS precision (B) separated for the three patterns. Error bars represent standard error across participants.

The ANOVA on mean asynchrony yielded a significant a main effect of pattern [$F_{(2,32)}$ = 15.67, p < 0.001]. Post-hoc pairwise comparisons [all p < 0.01] revealed that SMS accuracy was lower for pattern 3 compared to patterns 1 and 2 [all p < 0.01], while there was no significant difference in accuracy between patterns 1 and 2 (Figure 3.3A). A significant main effect of pattern was also found for the standard deviation of asynchronies [$F_{(2,32)}$ = 7.34, p < 0.005]. Pairwise comparisons confirmed that SMS was less precise for pattern 3 compared to pattern 1 and 2 [all p < 0.05] (Figure 3.3B), while differences between patterns 1 and 2 were non-significant.

3.3.1.2 Adaptation mechanisms

The amount of phase and period correction implemented by participants was estimated by means of the bGLS method following the 'Adaptation Model' to investigate adaptation mechanisms. These data were entered into a repeated-measures ANOVA with correction type (phase/period) and pattern (1-2-3) as within-subject variables.

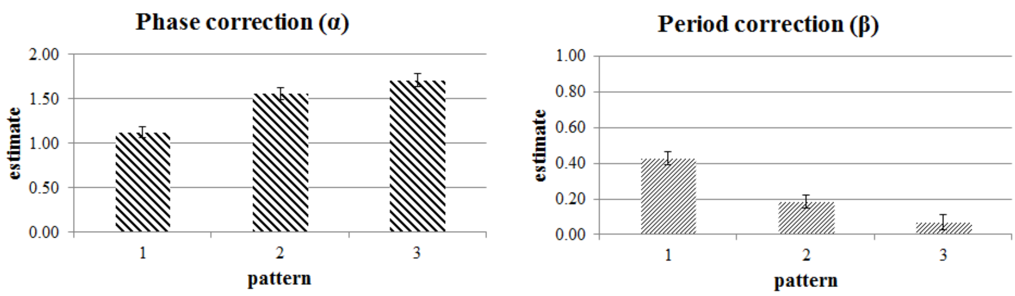


Figure 3.4 Estimated amount of phase **(A)** and period **(B)** correction reflecting adaptation mechanisms. Error bars represent standard error across participants.

The ANOVA revealed significant main effects of correction type [$F(1,16) = 368.17$, $p < 0.001$] and pattern [$F(2,32) = 5.50$, $p < 0.01$]. The effect of correction type indicated that phase correction estimates were generally higher than period correction estimates. The effect of pattern was qualified by a significant interaction between pattern and correction type [$F(2,32) = 57.41$, $p < 0.001$], reflecting the fact that phase correction estimates increased while the period correction estimates decreased as the frequency of tempo-change transitions increased from pattern 1 to 3. This interaction was explored further by analyzing the estimates for phase and period correction separately. A significant main effect of pattern was found for phase correction estimates [$F(2,32) = 40.02$, $p < 0.001$]. Pairwise comparisons revealed that phase correction estimates for pattern 1 were lower than for pattern 2 and 3 [all $p < 0.001$], while patterns 2 and 3 did not differ significantly (Figure 3.4A). A significant main effect of pattern was also found for period correction estimates [$F(2;32) = 29.12$, $p < 0.001$]. Pairwise comparisons revealed that period correction estimates for pattern 1 was higher than for pattern 2 and 3 [all $p < 0.001$] and pattern 2 was higher than pattern 3 [$p < 0.05$] (Figure 3.4B).

3.3.1.3 Anticipation mechanisms

Anticipation mechanisms were investigated by examining the lag-0, lag-1 cross-correlations, the PT-ratio and the PT-index. The repeated measures ANOVAs included pattern (1-2-3) and if applicable lag (0/1) as within subject variables. Furthermore, Pearson's correlations between the PT-ratio and the PT-index were calculated separately for the three patterns across participants to assess the degree to which the two measures reflect similar processes.

The ANOVA on cross-correlation coefficients yielded significant main effects of pattern [$F(2,32) = 59.94$, $p < 0.001$] and lag for the cross-correlations [$F(1,16) = 286.80$, $p < 0.001$]. Pairwise comparisons revealed that cross-correlations were generally lower for pattern 3 compared to pattern 1 and 2, and for pattern 2 compared to pattern 1. Furthermore, the lag-0 cross-correlation was found to be higher than the cross-correlation at lag-1. This is also reflected in the PT-ratios, which were all greater than 1. The interaction between pattern and lag also turned out to be significant for the cross-correlations [$F(1.13,18.03) = 108.08$, $p < 0.001$], as pattern had a stronger effect on lag-1 than lag-0 cross-correlation (Figure 3.5A).

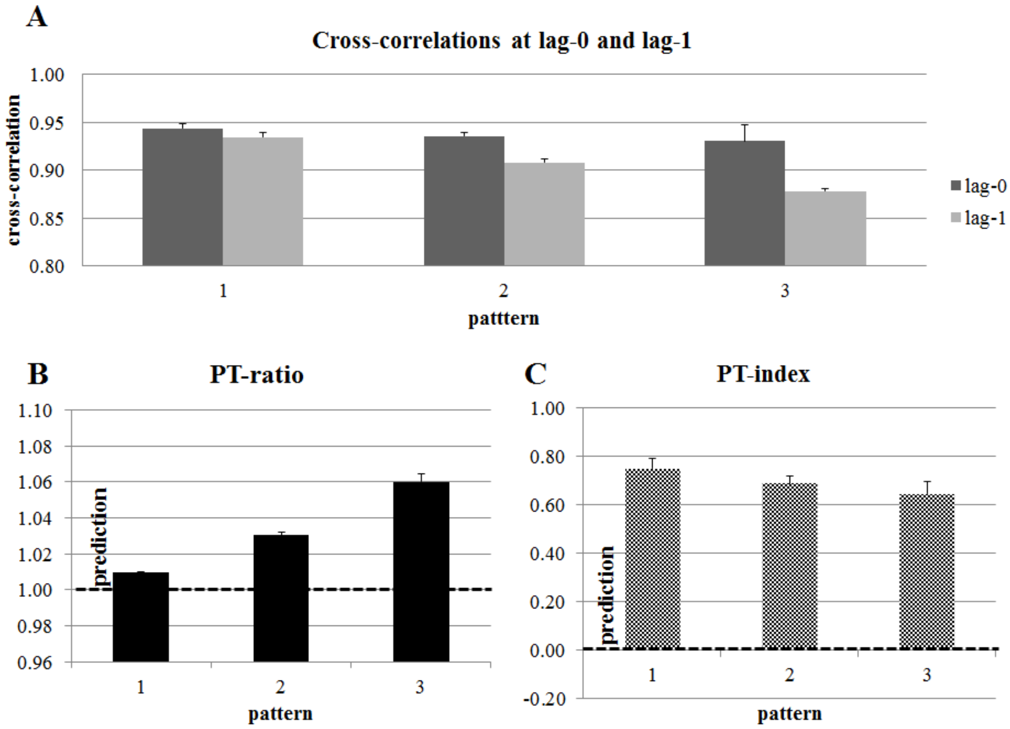


Figure 3.5 The cross-correlations at lag-0 and lag-1(**A**), PT-ratio (**B**), and PT-index (**C**) reflecting anticipation. PT-ratios bigger than 1 and PT-indices bigger than 0 indicate participants are predicting the tempo changes. Error bars represent standard error across participants

As already mentioned, all PT-ratios were greater than 1, suggesting that participants were predicting the tempo changes (Figure 3.5B). The ANOVA on PT-ratios yielded a significant effect of pattern [$F(1.11,17.79) = 107.51$, $p < 0.001$]. Pairwise comparisons revealed that the PT-ratio was higher for pattern 3 compared to pattern 1 and 2, and that the PT-ratio was higher for pattern 2 than for pattern 1 [all $p < 0.001$].

All PT-indices were positive indicating that, also according to the auto-regression method, participants were predicting the tempo changes in the stimulus sequences (Figure 3.5C). The ANOVA on PT-indices yielded a significant effect of pattern [$F(2,32) = 4.15$, $p < 0.05$], reflecting a decrease in PT-indices (suggesting less prediction) from pattern 1 to pattern 3. This effect goes in the opposite direction to the effect found for PT-ratios. Despite this, the two measures were positively correlated across participants at the level of each pattern. Pearson's correlations between PT-ratio and PT-index were 0.69, 0.94, and 0.99 for pattern 1, 2, and 3, respectively [all $p < 0.001$]. Thus, there was a moderately strong correlation between both measures for pattern 1 and a strong correlation for patterns 2 and 3.

3.3.2 Models

3.3.2.1 Simulations

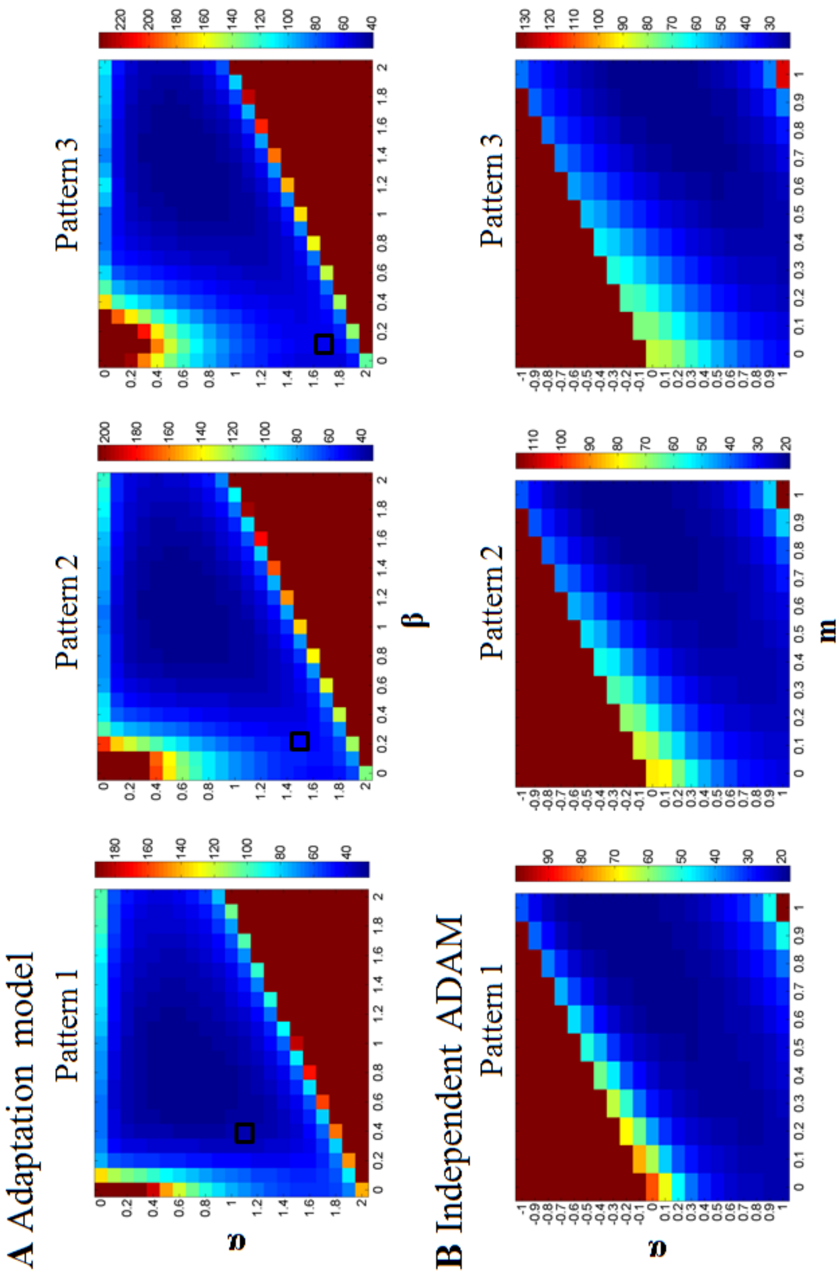
The results of simulations using the four versions of ADAM are shown in Figure 3.6. For the three tempo-changing synchronization patterns the 'Adaptation model' (Figure 3.6A) performed best when both phase correction (α) and period correction (β) were employed. When the rate of tempo change and number of turning points were high [pattern 2 and 3 compared to pattern 1], SMS precision was best when the model implemented higher levels of β. It can also be noted that several combinations of parameters, especially border parameters [e.g. $\alpha > 1$ in combination with larger β], led to extremely large and variable asynchronies due to drift. If the mean phase and period correction estimates of the participants (black boxes in Figure 3.6A) are compared with the results of the simulations with the adaptation model, we find a simulated SMS precision of 32.35 ms for pattern 1, 55.05 ms for pattern 2, and 57.48 ms for pattern 3. Participants were found to be more precise than these simulated values particularly for patterns 2 and 3 (Figure 3.3B), suggesting that adaptation mechanisms alone cannot account for all aspects of SMS behavior when tempo changes are large.

The 'Independent ADAM' and 'Joint ADAM (α | β)' models included adaptation and anticipation mechanisms. Anticipation is reflected in the prediction/tracking parameter *m*, which ranges from 0 to 1. This parameter is based on the assumption that humans engage in predictive and tracking behavior at the same time (Pecenka & Keller, 2011). The closer *m* is to 1, the more prediction takes place. When $m = 0.5$ the model relies equal on prediction and tracking behavior to determine the timing of the next tone. An *m* smaller than 0.5 indicates that the model relies more on tracking than prediction.

Adaptation in the 'Independent ADAM' model is restricted to phase correction. As can be seen in Figure 3.6B, negative phase correction settings (α) resulted in high variability of asynchronies due to drift (Figure 3.6B). The simulation results illustrate that SMS precision increased with increases in the degree to which the models relied on prediction [higher *m*] to determine the timing of the next tone (Figure 3.6B).

Finally, in the 'Joint ADAM (α | β)' models, adaptation and anticipation mechanisms were linked in a joint internal module that implements an anticipatory phase correction process (γ). This process uses the output of adaptation and anticipation modules to simulate what the asynchrony would be if the planned tap were to be produced, and then corrects for this anticipated error by the proportion γ. Simulations indicated that implementing more anticipatory phase correction had a positive effect on SMS precision (Figure 3.6C-D). For the

'Joint ADAM (α | β)' models, Figure 3.6 (C-D) show the effect of m in the anticipation module and the error correction component (α | β) in the adaptation module for the mean obtained γ estimate (see below). Negative period correction (β) settings in the adaptation module had a deteriorating effect on SMS precision, with settings beyond -0.2 resulting in large variability (Figure 3.6D).



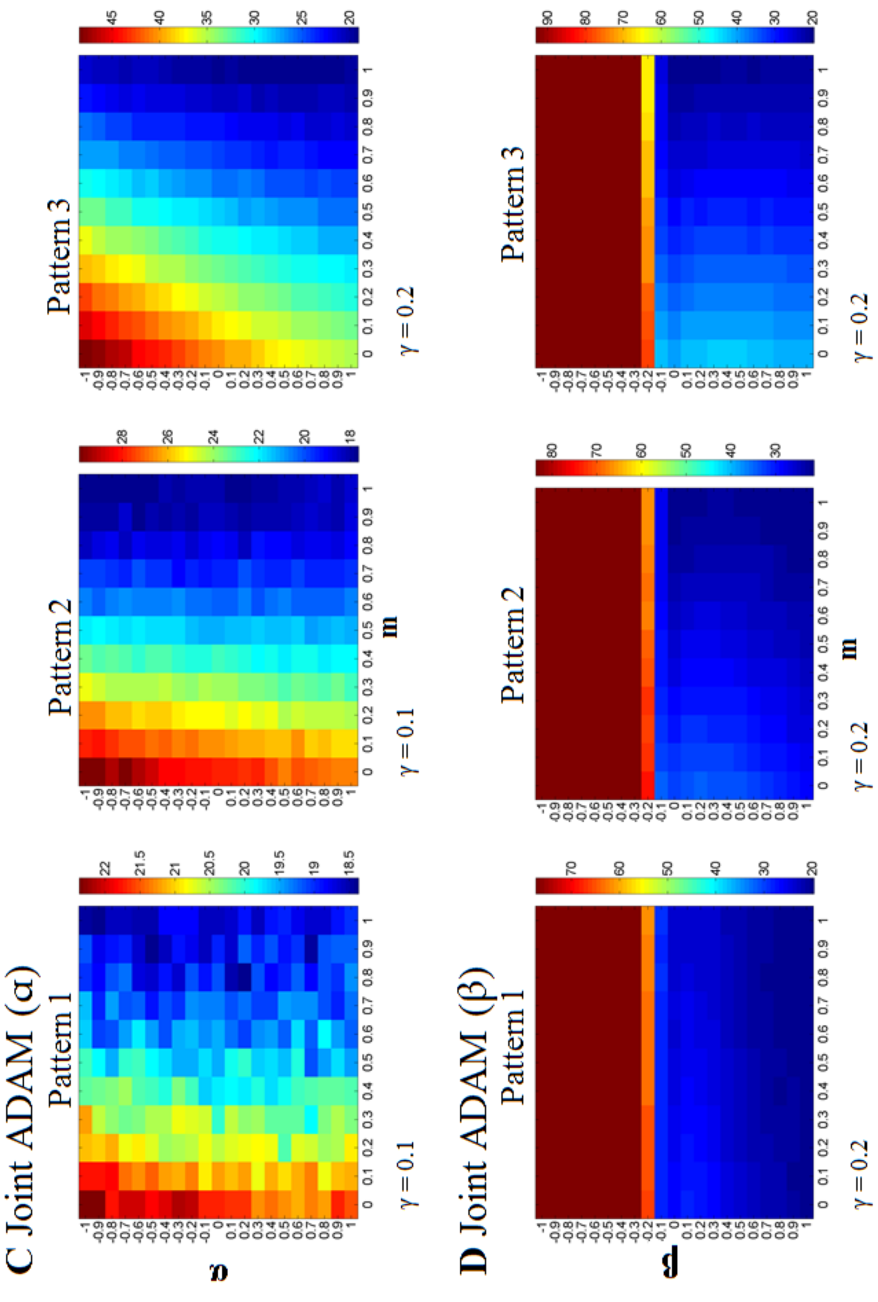


Figure 3.6 Heat-maps showing the SD of the signed asynchronies resulting from simulations across the parameter settings for the 'Adaptation Model' (A), 'Independent ADAM' model (B) 'Joint ADAM (α)' model (C), and 'Joint ADAM (β)' model (D). Dark blue represents the highest SMS precision (low standard deviation of asynchronies). Extreme values (larger than three times the mean of the medians of the simulated standard deviation of asynchronies) were replaced by the mean of the median for presentation purposes. The black boxes in panel A reflect the mean phase and period estimates for the participants from the behavioral experiment.

3.3.2.2 Parameter estimates

Model parameters for the 'Independent ADAM' and 'Joint ADAM (α | β)' models were estimated from the behavioral data by means of the bGLS-method. Estimates for the 'Adaption' model were already presented in paragraph 3.3.1.2 and Figure 3.3. For each parameter type, a separate repeated measures ANOVA with pattern (1, 2, 3) as the within subject variable was performed.

The ANOVAs on estimates from the 'Independent ADAM' model yielded a significant main effects of pattern for α [$F(1.35,21.60) = 78.03$, $p < 0.001$] and *m* estimates [$F(1.32;21.11) = 69.02$, $p < 0.001$]. Pairwise comparisons revealed that α and *m* estimates for pattern 1 differed from estimates for pattern 2 and 3 (all $p < 0.001$), while pattern 2 and 3 estimates did not differ significantly. Specifically, for pattern 1, estimates of *m* were low (indicating tracking), while α-estimates were high (phase correction). For pattern 2 and 3, when tempo changes are bigger, estimates of *m* were high (indicating prediction) and α estimates were negative (suggesting correction in opposite direction) (Figure 3.7).

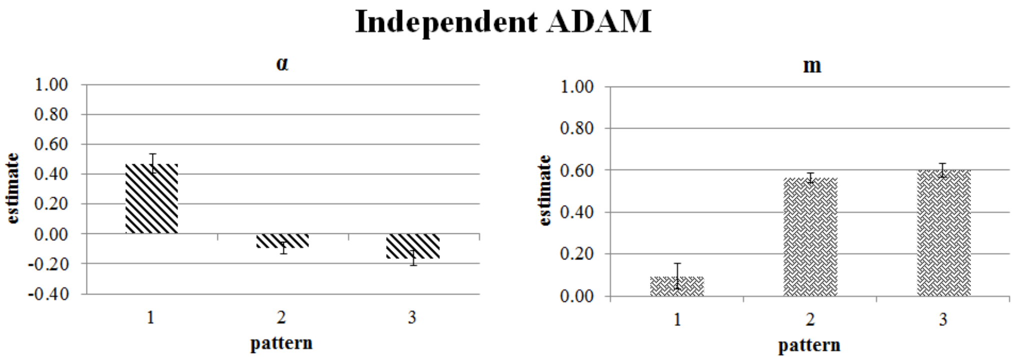


Figure 3.7 Parameter estimates based on the 'Independent ADAM' model. Where α reflects a phase correction parameter, while *m* indicates the prediction/tracking parameter. Error bars represent standard error across participants.

For the 'Joint ADAM (α)' model[2], the ANOVAs yielded significant main effects of pattern for all three parameters. (α: [$F(2,32) = 8.89$, $p = 0.001$], γ: [$F(2,32) = 70.85$, $p < 0.001$], *m*: [$F(1.47, 23.15) = 56.73$, $p < 0.001$]). Pairwise comparisons for α revealed that estimates for pattern 3 differed from the estimates of pattern 1 ($p < 0.005$). For γ, pairwise comparisons showed that estimates were lower for pattern 1 compared to pattern 2 and 3, and for pattern 2 compared to pattern 3 (all $p < 0.001$). Pairwise comparisons for *m* revealed that estimates for pattern 3 were higher compared to the estimates of pattern 1 ($p < 0.001$). These results

[2] Due to parameter interdependence, it was necessary to restrict the parameter space of α between -0.8 and -.1 in order to obtain reliable and unbiased estimates. This range was based on the results of Monte-Carlo simulations.

indicate that, compared to pattern 1, α estimates were less negative for patterns 3 (less phase correction in opposite direction in the adaptation module). Estimates of γ increased across patterns, indicating that the proportion of the asynchrony that was corrected by means of the anticipatory phase correction was smaller. Furthermore, for pattern 1 estimates for *m* were low (indicating tracking), while for pattern 2 and 3, when tempo changes are bigger, estimates of *m* were high (indicating prediction) (Figure 3.8). Note that this is consistent with the behavioral results for PT-ratios rather than PT-indices.

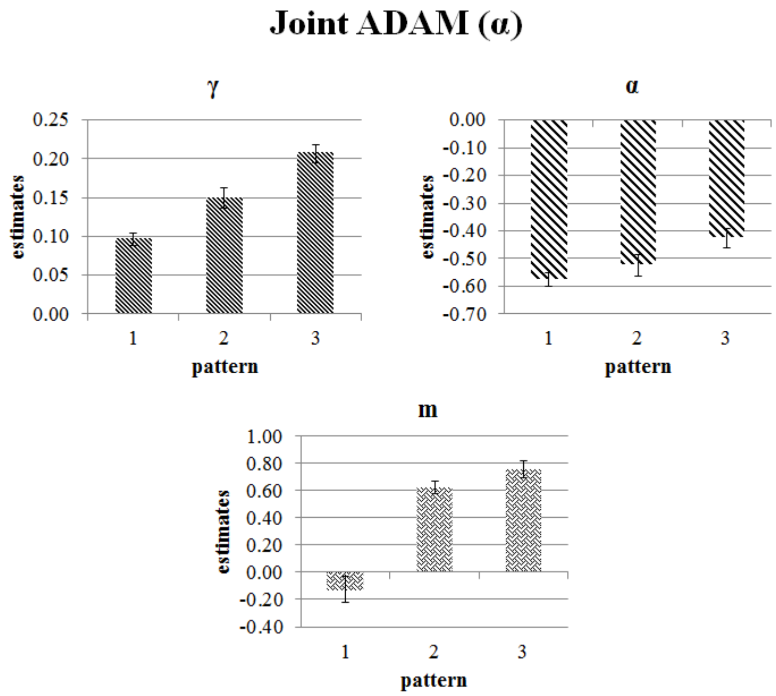


Figure 3.8 Parameter estimates based on the 'Joint ADAM (α)' model. Where γ reflects an anticipatory phase correction process in the link module, α reflects the phase correction parameter of the adaptation module, while *m* indicates the prediction/tracking parameter of the anticipation module. Error bars represent standard error across participants.

The repeated measures ANOVA on the three parameter estimates for the 'Joint ADAM (β)' [3] model yielded significant main effects of pattern for γ estimates [$F(2;32) = 49.68$, $p < 0.001$] and estimates of *m* [$F(2;32) = 65.79$, $p < 0.001$]. Pairwise comparisons revealed that both the γ and *m* estimates for pattern 1 differed from estimates for pattern 2 and 3, and that estimates for pattern 2 differed from the estimates of pattern 3 (all $p < 0.05$). These results suggest that

[3] Due to parameter interdependence, it was necessary to restrict the parameter space of α between 0 and 1 (based on the results of the simulations) in order to obtain reliable and unbiased estimates. Furthermore, the parameter space for *m* was restricted between 0 and 1, which covers complete tracking to complete prediction.

the γ estimates increased (less phase correction [1- γ] in the joint model) and the estimate for *m* increased (more prediction) across patterns. Estimates of β did not show significant difference across the three patterns (Figure 3.9).

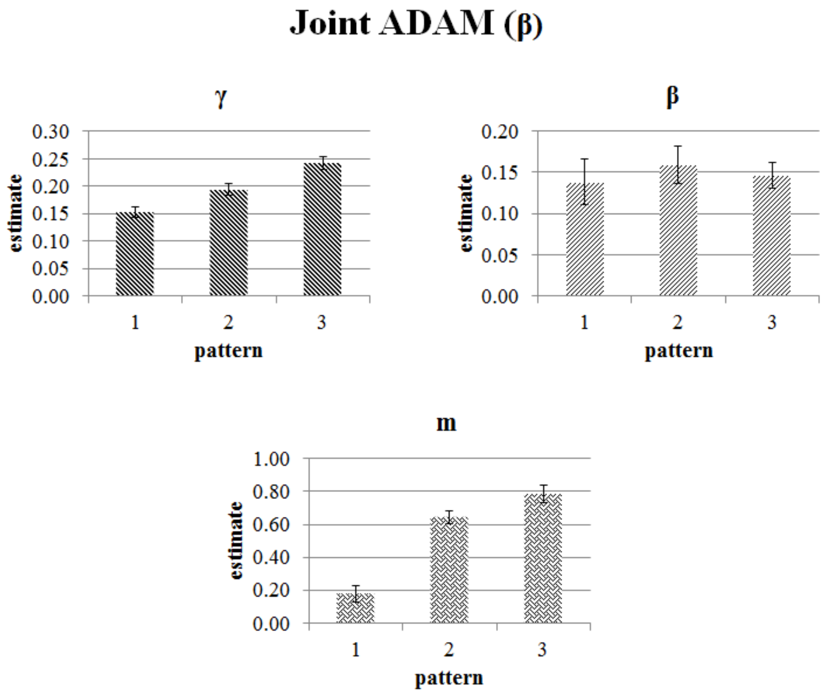


Figure 3.9 Parameter estimates based on the 'Joint ADAM (β) model. Where γ reflects an anticipatory phase correction process in the link module, β reflects the period correction parameter of the adaptation module, while *m* indicates the prediction/tracking parameter of the anticipation module. Error bars represent standard error across participants.

3.3.2.3 Comparison of the models

The fit of the models to the behavioral data was assessed by a likelihood estimation procedure. Values that are less negative and smaller in absolute magnitude indicate better fit (Figure 3.10). Likelihood estimates were entered into a repeated-measures ANOVA with pattern (1-2-3) and model ('Adaptation Model', 'Independent ADAM' 'Joint ADAM (α)', and 'Joint ADAM (β)') as within subject variables.

This ANOVA revealed significant main effects of model [$F(1.01;16.09) = 211.65$, $p < 0.001$] and pattern [$F(2;32) = 22.35$, $p < 0.001$], as well as a significant interaction between both variables [$F(1.88;30.05) = 13.73$, $p < 0.001$]. The larger, more negative likelihood estimates observed for adaptation model indicated that its fit was poor compared to the other models, especially for pattern 2 and 3 (Figure 3.10A). The fit of the three models that included adaptation and anticipation mechanisms was further investigated with a separate repeated-measures ANOVA per pattern, with model ('Independent ADAM', 'Joint ADAM (α)', and 'Joint ADAM (β)') as the only within subject variable. For pattern 1, no significant difference between the three models was found [$F(1.44;23.14) = 2.29$, $p > 0.05$]. For pattern 2 and 3 a significant effect of model was found [pattern 2: $F(1.18;18.80) = 27.49$, $p < 0.001$; pattern 3: $F(1.26;20.16) = 87.38$, $p < 0.001$]. Pairwise comparisons for both patterns the 'Joint ADAM (β)' model had a better fit compared to the 'Independent ADAM' and 'Joint ADAM (α)' models (all $p < 0.001$). Furthermore the 'Joint ADAM (α)' model was found to have a better fit compared to the 'Independent ADAM' model (all $p < 0.001$). These results indicate that for pattern 2 and 3, in which the tempo changes are relatively large, the models in which adaptation and anticipation mechanisms are linked via a joint internal module fit the behavioral data better than the 'Independent ADAM' model. Overall, the 'Joint ADAM (β)' model gives the best fit to the behavioral data (Figure 3.10B).

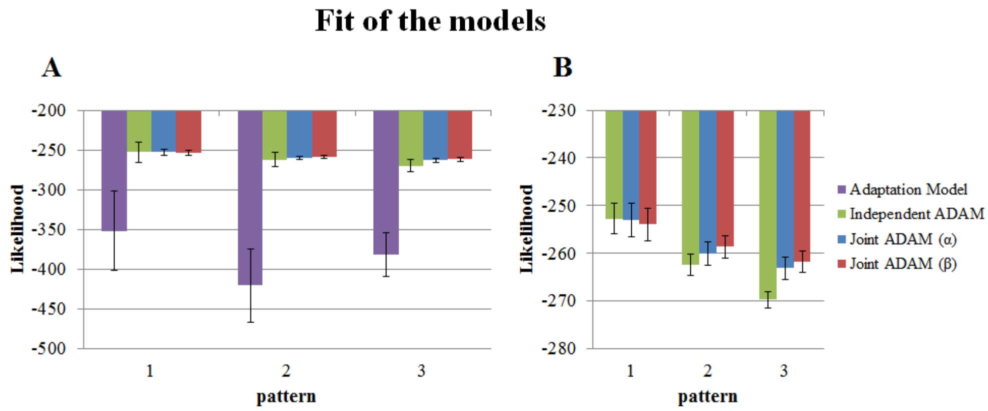


Figure 3.10 Likelihood estimates for the four models for each pattern (A); detail of likelihood estimates for the three models including both adaptation and anticipation (B). Error bars represent standard error across participants.

3.4 DISCUSSION

The aim of the current study was to test the contribution of temporal adaptation and anticipation mechanisms to sensorimotor synchronization with tempo-changing sequences. To this end, we conducted a behavioral finger tapping experiment along with simulations based on ADAM, a model of error correction (adaptation) and predictive processes (anticipation) developed by van der Steen and Keller (2013). The investigation centered on three continuously tempo changing stimulus sequences that contained global perturbations representative of scenarios found in expressively timed music. The sequences differed in the rate with which the tempo changed and the number of turning points. Results of the behavioral experiment showed that participants were capable of synchronizing their finger taps with the sequences with a high level of SMS accuracy and precision, although synchronization was less accurate and precise in pattern 3, which contained the most turning points and during which the tempo changes from interval to interval were the largest.

Four versions of ADAM were tested; a model that only implemented adaptation, one with independent contributions of adaptation and anticipation, and two models in which adaptation and anticipation were linked in a joint internal model. Applying the 'Adaptation model' (Schulze et al. 2005; Repp and Keller, 2008) yielded phase correction estimates that were larger than 1. This suggests over-correction in the sense that participants adjusted the timing of their taps by a larger amount than the asynchrony. If the timekeeper controlling tap timing does not adapt to a stimulus sequence that speeds up or slows down, the size of the tempo change is also reflected in the asynchrony (Repp, 2005). Over-correction can thus be beneficial when dealing with continuous tempo changes. Theoretically it has been argued that period correction is relevant when dealing with tempo changes, as changing the interval of the timekeeper allows adaptation to the tempo change (Repp, 2001b). In the standard adaptation model the timekeeper is adjusted every cycle (Schulze et al. 2005; Repp and Keller, 2008). Simulations produced this positive effect of period correction on SMS, but period correction estimates from participants' data were low and decreased when the rate of tempo change was large and turning points were frequent. The discrepancy between what the model predicts and what participants seem to do is also reflected in the difference of the standard deviation of the asynchrony. Participants' precision decreased when the stimulus sequence contained larger tempo changes and more turning points, but not by as much as the simulations suggested. The relatively small amount of applied period correction and the high amount of phase correction might hint at a different role of phase and period in relation to synchronization with continuous tempo-changing sequences. An option suggested previously is stepwise or intermittent adaptation to the tempo change, in which period correction only updates the timekeeper if the tempo change exceeds a certain threshold and in the meantime relies on phase correction (Michon 1967; Madison and Merker, 2005; Repp, 2005). This would suggest a large contribution of phase correction and a small but crucial role of period correction when maintaining synchronization with continuous tempo-changing stimulus sequences.

Participants were found to anticipate the tempo changes for all three patterns. However, PT-ratio's increased with increasing degree of tempo change between successive intervals, indicating that there was a tendency to engage in more predictive behavior when differences in tempo were more salient. This is in line with previous research showing that, when tempo changes are detectible, humans tend to predict the tempo changes (e.g., Rankin et al., 2009, Pecenka and Keller, 2011). The high correlations between the PT-ratios and the PT-indices suggest that both measures generally reflect the tendency to predict tempo changes in a similar way. However, the PT-ratios turned out to behave more consistently with the *m* parameter controlling prediction and/or tracking behavior in the anticipation component of the models. This might be seen as a reason to favor the PT-ratios over PT-indices, or at least to consider both measures, when describing anticipatory behavior in human SMS across different types of tempo-changing sequences.

In the versions of ADAM that combined adaptation and anticipation mechanisms, we introduced *m* as a prediction/tracking parameter. This parameter regulates the balance between predictive behavior, implemented as an extrapolation process based on two most recent IOIs, and tracking behavior, implemented as a copy of the previous interval. Although in our models anticipation is not used explicitly to set the timekeeper, *m* has some overlap with the concept of anticipatory period correction (Repp, 2006). According to Repp (2006), expectations and active prediction of learned timing are employed to adjust the timekeeper period. On this view, anticipatory period correction improves with exposure to a specific pattern due to learning, which results in smaller asynchronies and thus better synchronization.

The negative α estimates for the 'Independent ADAM' and especially the 'Joint ADAM (α)' model were unexpected and remain puzzling. For the 'Joint ADAM (α)' model, estimates had to be restricted (according to Monte-Carlo simulations) to a negative range in order to obtain reliable estimates with the bGLS-method. According to Vorberg and Schulze (2002), phase correction in a range between 0 and 2 facilitates the stabilization of asynchronies. Negative phase correction suggests a local correction in a direction opposite to the asynchrony, which normally does not contribute to successful SMS. However, anticipation mechanisms tend to lead to predictions that over- and undershoot at turning points. During synchronization with tempo changing sequences that contain turning points, implementing corrections in the opposite direction could thus have a positive effect on SMS because it correct for this imprecision in predictions. The slightly negative α estimates for the 'Independent ADAM' model, in conjunction with *m* estimates that indicate prediction, might thus in fact have been beneficial.

Adding timekeeper and motor noise to the simulations influences the variability of the simulated asynchrony and the fit of the models to the data. The current simulations included motor and timekeeper noise, for which values were drawn from the same distributions for all four models. There are, nevertheless, some noise-related issues that our simulations did not address. First, we did not take into account that timekeeper variance increases with interval length (Wing, 1980). Such dependence could have led to the scaling of SMS precision as intervals became progressively longer or shorter in each pattern. Second, we did not include perceptual noise, which affects the perceived time of occurrence of the stimulus, the participants' own taps, and therefore the perceived asynchrony (Repp and Keller, 2004). Perceptual variability also increases with interval length (Friberg and Sundberg, 1995; Repp, 2006). Notwithstanding these issues, it is still possible to determine model fits with respect to the behavioral data since we applied noise in a similar way for all four models.

In terms of fit, the adaptation model turned out to be inferior to the models that combined adaptation and anticipation for the types of tempo change that we investigated. The 'Joint ADAM (β) model was found to have the best fit, but due to parameter interdependence for both joint models, the parameter space needed to be restricted in order to be able to obtain reliable estimates [especially for pattern 1]. For the 'Joint ADAM (β) model, the *m* estimate for pattern 1 was set to zero (complete tracking) in 63% of the trials, indicating that the *m* estimate reached the restriction. For pattern 2 and 3, this happened in 3% and 1.5% of the trials, respectively. This suggests that the joint model had some difficulties when dealing with relatively small tempo changes (for pattern 1, where the range between two successive IOIs was only 1 - 14 ms) and might suggest that prediction then does not play a big role. Furthermore, for both 'Joint ADAM (α | β)' and the 'Independent ADAM' model, *m* estimates close to zero were found for pattern 1. This implied tracking behavior instead of the prediction of the tempo changes suggested by the PT-ratios computed from the behavioral data. It might be the case that adaptation and anticipation mechanisms are linked differently, and that adaptation plays a bigger role, when dealing with small tempo changes than when tempo changes are larger and easier to detect. Previous studies have shown that tempo changes are not fully predicted if these changes are small enough to be subliminal (Thaut et al., 1998b; Madison and Merker 2005). Nevertheless, synchronization can be established in these situations most likely as a result of adaptation mechanisms.

The anticipation module of ADAM contains a temporal extrapolation process that generates predictions based on the preceding intervals in the pacing sequence. The number of intervals used influences the predictions and can be controlled in the anticipation module by varying the parameter *k* (van der Steen and Keller, 2013). In the current simulations, *k* was set to 2, indicating that the predictions were an extrapolation based on the previous two intervals. Although using more intervals would make predictions more robust against outliers, this also means it takes longer before a change in direction of the tempo change (i.e., turning point) is detected and processed. Since the current patterns followed a clear sigmoidal function, basing predictions on just two intervals led to the most accurate results. If less predictable or more variable human sequences were to be used, then a higher value of k might be necessary for optimal anticipation.

Related to the previous point is the current usage of a first-order linear extrapolation process. This process detects and works with the direction and magnitude of a tempo change in such a way that an accelerating sequence (with intervals that decrease in duration) will result in a prediction that the next event will occur after an even shorter interval, and vice versa for tempo deceleration. It has been demonstrated that recognizing and predicting such tempo changes is beneficial during SMS (Pecenka & Keller, 2011; Pecenka et al., 2013). But it is not said that humans implement predictions per definition following a first order linear extrapolation process. More complex prediction processes —such as higher-order fitting and long-range correlations, or, when dealing with music, processes that take into account hierarchically nested timescales associated with metrical structure— might be applied during synchronization (e.g., Drake et al., 2000; Rankin et al., 2009).

Overall, we conclude that adaptation mechanisms alone cannot account for all aspects of SMS behavior. Both adaptation and anticipation mechanisms contribute to successful SMS, specifically for SMS with tempo changes such as those found in expressively performed music. How the adaptation and anticipation mechanisms are combined remains a question, but our results are consistent with the proposal that joint internal models that evaluate the degree of discrepancy between adaptation and anticipation, and allow any error to be compensated for before it occurs, play a role in linking these mechanism. ADAM has proven to be a useful framework to investigate the role of adaptation and anticipation during SMS, and how these mechanisms might interact. It would be fruitful in future research with ADAM to explore different types of linkage between the adaptation and anticipation modules (e.g., by include phase and period correction in a joint model), focus on the role of the different noise components (e.g., perceptual noise) involved with SMS, or include other (visual) synchronization cues associated with body movements and hierarchical temporal structures, such as those occurring in music performance.

3.5 EXPERIMENTAL PROCEDURE

3.5.1 Experiment

3.5.1.1 Participants

Twenty amateur musicians (11 female / 9 male, age: 25.83 ± 4.25 years, musical experience: 18.15 ± 3.98 years) participated in this study. None of the participants reported any neurological or psychiatric disorders. Participants received written descriptions of all procedures and signed an informed consent form before the experiment started. Data from three participants were excluded from the final sample (N = 17) due to technical problems (n = 2) and failure to reach criterion performance (n = 1).

3.5.1.2 Materials

Three different patterns served as stimulus sequences (Figure 3.2). All patterns started with a section in which the tempo was stable, consisting of 16 tones (woodblock, 25 ms duration) with IOIs of 600 ms. This section was included in order to allow synchrony to be established between the stimulus sequence and the participants' taps. The IOIs of the following 48 sequence tones gradually changed between 600 ms and 400 ms. The tempo changes were designed to resemble musical accelerando and ritardando and followed a sigmoidal function[4] (cf. Schulze et al., 2005). The three patterns differed in the number of steps (N_{steps}) required to cover the 200 ms change in IOI. Since the tempo-changing section of all patterns contained the same number of beats (48), the number of steps used to cover the change meant that the three patterns differed in the number of cycles that contained this tempo change. An accelerando phase followed by a successive ritardando phase constituted one cycle of tempo change from an IOI of 400 ms to 600 ms and back to 400 ms (Figure 3.2).

In Pattern 1, the accelerando and ritardando phases of the tempo change each spanned 24 steps. This led to one cycle per trial that changed tempo smoothly and slowly, with the difference between successive IOIs being small (range: 1 - 14 ms). Pattern 2 had 12 steps for each accelerando and ritardando phase, and hence contained two cycles (each of 24 steps) of speeding up and slowing down (the difference between successive IOIs ranged between 4 and

[4] The sigmoidal function was defined by:

$$IOI_i = tempo_{start} + (tempo_{start} - tempo_{goal}) * frac \quad \text{eq. 1}$$

$$frac = \frac{1}{2}\left[1 + \cos\frac{i-1}{N_{steps}-1}\pi\right] \quad \text{eq. 2}$$

For the accelerando part of each cycle $tempo_{start}$ was set to 600 and $tempo_{goal}$ was 400. For the ritardando part of each cycle $tempo_{start}$ was set to 600 and $tempo_{goal}$ was 400.

28 ms). In Pattern 3, there were 8 steps for each accelerando and ritardando phase, leading to three cycles (consisting of 16 steps each) of rapid and large tempo changes (successive IOI differences ranged from 10 to 44 ms) (Figure 3.2).

3.5.1.3 Procedure

The current dataset was obtained as part of a large-scale experiment examining participant's abilities to learn to tap the three different patterns of tempo change. In the experiment participants tapped the three patterns under three conditions that were presented in a fixed order. First, in a 'Melody' condition, participants tapped along with the melody line of a Bach chorale presented in a piano timbre[5]. The tempo of melody line was set to follow the tempo-changing pattern as described above (Figure 3.2). Second, in a 'Pacing signal' condition, participants synchronized their taps with the tempo-changing stimulus signals that contained a woodblock tone for each note of the chorale. Third, in a 'Free' condition, participants tapped the tempo-changing pattern by themselves in a self-paced manner without an auditory synchronization aid. All conditions started with 4 initiation tones indicating the initial tempo (600 ms IOI). During all conditions the musical notation of the chorale including the tempo changes was displayed on a computer monitor in front of to the participants. The three patterns were presented in a randomized order across participants. Each condition of each pattern started with a practice trial, followed by 15 experimental trials, each lasting 35 seconds.

Participants were seated in a quiet laboratory room and were instructed to tap the tempo changing sequences as accurately and precisely as possible. The experiment was run in Presentation (Neurobehavioral Systems, www.neurobs.com) on a Windows computer. Participants' timing was registered using a custom built tapping device that was connected to the computer via a serial connection. Auditory information was presented over headphones. Participants started each trial by pressing a key on a keyboard and could therefore pace their progression through the experiment. Short breaks between patterns were allowed. In total the experiment took 1.5-2 hours. The current article is based on the synchronized tapping data obtained in the 'Pacing signal' condition.

[5] Half, dotted, and 8th notes in the chorale were transformed, using Finale® software, into quarter notes to end up with 64 events of equal length.

3.5.1.4 *Data-analyses*

The onset times of taps were aligned offline to the closest tones of the target sequence within a ± 200 ms asynchrony window[6]. 2.6% of the recorded taps fell outside this window and were excluded from the analyses. Data analyses focused on the tempo-changing phase of the trials (grey dashed box Figure 3.2), the stable phase was used to establish synchrony between the stimulus sequence and the participants' taps [mean / standard deviation signed asynchrony (mean±sd): -18.4±16.1 / 19.1±3.5 ms (pattern 1), -17.9±16.1 / 19.3±3.8 ms (pattern 2); -24.3±16.1 / 19.0±3.3 ms (pattern 3)]. The mean signed asynchrony was calculated as an inverse measure of SMS accuracy, while the standard deviation of the signed asynchronies was used as an inverse measure of SMS precision. SMS accuracy and SMS precision measures were calculated for each trial and then averaged across repetitions of each pattern for each participant.

Before measures related to the hypothesized underlying adaptation and anticipation mechanisms were calculated, linear interpolation was used to fill missing asynchronies, unusually large ITIs, and missing ITIs resulting from skipped taps. This affected less than 1% of data. To investigate adaptation while synchronizing with tempo-changing sequences, the amount of phase and period correction implemented by the participant was estimated by means of the bGLS method (cf., Jacoby and Repp, 2012 see also Jacoby et al. *submitted* for further analysis of the method) based on the adaptation model (Schulze et al. (2005), Repp & Keller, 2008). In this model, both correction mechanisms depend on the preceding asynchrony. The bGLS method used the interpolated inter-tap intervals and corresponding asynchronies as input (A detailed description of the method can be found in Appendix I). Anticipation during synchronization with tempo changing sequences was quantified using two methods. The first was based on the lag-1 and lag-0 cross-correlations between the inter-stimulus and inter-tap intervals and the prediction/tracking ratio. The lag-0 cross-correlation between the IOIs and ITIs is high to the extent that participants anticipate the tempo changes, while the lag-1 cross-correlation is high to the extent that participants copy, or 'track', the tempo changes. This relationship reflected in the PT-ratio (lag-0/lag-1 cross-correlation) used by Pecenka and Keller (2009; 2011). A ratio bigger than 1 reflects the participant's tendency to predict the tempo change, while ratio smaller than 1 indicates that the participant tend to copy (track) the tempo changes. It has been shown that autocorrelations of time series might influence cross-correlation estimates (Dean and Bailes, 2010). Therefore, we also investigated

[6] There was a transmission delay of 10 ms between the tapping device and the registration software, which was subtracted from the recorded tap times before data analysis

the anticipation mechanisms by means of alternative PT-indices (Mills et al., *submitted*). PT-indices are based on the difference between the coefficients of two autoregressive components of the autoregressive model (Dean and Bailes, 2010; Launay et al., 2013). Prior to applying the autoregressive model, IOI and ITI time series were pre-whitened. Pre-whitening consists of identifying the autoregressive lag structure of one series, and calculating residuals after the influence of the autoregressive structure has been modeled (Dean and Bailes, 2010). The autoregressive model was then used to calculate the coefficients representing the strength of the relationship between IOIs and ITIs using pre-whitened IOI series at lag-0 and lag-1 as predictors for the pre-whitened ITI series. In a final step, the lag-1 coefficient was subtracted from the lag-0 coefficient, resulting in an index with values greater than 0 reflecting anticipation of the tempo changes in the patterns and values smaller than 0 reflecting tracking behavior (Mills et al., *submitted*).

The data were processed with MATLAB (The Mathworks Inc, MA, USA R 2011a). Statistical analyses were performed with SPSS (IBM SPSS Statistics 21). In addition to descriptive statistics, repeated measures ANOVAs were conducted to test for effects of the factors (e.g., pattern). If the assumption of sphericity was violated, the Greenhouse–Geisser correction was applied.

3.5.2 Simulations

To investigate the effect of adaptation and anticipation mechanisms on SMS precision, we ran simulations with ADAM in which parameter settings were systematically varied. We focused on SMS precision because in a previous study adaptation mechanisms were found to contribute more to SMS accuracy, while both adaptation and anticipation mechanisms predicted SMS precision (Mills et al., *submitted*). Possible links between the adaption and anticipation mechanisms were explored by creating four different versions of ADAM. The 'Adaptation Model' only implements adaptation, in the 'Independent ADAM' model adaption and anticipation mechanisms contribute independently of each other to SMS, in the 'Joint ADAM (α)' and 'Joint ADAM (β)' models adaptation and anticipation mechanisms were linked in a joint internal model. Simulations were run using MATLAB (The Mathworks Inc, MA, USA R 2011a).

3.5.2.1 Background

ADAM comprises an adaptation and anticipation module (van der Steen and Keller, 2013). The adaptation module of ADAM implements phase and period correction following the equations[7]:

$$t_{n+1} = t_n + T_n - (\alpha + \beta) * asyn_n + TK_n + M_n - M_{n-1} \quad (1)$$

$$T_{n+1} = T_n - \beta * asyn_n \quad (2)$$

The most recent asynchrony $(asyn_n)$ is multiplied by the sum of the phase (α) and period (β) correction parameters and the result is added to the current timekeeper period (T_n) (eq. 1). The timing of the next tap (t_{n+1}) by ADAM is then determined by adding this to the timing of the most recent event (t_n). Timekeeper (TK) and motor noise (M) is added so that ADAM produces human-like asynchronies (Repp and Keller, 2008). The current timekeeper period is affected by the period correction parameter (β) (eq. 2). The next timekeeper period (T_{n+1}) is given by the last asynchrony $(asyn_n)$ multiplied by the period correction parameter (β) added to the current timekeeper (T_n).

The anticipation module of ADAM bases the timing of the next tap on a temporal extrapolation process that generates a prediction about the timing of the next tone based on the most recent series of IOIs that ADAM receives as input. The predicted time of the next tone $(tone_{n+1})$ is based on Equation 3[8], where Equation 4[9] is used to determine the predicted interval (Int_{n+1}):

---

[7] The difference in sign compared to the equations in van der Steen & Keller (2013) is because in this case ADAM takes the role of participant while in the other paper ADAM presents the pacing tones.

[8] Again since the perspective of ADAM is this time from the participant's point of view the equations are slightly modified.

[9] Following the method of least squares, the line of the form $Int = a + b \cdot x$ has the smallest sum of squared errors if

$$a \cdot k + b \cdot \sum_{i=1}^{k} x_{n-k+i} = \sum_{i=1}^{k} Int_{n-k+i}$$

and

$$a \cdot \sum_{i=1}^{k} x_{n-k+i} + b \cdot \sum_{i=1}^{k} (x_{n-k+i})^2 = \sum_{i=1}^{k} (x_{n-k+i} \cdot Int_{n-k+i}) .$$

The smallest sum of squared errors is obtained if

$$b = \frac{k \cdot \sum_{i=1}^{k} x_i \cdot Int - \sum_{i=1}^{k} x_i \cdot \sum_{i=1}^{k} Int}{k \cdot \sum_{i=1}^{k} {x_i}^2 - \sum_{i=1}^{k} x_i \cdot \sum_{i=1}^{k} x_i}$$

and

$$a = \frac{1}{k} \cdot \sum_{i=1}^{k} Int_i - \frac{1}{k} \cdot b \cdot \sum_{i=1}^{k} x_i .$$

$$tone_{n+1} = tone_n + Int_{n+1} \quad (3)$$

$$Int_{n+1} = a + b * (n + 1) \quad (4)$$

$$t_{n+1} = tone_{n+1} - \alpha * asyn_n + TK_n + M_n - M_{n-1} \quad (5)$$

In equation 4, a represents the intercept and b stands for the slope of the best fitting line. Both parameters a and b depend on the number in intervals (k) used to determine the best-fitting straight line. The onset time of the next tap is set to match the predicted tone onset time. Like in the adaptation module the tap is subject to noise (eq. 5).

3.5.2.2 Models

In the 'Adaptation Model', only the adaptation module of ADAM implementing phase and period correction is active (eq. 1-2).

In the 'Independent ADAM' model, the adaptation and anticipation modules are both present but they act independently (Figure 3.11). In this model, the interval of the tap is set by means of a prediction with the anticipation module. Because predictions are not necessarily correct and the system is subject to noise, a local correction is applied to simulate the process of counteracting unintentional variability. Again it is taken into account that humans can engage in predictive (eq. 6-8) and tracking behavior at the same time (eq. 9). The interval between the current and next tone is based on an extrapolation process (as described above) based on two most recent IOIs (k = 2) (eq. 7). The anticipation module is used to determine the timing of the next tap but this tap is also subjected to phase correction (eq. 10).

In the 'Joint ADAM (α)' and 'Joint ADAM (β)' models, again both the adaptation and the anticipation modules of ADAM were active (Figure 3.11). Within a 'Joint ADAM' model the adaptation module simulates the next tap (t'_{n+1}) (eq. 11-12). In the 'Joint ADAM (α)' model this tap is only subjected to phase correction (α), while in the 'Joint ADAM (β)' model, this tap is only subjected to period correction (β) (Eq. 11-12). The anticipation module predicts when the next tone ($tone'_{n+1}$) will occur (eq. 15). This next tone is a combination of predictive behavior, i.e., extrapolation based on two most recent IOIs (k = 2) (eq. 13), and tracking behavior, which copies of the previous interval (eq. 14). Predictive and tracking processes are regulated by the prediction/tracking parameter (m) (eq. 15). Theoretically, this parameter ranges from 0 to 1, with m = 0 indicating that the model fully relied on tracking, while with an m of 1 the next tone is purely based on the prediction. The link of the adaptation and anticipation module simulates what the asynchrony (asyn'_{n+1}) between the planned next tap (t'_{n+1}) and the predicted next tone ($tone'_{n+1}$) would be (eq. 16). This simulated asynchrony is then minimized by means of an anticipatory phase correction process (γ), that influences occurrence of the next tap (t_{n+1}) (eq. 17). The appropriate motor command is then selected to execute this next tap(t_{n+1}). In both 'Joint ADAM' models potential errors are thus predicted and corrected before they could occur. The adaptation and anticipation modules are subjected to timekeeper noise (*TK*), while motor noise (*M*) affects the next tap in the link module of the joint model.

Independent ADAM

Interval prediction:

$tone'_{n+1} = tone_n + Int_{n+1}$ (6)

$Int_{n+1} = a + b * (n+1)$ (7)

$PRED_{n+1} = tone'_{n+1} - t_n$ (8)

Interval tracking:

$TRACK_{n+1} = tone_n - tone_{n-1}$ (9)

$$t_{n+1} = t_n + (m * PRED_{n+1} + (1-m) * TRACK_{n+1}) - \alpha * asyn_n + TK_n + M_n - M_{n-1} \quad (10)$$

Joint ADAM

Adaptation module*:

$t'_{n+1} = t_n + T_n - (\alpha + \beta) * asyn_n + \mathrm{TK1}_n$ (11)

$T_{n+1} = T_n - \beta * asyn_n$ (12)

* Joint ADAM (α), we assume $\beta = 0$
  Joint ADAM (β), we assume $\alpha = 0$

Anticipation module:

$IOI\_pred_{n+1} = Int_{n+1} = a + b * (n+1)$ (13)

$IOI\_track_{n+1} = tone_n - tone_{n-1}$ (14)

$tone'_{n+1} = tone_n + (m * IOI\_pred_{n+1} + (1-m) * IOI\_track_{n+1}) + \mathrm{TK2}_n$ (15)

Link module:

$\mathrm{asyn}'_{n+1} = t'_{n+1} - tone'_{n+1}$ (16)

$t_{n+1} = t'_{n+1} - ((1-\gamma) * \mathrm{asyn}'_{n+1}) + M_n - M_{n-1}$ (17)

Figure 3.11 Equations describing the 'Independent ADAM' and 'Joint ADAM (α | β)' models. α = phase correction, β = period correction, γ = anticipatory phase correction, *m* = prediction/tracking parameter. See text for explanation.

3.5.2.3 Evaluation of the models

Input values for the simulations were the onset times that correspond to three different tempo-changing patterns. For each pattern and parameter setting combination, 100 trials are simulated in MATLAB (The Mathworks Inc, MA, USA R 2011a). Timekeeper noise was sampled from a normal distribution, while motor noise was drawn from a gamma distribution (Repp and Keller, 2008). The standard deviation of asynchronies was taken as a measure of a SMS precision in simulated data. Asynchronies were computed as the difference between the onset times of simulated tones in the tempo-changing pattern and the simulated tap times, and were, by convention, negative if the simulated tap preceded the tone onset time. Parameter estimates were obtained by means of the bGLS method (Repp et al., 2012; Jacoby et al., 2013; Jacoby et al. *submitted*). The method is based on re-writing each model in a matrix notation. Based on this notation a solution to a generalized regression problem is found, with certain constraints imposed on the parameter spaces (Appendix I). Furthermore, we used an adjusted asynchrony that is the asynchrony minus the mean asynchrony. Due to parameter interdependence in the joint models it was necessary to restrict the parameter space in order to obtain reliable and unbiased estimates. For the 'Joint ADAM (α)' model, α values were restricted to the range $-0.8 < \alpha < -0.1$.For the 'Joint ADAM (β)' both β and m were restricted ($0 < \beta, m < 1$, see Appendix I). The fit of the model is determined by the likelihood estimate. The likelihood of the model is related to the generalized sum of squares and defined as $LL=\log_2(p(data|model))$, where p is the probability. A less negative and smaller in absolute value indicated a better fit between the behavioral data and the model. When calculating the likelihood, the same data and number of estimated parameters were included for all models. Therefore, for both joint models, the motor noise parameter was set to zero.

3.6 ACKNOWLEDGMENTS

We thank Felix Haiduk, Kerstin Traeger, and Maria Bader for their help preparing and running the behavioral experiment. We thank Twan Dollevoet for his help with re-formulating the equations for the bGLS method and his comments on an earlier version of the manuscript.

This work was supported by funding from the European Community's Seventh Framework Programme under the EBRAMUS project - grant agreement n° 238157. The funders had no role in study design, data collection and analysis, decision to publish, or preparation of the manuscript.

3.7 REFERENCES

Dean, R.T., Bailes, F., 2010. Time series analysis as a method to examine acoustical influences on real-time perception of music. Empir. Musicol. Rev. 5, 152-175.

Drake, C., Penel, A., Bigand, E., 2000. Tapping in time with mechanically and expressively performed music. Music Percept. 18, 1-23.

Friberg, A., Sundberg, J., 1995. Time discrimination in a monotonic, isochronous sequence. *J. Acoust. Soc. Am.* 98, 2524-2531.

Hary, D., Moore, G.P., 1987. Synchronizing human movement with an external clock source. Biol. Cybern. 56, 305-311.

Jacoby, N., Repp, B.H., 2012. A general linear framework for the comparison and evaluation of models of sensorimotor synchronization. Biol. Cybern. 106, 135-154.

Jacoby, N., Keller, P.E., Repp, B.H., Ahissar, M., Tishby N., (*submitted*). Parameter estimation of linear sensorimotor synchronization models: phase correction, period correction and ensemble synchronization.

Keller, P.E., 2008. Joint action in music performance, in: Morganti, F., Carassa, A., Riva, G. (Eds.), Enacting intersubjectivity: a cognitive and social perspective to the study of interactions. IOS Press, Amsterdam, the Netherlands, pp. 205-221.

Large, E.W., Fink, P., Kelso, J.A.S., 2002. Tracking simple and complex sequences. Psychol. Res. 66, 3-17.

Launay, J., Dean, R.T., Bailes, F., 2013. Evidence for multiple strategies in off-beat tapping with anisochronous stimuli. Psychol. Res. doi: 10.1007/s00426-013-0513-9 [Epub ahead of print].

Madison, G., Merker, B., 2005. Timing of action during and after synchronization with linearly changing intervals. Music Percept. 22, 441–459.

Mates, J., 1994a. A model of synchronization of motor acts to a stimulus sequence: I. Timing and error corrections. Biol. Cybern. 70, 463-473.

Mates, J., 1994b. A model of synchronization of motor acts to a stimulus sequence: II. Stability analysis, error estimation and simulations. Biol. Cybern. 70, 475-484.

Michon, J.A., 1967. Timing in temporal tracking. Van Gorcum, Assen, the Netherlands.

Mills, P.F., Van der Steen, M.C., Schultz, B.G., Keller, P.E. (*submitted*). The relationship between temporal anticipation and adaptation during sensorimotor synchronization.

Palmer, C. (1997). Music performance. *Annu. Rev. Psychol. 48,* 155-138.

Pecenka, N., Keller, P.E., 2009. Auditory pitch imagery and its relationship to musical synchronization. Ann. NY. Acad. Sci. 1169, 282-286.

Pecenka, N., Keller, P.E., 2011. The role of temporal prediction abilities in interpersonal sensorimotor synchronization. Exp. Brain Res. 211, 505-515.

Pecenka, N., Engel, A., Keller, P.E., 2013. Neural correlates of auditory temporal predictions during sensorimotor synchronization. Front. Hum. Neurosci. 7:380. doi: 10.3389/fnhum.2013.00380

Rankin, S.K., Large, E.W., Fink, P.W., 2009. Fractal tempo fluctuation and pulse prediction. Music Percept. 26, 401-413.

Repp, B.H., 1998. A microcosm of musical expression. I. Quantitative analysis of pianists' timing in the initial measures of Chopin's Etude in E major. J. Acoust. Soc. Am. 104, 1085-1100.

Repp, B.H., 2001a. Phase correction, phase resetting, and phase shifts after subliminal timing perturbations in sensorimotor synchronization. J. Exp. Psychol. Hum. Percept. Perform. 27, 600-621.

Repp, B.H., 2001b. Processes underlying adaptation to tempo changes in sensorimotor synchronization. Hum. Movement Sci. 20, 277-312.

Repp, B.H., 2002a. The embodiment of musical structure: Effects of musical context on sensorimotor synchronization with complex timing patterns, in: Prinz, W., Hommel, B. (Eds.), Common mechanisms in perception and action: Attention and Performance XIX. Oxford University Press, Oxford, U.K., pp. 245-265.

Repp, B.H., 2002b. Automaticity and voluntary control of phase correction following event onset shifts in sensorimotor synchronization. J. Exp. Psychol. Hum. Percept. Perform. 28, 410-430.

Repp, B.H., 2005. Sensorimotor synchronization: A review of the tapping literature. Psychon. B. Rev. 12, 969-992.

Repp, B. H., 2006. Musical synchronization, in: Altenmüller, E., Wiesendanger, M., Kesselring, J. (Eds.), *Music, motor control, and the brain*. Oxford University Press, Oxford, UK, pp. 55–76.

Repp, B.H., 2008. Metrical subdivision results in subjective slowing of the beat. *Music Percept. 26,* 19-39.

Repp, B.H., Bruttomesso, M., 2009. A filled duration illusion in music: Effects of metrical subdivision on the perception and production of beat tempo. *Adv. Cogn. Psychol. 5,* 114-134.

Repp, B. H., Keller, P.E., 2004. Adaptation to tempo changes in sensorimotor synchronization: Effects of intention, attention, and awareness. Q. J. Exp. Psychol. 57A, 499-521.

Repp, B.H., Keller, P.E., 2008. Sensorimotor synchronization with adaptively timed sequences. Hum. Movement Sci. 27, 423-456.

Repp, B.H., Keller, P.E., Jacoby, N., 2012. Quantifying phase correction in sensorimotor synchronization: empirical comparison of three paradigms. Acta Psychol. 139, 281-290.

Schulze, H.-H., Cordes, A., Vorberg, D., 2005. Keeping synchrony while tempo changes: accelerando and ritardando. Music Percept. 22, 461-477.

Schmidt, R.A. 1968. Anticipation and timing in human motor performance. Psychol. Bull. 70, 631-646.

Semjen, A., Vorberg, D., Schulze, H.-H., 1998. Getting synchronized with the metronome: Comparisons between phase and period correction. Psychol. Res. 61, 44-55.

Thaut, M.H., Miller, R.A., Schauer, L.M., 1998a. Multiple synchronization strategies in rhythmic sensorimotor tasks: phase vs period correction. Biol. Cybern. 79, 241-250.

Thaut, M.H., Tian, B., Azimi-Sadjadi, 1998b. Rhythmic finger tapping to cosine-wave modulated metronome sequences: Evidence of subliminal entrainment. Hum. Mov. Sci. 17, 839-863.

Thaut, M.H., Stephan, K.M., Wunderlich, G., Schicks, W., Tellmann, L., Herzog, H., McIntosh, G.C., Seitz, R.J., Hömber, V., 2009. Distinct cortico-cerebellar activations in rhythmic auditory motor synchronization. Cortex. 45, 44-53.

Van der Steen, M.C., Keller, P.E., 2013. The Adaptation and Anticipation Model (ADAM) of sensorimotor synchronization. Front. Hum. Neurosci. 7:253. doi: 10.3389/fnhum. 2013.00253

Vorberg, D., Wing, A., 1996. Modeling variability and dependence in timing, in Heuer, H., Keele, S.W. (Eds.), Handbook of perception and action Vol. 2. Academic Press, London, UK, pp. 181-262.

Vorberg, D., Schulze, H-H., 2002. A two-level timing model for synchronization. J. Math. Psychol. 46, 56-87.

Wing, A.M., 1980. The long and short of timing in response sequences, in: Stelmach, G.E., Requin, J. (Eds.), Tutorials in motor behavior. North-Holland, Amsterdam, pp. 469-486.

Wing, A.M., Kristofferson, A.B., 1973. Response delays and the timing of discrete motor responses. Percept. Psychophys. 14, 5-12.

Wing, A.M., Endo, S., Bradbury, A., Vorberg, D., 2014. Optimal feedback correction in string quartet synchronization. J. R. Soc. Interface, 11, 20131125. http://dx.doi.org/10.1098/rsif.2013.1125

Wolpert, D. M., Doya, K., Kawato, M., 2003. A unifying computational framework for motor control and social interaction. Philos. T. Roy. Soc. B. 358, 593-602.

Wolpert, D. M., Kawato, M., 1998. Multiple paired forward and inverse models for motor control. Neural Networks. 11, 1317-1329.

Appendix I – estimating the model parameters with the bGLS method.

We used the bGLS method to estimate the models' parameters (Repp et al., 2012; Jacoby et al., 2013; Jacoby et al. *submitted*). The method is based on re-writing the model in matrix notation. Based on this notation a generalized regression problem is solved, with certain constraints imposed on the parameter space.

In order to match the notation of Jacoby et al. (*submitted*) we will introduce slightly different notation to that used in the main body of the article.

We denote by $S(n)$, $R(n)$ the stimulus and response onsets at time n, respectively. We denote by $s(n)$ and $r(n)$ the inter-stimulus and inter-response intervals, respectively. We denote by $e(n)$ the asynchrony: $e(n)=R(n)-S(n)$. This leads to the following relations:

A1) $tone_n = S(n),$
A2) $IOI = s(n),$
A3) $t_n = R(n),$
A4) $ITI = r(n),$
A5) $asyn_n = e(n).$

We denote by $z(n)$ the noise at time n. The assumption is that z has two components: a motor and a time keeper variance, similar to the model of Vorberg and Wing (1996).

A6) $z(n) = TK(n) + M(n) - M(n-1),$

where $TK(n)$ and $M(n)$ are the timekeeper and motor noises with variance σ_T^2 and σ_M^2, respectively.

We will focus on the model where the prediction is based on the two recent intervals (k=2). In this case it follows that the slope the best fit equals $s(n) - s(n-1)$. Hence,

A7) $Int_{n+1} = s(n) + \big(s(n) - s(n-1)\big) = 2 * s(n) - s(n-1).$

In what follows we rewrite Joint ADAM (α), Joint ADAM (β), and Independent ADAM as a bGLS regression model.

Joint ADAM (α)

ADAPTATION module:

$t\_adap_{n+1} = t_n + T_n - (\alpha + \beta) * asyn_n + \mathrm{TK1}_n$

$T_{n+1} = T_n - \beta * asyn_n$

We assume $[\beta = 0]$, thus $T_{n+1} = T_n = T_0$

ANTICIPATION module:

$IOI\_pred_{n+1} = Int_{n+1} = a + b * (n+1)$

$IOI\_track_{n+1} = tone_n - tone_{n-1}$

$tone\_anti_{n+1} = tone_n + (m * IOI\_pred_{n+1} + (1-m) * IOI\_track_{n+1}) + \mathrm{TK2}_n$

LINK module:

$\mathrm{asyn_{joint}} = t\_adap_{n+1} - tone\_anti_{n+1}$

$t_{n+1} = \mathrm{t}_{adap_{n+1}} - ((1-\gamma) * \mathrm{asyn_{joint}}) + M_{noise}$

Using the new notation and $T_n = T_0$ for all n, we write:

ADAPTATION module:

A8) $t\_adap_{n+1} = R(n) + T_0 - \alpha * e(n) + TK1(n)$

ANTICIPATION module:

A9) $IOI\_pred_{n+1} = Int_{n+1} = a + b * (n+1) = 2s(n) - s(n-1)$

A10) $IOI\_track_{n+1} = tone_n - tone_{n-1} = s(n)$

A11) $tone\_anti_{n+1} = \mathrm{S(n)} + \big(m * (2s(n) - s(n-1)) + (1-m) * s(n)\big) + TK2(n)$
$= S(n) + (m+1)s(n) - m * s(n-1) + TK2(n)$

LINK module:

A12) $\mathrm{asyn_{joint}} = t_{adap_{n+1}} - tone_{anti_{n+1}}$
$= [R(n) + T_0 - \alpha * e(n) + TK1(n)]$
$-[S(n) + (m+1)s(n) - m * s(n-1) + TK2(n)]$
$= (1-\alpha)e(n) + T_0 - (m+1)s(n) + m * s(n-1) + TK1(n) - TK2(n)$

A13) $t_{n+1} = \mathrm{t}_{adap_{n+1}} - \big((1-\gamma) * \mathrm{asyn_{joint}}\big) + M_{noise}$
$= [R(n) + T_0 - \alpha * e(n) + TK1(n)] + M(n) - M(n-1)$
$-\big((1-\gamma)$
$* [(1-\alpha)e(n) + T_0 - (m+1)s(n) + m * s(n-1) + TK1(n) - TK2(n)]\big)$

This can be written as:

A14) $r(n+1) + (-\gamma)\mathrm{T_0}$
$= (-1 + \gamma - \alpha\gamma)\mathrm{e(n)} + [(1-\gamma)(1+m)]\mathrm{s(n)}$
$+[(-1+\gamma)m] * s(n-1) + [\gamma\, TK1(n) + (1-\gamma)\, TK2(n) + M(n) - M(n-1)]$
$= (1-\gamma)m * [s(n) - s(n-1)] + (1-\gamma)\,[s(n) - e(n)] + (\alpha\gamma)\big(-e(n)\big) + z(n)$,

where $z(n) = [\gamma TK1(n) + (1-\gamma)TK2(n) + m(n)] = TK3(n) + m(n)$.

Define now:

A15) $x_1 = (1-\gamma)m$,

A16) $x_2 = (1-\gamma)$,

A17) $x_3 = \alpha\gamma$,

A18) $\sigma^2_{TK3} = (1 + 2\gamma^2 - 2\gamma)\sigma^2_T$.

From this it follows that:

A19) $\gamma = (1 - x_2)$,

A20) $m = \frac{x_1}{1-\gamma} = x_1/x_2$,

A21) $\alpha = \frac{x_3}{\gamma} = \frac{x_3}{1-x_2}$,

A22) $\sigma^2_T = \sigma^2_{TK3}/(1 + 2\gamma^2 - 2\gamma)$.

In this model it is essential to assume that *mean(e)=0* and that *mean(s)=mean(r)=T_0*. To ensure that this holds we subtract the empirical mean of e from e before we start.

Now we can write the Joint ADAM (α) with the new parameterization as:

$$b = \begin{bmatrix} r'(3) \\ \vdots \\ r'(n+1) \end{bmatrix} = A * x + z = \begin{bmatrix} s'(2) - s'(1) & s'(2) - e'(2) & -e'(2) \\ \vdots & \vdots & \vdots \\ s'(n) - s'(n-1) & s'(n) - e'(n) & -e'(n) \end{bmatrix} \begin{bmatrix} x_1 \\ x_2 \\ x_3 \end{bmatrix} + \begin{bmatrix} z(2) \\ \vdots \\ z(n) \end{bmatrix}$$

In this equation we assume that we reduced the empirical mean from the vectors so that: *mean(e')=mean(s')=mean(r')=0*.
We can solve this model using the bGLS method, and then project back to original parameters space using equations (A19)-(A22).
Note that in the bGLS method we use the assumption that: $\sigma_T^2 > \sigma_M^2$. This assumption is essential because otherwise parameter interdependence deteriorate the estimation accuracy (Jacoby et al. *submitted)*.
However, for this model, this assumption is not enough to avoid parameter interdependence. This causes relatively large estimation errors for the parameter alpha. The negative effect of this problem can be reduced using further assumptions on the parameter space, similar to the assumption that $\sigma_T^2 > \sigma_M^2$ used in the original bGLS method (e.g Repp, Keller and Jacoby 2012). The idea is to restrict the possible α values to a smaller range for example:

$$L < \alpha < H,$$

where L=-0.8 and H=-0.1. This range is determined based on simulations. This, therefore, implies that:

$$L < \frac{x_3}{1 - x_2} < H.$$

Within the bGLS iterations, if $\frac{x_3}{1-x_2} < L$ or $\frac{x_3}{1-x_2} > H$, we change x_3 so that the result is in the right range. This of course imposes further restrictions on the parameters that the estimation method can detect, but significantly reduces the estimation error variance.

Joint ADAM (β)

ADAPTATION module:

$t\_adap_{n+1} = t_n + T_n - (\alpha + \beta) * asyn_n + TK1_n$

$T_{n+1} = T_n - \beta * asyn_n$

We assume $[\alpha = 0]$.

ANTICIPATION module:

$IOI\_pred_{n+1} = Int_{n+1} = a + b * (n + 1)$

$IOI\_track_{n+1} = tone_n - tone_{n-1}$

$tone\_anti_{n+1} = tone_n + (m * IOI\_pred_{n+1} + (1 - m) * IOI\_track_{n+1}) + TK2_n$

LINK module:

$\mathrm{asyn_{joint}} = t\_adap_{n+1} - tone\_anti_{n+1}$

$t_{n+1} = \mathrm{t}_{adap_{n+1}} - ((1 - \gamma) * \mathrm{asyn_{joint}}) + M_{noise}$

Using the new notation, we write:

ADAPTATION module:

A23) $t\_adap_{n+1} = R(n) + T_n - (\alpha + \beta) * e(n) + TK1(n),$

A24) $T_n = T_0 - \beta * \sum_{N=1}^{n-1} e(N)$

ANTICIPATION module:

A25) $IOI\_pred_{n+1} = Int_{n+1} = a + b * (n+1) = 2s(n) - s(n-1)$

A26) $IOI\_track_{n+1} = tone_n - tone_{n-1} = s(n)$

A27) $tone\_anti_{n+1} = S(n) + \Big(m * \big(2s(n) - s(n-1)\big) + (1-m) * s(n)\Big) + TK2(n)$

$= S(n) + (m+1)s(n) - m * s(n-1) + TK2(n)$

LINK module:

A28) $\text{asyn}_{\text{joint}} = t_{adap_{n+1}} - tone_{anti_{n+1}}$

$= [\mathrm{R(n)} + T_n - (\alpha + \beta) * \mathrm{e(n)} + \mathrm{TK}_1(n)] - [S(n) + (m+1)s(n) - m * s(n-1) +$
$TK2(n)]$

$= (1-\alpha)e(n) + T_n - \beta e(n) - (m+1)s(n) + m * s(n-1) + TK1(n) - TK2(n)$

$=(1-\alpha)e(n) + T_0 - \beta * \sum_{N=1}^{n-1} e(N) - \beta e(n) - (m+1)s(n) + m * s(n-1)$
$+TK1(n) - TK2(n)$

A29) $t_{n+1} = \mathrm{t}_{adap_{n+1}} - ((1-\gamma) * \text{asyn}_{\text{joint}}) + M_{noise}$

$= R(n) + T_0 - \beta * \sum_{N=1}^{n-1} e(N) - (\alpha + \beta) * e(n) + TK1(n) + M(n) - M(n-1)$
$-((1-\gamma) * (1-\alpha)e(n) + T_0 - \beta * \sum_{N=1}^{n-1} e(N) - \beta e(n)$
$-(m+1)s(n) + m * s(n-1) + TK1(n) - TK2(n))$

This can be written as:

A30) $r(n+1) + (-\gamma)T_0 = (1-\gamma)m * [s(n) - s(n-1)] + (1-\gamma)\,[s(n) - e(n)] +$
$(\alpha\gamma)\big(-e(n)\big)$

$$-\gamma\beta \sum_{N=1}^{n} e(N) + z(n),$$

where $z(n) = [\gamma\, TK1(n) + (1-\gamma)TK2(n) + m(n)] = TK3(n) + m(n)$.

Define now

A31) $x_1 = (1-\gamma)m,$

A32) $x_2 = (1-\gamma),$

A33) $x_3 = \beta\gamma,$

A34) $\sigma_{TK3}^2 = (1 + 2\gamma^2 - 2\gamma)\sigma_T^2.$

From this it follows that:

A35) $\gamma = (1 - \mathrm{x}_2),$

A36) $m = \frac{x_1}{1-\gamma} = x_1/x_2,$

A37) $\beta = \frac{x_3}{\gamma} = \frac{x_3}{1-x_2},$

A38) $\sigma_T^2 = \sigma_{TK3}^2/(1 + 2\gamma^2 - 2\gamma).$

In this model it is essential to assume that *mean(e)=0* and that *mean(s)=mean(r)=*T_0. To ensure that this holds we reduce the empirical mean of e from e before we start.

Now we can write the Joint ADAM (β) with the new parameterization as:

$$b = \begin{bmatrix} r'(3) \\ \vdots \\ r'(n+1) \end{bmatrix} = A * x + z = \begin{bmatrix} s'(2) - s'(1) & s'(2) - e'(2) & -\sum_{n=1}^{2} e'(n) \\ \vdots & \vdots & \vdots \\ s'(n) - s'(n-1) & s'(n) - e'(n) & -\sum_{n=1}^{n} e'(n) \end{bmatrix} \begin{bmatrix} x_1 \\ x_2 \\ x_3 \end{bmatrix} + \begin{bmatrix} z(2) \\ \vdots \\ z(n) \end{bmatrix}$$

In this equation we assume that we reduced the empirical mean from the vectors so that: *mean(e')=mean(s')=mean(r')=0*.
We can solve this model using the bGLS method, and then project back to original parameters space using equations (A35)-(A38). Unfortunately this gives relatively large estimation error for the parameter β (as was the case with α).

Again, this problem is generated because of the parameter interdependence of the model. The negative effect of this problem can be reduced by restricting the possible β values to a smaller range for example:

$$L < \beta < H,$$

where $L = 0$ and $H = 1$

This, therefore, implies that:

$$L < \frac{x_3}{1 - x_2} < H$$

Within the bGLS iterations, if $\frac{x_3}{1-x_2} < L$ or $\frac{x_3}{1-x_2} > H$, we change x_3 so that the result is in the right range. Furthermore, we restrict m to the same range.

$$L < m < H$$

$$L < x_1/x_2 < H$$

If x_2 is positive:

$$x_2 L < x_1 < x_2 H$$

This of course imposes further restrictions on the parameters that the estimation method can detect but significantly reduces the estimation error variance.
Note that like any bGLS estimates we also assume that $\sigma_T^2 > \sigma_M^2$.

Independent ADAM

Interval prediction:

$Int_{n+1} = a + b * (n+1)$

$PRED_{n+1} = tone'_{n+1} - t_n$

$tone'_{n+1} = tone_n + Int_{n+1}$

Interval tracking:

$TRACK_{n+1} = tone_n - tone_{n-1}$

$$t_{n+1} = t_n + (m * PRED_{n+1} + (1-m) * TRACK_{n+1}) - \alpha * asyn_n + TK_n + M_n - M_{n-1}$$

Using the new notation we write:

A39) $PRED_{n+1} = tone'_{n+1} - t_n = S(n) + 2s(n) - s(n-1) - R(n) = 2s(n) - s(n-1) - e(n)$

A40) $tone'_{n+1} = tone_n + Int_{n+1} = S(n) + 2s(n) - s(n-1)$

A41) $TRACK_{n+1} = tone_n - tone_{n-1} = S(n) - S(n-1) = s_n$

A42) $$t_{n+1} = t_n + (m * PRED_{n+1} + (1-m) * TRACK_{n+1}) - \alpha * asyn_n + noise$$
$$= R(n) + (m * (2s(n) - s(n-1) - e(n)) + (1-m) * s(n)) - \alpha * e(n) + z(n)$$

This can be written as:

A43) $r(n+1) = m\,[s(n) - s(n-1) - e(n)] + \alpha(-e(n)) + s(n) + z(n)$

The hybrid model can be written therefore in matrix notation as:

$$b = \begin{bmatrix} r(3) - s(2) \\ \vdots \\ r(n+1) - s(n) \end{bmatrix} = A * x + z = \begin{bmatrix} s(2) - s(1) - e(1) & -e(2) \\ \vdots & \vdots \\ s(n) - s(n-1) - e(n) & -e(n) \end{bmatrix} \begin{bmatrix} m \\ \alpha \end{bmatrix} + \begin{bmatrix} z(2) \\ \vdots \\ z(n) \end{bmatrix}$$

This formulation can be again solved with the bGLS method.

For one block of the experiment, the method provided unbiased estimates for large values of *m*. For small values of *m* more bias is observed in the α parameters and the estimation error is relatively large. We increased the accuracy of estimates by averaging over the 15 repetitions for each pattern.

Chapter 4

MANUSCRIPT 3

Basic timing abilities stay intact in patients with musician's dystonia

M.C. (Marieke) van der Steen[1,2], Floris T. van Vugt[2,3], Peter. E. Keller[1,4], Eckart Altenmüller[2]

[1] Max Planck Institute for Human Cognitive and Brain Sciences, Research Group "Music Cognition & Action", Leipzig, Germany

[2] Institute of Music Physiology and Musicians' Medicine, University of Music, Drama and Media, Hanover, Germany

[3] Lyon Neuroscience Research Center CNRS-UMR 5292, INSERM U1028, University Lyon-1, Lyon, France

[4] The MARCS Institute, University of Western Sydney, Sydney, Australia

Published in

***PLoS ONE,* 9(3): e92906. doi: 10.1371/journal.pone.0092906**

4.1 ABSTRACT

Task-specific focal dystonia is a movement disorder that is characterized by the loss of voluntary motor control in extensively trained movements. Musician's dystonia is a type of task-specific dystonia that is elicited in professional musicians during instrumental playing. The disorder has been associated with deficits in timing. In order to test the hypothesis that basic timing abilities are affected by musician's dystonia, we investigated a group of patients (N=15) and a matched control group (N=15) on a battery of sensory and sensorimotor synchronization tasks. Results did not show any deficits in auditory-motor processing for patients relative to controls. Both groups benefited from a pacing sequence that adapted to their timing (in a sensorimotor synchronization task at a stable tempo). In a purely perceptual task, both groups were able to detect a misaligned metronome when it was late rather than early relative to a musical beat. Overall, the results suggest that basic timing abilities stay intact in patients with musician's dystonia. This supports the idea that musician's dystonia is a highly task-specific movement disorder in which patients are mostly impaired in tasks closely related to the demands of actually playing their instrument.

Keywords: musician's dystonia – timing abilities – sensorimotor synchronization – perceptual timing – machine learning

4.2 INTRODUCTION

Task-specific focal dystonia is a movement disorder that manifests itself as a loss of voluntary motor control in extensively trained movements [1-4]. Although this type of dystonia clearly impairs patients' ability to perform certain movements, it has been suggested that movement processing, planning, somatosensory functions and aspects of timing are also affected [5-6]. A well-known example of task-specific focal hand dystonia is writer's cramp. When picking up a pen or writing some words, dystonic postures of the hand occur that disrupt the speed and accuracy of writing [7]. Another form of task-specific dystonia is musician's dystonia (MD), which is characterized by impairments related to instrumental playing in professional musicians. With an estimated one percent of professional musicians being affected by MD, the prevalence of MD is much higher compared to other forms of focal dystonia in the general population [1]. This article focusses on the form of MD that affects the fingers and/or hand, leaving aside embouchure dystonia that affect the coordination of lips, tongue, facial and cervical muscles of brass and wind players. Typically the cramping, co-contractions of antagonist muscle groups that accompany the loss of motor control, as well as the dystonic postures during instrumental playing, occur without pain (although muscle aching can occur after lasting spasms) [1, 8]. In piano playing MD disrupts the fluidity of movements related to instrumental playing [9]. Furthermore, MD affects individuated finger movements, as evidenced by more forceful keystrokes and abnormal temporal control of the keystrokes [10]. For the affected musicians the disorder is very disabling and often signifies the end of a musical career [8]. Furthermore, as time passes, MD patients may show overflow of impairments to other tasks, such as hand writing or typing on a keyboard [11-13]. Several therapies are available to MD patients such as botulinum toxin injections [14] and behavioural retraining [13]. These therapies seem to have positive effect in about half of the patients but, unfortunately, the disorder often forces musicians to change profession [14].

The pathophysiology of MD is still unclear but both functional and structural abnormalities (i.e., maladaptive plasticity) in motor-related cortical and subcortical regions (e.g., primary motor cortex, supplementary motor area, basal ganglia and cerebellum) have been linked with focal hand dystonia [15-18]. For example, blurred or even overlapping somatosensory representations of the single fingers have been found in MD-patients [1]. Functional abnormalities have been shown both in relation to task-specific movements (guitar playing, writing) [19-20] and more general tasks, like finger tapping [21]. Furthermore, focal hand dystonia (MD and writer's cramp) patients showed reduced central nervous surround inhibition in the finger muscles when investigated with motor cortex stimulation [22-23]. In addition to these altered inhibition patterns at different levels of the central nervous system, alterations in sensorimotor integration play a role in focal hand dystonia [24-26].

The brain areas that show abnormalities in MD patients have previously been shown to be critical for different aspects of timing. Extensive networks of brain regions have been linked with sensorimotor synchronization, temporal processing, and the evaluation of temporal structures. Brain areas typically implicated with these types of timing behavior are the primary sensorimotor cortices, the inferior parietal cortex, supplementary motor area, the cerebellum, and the basal ganglia [e.g., 27-28]. Problems due to disorders (e.g. Parkinson's disease) and lesions in these areas (e.g., the basal ganglia) have shown to compromise timing behavior [29-30]. The overlap in brain areas that show abnormalities in focal hand dystonia patients and the brain areas involved in sensorimotor synchronization-timing tasks made us hypothesize that MD patients might show impaired timing abilities.

Indeed, some previous studies found that focal hand dystonia patients have impaired perceptual timing and temporal processing abilities. For example, Lim and colleagues [3] had healthy controls, writer's cramp and MD patients, away from their instrument, judge whether a sequence of six brief pulses (auditory and tactile stimuli) appeared to be regular or not. The interval between the fifth and sixth pulse varied, creating regular and irregular sequences. Results showed that compared to controls, MD patients were less sensitive to these timing irregularities, both in the tactile and auditory domain. The writer's cramp patients did not show this impairment. A large study investigated somatosensory temporal discrimination in patients with various forms of focal dystonia by means of paired stimuli with an increasing inter-stimulus interval to the skin on different body parts. Like other groups of patients with focal dystonia, the patients with writer's cramp showed higher discrimination thresholds compared to healthy control subjects [31]. Further abnormalities of tactile temporal discrimination have been reported in writer's cramp patients [32]. However, it remains unclear what aspects of timing are affected by dystonia. Especially considering that timing is a multifaceted capacity that ranges from purely perceptual discrimination abilities to sensorimotor synchronization [33].

The extent to which dystonia is task-specific is a matter of debate. On the one hand, writer's cramp and MD patients have been found to show impairments in fine motor control tasks other than instrumental playing [11-13, 34, 35]. Furthermore, differences in brain activations have been found without the occurrence of dystonic movements [21]. On the other hand, MD is mainly seen as a task-specific disorder that impairs instrumental playing severely [1]. The disturbed temporal accuracy found in MD-patients during piano playing is most likely due to dystonic movements and not due to timing errors in temporal processing [9]. Furthermore, significant different activations between writer's cramp patients and healthy controls in writing with a pencil have been shown; whereas no difference between the patients and controls during writing with their finger were found [36]. This finding shows that dystonic symptoms may only be evoked during particular tasks.

The foregoing raises two mutually exclusive hypotheses. Firstly, if MD is also characterized by basic timing problems, then these problems should also occur when we test patients' timing abilities away from the instrument. Alternatively, if MD patients' impairments are mostly related to instrumental playing, then their basic timing perception and production capacities should be intact. The current study employs a battery of auditory-motor tasks to investigate basic timing-abilities of MD patients away from their instrument. If MD patients do not show impaired behavior on these tasks, this would support the task-specific nature of MD.

To test these hypotheses, we employed battery of auditory-motor tasks focusing on basic perceptual and action aspects of timing relevant for music making. The battery aims to separate purely perceptual timing capacities from timing production. Although the tasks included in the battery are not standard in clinical practice, all of them have been successfully employed in basic research on individual differences in perceptual and action aspects of sensorimotor timing in musicians [37-42].

Sensorimotor synchronization is the temporal coordination of an action with events in a predictable external rhythm. This fundamental human skill contributes to successful motor control in daily life and is important for musicians, because it plays an important role during ensemble music production. Precise and flexible sensorimotor synchronization requires mechanisms that enable an individual to adapt to timing variations and to anticipate tempo changes [43-45]. These underlying mechanisms were assessed in our task battery.

Furthermore, we used machine learning techniques to investigate whether MD patients are characterized by non-linear combinations of the timing abilities assessed in the battery. It has been suggested previously that instrument-specific performance differences between dystonia and control participants exist in particular combinations of timing variables instead of individual variables [10]. We extend this result to non-instrument-specific timing variables, investigating whether (non-linear) combinations of the timing variables measured here would identify patients and controls. To this end, we tested various supervised machine learning approaches in order to ascertain whether we could recognize patients by a signature consisting of various timing ability scores. If patients show the hypothesized timing impairments, the present battery of tests would enable us to pinpoint at what stage of auditory-motor processing the deficit occurs. Furthermore, the machine learning approaches should be able to differentiate between MD patients and healthy controls based on the hypothesized pathological behaviors. If, on the contrary, no differences between MD patients and the matched control group are found, this would be in favor of the view that MD is mostly a task-specific motor impairment.

4.3 METHODS

4.3.1 Participants

Fifteen patients (age 36.47 ± 12.01 yrs., four females) with musicians' dystonia participated in the study. Patients were recruited from the outpatient clinic of the Institute of Music Physiology and Musicians' Medicine at the Hannover University of Music, Drama, and Media between February and June 2013. All patients were professional musicians between 18 and 65 years old. Inclusion criteria were right-handed patients with focal hand dystonia and isolated curling of the thumb, middle, ring or little finger when playing their instruments. Excluded were patients with embouchure dystonia, additional neurological problems or patients in which the right index finger was affected. All patients were diagnosed by a neurologist (author E.A.) specialised in movement disorders of musicians. For those patients who, prior to the experiment, received a botulinum toxin treatment (n = 6), the last injection was two to 24 months ago (8.6 ± 8.3 months). This amount of time suggests that the effect of the injection had worn off by time the experiment took place. A description of the patients can be found in Table 4.1. The control group of 15 professional musicians without musicians' dystonia (age 36.13 ± 12.59 yrs., five females) were matched to the patients as closely as possible for age, gender, handedness and musical instrument (Table 4.1).

According to the laterality score from the Edinburgh Handedness Inventory all participants except one control participant (-100, fully left handed) were right handed (patients: 75.33 ± 13.98 / controls: 79.90 ± 18.77). The study was approved by the local ethics committee of the Hannover Medical University. Following the Declaration of Helsinki, experimental procedures were explained to all participants and written informed consent was obtained prior to participation in the experiment. Control participants received a compensatory fee for their participation in the study.

Table 4.1 Description of the participants.

Participant	Gender	Age	Main instrument	Cumulative practice time ($x10^3$ hours)	Experience (years)	Affected finger*		Months affected	Severity Score**	Self-rated playing ability***
p1	Male	40	Clarinet	13.10	30	4	Right hand	238	60%	80%
p2	Male	40	Clarinet	33.60	31	3	Left hand	150	90%	75%
p3	Female	23	Violin	20.20	18	4	Left hand	24	70%	60%
p4	Male	29	Piano	33.42	24	1	Right hand	27	70%	10%
p5	Male	19	Flute	9.04	12	4	Left hand	20	80%	50%
p6	Male	31	Guitar	26.21	20	3	Left hand	47	70%	65%
p7	Male	26	Cembalo	20.08	20	4	Right hand	20	80%	50%
p8	Male	43	Piano	24.20	30	3	Left hand	211	80%	80%
p9	Male	35	Guitar	23.10	22	4	Left hand	15	60%	20%
p10	Male	31	Piano	21.37	15	3	Right hand	19	90%	65%
p11	Male	55	Flute	78.35	45	4	Left hand	110	90%	70%
p12	Male	51	Guitar	50.04	39	4	Left hand	58	80%	70%
p13	Female	58	Violin	81.18	54	4	Left hand	125	90%	80%
p14	Female	52	Piano	51.50	38	4	Left hand	15	70%	30%
p15	Female	23	Guitar	5.57	13	3	Right hand	24	60%	25%
c1	Male	44	Clarinet	20.98	37					
c2	Male	42	Clarinet	9.33	32					
c3	Female	21	Violin	11.51	15					
c4	Male	30	Piano	30.43	23					
c5	Female	20	Flute	5.75	13					
c6	Male	29	Guitar	8.58	20					
c7	Male	25	Piano	11.28	20					
c8	Male	40	Piano	61.45	33					
c9	Male	35	Guitar	20.82	25					
c10	Male	31	Piano	14.70	26					
c11	Male	56	Flute	36.34	44					
c12	Male	55	Guitar	70.86	45					
c13	Female	54	Violin	20.64	46					
c14	Female	38	Piano	67.62	34					
c15	Female	22	Guitar	8.76	13					

* 1 = Thumb, 3 = Middle finger, 4 = Ring finger

** The severity score is based on expert rating: 100%=healthy, 0 % playing impossible.

*** Self-rated playing ability is judged by the patient self: 100% = level before onset dystonia.

4.3.2 Tasks, procedures & measures

A battery of five auditory-motor tasks was employed to investigate at what stage of auditory-motor processing deficits occurs. The battery includes sensorimotor synchronization and perceptual tasks. The tasks were presented to the participants in a randomized order. Participants received oral and written instructions before each task. After the experiment, participants filled in a short questionnaire. In total the experiment took about 1-1.5 hours.

4.3.2.1 Sensorimotor synchronization tasks: Adaptive tapping

The adaptive tapping task contained both, fixed and adaptive trials [46]. During the fixed trials participants synchronized their taps with a non-responsive metronome. During the adaptive trials the sequences responded to the participants' tap timing by implementing error correction [45-46]. In brief, the pacing sequence adjusted its timing during each trial based on the registered asynchrony between its previous tone and the participants' tap (phase correction). Two levels of error correction (α) were employed: 0.3 and 0.7. Each value indicates the proportion of each asynchrony that is corrected for by local adjustments to the timing of pacing events (Figure 4.1), resulting in an adaptive pacing sequence with which the participants synchronized their taps. The two levels of α were chosen to result in a hypothesized helpful (α=0.3) metronome, that has previously been shown to boost sensorimotor synchronization and a hypothesized unhelpful (α=0.7) metronome, leading to a more challenging synchronization task [46-47]. The non-responsive metronome in the fixed trials could be referred to as an adaptive metronome of which alpha is set to 0.

Stimulus presentation and tap recording was controlled by a MaxMSP program running PC with Windows. Participants tapped with their right index finger on a custom built tapping device, which was connected to PC and MaxMSP via a MIDI-connection. Stimulus sounds, sampled as a woodblock sound, were generated by a Roland SPD-S sampling pad. Sounds were presented over headphones and participants' taps did not trigger sounds.

The different conditions of the stable tapping task (α=0 [fixed], α=0.3, and α=0.7) were presented in a randomized block of 10 trials. All trials had a base inter-onset interval of 500 ms and consisted of 42 tones. Participants were instructed to start tapping from the third tone onwards and to synchronize their taps as accurately as possible with the pacing signal, while maintaining the initial tempo. Prior to the experimental blocks participants performed one trial for each of the three conditions to familiarize themselves with the experimental procedure.

As a measure of sensorimotor synchronization accuracy the mean signed asynchrony between the metronome's tones and the participants' taps was calculated. The standard deviation of the signed asynchrony functioned as a measure of sensorimotor synchronization precision, indicating how consistent the taps were in relation to the tones [48]. The standard deviation of the signed asynchrony is also used as a measure of coupling-strength [46-47]. A lower standard deviation of the signed asynchrony reflects a stronger coupling between the pacing signal's tones and the participant's taps. Based on the stable tapping task, the amount of phase correction implemented by the participant was estimated as a measure of adaptation during sensorimotor synchronization [39]. The amount of human alpha can be determined based on the lag 1 autocorrelation of asynchronies in the conditions of stable tapping (α=0 [fixed], α=0.3, and α=0.7). Based on a regression line, the alpha corresponding to a lag-1 autocorrelation of 0 was determined. To obtain an estimate of the amount of phase correction implemented by the participant this alpha value was subtracted from the hypothesized optimal amount of error correction, namely 0.9 [46, 49].

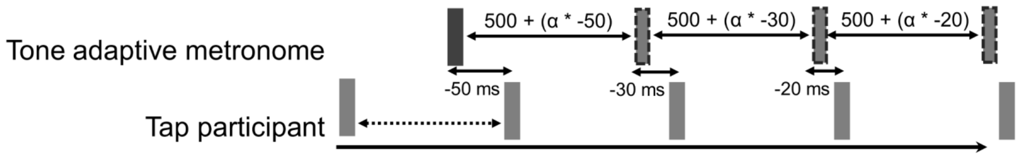


Figure 4.1 Pacing signal for the adaptive tapping task. The timing of the pacing signal was determined by the following equation: tn+1 = tn + 500 + α × asynn. In the current experiment α was set to 0, 0.3 or 0.7, thus the pacing signal corrected 0 (non- responsive metronome in fixed trials), 30 or 70 % of the asynchrony by shifting the next tone in the opposite direction.

4.3.2.2 Sensorimotor synchronization tasks: Tempo changing tapping

During the tempo changing tapping task participants were instructed to tap in synchrony with the tempo changing stimulus sequence. Twelve tempo changing sequences were employed [38]. The stimulus sequences consisted of 68 tones, starting with five tones with an inter-onset interval of 600 ms followed by tempo changes of which the inter-onset interval varied between 600 and 387 ms inter-onset interval. Tempo changes proceeded over the course of five to nine intervals, resulting in 12 slightly different sequences with nevertheless a similar character. All sequences contained eight continuous tempo changes resembling those found in performed music (i.e., accelerando and ritardando). Stimulus presentation and tap recording were controlled in the same way as during the stable tapping task. The order of the 12 sequences was randomized across participant. Participants performed two randomly chosen sequences as practice and to familiarize themselves with the experimental procedure.

The absolute mean asynchrony and the standard deviation of the signed asynchrony were calculated as measures of sensorimotor synchronization accuracy and precision, respectively [38]. The cross correlations between the inter-stimulus and inter-tap intervals at lag 0 and lag 1 and the prediction/tracking ratio (PT-ratio) were calculated as indicators of anticipation mechanisms during sensorimotor synchronization. The PT-ratio is computed by dividing the lag 0 by the lag 1 cross correlation between inter-tap and inter-stimulus interval [38, 50]. If this ratio is greater than 1, it reflects the participant's tendency to predict the tempo change, while a ratio smaller than 1 indicates the participants tend to copy (track) the tempo changes. The PT-ratio has been shown to classify individual differences reliably and has been found to correlate positively with musical experience, tapping abilities and neural activation in different brain networks [38, 40, 50].

4.3.2.3 Perceptual task: Beat Alignment Test

The Beat Alignment Test was an adapted version of the Beat Alignment Test developed by Iversen & Patel [37]. Since our participants were professional musicians, the adjustments were made to make the task more challenging (see supplementary materials for details). We chose five extracts (10-20 sec each) of musical recordings of various styles from Iversen and Patel's stimuli. After five seconds, a metronome was superimposed on the music. In half of the trials, the metronome was aligned with the beat of the musical piece. In the other trials, the metronome was phase-shifted to be either too late or too early by 10 or 15% of the average metronome click interval. A total of 40 stimuli (20 aligned, 20 misaligned) were randomly presented in four blocks of 10 trials. In between blocks, participants could take a short break. Participants were instructed to judge if the metronome was aligned with the beat of the musical piece or not.

The stimuli were generated offline and saved as wave files. A python-pygame graphical interface presented the instructions and stimuli and collected key press responses. Stimuli were presented through headphones. This task was used as a purely perceptual task to probe patients' capacity to align a metronome with the beat of a musical extract independently of their motor capacities [37]. Therefore, participants were explicitly instructed not to move or tap along while they were listening.

Prior to the experimental blocks, participants were presented an example with aligned metronome and one during which the metronome was shifted, i.e. misaligned trial. Next, participants completed a training block with four training trails (two aligned and two in which the metronome was shifted; +15% and -15% of the metronome interval). Participants responded whether the metronome was aligned or not. During the training block, but not during the experimental blocks, participants received accuracy feedback.

The summed correct responses divided by the total number of responses across extracts for each metronome shift (-15, -10, 0, +10, +15%) was calculated as an accuracy score for each participant.

4.3.2.4 Perceptual task: Keystroke-sound delay detection task

At each trial, the participant pressed the "zero" key on the keypad at a time of her/his choosing and heard a tone. This tone was either played at the same time of the keystroke or delayed by a number of milliseconds [42]. The Maximum Likelihood Procedure (MLP) algorithm [51-52] was used to detect the threshold for the detection of the asynchrony between movement (keystroke) and the tone. The algorithm is designed to adaptively select the stimulus level (tone delay) on each trial so as to converge to the participant's threshold. For each block, the algorithm outputs an estimate for the participant's threshold. In short, the applied MLP algorithm works as follows: A set of candidate psychometric curves are maintained in parallel and for each, the likelihood of the set of the participants' responses is calculated. The psychometric curve that makes the participant's responses maximally likely is used to determine the stimulus level (the delay between the keystroke and the sound) on the next trial. We used 600 candidate psychometric curves with midpoints linearly spread between 0 and 600 ms delay, each combined with the five false alarm rates (0, 10, 20, 30, and 40%). Hence, a total of 3000 candidate psychometric curves were used. The source code for the MLP is freely available online on https://github.com/florisvanvugt/PythonMLP.

A USB keypad (Hama Slimline Keypad SK110) interfaced through HDI protocols with a python script was used to detect the keystroke onset and playing a woodblock wave sound (duration: 63 ms) through headphones.

Three experimental blocks were administered. These blocks consisted of 36 trials and contained six catch trials. Catch trials are trials on which the delay was set to 0 ms (regardless of the delay that was suggested by the MLP algorithm). The function of catch trials is to prevent participants from always responding "delayed" (which would cause the MLP algorithm to converge to a zero threshold). Catch trials were inserted randomly with the following constraints: the first 12 trials of each block contained 2 catch trials and the next 24 trials contained 4 catch trials.

Prior to the experimental blocks, participants first performed four training trials (two with no delay and two with a delay of 600 ms) to make clear the difference between when the sound came immediately and when it was delayed. During these practice trails participants received accuracy feedback about the given answers. Next, they performed a training block of 10 trials, starting at 600 ms delay but then using MLP to determine the stimulus levels of the following trials.

This task measured participants' sensitivity to asynchronies between motor (keystroke) and auditory (tone) events [42].

4.3.2.4 Perceptual task: Anisochrony detection

Participants heard a five-tone sequence over headphones. The base sequence consisted of five isochronous sine wave tones (100 ms duration) presented with an IOI of 350 ms. In some trials, the fourth tone was delayed by a certain amount but the fifth tone was always on time [53-54]. That is, when the tone was delayed by an amount *d*, the third interval was longer by *d* ms and the fourth interval was shorter by *d* msec. The amount of delay depended on the participant's threshold, which was established adaptively using the MLP. The basic procedure was the same as for the delay detection task but for this task 200 logistic psychophysical curves were used. Midpoints of these curves were linearly spread over the 0 to 200 ms delay range (0% to 57% of the inter-tone intervals) and combined with the five false alarm rates (0, 10, 20, 30, and 40%). A python-pygame graphical interface presented the instructions and stimuli and collected keystroke responses.

Three experimental blocks of 36 trials, including six catch trials, were presented to the participants.

Participants were instructed to judge if the five-tone sequence was regular or irregular. Prior to the experimental blocks, four example stimuli (two regular, two irregular) were presented. For these trials participant received accuracy feedback. Next, a training block with 10 trials was administered.

The obtained threshold was used as an estimator of the precision of participants' auditory temporal perception [42, 53-54].

4.3.3 Machine learning

4.3.3.1 Non-linear classification of patients and controls

In order to investigate whether the patient group was characterized by particular non-linear combinations of scores on the variables measured in this study, we performed supervised machine learning analyses as follows [for a similar procedure, see 10]. The variables that were fed into these analyses are outcome measures of the five tasks. From the stable tapping task we used the following variables. The mean signed asynchronies (ms) and the standard deviation of the asynchronies (ms) on the different levels of alpha (α=0 [fixed], α=0.3, and α=0.7) were used, amounting to 6 data points (2 variables for each of the 3 levels of alpha) per participant. Furthermore, the error correction estimate (unit-less; see stable tapping methods) was used. From the tempo changing tapping task the mean absolute asynchrony (ms), the standard deviation of the signed asynchronies (ms), and the PT-ratio (unit-less) were included. For the perceptual tasks the score on the beat alignment test (%), the delay detection threshold (ms), and the anisochrony threshold (% of IOI) were fed into the supervised machine learning analyses.

Prior to running the machine learning analyses, each of the variables was rescaled and centred so that their mean was zero and standard deviation equal to one. Three established machine learning algorithms were tested (details below): Naive Bayesian classification, Linear Discriminant Analysis (LDA) and Support Vector Machines (SVM). Each model was given the variables as predictors and is trained to categorise participants as patient or control.

We first trained the models on the entire dataset, then removed the labels, and asked the model to predict which participants are patients and which are controls. We expected the models to do very well on this classification task, because the models have a large number of degrees of freedom. The risk of this great number of degrees of freedom is that we could over-fit the data, essentially fitting noise. In order to assess the models without risking over-fitting, we used leave-one-out-cross-validation (LOOCV). In this procedure, we trained each of the three models on all the data (training data) except one participant. The model is then tested on classifying this one participant (the test data). By repeating this procedure for each participant in the sample, we get an overall classification accuracy which is corrected for over-fitting. We then tested its overall success rate using binomial testing.

To perform naive Bayesian classification, the naiveBayes function from the e1071 machine learning package as part of the R package for statistical computing (version 3.0.2) was used. This function implements the standard Bayes classifier. To perform LDA, we used the lda function from the MASS package as part of the R package for statistical computing (version 3.0.2). Finally, SVM was implemented using the svm function from the e1071 machine learning package as part of the R package for statistical computing. We performed C-classification using a radial basis SVM kernel. Hyperparameter's cost and gamma were set to 10000 and 1e-4, respectively. These hyperparameter values were chosen from a range of possible values as those minimising the classification error. The machine used 22 support vectors.

4.3.4 Data-analyses

The tapping data were processed with MATLAB (The Mathworks Inc, MA, USA R2011a). In addition to descriptive statistics, we performed mixed design ANOVAs (see below). If the assumption of sphericity was violated, the Greenhouse–Geisser correction was applied. To interpret the significant effects of the ANOVAs, the generalized η^2 effect size was used. The effect sizes were interpreted according to Cohen's recommendation of 0.02 for a small effect, .13 for a medium effect, and .26 for a large effect [55]. The analyses were performed with SPSS (IBM SPSS Statistics 21) and R package for Statistical Computing (version 2.15.1).

4.4 RESULTS

Across the different tasks, no differences between left and right hand affected patients were observed. Therefore, in the analyses reported below all fifteen patients were included as a single level of the group factor.

4.4.1 Sensorimotor synchronization tasks

4.4.1.1 Adaptive tapping

Two-way mixed design ANOVAs with group (patient or control) as between-participant factor, and level of alpha (three levels: $\alpha=0$ [fixed], $\alpha=0.3$, and $\alpha=0.7$) as within-participant factor were run to investigate differences between groups and the effect of the adaptive metronome on the mean and standard deviation of the signed asynchrony. In order to investigate whether the estimated amount of human phase correction differed between groups, an ANOVA with group (patient or control) as between-participant factor was run.

For the mean signed asynchrony there was no main effect of group [$F(1,28)=1.76$, $p=0.20$]. One control participant had unusual positive mean asynchrony, which was further than 2.5 SD away from the sample mean, for two of the three levels of alpha. When the analysis was repeated without this outlier a moderate significant main effect of group was found [$F(1,27)=4.61$, $p=0.04$, $\eta^2=0.15$], indicating that the patients were more accurate in synchronizing their taps with the pacing sequence. In the analysis without the outlier, a moderate main effect of alpha was also found [$F(1.63;44.05)=9.31$, $p=0.001$, $\eta^2=0.25$]. Pairwise comparisons revealed that synchronization was more accurate when the metronome implemented 70% phase correction compared to the fixed metronome ($p<0.001$) and the metronome that implemented 30% phase correction ($p=0.029$). No significant interaction effect between group and alpha was found [$F(1.63;44.05)=0.41$, $p=0.66$] (Figure 4.2).

For the standard deviation of the signed asynchrony no significant main effects of group [F(1.28)=0.10, p=0.75] or alpha [F(2,56)=2.75, p=0.07], nor interaction effects [F(2,56)=1.11, p=0.33] were found. This indicates that the precision of synchronization did not differ between groups or levels of alpha (Table 4.2).

There was also no significant difference in the estimated amount of error correction implemented by the patients and controls [F(1;28)=2.60, p=0.12] (Table 4.2).

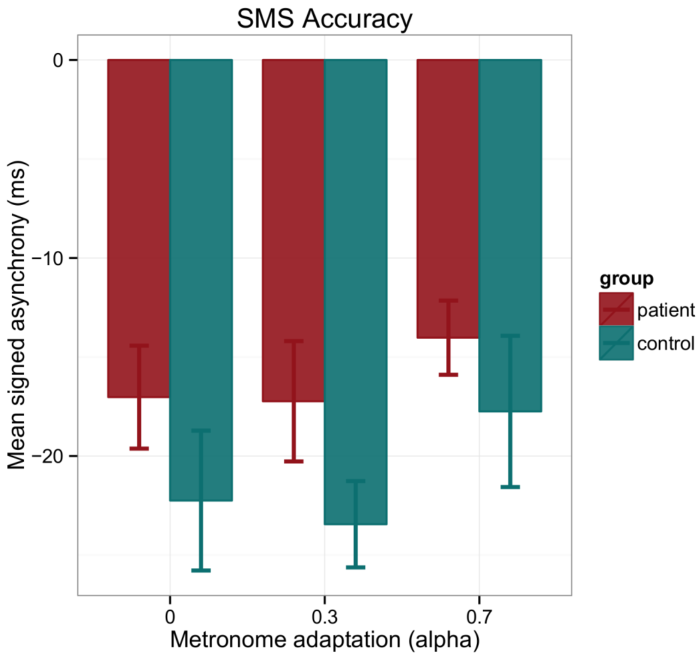


Figure 4.2 Adaptive tapping task accuracy results. Mean signed asynchronies as a measure of sensorimotor synchronization accuracy separated for group and levels of alpha. By convention negative values indicate that the tap preceded the tone. Error bars indicate standard error of the mean.

4.4.1.2 Tempo changing tapping

Group differences between patients and controls for the absolute mean asynchrony, the standard deviation of the signed asynchrony and PT-ratio were statistically investigated by means of separate ANOVAs with the mentioned outcome measures as dependent variable and as between-factor group (patient or control). For all three measures no significant main effect of group was found (mean asynchrony [F(1;28)=0.30, p=0.59], standard deviation of asynchronies [F(1;28)=0.01, p=0.93]; PT-ratio [F(1;28)=0.94, p=0.34]) (Table 4.2). Furthermore, PT-indices estimated based on an autoregressive method [56] did not show a significant group difference [F(1;28)=0.80, p=0.38]. The correlation between the PT-index and PT-ratio was ρ=0.97, p<0.001. These findings indicate that patients' synchronization abilities did not differ from controls for tempo changing sensorimotor synchronization accuracy and precision. Furthermore, both groups predicted the tempo changes to a similar degree (able 4.2).

4.4.2 Perceptual tasks

4.4.2.1. Beat Alignment Test

In order to investigate whether beat alignment performance was different between groups, a mixed design ANOVA with between-participant factor group (patient or control) and within-participant factor metronome alignment (aligned or misaligned) was performed. The two groups had identical overall accuracy scores (84.3%). Therefore the main effect of group was not significant [$F(1,28)=0.00$, $p=1.00$]. The main effect of metronome alignment was not significant [$F(1,28)=0.17$, $p=0.68$], which indicated that participants were equally good at detecting aligned and misaligned metronomes. The interaction between metronome alignment and group was also not significant [$F(1,28)=0.07$, $p=0.79$] (Figure 4.3A).

In order to test whether the different metronome shifts differentially influenced performance, we proceeded to analyze the misaligned stimuli as follows. A mixed design ANOVA with within-factors shift direction (metronome lead or metronome lag), shift amount (10% or 15% of the inter-beat-interval) and between-factors group (patient or control) was performed. The dependent variable was the proportion "aligned" responses. The main effect of group was not significant [$F(1,28)=0.04$, $p=0.85$]. Shift direction revealed a small significant main effect [$F(1,28)=22.02$, $p<0.0001$, $\eta^2=0.09$], which indicated that participants responded "aligned" more often (erroneously) when the metronome preceded the beat (M=23%, SD=21%) than when the metronome came after the beat (M=10%, SD=14%). That is, participants more readily detected a metronome as misaligned when it came late than when it came early relative to the underlying musical beat. There was a moderate main effect of shift magnitude [$F(1,28)=30.86$, $p<0.001$, $\eta^2=0.19$], which revealed that participants judged the metronome aligned less often when it was shifted by 15% of the inter-beat-interval (M=7%, SD=8% "aligned" responses) than when it was shifted by 10% (M=26%, SD=25% "aligned" responses). The interaction between shift magnitude and direction was not significant [$F(1,28)=1.17$, $p=0.29$]. The interactions between group and shift magnitude or shift direction were not significant and there was no significant three-way interaction [all interactions $F(1,28)<1.34$, $p>0.26$] (Figure 4.3B).

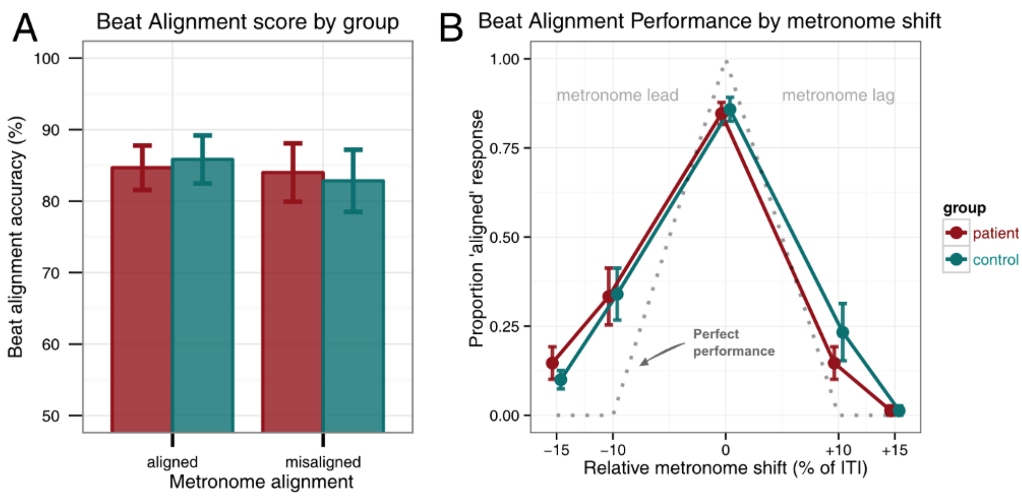


Figure 4.3 Beat alignment test results (A) Overall accuracy scores. Error bars indicate standard error of the mean. (B) Aligned responses according to relative metronome shifts. Error bars indicate standard error of the mean.

4.4.2.2 Keystroke-sound delay detection task

Blocks in which participants responded "delayed" to more than 30% of catch trials were classified as invalid and eliminated from the analysis. This was the case of 14.9% of all blocks. A further 4.2% of blocks were discarded because they had not properly converged on a threshold. The criterion for non-convergence was if threshold estimates varied more than 2 ms/trial over the last ten trials (based on previous datasets [42]). After discarding blocks, participants had on average 2.5 (SD=0.73) valid blocks remaining. The average threshold (in ms) for these remaining blocks was calculated.

In order to investigate whether keystroke-sound delay detection differed between groups, we performed an ANOVA with delay detection threshold as dependent variable and between-factor group (patient or control). There was no effect of group [$F(1,28)=0.55$, $p=0.46$], which indicated that delay detection thresholds did not differ between patients and controls. One participant (control group) had an unusually high delay detection threshold (314.5 ms), which was further than 3 SD away from the mean of the sample. Repeating our analysis without this participant, we still found no effect of group [$F(1,27)=0.02$, $p=0.90$] on delay detection threshold (Table 4.2). The thresholds for both controls and patients were comparable to previously observed thresholds for delay detection in musician populations [42].

4.4.2.3 *Anisochrony detection*

Blocks in which participants responded "irregular" to more than 30% of catch trials were eliminated. This was the case in all three blocks of one participant (3.2% of all blocks). This control participant was eliminated from further analysis. All blocks had properly converged according to the non-convergence criterion (less than 1.18 ms/trial threshold change over the last ten trials). After discarding, all remaining participants had all 3 blocks remaining. The average threshold (in % of the inter-tone-interval) was calculated for these remaining blocks.

In order to investigate whether anisochrony detection differed between groups, an ANOVA with anisochrony threshold as dependent variable and between-factor group (patient or control) was performed. There was no significant main effect of group [$F(1,27)=0.07$, $p=0.80$] which revealed that anisochrony thresholds were identical for patients and controls (Table 4.2). The thresholds for both controls and patients were comparable to previously found thresholds for anisochrony in musician populations [42, 53].

Table 4.2 Mean (SD) of the non-significant results for the different tasks and outcome measure separated per group and if applicable level of alpha.

Task	Measure	Patient group	Control group
Adaptive tapping task	Precision SD signed asyn (ms) alpha = 0 [fixed]	15.93 (3.05)	16.59 (4.45)
	Precision SD signed asyn (ms) alpha = 0.3	15.36 (2.58)	14.90 (3.23)
	Precision SD signed asyn (ms) alpha = 0.7	15.26 (2.03)	16.15 (4.65)
	Error correction estimate	0.61 (0.15)	0.53 (0.13)
Tempo changing tapping task	Accuracy mean abs asyn (ms)	36.47 (5.83)	37.90 (8.38)
	Precision SD sign asyn (ms)	36.67 (4.61)	36.50 (6.58)
	PT-ratio	1.04 (0.04)	1.05 (0.03)
Keystroke-sound delay detection task	Keystroke-sound delay detection threshold (ms)	86.8 (43.7)	104.3 (79.6)
Anisochrony detection	Anisochrony threshold (% of inter-tone-interval)	4.5 (2.2)	4.7 (2.7)

4.4.3 Machine Learning

4.4.3.1 *Non-linear classification of patients and controls*

One participant from the control group was not included in this analysis due to a lack of valid blocks for anisochrony threshold (see anisochrony results above).

All three methods of machine learning (Naive Bayes, LDA and SVM) were able to classify participants as patient or control above chance level (all binomial test p<=0.001; Table 4.3) when they were trained on the entire dataset. However, when controlling for over-fitting using leave-one-out-cross validation (LOOCV), all models performed at chance level (all binomial test p>0.36; Table 4.3). This indicated that combinations of variable scores that separated patients and controls could be identified, but that these combinations were based on individual differences unrelated to MD.

Table 4.3 Classification accuracy for each of the machine learning approaches: Naive Bayesian, Linear Discriminant analysis (LDA) and Support Vector Machines (SVM).

Method	Accuracy	Patient predictive value	Control predictive value	Sensitivity	Specificity	Binomial test p-value
SVM.all	86.2%	86.7%	85.7%	86.7%	85.7%	<0.001*
SVM.LOOCV	44.8%	47.1%	41.7%	53.3%	35.7%	0.771
LDA.all	82.8%	85.7%	80.0%	80.0%	85.7%	<0.001*
LDA.LOOCV	55.2%	55.6%	54.5%	66.7%	42.9%	0.356
NaiveBayes.all	79.3%	76.5%	83.3%	86.7%	71.4%	0.001*
NaiveBayes.LOOCV	51.7%	52.9%	50.0%	60.0%	42.9%	0.500

For each approach, the classification rate for the model that was trained on all data (all) and the model that was tested using leave-one-out-cross validation (LOOCV) is reported. We report accuracy (number correct divided by total number of participants), patient-predictive-value (the proportion of true patients among those classified as patients by the model), control-predictive-value (the proportion of true controls among those classified as controls by the model), sensitivity (the proportion of participants classified as patients relative to the total number of patients), specificity (the proportion of participants classified as controls relative to the total number of controls), binomial test p-value.

4.5 DISCUSSION

This study investigated MD patients' timing perception and production capacities away from their instrument. Previous studies showed that beside the task specific problems, MD patient are also impaired in more general tasks and processes [5, 12]. Results of the current study suggest that basic movement and timing capacities relevant for music making are unaffected in MD patients. Both for purely auditory perception tasks as well as for the sensorimotor synchronization tapping tasks, no impairments were found in MD-patients. Furthermore, state-of-the-art machine learning algorithms could not separate patients and controls based on the outcome measures of the five timing tasks. Overall, these results suggest that MD-patients show intact auditory-motor processing related to the basic timing tasks studied here. Therefore, the present results support the claim that MD is a task-specific movement disorder.

The finding that patients are more accurate in synchronizing their taps with the tones in the stable tapping task is most likely related to their amount of practice. Patients reported on average a higher amount of accumulated hours of practice [patients: 32.7 (23.0) / controls:

26.6 (22.4) x10^3 hours], indicating that they practiced more than the tested controls. It has been shown that practice is associated with high sensorimotor synchronization accuracy [50, 57]. The positive effect of the adaptive timing of the pacing signal on sensorimotor synchronization was only visible for sensorimotor synchronization accuracy. The coupling between the pacing signal and the participants' taps was very high, indicated by the small asynchronies. This tight coupling is not very surprising considering we tested professional musicians but also did not leave much room for improvement in sensorimotor synchronization behavior. This might also be the reason why the hypothesized unhelpful metronome (alpha=0.7) did show a positive effect of sensorimotor synchronization accuracy but the hypothesized helpful metronome (alpha=0.3) did not reveal a difference compared to the unresponsive metronome (alpha=0 [fixed]). On the small asynchronies only a 70% correction led to a meaningful adjustment of the timing of the metronome's tones.

The Beat Alignment Test was used to measure participants' perceptual precision in detecting whether a metronome was aligned with a musical beat. Humans perceive a regular pulse of the rhythm of the musical pieces [58]. Not surprisingly the bigger (15%) metronome misalignments were easier to detect for participants than the more subtle 10% phase-shifted metronome. Furthermore, the finding that late, positive shifts are easier to detect than early, negative shifts might be explained by means of the oscillator-based dynamic theory of attending [59]. According to this theory, regular sequences establish internal oscillators that resonate in phase with the regular external stimulus. The attention of the listener is not equally distributed of the entire time span but follows attentional cycles that are linked to the internal oscillators. The perception (and production) of events is more accurate when the event coincides with the peak of the attentional cycle [59-60]. In case of the phase-shifted metronome the clicks do not coincide with the expected pulse of the music. In case of the late shifted metronome, the narrowed focus around anticipated events may increase attention as time progresses, because the expected click has not yet occurred [59, 61]. Furthermore, in trials where the metronome was shifted earlier the internal oscillator is disturbed by one cue. This cue is the result of the pulse of the too early occurring metronome click. Trials during which the metronome was shifted later two cues are available, namely the missing click when a click was expected and then the click that happens after the perceived pulse [62]. Late shifts might therefore be easier to detect and classify as misaligned, than early shifts [59, 62]. Surprisingly, Lim and colleagues [3] showed that if the last tone in a five tone sequences occurred earlier this was more easily detectable than if the fifth tone was delayed. Furthermore, they concluded that this difference was bigger in MD patients. The anisochrony task employed here, with an adaptively delayed tone, has strong resemblances with the task employed by Lim and colleagues [3]. However, the anisochrony task did not reveal this difference in detecting delayed tones between the MD patients and healthy controls. The effect found by Lim and colleagues [3] might arise because musicians perhaps link delays at the end of the five tone sequence to the final tone of a musical phrase. In expressively timed musical performances this final tone is often delayed. It was previously found that detecting delays at the end of a musical phrase is difficult, because musicians expect delays at this point [63-64]. In the anisochrony task the one-but-last tone was delayed instead of the last tone, this phrase-final lengthening effect did not occur. Here, we aimed to purely measure participants' auditory temporal perception and there we eliminated potential interference from high-level musical processing by measuring sensitivity to the fourth (i.e. one-but-last) instead of fifth (last) tone.

In summary, the observed significant effects are all related to the applied experimental manipulations but did not differ between patients and controls. Furthermore, even state-of-the-art machine learning algorithms were not able to pick up pathological behaviors that would tease apart patients and controls. The results suggest that basic timing abilities, both perception and production, are intact in patients that suffer from MD. Although this finding supports the claim that MD is a task-specific movement disorder our main hypothesis was that, due to the assumed maladaptive plasticity in brain areas that are highly relevant for timing, patients would show impaired timing abilities compared to a matched healthy control group.

A possible explanation for the lack of the effect of MD on timing might be related to the nature of the task. The tasks employed in the current study are less complex than the movements involved in music making. The tasks were specifically developed and successfully employed in previous studies addressing basic perceptual and action aspects of timing that are important for playing music [37-42]. Although differences in brain activations have been shown by very basic tasks that did not evoke dystonic symptoms (e.g., finger tapping), the functional maladaptive plasticity underlying focal hand dystonia was more pronounced in more complex tasks (e.g., Luria apposition task) [21, 26]. It would therefore be interesting to test MD-patients' timing abilities using more complex tasks.

A second explanation might be found in the role of the affected finger. In the current experiment, focussing on basic timing abilities, participants of whom the right index finger was affected were excluded from the study. The reason to do this was to be sure that no dystonic movements would be evoked during the tasks, which often required participants to use their right index finger. Dystonic movements most likely would disturb the temporal accuracy. Previous studies reporting timing anomalies in MD-patients during piano playing [9] and individuated finger movements [10] indicated the role of the affected finger(s). Jabusch and colleagues [9] found no difference in timing parameters between the unaffected hands of the MD patients and the reference hands of the healthy controls. Obviously, in the affected hands of the tested pianists, dystonic cramping was present during the task. The results by Furuya and Altenmüller [10] were also obtained by means of a finger-tapping task. But in this case participants were instructed to depress the piano keys with all fingers, while tapping with one of the fingers. This made the task more complex, but more importantly also included the affected finger in the position of the hand, like during real piano playing. Furthermore, patients were directly tested at their instrument (like in [9]).

The latter two points brought up in relation to the Furuya and Altenmüller [10] study link to a final and most likely reason why no general basic timing deficits were found in MD-patients, namely the task-specific nature of this movement disorder. Hu and colleagues (2006) found differences in brain activation in writer's cramp patients compared to healthy controls only for writing with a pencil. However, no differences between patients and controls were found for the same writing task when performed with the finger [36]. This finding pin-points the specific role of the task in task-specific hand dystonia. The problems patients suffering from MD encounter are most strongly related to instrumental playing [1]. However, a recent study found that 98% of the patients also report problems with other fine motor control daily life activities, such as computer keyboard typing and hand writing [13]. Similarly, in our sample 9 out of 15 patients reported (subtle) problems with non-musical fine motor tasks. But the loss of voluntary motor control in MD-patients is most pronounced in the over-practiced task, for these professional musicians playing their instrument. The timing abilities of MD-patients were tested away from their instrument, since we were interested in the basic aspect of timing. The question remains if problems with timing are present in MD-patients when basic features of timing are investigated at the instrument without evoking dystonic movements that disturb temporal aspects of the movement.

Furthermore, we did not measure brain activation patterns during the tasks. Therefore, it remains unclear whether the previously found maladaptive plasticity [20-21] played a role during the experiment. Moreover, a recent study found that focal hand dystonia patients exhibited decreased activations and increased connectivity in different brain regions (e.g., cerebellum, putamen, and sensorimotor cortex). Nevertheless, identical motor performance in the patient and the healthy control group was found, suggesting that differences in activation and connectivity may reflect beneficial compensatory processes [65]. The tasks employed in the current experiment focus on basic perceptual and action aspects of timing that have been found to be important for playing music and ensemble music making [42, 48]. Due to importance of movement timing for musicians, it might be that MD patients have developed compensatory mechanisms to maintain their extraordinary level of timing. We addressed this issue by examining the amount of phase correction and the PT-ratio, as indicators of the underlying mechanisms of successful sensorimotor synchronization [45]. The finding that these measures also did not differ between groups speaks against the use of compensatory processes by patients, but further research is necessary to definitively exclude this possibility.

The timing of movements is obviously a complex multifaceted capacity that entails both perceptual and action components, also seems to differ between types of movements (e.g., continuous vs discrete tasks). Although the employed battery of auditory-motor tasks covers a wide range of processes relevant to motor timing, it is impossible to test all aspects exhaustively. The aspects that we investigated are mostly relevant to discrete movement tasks, such as finger tapping. It is therefore unknown whether our findings generalize to timing abilities most relevant in other tasks, such as emergent timing in continuous movements [66-67].

Further experiments could further clarify the task-specific nature of MD and the generalizability of our results to other types of timing tasks. In these experiments the above-mentioned points could be tested. For example, sensorimotor synchronization abilities of right index finger affected pianists could be addressed via a similar paradigm both at the piano as well as using the current experiment set up. Also more complex tasks, such as tapping tasks that include multiple fingers or even both hands, and continuous tasks could be administrated while timing measures are recorded. The tasks could be administrated in an fMRI scanner to reveal the brain activation patterns of patients and controls during the tasks.

Overall, results of the current study suggest that basic timing abilities stay intact in patients that suffer from MD. This finding supports the idea that MD is a task-specific movement disorder and that problems in this patient population are most pronounced in relation to instrumental playing. The current study raises the question how patients' basic timing capacities can be intact although they are impaired at a variety of fine motor tasks. Our results suggest that MD patients may maintain their musical timing skills by practicing sensorimotor timing tasks away from their instrument. Also, the finding that these basic musical skills are intact might suggest that if musical instruments are adapted in such a way as to not evoke dystonic movements, musical performance in these patients may be restored.

4.6 ACKNOWLEDGMENTS

The authors thank Caroline Seer, Matthias Klaus, Marlehn Lübbert, and Johann Schneider for their help running the experiment. This work was supported by funding from the European Community's Seventh Framework Programme under the EBRAMUS project - grant agreement n° 238157.

4.7 REFERENCES

1. Altenmüller E, Jabusch HC (2010) Focal dystonia in musicians: phenomenology, pathophysiology, triggering factors, and treatment. Med Probl Perform Art, 25: 3-9.
2. Hallett M (1995). Is dystonia a sensory disorder? Ann Neurol 38: 139-140.
3. Lim VK, Bradshaw JL, Nicholls MER, Altenmüller EA (2003) Perceptual differences in sequential stimuli across patients with musician's and writer's cramp. Mov Disord 18: 1286-1293.
4. Tinazzi M, Rosso T, Fiaschi A (2003) Role of the somatosensory system in primary dystonia. Mov Disord 18: 605-622.
5. Avanizo L, Martine D, Martine I, Pelosin E, Vicario CM, Bove M, Defazio G, Abbruzzese G (2013) Temporal expectation in focal hand dystonia. Brain 136: 444-454.
6. Stamelou M, Edwards MJ, Hallett M, Bhatia, KP (2012) The non-motor syndrome of primary dystonia: clinical and pathophysiological implications. Brain 135: 1668-1681.
7. Marsden CD, Sheehy MP (1990) Writer's cramp. Trends Neurosci 13: 148-153.
8. Jankovic J, Shale H (1989) Dystonia in musicians. Seminars in Neurol 9: 131-135.
9. Jabusch HC, Vauth H, Altenmüller E (2004) Quantification of focal dystonia in pianists using scale analysis. Mov Disord 19: 171-180.
10. Furuya S, Altenmüller E (2013) Finger-specific loss of independent control of finger movements in musician's dystonia. Neuroscience 247C: 152-163.
11. Chang FCF, Frucht SJ (2013) Motor and sensory dysfunction in musician's dystonia. Curr Neuropharmacol 11: 41-47.
12. Rosset-Llobet J, Candia V, Fàbregas S, Ray W, Pascual-Leone Á (2007) Secondary motor disturbances in 101 patients with musician's dystonia. J Neurol Neurosurg Psychiatry 78: 949-953.
13. van Vugt FT, Boullet L, Jabusch HC, Altenmueller E (2013) Musician's dystonia in pianists: long-term evaluation of retraining and other therapies. Parkinsonism Relat D doi: 10.1016/j.parkreldis.2013.08.009.
14. Jabusch HC, Zschucke D, Schmidt A, Schuele S, Altenmüller E (2005) Focal dystonia

in musicians: Treatment strategies and long-term outcome in 144 patients. Mov Disord 20: 1623-1626.

15. Breakefield XO, Blood AJ, Li Y, Hallett M, Hanson PI, Standaert, DG (2008) The pathophysiological basis of dystonias. Nat Rev Neurosci 9: 222-234.
16. Delmaire C, Vidailhet M, Elbaz A, Bourdain F, Bleton JP, Sangla S, Meunier S, Terrier A, Lehéricy S (2007) Structural abnormalities in the cerebellum and sensorimotor circuit in writer's cramp. Neurology 69: 376-380.
17. Granert O, Peller M, Jabusch HC, Altenmüller A, Siebner HR (2011) Sensorimotor skills and focal dystonia are linked to putaminal grey-matter volume in pianists. J Neurol Neurosurg Psychiatry 82: 1225-1231.
18. Quartarone A, Siebner HR, Rothwell JC (2006) Task-specific hand dystonia: can too much plasticity be bad for you? Trends Neurosci, 29: 192-199.
19. Preibisch C, Berg D, Hofmann E, Solymosi L, Naumann M (2001) Cerebral activation patterns in patients with writer's cramp: a functional magnetic resonance imaging study. J Neurol 248: 10-17.
20. Pujol J, Roset-Llobet J, Rosine´s-Cubells D, Deus J, Narberhaus B, Valls-Sole´ J, Capdevila A, Pascual-Leone A (2000) Brain Cortical Activation during Guitar-Induced Hand Dystonia Studied by Functional MRI. NeuroImage 12: 257-267.
21. Kadota H, Nakajima Y, Miyazaki M, Sekiguchi H, Kohno Y, Amako M, Arino H, Nemoto K, Sakai N (2010) An fMRI study of musicians with focal dystonia during tapping tasks. J Neurol 257: 1092-1098.
22. Beck S, Hallett M (2010) Surround inhibition in the motor system. Exp Brain Res 210: 165-172.
23. Rosenkranz K, Williamon A, Butler K, Cordivari C, Lees AJ, Rothwell JC (2005) Pathophysiological differences between musician's dystonia and writer's cramp. Brain 128: 918-931.
24. Abbruzzese G, Marchese R, Buccolieri A, Gasparetto B, Trompetto C, (2001) Abnormalities of sensorimotor integration in focal dystonia: a transcranial magnetic stimulation study. Brain 124: 537-45.
25. Lim VK, Bradshaw JL, Nicholls MER, Kirk IJ, Hamm JP, Grossbach M, Altenmüller E (2003) Aberrant sensorimotor integration in patients with musicians' cramp. J Psychophysiol 17: 195-202.
26. Wu CC, Fairhall SL, McNair NA, Hamm JP, Kirk IJ, Cunnington R, Anderson T, Lim VK (2010) Impaired sensorimotor integration in focal hand dystonia patients in the

absence of symptoms. J Neurol Neurosurg Psychiatry 81: 659-665.
27. Coull JT, Cheng R, Meck WH (2011) Neuroanatomical and neurochemical substrates of timing. Neuropsychopharmacol 36: 3-25.
28. Witt ST, Laird AR, Meyerand ME (2008) Functional neuroimaging correlates of finger-tapping task variations: an ALE meta-analysis. NeuroImage 42: 343-356.
29. Grahn JA, Brett M (2009). Impairment of beat-based rhythm discrimination in Parkinson’s disease. Cortex 45: 54-61.
30. Schwartze M, Keller PE, Patel AD, Kotz SA (2011) The impact of basal ganglia lesions of sensorimotor synchronization, spontaneous motor tempo and the detection of tempo changes. Behav Brain Res 216: 685-691.
31. Scontrini A, Conte A, Defazio G, Fiorio M, Fabbrini G, Suppa A, Tinazzi M, Berardelli A. (2009) Somatosensory temporal discrimination in patients with primary focal dystonia. J Neurol Neurosurg Psychiatry 80: 1315-1319.
32. Sanger TD, Tarsy D, Pascual-Leone A (2001) Abnormalities of spatial and temporal sensory discrimination in writer’s cramp. Mov Disord 16: 94-99.
33. Fujii S, Schlaug G (2013) The Harvard Beat Assessment Test (H-BAT): a battery for assessing beat perception and production and their dissociation. Front Hum Neurosci 7:771. doi:10.3389/fnhum.2013.00771
34. Sheehy MP, Marsden CD (1982). Writers’ cramp – a focal dystonia. Brain, 105: 461-480.
35. Jedynak PC, Tranchant C, de Beyl DZ (2001) Prospective clinical study of writer’s cramp. Mov Disord 16: 494-499.
36. Hu XY, Wang L, Liu H, Zhang SZ (2006) Functional magnetic resonance imaging study of writer's cramp. Chin Med J (Engl) 119: 1263-1271.
37. Iversen JR, Patel AD (2008) The Beat Alignment Test (BAT): Surveying beat processing abilities in the general population. In: Miyazaki K, Hiraga Y, Adachi M, Nakajima Y, Tsuzaki M, editors. Proceedings of the 10th International Conference on Music Perception & Cognition (ICMPC10) Sapporo, Japan. Adelaide: Causal Productions. pp. 465-468.
38. Pecenka N, Keller PE (2011) The role of temporal prediction abilities in interpersonal sensorimotor synchronization. Exp Brain Res 211: 505-515.
39. Repp BH, Keller PE, Jacoby N (2012) Quantifying phase correction in sensorimotor synchronization: empirical comparison of three paradigms. Acta Psychol 139: 281-329.
40. Pecenka N, Engel A, Keller PE (2013) Neural correlates of auditory temporal

predictions during sensorimotor synchronization. Front Hum Neurosci 7:380. doi: 10.3389/fnhum.2013.00380
41. Fairhurst MT, Janata P., Keller PE (2014) Leading the follower: An fMRI investigation of dynamic cooperativity and leader-follower strategies in synchronization with an adaptive virtual partner. NeuroImage 84: 688-697.
42. van Vugt FT, Tillmann B (2014) Thresholds of auditory-motor coupling measured with a simple task in musicians and non-musicians: was the sound simultaneous to the key press? PLoS ONE 9(2): e87176. doi:10.1371/journal.pone.0087176
43. Keller PE (2008) Joint action in music performance. In: Morganti F, Carassa A, and Riva G, editors. Enacting Intersubjectivity: a Cognitive and Social Perspective to the Study of Interactions. Amsterdam: IOSPre. pp. 205-221.
44. Konvalinka I,Vuust P, Roepstorff A, Frith CD (2010) Follow you, follow me: continuous mutual prediction and adaptation in joint tapping. Q J Exp Psychol 63: 2220-2230.
45. van der Steen MC, Keller PE (2013) The Adaptation and Anticipation Model (ADAM) of sensorimotor synchronization. Front Hum Neurosci 7:253. doi: 10.3389/fnhum. 2013.00253
46. Repp BH, Keller PE (2008) Sensorimotor synchronization with adaptively timed sequences. Hum Mov Sci 27: 423-456.
47. Fairhurst MT, Janata P, Keller PE (2012) Being and feeling in sync with an adaptive virtual partner: Brain mechanisms underlying dynamic cooperativity. Cereb Cortex 67: 313-321.
48. Repp BH, Su Y-H (2013) Sensorimotor synchronization: a review of recent research (2006– 2012). Psychon Bull Rev doi: 10.3758/s13423-012-0371-2. [Epub ahead of print].
49. Vorberg D, Schulze HH (2002) A two-level timing model for synchronization. J Math Psychol 46: 56-87.
50. Pecenka N, Keller PE (2009) Auditory pitch imagery and its relationship to musical synchronization. Ann NY Acad Sci 1169: 282-286.
51. Green DM (1995) Maximum-likelihood procedures and the inattentive observer. J Acoust Soc Am 97: 3749-3760.
52. Gu X, Green DM (1994) Further studies of a maximum-likelihood yes–no procedure. J Acoust Soc Am 96: 93-101.
53. Ehrlé N, Samson S (2005) Auditory discrimination of anisochrony: influence of the

tempo and musical backgrounds of listeners. Brain Cognition 58, 133-147.

54. Hyde KL, Peretz I (2004) Brains that are out of tune but in time. Psychol Sci 15, 356-360.
55. Bakeman R (2005) Recommended effect size statistics for repeated measures designs. Behav Res Methods 37: 379-384.
56. Launay J, Dean RT, Bailes F (2013) Evidence for multiple strategies in off-beat tapping with anisochronous stimuli. Psychol Res doi: 10.1007/s00426-013-0513-9 [Epub ahead of print].
57. Repp BH (2010) Sensorimotor synchronization and perception of timing: Effects of music training and task experience. Hum Mov Sci 29: 200-213.
58. Large EW (2008) Resonating to musical rhythm: Theory and experiment. In. Grondin S, editors. Psychology of time. Bingley, U.K.: Emerald Group. pp. 189-232.
59. Large EW, Jones MR (1999) The dynamics of attending: How people track time-varying events. Psychol Rev 106: 119-159.
60. Jones MR, Moynihan H, MacKenzie N, Puente J (2002) Temporal aspects of stimulus-driven attending in dynamic arrays. Psychol Sci 13: 313-319.
61. McAuley JD, Kidd GR (1998) Effect of deviations from temporal expectations on tempo discrimination of isochronous tone sequences. J Exp Psychol Human 24: 1786-1800.
62. Lebrun-Guillaud G, Tillmann B (2007) Influence of a tone's tonal function on temporal change detection. Percept Psychophys 69: 1450-1459.
63. Repp BH (1999) Detecting deviations from metronomic timing in music: Effects of perceptual structure on the mental timekeeper. Percept Psychophys 61: 529-548.
64. Penel A, Drake C (1998) Sources of timing variations in music performance: a psychological segmentation model. Psychol Res 61: 12-32.
65. Moore RD, Gallea C, Horovitz SG, Hallett M (2012) Individuated finger control in focal hand dystonia: An fMRI study. NeuroImage 61: 823-831.
66. Zelaznik HN, Spencer RM, Ivry RB (2002) Dissociation of explicit and implicit timing in repetitive tapping and drawing movements. J Exp Psychol Hum Percept Perform 28: 575-588.
67. Zelaznik HN, Spencer RM, Ivry RB, Baria A, Bloom M, Dolansky L, Justice S, Patterson K, Whetter E (2005) Timing variability in circle drawing and tapping: probing the relationship between event and emergent timing. J Mot Behav 37: 395-403.

Summary of the dissertation

Temporal adaptation and anticipation mechanisms in sensorimotor synchronization

Dissertation submitted to Faculty of Biosciences, Pharmacy and Psychology
University of Leipzig
Submitted by Maria Christine van der Steen, M.Sc.
Leipzig, 10 July 2014

INTRODUCTION

A constantly changing environment requires precise yet flexible timing of movements. Sensorimotor synchronization (SMS) is the temporal coordination of an action with an external event. This basic and fundamental human skill contributes to optimal sensory-motor control in daily life. SMS can occur more or less spontaneously, for example when our steps become synchronized to the steps of the person with whom one is walking. On the other hand, SMS can also be the goal of extensive practice, for example a musical ensemble practices to reach an extraordinary level of SMS among co-performers. Adaptive error correction mechanisms that support synchronization have traditionally been the focus of research investigating SMS. Recently, an emerging line of research has highlighted the additional importance of anticipatory mechanisms for SMS. The goal of this dissertation was to gain a better understanding of the underlying temporal adaptation (reactive error correction processes) and anticipation (predictive processes) mechanisms that are hypothesized to play a role in the precise yet flexible nature of SMS. To this end, an Adaptation and Anticipation Model (ADAM) was developed and experiments focusing on different aspects of timing with healthy participants and patients were performed.

CHAPTER 2

In chapter 2, an overview of the existing literature on adaptation and anticipation mechanisms in SMS is given and ADAM is introduced. Humans are normally highly capable of synchronizing their movements with auditory sequences. Nevertheless, during synchronization, timing errors (asynchronies) between the action and the stimulus sequence occur due to biological noise and because of intentional deviations from regularity (as in expressive timed musical performances). Error correction processes, including phase and period correction, compensate for timing errors in a reactive fashion. Without these adaptation mechanisms, asynchronies would increase over time, which in turn could eventually lead to the loss of synchrony between the stimulus sequence and the movement. Although successful SMS requires adaptation mechanisms, phase and period correction alone are not capable of accounting for all aspects of SMS, for example, the ability to move precisely in synchrony with a tempo-changing sequence. In such situations, anticipatory mechanisms enable the onset of stimulus events to be predicted, therefore allowing the movement to start in time so that it coincides with the actual stimulus event.

Anticipation mechanisms have been linked with internal models. Internal (forward and inverse) models represent the sensorimotor transformations that mediate intentions, motor commands, and behavioral effects and can be run without actually performing the action. Forward models predict the outcome of a motor command based on the current state of the action control system and therefore represent the causal relationship between input and output of the system. Inverse models, on the other hand, serve as a controller by providing the motor command that is necessary to change the system from the current state to the desired end state. Paired forward and inverse internal models facilitate successful SMS by allowing potential errors to be corrected before they actually occur.

Typically, the involvement of adaptation and anticipation mechanisms in SMS has been investigated with separate paradigms. Here it is argued that it is desirable to consider both mechanisms within a unified framework in order to develop a more complete understanding of these mechanisms, how they are linked, and how they influence each other. Such a unified framework was pursued by creating ADAM, an Adaptation and Anticipation Model that combines reactive error correction processes (adaptation) with predictive temporal extrapolation processes inspired by the notion of internal models (anticipation). One goal in creating ADAM is to shed light on adaptation and anticipation mechanisms involved in SMS by means of simulations, during which parameters can systematically be varied and by using ADAM to drive a virtual partner, with which participants can interact directly.

CHAPTER 3

A common paradigm to investigate SMS and its underlying mechanisms involves a paced finger tapping task. During this simple task participants are asked to tap their finger in synchrony with a pacing stimulus, often consisting of an auditory sequence. The study presented in chapter 3 aimed to understand how participants synchronize their movements with sequences containing continuous tempo changes. To this end, the results of a behavioral experiment were combined with simulations with ADAM. Seventeen healthy participants synchronized their finger taps with three auditory tempo changing stimulus sequences. The pattern of the stimulus sequences differed in the rate with which the tempo changed and the number of turning points. The tempo changes were designed to resemble musical accelerando and ritardando. The mean asynchrony and the standard deviation of the signed asynchrony were calculated as measures of SMS accuracy and precision, respectively. Furthermore, measures pertaining to the underlying adaptation and anticipation mechanisms were derived. The simulations focused on the effect of adaptation and anticipation mechanisms underlying SMS and possible links between both mechanisms. Four models were created: one with adaptation only, one with independent contributions of adaptation and anticipation, and two models in which adaptation and anticipation were linked in a joint internal model. Results of the behavioral experiment indicated that sensorimotor synchronization accuracy and precision, while generally high, decreased with increases in the rate of tempo change and number of turning points. Simulations and model-based parameter estimates showed that adaptation mechanisms alone could not fully explain the observed sensorimotor synchronization behavior. Including the anticipation process in the model increased the precision of simulated sensorimotor synchronization and improved the fit of model to behavioral data. Overall, the results suggested that both adaptation and anticipation mechanisms play an important role during sensorimotor synchronization with tempo changing sequences. While the exact link between adaptation and anticipation remains an open question, joint internal models provide a possible mechanism that might play a role in this link.

CHAPTER 4

Chapter 4 describes a study investigating timing abilities in patients with musician's dystonia. Musician's dystonia is a form of focal dystonia and is characterized by a loss of voluntary motor control of skilled hand movements during instrumental playing. The pathophysiology of this movement disorder is still unclear but research suggests that in addition to altered inhibition patterns at different levels of the central nervous system, maladaptive plasticity in areas that are important for timing (e.g. basal ganglia and sensorimotor cortices), as well as alterations in sensorimotor integration play a role in this disorder. Several studies have reported that besides the loss of control of movements necessary to successfully play their instrument, patients also show impaired perceptual timing and temporal processing abilities. The current study employed a battery of tasks aiming to separate the purely perceptual capacity from production abilities necessary for SMS, and thereby to provide a picture of the timing abilities of musician's dystonia patients. Participants (15 patients / 15 matched controls) synchronized their tapping with tempo changing and adaptive auditory sequences, so as to address SMS abilities and underlying anticipation and adaptation mechanisms. In addition, precision of beat synchrony perception was examined with an adjusted version of the Beat Alignment Test. Performance on these tasks was compared with elementary perceptual tasks, namely anisochrony detection and auditory-motor delay detection. Results did not show any deficits in auditory-motor processing for patients relative to controls. Both groups benefited from a pacing sequence that adapted to their timing during SMS. Furthermore, in the Beat Alignment Test both groups were able to detect a misaligned metronome when it was late rather than early relative to a musical beat. In sum, the results suggest that timing abilities are intact in patients with musician's dystonia. This supports the idea that musician's dystonia is a highly task-specific movement disorder in which patients are mostly impaired in tasks closely related to the demands of actually playing their instrument.

CONCLUSION

The research presented in this dissertation investigated the timing of movements during SMS, focusing on the underlying adaptation and anticipation mechanisms. ADAM was found to be a useful framework to investigate adaptation and anticipation mechanisms and possible links between these mechanisms. Hypothesized relationships between adaptation and anticipation were investigated by comparing computer simulations based on ADAM with data from behavioral experiments, leading to novel insights into SMS. Notably, it was shown not only that both adaptation and anticipation mechanisms play a role during SMS with tempo changing sequences, but also that internal models may provide a link between the mechanisms. The research in this dissertation was motivated by the assumption that, once a better understanding of the mechanisms underlying temporal sensorimotor synchronization and related deficits in patient populations is acquired, it will be possible to set up targeted rehabilitation programs focusing on the timing of movements. Musician's dystonia patients did not display impaired SMS but nevertheless benefited from synchronizing with adaptive stimulus sequences. This finding is generally promising for the development of rehabilitation programs. Musician's dystonia patients could maintain their timing skills by practicing sensorimotor timing tasks away from their instrument. For this and other clinical populations (e.g., stroke patients), challenging synchronization tasks could be developed involving adaptive virtual partners that could be driven by ADAM.

Zusammenfassung der Dissertation

Zeitliche Adaptations- und Antizipationsmechanismen sensomotorischer Synchronisation

Dissertation eingereicht bei der Fakultät für Biowissenschaften, Pharmazie und Psychologie der Universität Leipzig

Eingereicht von Maria Christine van der Steen, M.Sc.

Leipzig, 10. Juli 2014

EINLEITUNG

Eine sich ständig ändernde Umwelt erfordert die präzise und doch flexible zeitliche Koordination (Timing) von Bewegungen. Sensomotorische Synchronisation (SMS) ist die zeitliche Koordination einer Handlung mit einem externalen Ereignis. Diese basale und fundamentale menschliche Fähigkeit trägt zu optimaler sensorisch-motorischer Kontrolle im Alltag bei. SMS kann mehr oder weniger spontan auftreten, beispielsweise wenn sich unsere Schritte mit der Person synchronisieren, die neben uns läuft. SMS kann aber auch Ziel ausgiebigen Übens sein; z.B. übt ein Musikensemble, um ein sehr hohes Niveau an SMS zwischen den Musikern zu erreichen. Im Fokus der Forschung zu SMS standen traditionell adaptive Fehlerkorrekturmechanismen, die Synchronisation unterstützen. Seit Kurzem hat eine wachsende Zahl von Studien die zusätzliche Wichtigkeit antizipatorischer Mechanismen für SMS hervorgehoben. Ziel dieser Dissertation war es, ein besseres Verständnis dieser zugrundeliegenden Mechanismen zeitlicher Adaptation (Prozesse reaktiver Fehlerkorrektur) und Antizipation (prädiktive Prozesse) zu gewinnen, von denen angenommen wird, dass sie bei der für SMS charakteristischen Verknüpfung von Präzision und Flexibilität eine Rolle spielen. Dazu wurde ein Adaptations- und Antizipationsmodell (ADAM) entwickelt sowie Experimente mit Fokus auf verschiedene Aspekte von Timing sowohl mit gesunden Probanden, als auch mit Patienten durchgeführt.

KAPITEL 2

Kapitel 2 gibt einerseits eine Übersicht über existente Literatur zu Adaptations- und Antizipationsmechanismen der SMS und stellt zum Anderen ADAM vor. Menschen sind normalerweise in hohem Grad dazu fähig, ihre Bewegungen mit auditiven Sequenzen zu synchronisieren. Aufgrund biologischen Rauschens und intentionaler Abweichungen von

Regelhaftigkeit (etwa in Musik, die zeitliche Variationen wie Verlangsamung oder Tempoerhöhung als expressives Mittel nutzt) treten nichtsdestotrotz während der Synchronisation zwischen Handlung und Stimulus Fehler im Timing auf (Asynchronitäten). Prozesse der Fehlerkorrektur, einschließlich Phasen- und Periodenkorrektur, kompensieren Fehler im Timing auf reaktive Art und Weise. Ohne diese Adaptationsmechanismen würden Asynchronitäten über die Zeit zunehmen, was wiederum schließlich zum Verlust von Synchronität zwischen Stimulussequenz und Bewegung führen würde.

Obwohl erfolgreiche SMS Adaptationsmechanismen voraussetzt, können Phasen- und Periodenkorrektur nicht alle Aspekte von SMS erklären, beispielsweise die Fähigkeit, präzise und synchron einer Sequenz zu folgen, die sich im Tempo ändert. In solchen Situationen ermöglichen Antizipatorische Mechanismen die Vorhersage des Auftretens der Stimulusereignisse (Stimulus Onset), und damit der Bewegung, rechtzeitig zu beginnen, so dass sie mit dem eigentlichen Stimulusereignis zusammenfällt. Antizipationsmechanismen wurden und werden mit internalen Modellen verbunden. Internale, nämlich vorwärtsgerichtete und inverse Modelle, repräsentieren die sensomotorischen Transformationen, welche Intentionen, motorische Befehle und Verhaltenseffekte vermitteln, und können ausgeführt werden, ohne die Handlung tatsächlich durchzuführen. Vorwärtsgerichtete Modelle sagen das Ergebnis eines motorischen Befehls auf Grundlage des momentanen Zustand des Systems vorher und repräsentieren somit den kausalen Zusammenhang zwischen Input und Output des handlungskontrollierenden Systems.

Inverse Modelle andererseits dienen als Kontrollinstanz, indem sie den motorischen Befehl zur Verfügung stellen, der nötig ist, um das System vom momentanen auf den angestrebten Endzustand zu ändern. Gepaarte vorwärtsgerichtete und inverse internale Modelle ermöglichen erfolgreiche SMS, indem durch sie potentielle Fehler bereits vor ihrem eigentlichen Auftreten korrigiert werden können.

Typischerweise wurden die Rollen von Adaptations- und Antizipationsmechanismen in SMS mit getrennten Paradigmen untersucht. In dieser Dissertation werden Argumente dafür angeführt, dass es erstrebenswert ist, beide Mechanismen innerhalb eines gemeinsamen theoretischen Rahmens zu betrachten, um ein vollständigeres Verständnis dieser Mechanismen, ihrer Verbindung und ihres wechselseitigen Einflusses entwickeln zu können. Solch ein gemeinsamer Rahmen wurde mit der Entwicklung des ADAM verfolgt, einem Adaptations- und Antizipationsmodell, dass reaktive Fehlerkorrekturprozesse (Adaptation) mit prädiktiven zeitlichen Extrapolationsprozessen, entsprechend dem Konzept internaler Modelle (Antizipation), verbindet. Durch Simulationen, während derer Parameter systematisch variiert werden können, und durch die Nutzung von ADAM zur Erstellung eines virtuellen Partners, mit dem Probanden direkt interagieren können, soll ADAM Erkenntnisse über die an SMS beteiligten Adaptations- und Antizipationsmechanismen bereitstellen.

KAPITEL 3

Ein gängiges Paradigma zur Untersuchung von SMS und ihrer zugrunde liegenden Mechanismen beinhaltet eine Tapping-Aufgabe. Während dieser einfachen Aufgabe werden Probanden darum gebeten, ihren Finger synchron mit einer Stimulussequenz, oft einer auditiven Sequenz, zu bewegen. Das Ziel der in Kapitel 3 vorgestellten Studie war, zu verstehen wie Probanden ihre Bewegungen mit Sequenzen synchronisieren, die konstant ihr Tempo ändern. Zu diesem Zweck wurden die Ergebnissen eines Verhaltensexperiments mit Simulationen mittels ADAM verglichen. 17 gesunde Probanden synchronisierten ihr Tapping mit auditiven, ihr Tempo ändernden Stimulussequenzen.

Die Muster dieser Stimulussequenzen unterschieden sich hinsichtlich der Schnelligkeit der Tempowechsel und der Anzahl der Wendepunkte. Die Tempowechsel wurden so konzipiert, dass sie musikalischem Accelerando und Ritardando ähnelten.

Die durchschnittliche Asynchronität (arithmetisches Mittel) und die Standardabweichung der Asynchronität wurden als Maße für die Genauigkeit und Präzision der SMS verwendet. Weiterhin wurden Maße abgeleitet, welche die zugrunde liegenden Adaptations- und Antizipationsmechanismen betreffen. Die Simulationen fokussierten auf den Effekt dieser Mechanismen, sowie auf mögliche Verbindungen zwischen beiden Mechanismen.

Es wurden vier Modelle entwickelt: eines, das nur Adaption beinhaltete, eines mit voneinander unabhängigen Beiträgen der Adaption und Antizipation, und zwei Modelle, in denen Adaption und Antizipation in einem gemeinsamen internalen Modell gekoppelt waren. Ergebnisse des Verhaltensexperiments deuteten darauf hin, dass die Genauigkeit und Präzision der sensomotorischen Synchronisation, auch wenn sie durchgehend hoch waren, mit Zunahme der Schnelligkeit der Tempowechsel und der Anzahl der Wendepunkte abnahmen. Auf Simulationen und dem Modell basierende Parameterschätzungen zeigten, dass Adaptionsmechanismen alleine das beobachtete sensomotorische Synchronisationsverhalten nicht vollständig erklären können. Die Berücksichtigung des Antizipationsprozesses im Modell erhöhte die Präzision der simulierten sensomotorischen Synchronisation und verbesserte den Fit des Modells auf die Verhaltensdaten. Insgesamt legten die Ergebnisse nahe, dass sowohl Adaptations- als auch Antizipationsmechanismen während der sensomotorischen Sycnhronisation mit Tempowechseln eine wichtige Rolle spielen. Obwohl die exakte Verbindung zwischen Adaption und Antizipation eine offene Frage bleibt, bieten internale Modelle, die beide Prozesse verbinden, einen möglichen Mechanismus, der eine Rolle in dieser Verbindung spielen könnte.

KAPITEL 4

Kapitel 4 beschreibt eine Studie zu Timing bei Musikern mit fokaler Dystonie (Musikerdystonie, Musician's Hand Dystonia), gekennzeichnet durch Verlust willentlicher motorischer Kontrolle über geübte Handbewegungen beim Instrumentalspiel. Die Pathophysiologie dieser Bewegungseinschränkung ist noch unklar, aber Studien deuten darauf hin, dass neben veränderten Inhibitionsmustern auf verschiedenen Ebenen des Zentralnervensystems auch fehladaptive Plastizität in Timing verarbeitenden Arealen (z.B. Basalganglien, Sensomotorische Cortices), sowie Änderungen der sensomotorischen Integration eine Rolle spielen. Verschiedene Studien haben dargelegt, dass neben dem Verlust über die Kontrolle von für das Instrumentalspiel notwendigen Bewegungen die Patienten auch eingeschränkte Fähigkeiten in der Wahrnehmung und Verarbeitung zeitlicher Koordination zeigen. Die aktuelle Studie gab eine Vielzahl von Aufgaben vor mit dem Ziel, die rein perzeptuelle Kapazität von für SMS notwendigen produktiven Fähigkeiten zu trennen und dadurch ein Bild des Timings von Patienten mit Musikerdystonie zu gewinnen. Die Probanden (15 Patienten und 15 angepasste Kontrollprobanden) synchronisierten ihr Tapping mit sich im Tempo ändernden und adaptiven auditiven Sequenzen, um SMS-Fähigkeiten und zugrundeliegende Adaptations- und Antizipationsmechanismen anzusprechen. Eine angepasste Version des Beat Alignment Tests wurde benutzt, um die Präzision in der Wahrnehmung der Synchronizität eines Metrums zu untersuchen. Die Performanz in diesen Aufgaben wurde mit elementaren Wahrnehmungsaufgaben verglichen, namentlich Anisochroniedetektion und Entdeckung auditiv-motorischer Verzögerungen (Auditory-motor delay detection). Die Ergebnisse zeigten keine Defizite in auditorisch-motorischer Verarbeitung zwischen Patienten- und Kontrollgruppe. Beide Gruppen profitierten von einer Stimulussequenz, die sich an ihr Timing während einer stabilen SMS-Aufgabe (ohne Änderung des IOI) anpasste.

Weiterhin waren beide Gruppen im Beat Alignment Test in der Lage, ein zeitlich falsch ausgerichtetes Metronom zu detektieren, wenn dieses relativ zum musikalischen Schlag zu spät (gegenüber zu früh) war. Insgesamt lassen die Resultate darauf schließen, dass Timing-Fähigkeiten in Patienten mit Musikerdystonie intakt sind. Das weist darauf hin, dass

Musikerdystonie eine hoch aufgabenspezifische Bewegungseinschränkung ist, die Patienten am meisten bei Aufgaben einschränkt, die denen beim Spielen ihres Instrumentes ähnlich sind.

SCHLUSSFOLGERUNG

Die in dieser Dissertation präsentierte Forschung untersuchte das Timing von Bewegungen während SMS mit Fokus auf die zugrunde liegenden Adaptations- und Antizipationsmechanismen... ADAM erwies sich bei der Untersuchung der Adaptions- und Antizipationsmechanismen, sowie der möglichen Verbindung dieser Mechanismen, als nützlicher Rahmen. Angenommene Beziehungen zwischen Adaption und Antizipation wurden durch Vergleiche von auf ADAM basierenden Computersimulationen mit Verhaltensdaten untersucht, was zu neuen Erkenntnissen hinsichtlich SMS führte. Insbesondere konnte nicht nur gezeigt werden, dass sowohl Adaptations- als auch Antizipationsmechanismen eine Rolle während SMS mit Sequenzen, die das Tempo verändern, spielen, sondern auch, dass internale Modelle eine Verbindung zwischen diesen Mechanismen bieten könnten. Die Untersuchungen in dieser Dissertation waren durch die Annahme motiviert, dass es möglich sein wird ein zielgerichtetes Rehabilitationsprogramm mit Fokus auf das Timing von Bewegungen zu erstellen, sobald ein besseres Verständnis der zugrunde liegenden Mechanismen von zeitlicher sensomotorischer Synchronisation und entsprechenden Defiziten bei Patienten erlangt wurde. Patienten mit fokaler Dystonie zeigten keine beeinträchtigte SMS, profitierten aber trotzdem von der Synchronisierung mit adaptiven Stimulussequenzen. Dieses Ergebnis ist aussichtsreich im Hinblick auf die Entwicklung von Rehabilitationsprogrammen. Patienten mit fokaler Dystonie konnten ihre Timing-Fähigkeiten erhalten, indem sie sensomotorische Timing-Aufgaben ohne ihr Instrument übten. Es könnten anspruchsvolle Synchronisationsaufgaben entwickelt werden, die adaptive virtuelle Partner einbeziehen, welche von ADAM gesteuert werden könnten.

List of figures

Chapter 1

Figure 1.1 _ p 9

Standard variables related to a finger tapping task. asyn, asynchrony; ITI, interval between successive actions; IOI, interval between the onsets of the stimulus sequence.

Figure 1.2 _ p 13

Implementation of adaptation (**A**) and anticipation (**B**, **C**) in ADAM. asyn, asynchrony; Int, interval; T, Timekeeper period; α, phase correction parameter; β, period correction parameter; k, number of intervals. (**A**) The time of the occurrence of the next tone is determined based on the asynchrony and the settings of the error correction parameters α and β. (**B**, **C**) A curve-fitting process, applied to the preceding intervals, predicts the next tap [Reprinted from "The Adaptation and Anticipation Model (ADAM) of sensorimotor synchronization," by M.C. van der Steen and P.E. Keller, *Frontiers in Human Neuroscience, 7*:253, p. 9]

Chapter 2

Figure 2.1 _ p 27

(**A**) The proposed architecture of the ADaptation and Anticipation Model, ADAM. The main components that are illustrated include auditory and visual input, internal mechanisms that support adaptation to and anticipation of this input, and —by communing with internal models of one's own actions, others' actions, and collective joint actions— control behavioral output. In addition, three sources of noise (perceptual, timekeeper, and motor) can affect ADAM's SMS accuracy and precision. Components illustrated in grey have not been implemented in the current version of ADAM, though their relevance to SMS is discussed in this article.

(**B**) An example of a bi-directional experimental set up in which the participant and ADAM influence each other in the context of a joint drumming task.

Figure 2.2 _ p 33

Adaptation processes based on the asynchrony following the information-processing theory. In the examples, α and β are both equal to 0.5, which is a value that fits within the typical range of empirical α and β estimates (0.2-0.8). The examples given show how the timing of the next tap is adjusted to compensate for the asynchrony. As a result of the timekeeper setting, the asynchrony (asyn) in combination with error correction mechanisms, and motor and timekeeper noise (N [which is set to zero in the present example]) the next tap is shifted in the opposite direction of the asynchrony.

(**A**) Phase correction (α = 0.5): half of the asynchrony is corrected. Phase correction is a local adjustment; the setting of the timekeeper (in this example 500 ms) is not affected.

(**B**) Period correction (β = 0.5): the correction of the asynchrony has a cumulative effect on the setting of the timekeeper (in this example the base timekeeper is 500 ms), leading to tempo drift.
(**C**) In practice, phase and period correction can be both active during SMS. As a result of the combination of both error correction mechanisms, the timing of the next tap is adjusted based on a percentage of the asynchrony.

Figure 2.3 ____ p 42
Implementation of adaptation (A) and anticipation (B + C) in ADAM. asyn = asynchrony | Int = interval | T = Timekeeper period
(**A**) The time of occurrence of the next tone is determined based on the asynchrony and the settings of error correction parameters α and β (eq. 1). The setting of β affects the current timekeeper period (eq. 2). The interval produced by ADAM between t_n and t_{n+1} is equal to $T_n + (\alpha + \beta) \cdot asyn_n$.
(**B-C**) A curve-fitting process that is applied to the preceding intervals predicts the participant's next tap time (eq. 3 and 4). The timing of upcoming tone or the next interval produced by ADAM can be set to enable ADAM's next tone to coincide with the predicted next tap of the participant.

Figure 2.4 ____ p 44
A schematic overview of the joint internal model, where the adaptation and anticipation module interact via 'own' and 'other' internal models. The difference between the outputs of the adaptation and anticipation module of ADAM is compared to a predefined threshold. Depending on this comparison, the motor command is either executed as planned or in accordance with a default setting. A detailed description of this process can be found in the text.

<u>Chapter 3</u>
Figure 3.1 ____ p 66
Schematic representation of phase and period correction. Equations governing phase and period correction are: $t_{n+1} = t_n + T_n - (\alpha + \beta) * asyn_n + noise$ and $T_{n+1} = T_n - \beta * asyn_n$. Where α reflects the phase correction parameter and β the period correction parameter, t_n is the timing of the next tap, and T_n the current timekeeper setting (see Experimental procedure). The timekeeper originally has an interval setting of 500ms. In blue standard variable related to a finger tapping task are presented; asyn, asynchrony; ITI, interval between successive actions; IOI, interval between the onsets of the stimulus sequence. Adapted from van der Steen and Keller, 2013.

Figure 3.2 ____ p 66
The three tempo changing patterns. Each trial started with four initiation tones with an IOI of 600 ms. The stimulus sequences consisted of 64 tones. The tempo of the first 16 tones was stable (IOI 600 ms)

[black dotted box], allowing synchrony to be established. The tempo during the following 48 tones varied between 600 and 400 ms IOI, following three sigmoidal patterns that resembled musical accelerando and ritardando. Data-analyses focuses on the tempo changing part of the trials [grey dashed box] (see Experimental procedure).

Figure 3.3 ____ p 68
The mean signed asynchrony as a measure of SMS accuracy (A) en the standard deviation of the signed asynchrony as a measure of SMS precision (B) separated for the three patterns. Error bars represent standard error across participants.

Figure 3.4 ____ p 68
Estimated amount of phase **(A)** and period **(B)** correction reflecting adaptation mechanisms. Error bars represent standard error across participants.

Figure 3.5 ____ p 70
The cross-correlations at lag-0 and lag-1(**A**), PT-ratio (**B**), and PT-index **(C)** reflecting anticipation. PT-ratios bigger than 1 and PT-indices bigger than 0 indicate participants are predicting the tempo changes. Error bars represent standard error across participants

Figure 3.6 ____ p 72-73
Heat-maps showing the SD of the signed asynchronies as a result of the parameter settings for the 'Adaptation Model' (A), 'Independent ADAM' model (B) 'Joint ADAM (α)' model (C), and 'Joint ADAM (β)' model (D). Dark blue represents the most successful SMS precision (low standard deviation of the signed asynchrony). Extreme values (larger than three times the mean of the medians of the simulated standard deviation of the signed asynchrony) were replaced by the mean of the median for presentation purposes. The black boxes in panel A reflect the mean phase and period estimates for the participants.

Figure 3.7 ____ p 74
Parameter estimates based on the 'Independent ADAM' model. Where α reflects a phase correction parameter, while *m* indicates the prediction/tracking parameter. Error bars represent standard error across participants.

Figure 3.8 ____ p 75
Parameter estimates based on the 'Joint ADAM (α)' model. Where γ reflects an anticipatory phase correction process in the link module, α reflects the phase correction parameter of the adaptation

module, while *m* indicates the prediction/tracking parameter of the anticipation module. Error bars represent standard error across participants.

Figure 3.9 _ p 76

Parameter estimates based on the 'Joint ADAM (β) model. Where γ reflects an anticipatory phase correction process in the link module, β reflects the period correction parameter of the adaptation module, while *m* indicates the prediction/tracking parameter of the anticipation module. Error bars represent standard error across participants.

Figure 3.10 _ p 77

Likelihood estimates for the four models for each pattern (A); detail of likelihood estimates for the three models including both adaptation and anticipation (B). Error bars represent standard error across participants.

Figure 3.11 _ p 88

Equations describing the 'Independent ADAM' and 'Joint ADAM (α | β)' models. α = phase correction, β = period correction, γ = anticipatory phase correction, *m* = prediction/tracking parameter. See text for explanation.

Chapter 4

Figure 4.1 _ p 107

Pacing signal for the adaptive tapping task. The timing of the pacing signal was determined by the following equation: tn+1 = tn + 500 + α × asynn. In the current experiment α was set to 0, 0.3 or 0.7, thus the pacing signal corrected 0 (non- responsive metronome in fixed trials), 30 or 70 % of the asynchrony by shifting the next tone in the opposite direction.

Figure 4.2 _ p 113

Adaptive tapping task accuracy results. Mean signed asynchronies as a measure of sensorimotor synchronization accuracy separated for group and levels of alpha. By convention negative values indicate that the tap preceded the tone. Error bars indicate standard error of the mean.

Figure 4.3 _ p 115

Beat alignment test results (A) Overall accuracy scores. Error bars indicate standard error of the mean. (B) Aligned responses according to relative metronome shifts. Error bars indicate standard error of the mean.

List of tables

Chapter 4

Table 4.1 _ p 105
Description of the participants.

Table 4.2 _ p 116
Mean (SD) of the non-significant results for the different tasks and outcome measure separated per group and if applicable level of alpha.

Table 4.3 _ p 117
Classification accuracy for each of the machine learning approaches: Naive Bayesian, Linear Discriminant analysis (LDA) and Support Vector Machines (SVM).

Curriculum Vitae

Name	Maria Christine (Marieke) van der Steen
Date of birth	03.12.1985
Place of birth	Veghel, the Netherlands
since October 2010	PhD candidate, Max Planck Research Group "Music Cognition and Action", Max Planck Institute for Human Cognitive and Brain Sciences, Leipzig
October 2012 – January 2014	Scientific collaborator Institute of Music Physiology and Musicians' Medicine University of Music, Drama and Media, Hanover
October 2010 – September 2013	Early stage researcher, EBRAMUS project, European Community's Seventh Framework Programme, grant agreement number 238157
September 2004 – August 2010	Bachelor & Master Human Movement Sciences, University of Groningen, Groningen, the Netherlands
July 2004	High school: Gymnasium, Gymnasium Bernrode, Heeswijk, the Netherlands

List of Publications

Publications

2014 Van der Steen, M.C., Molendijk, E.B.D., Altenmüller, E. & Furuya, S. Expert pianists do not listen: the expertise-dependent influence of temporal perturbation on the production of sequential movements. *Neuroscience*, 269, 290-298.

Van der Steen, M.C., Van Vugt, F.T, Keller, P.E. & Altenmüller, E. General timing abilities stay intact in patients with musician's dystonia. *PLoS ONE,* 9(3): e92906. doi: 10.1371/journal.pone.0092906.

2013 Van der Steen, M.C. & Keller, P.E. The ADaptation and Anticipation Model (ADAM) of sensorimotor synchronization. *Frontiers in Human Neuroscience*, 7:253.

2011 Van der Steen, M.C. & Bongers, R.M. Joint angle variability and co-variation in a reaching with a rod task. *Experimental Brain Research*, *208*(3), 411-422.

Submitted Mills, P.F., van der Steen, M.C., Schultz, B.G., & Keller, P.E. Individual differences in temporal anticipation and adaptation during sensorimotor synchronization.

Van der Steen, M.C., Jacoby, N, Fairhurst, M.T. & Keller, P.E. Sensorimotor synchronization with tempo changing auditory sequences

Presentations

2013 Van der Steen, M.C. Adaptation and anticipation in sensorimotor synchronization. Talk presented at New Perspectives for Stimulating Cognitive and Sensory Processes: EBRAMUS Network Final Conference, Pavia, Italy.

Van der Steen, M.C. Perception and production abilities in auditory-motor processing of musicians' dystonia patients. Talk presented at Sequence Production Lab. Montreal, QC, Canada.

Van der Steen, M.C. Sensorimotor synchronization in musicians' dystonia, cerebellum lesion and basal ganglia lesion patients. Talk presented at EBRAMUS Consortium Meeting Workshop 2013. Montpellier, France.

Van der Steen, M.C. ADAM, Max and patients. Talk presented at EBRAMUS Consortium Meeting. Warsaw, Poland.

2012 Van der Steen, M.C., Fairhurst, M.T., & Keller, P.E. Speeding up and slowing down with ADAM. Talk presented at EBRAMUS Consortium Meeting Workshop 2012. Leipzig, Germany.

Van der Steen, M.C., Fairhurst, M.T., & Keller, P.E. ADAM in action: Working with an adaptive and anticipatory virtual partner. Talk presented at EBRAMUS Consortium Meeting Springschool 2012. Ghent, Belgium.

2011 Van der Steen, M.C. Sensorimotor synchronization and ADAM. Talk presented at Music Dynamics Lab, Center for Complex Systems and Brain Sciences, Florida Atlantic University. Boca Raton, FL, USA.

Van der Steen, M.C. Developing an adaptive virtual synchronization partner. Talk presented at EBRAMUS Consortium Meeting Workshop 2011. Edinburgh, United Kingdom.

Van der Steen, M.C. Developing a virtual synchronization partner. Talk presented at EBRAMUS Consortium Meeting Springschool. Delmenhorst, Germany.

Posters

2013 Van der Steen, M.C., van Vugt, F.T., Keller, P.E., & Altenmueller, E. Separating perception and production abilities in auditory-motor processing of musicians' dystonia patients. Poster presented at Progress in Motor Control IX, Montreal, QC, Canada.

Van der Steen, M.C., van Vugt, F.T., Keller, P.E., & Altenmueller, E. Perception and production abilities of musicians' dystonia patients in auditory-motor processing. Poster presented at Second International Congress on Treatment of Dystonia, Hannover, Germany.

2012 Van der Steen, M.C., Fairhurst, M.T., & Keller, P.E. Investigating the role of adaptation and anticipation mechanisms on sensorimotor synchronization with ADAM and a tempo changing tapping task. Poster presented at The Donders Discussions, Nijmegen, the Netherlands.

Van der Steen, M.C., Fairhurst, M.T., & Keller, P.E. Meet ADAM: A model for investigating the effects of adaptation and anticipatory mechanisms on sensorimotor synchronization. Poster presented at 12th International Conference on Music Perception and Cognition (ICMPC) 8th Triennial Conference of the European Society for the Cognitive Sciences of Music (ESCOM), Thessaloniki, Greece.

Van der Steen, M.C., Fairhurst, M.T., & Keller, P.E. Investigating the role of adaptation and anticipatory mechanisms on sensorimotor synchronization using ADAM. Poster presented at PoRT Workshop, Glasgow, United Kingdom.

Van der Steen, M.C., Fairhurst, M.T., & Keller, P.E. Tapping along with ADAM: Synchronizing with an adaptive and anticipatory virtual partner. Poster presented at Annual Meeting of The Society for the Neural Control of Movement, Venice, Italy.

2010 Bongers, R.M., & van der Steen, M.C. The effect of length of the end-effector on arm synergies during pointing movements. Poster presented at 40th Annual Meeting of the Society for Neuroscience Conference, San Diego, CA, USA.

Zaal, F.T.J.M., Bongers, R.M., & van der Steen, M.C. The reaching component of prehension. Poster presented at 3rd International Congress Complex Systems in Medicine and Sport (ICCSMS2010), Kaunas, Lithuania.

Van der Steen, M.C., & Bongers, R.M. Joint angle variability in 3D tool reaching: uncontrolled manifold analysis. Poster presented at FENS 2010 Satellite Symposium on Motor Control, Nijmegen, the Netherlands.

Confirmation of contribution of co-authors

Title: **The Adaptation and Anticipation Model (ADAM) of sensorimotor synchronization**

Journal: Frontiers in Human Neuroscience

Authors: M.C. (Marieke) van der Steen, Peter E. Keller

Contribution of Maria Christine (Marieke) van der Steen:

- Project conception
- Creating model
- Writing of the manuscript

Contribution of Peter E. Keller:

- Project conception
- Writing of the manuscript

Maria Christine (Marieke) van der Steen

Peter E. Keller

Confirmation of contribution of co-authors

Title: **Sensorimotor synchronization with tempo changing auditory sequences**

Journal: Brain Research

Authors: M.C. (Marieke) van der Steen, Nori Jacoby, Merle T. Fairhurst, Peter E. Keller

---

Contribution of Maria Christine (Marieke) van der Steen:

- Project conception
- Experimental design
- Experimental set up and preparation of stimuli
- Data acquisition
- Data analyses
- Writing of the manuscript

Contribution of Nori Jacoby:

- Data analyses
- Writing of the manuscript

Contribution of Merle T. Fairhurst:

- Project conception
- Experimental design
- Writing of the manuscript

Contribution of Peter E. Keller:

- Project conception
- Experimental design

Maria Christine (Marieke) van der Steen

Nori Jacoby

Merle T. Fairhurst

Peter E. Keller

– Writing of the manuscript

Confirmation of contribution of co-authors

Title: Basic timing abilities stay intact in patients with musician's dystonia

Journal: PLoS ONE

Authors: M.C. (Marieke) van der Steen, Floris T. van Vugt, Peter E. Keller, Eckart Altenmüller

---

Contribution of Maria Christine (Marieke) van der Steen:

- Project conception
- Experimental design
- Experimental set up and preparation of stimuli
- Data acquisition
- Data analyses
- Writing of the manuscript

Contribution of Floris T. van Vugt:

- Project conception
- Experimental design
- Experimental set up and preparation of stimuli
- Data analyses
- Writing of the manuscript

Contribution of Peter E. Keller:

- Project conception
- Writing of the manuscript

Contribution of Eckart Altenmüller:

- Project conception
- Writing of the manuscript

Maria Christine (Marieke) van der Steen

Floris T. van Vugt

Peter E. Keller

Eckart Altenmüller

Selbständigkeitserklärung zum monographischen Kapitel 1

Hiermit erkläre ich, dass das monographische Kapitel 1 ohne unzulässige Hilfe und ohne Benutzung anderer als der angegebenen Hilfsmittel angefertigt wurde und dass die aus fremden Quellen direkt oder indirekt übernommenen Gedanken in der Arbeit als solche erkenntlich gemacht worden sind.

Leipzig, den 10.07.2014

Maria Christine van der Steen

Selbständigkeitserklärung

Hiermit erkläre ich, dass die vorliegende Arbeit ohne unzulässige Hilfe und ohne Benutzung anderer als der angegebenen Hilfsmittel angefertigt wurde und dass die aus fremden Quellen direkt oder indirekt übernommenen Gedanken in der Arbeit als solche erkenntlich gemacht worden sind.

Leipzig, den 10.07.2014

Maria Christine van der Steen

Bibliographic details

van der Steen, Maria Christine
Temporal adaptation and anticipation mechanisms in sensorimotor synchronization
Fakultät für Biowissenschaften, Pharmazie und Psychologie
Universität Leipzig
Dissertation
153 pages, references: 49 (introduction) / 108 (manuscript 1) / 45 (manuscript 2) / 67 (manuscript 3), 20 figures, 3 tables

---

A constantly changing environment requires precise yet flexible timing of movements. Sensorimotor synchronization (SMS) —the temporal coordination of actions with events in a predictable external rhythm— is a fundamental human skill that contributes to optimal sensory-motor control in daily life. A large body of research related to SMS has focused on adaptive error correction mechanisms that support the synchronization of periodic movements (e.g., finger taps) with events in regular pacing sequences. The results of recent studies additionally highlight the importance of anticipatory mechanisms that support temporal prediction in the context of SMS with sequences that contain tempo changes.

The goal of this dissertation was to gain a better understanding of the underlying temporal adaptation (reactive error correction processes) and anticipation (predictive processes) mechanisms that are hypothesized to play a role in the precise yet flexible nature of SMS. To this end, an Adaptation and Anticipation Model (ADAM) was developed in theoretical work, and then two experiments focusing on different aspects of movement timing with healthy participants and patients were performed. The first experiment combined simulations with ADAM and behavioral data from a tempo changing finger tapping experiment. Results indicated that both adaptation and anticipation mechanisms play a role in synchronization with tempo changes, and that these mechanisms may be linked in internal models. The second experiment revealed that patients with musician's dystonia (a movement disorder that is characterized by the loss of voluntary motor control related to instrumental playing in musicians) do not display impaired sensorimotor synchronization but nevertheless benefit from synchronizing with adaptive stimulus sequences. This finding is generally promising for developing rehabilitation programs targeted towards facilitating movement timing by employing adaptive virtual partners driven by ADAM (e.g., musician's dystonia patients could train and therefore maintain their timing skills).

MPI Series in Human Cognitive and Brain Sciences:

1 Anja Hahne
Charakteristika syntaktischer und semantischer Prozesse bei der auditiven Sprachverarbeitung: Evidenz aus ereigniskorrelierten Potentialstudien

2 Ricarda Schubotz
Erinnern kurzer Zeitdauern: Behaviorale und neurophysiologische Korrelate einer Arbeitsgedächtnisfunktion

3 Volker Bosch
Das Halten von Information im Arbeitsgedächtnis: Dissoziationen langsamer corticaler Potentiale

4 Jorge Jovicich
An investigation of the use of Gradient- and Spin-Echo (GRASE) imaging for functional MRI of the human brain

5 Rosemary C. Dymond
Spatial Specificity and Temporal Accuracy in Functional Magnetic Resonance Investigations

6 Stefan Zysset
Eine experimentalpsychologische Studie zu Gedächtnisabrufprozessen unter Verwendung der funktionellen Magnetresonanztomographie

7 Ulrich Hartmann
Ein mechanisches Finite-Elemente-Modell des menschlichen Kopfes

8 Bertram Opitz
Funktionelle Neuroanatomie der Verarbeitung einfacher und komplexer akustischer Reize: Integration haemodynamischer und elektrophysiologischer Maße

9 Gisela Müller-Plath
Formale Modellierung visueller Suchstrategien mit Anwendungen bei der Lokalisation von Hirnfunktionen und in der Diagnostik von Aufmerksamkeitsstörungen

10 Thomas Jacobsen
Characteristics of processing morphological structural and inherent case in language comprehension

11 Stefan Kölsch
Brain and Music
A contribution to the investigation of central auditory processing with a new electrophysiological approach

12 Stefan Frisch
Verb-Argument-Struktur, Kasus und thematische Interpretation beim Sprachverstehen

13 Markus Ullsperger
The role of retrieval inhibition in directed forgetting – an event-related brain potential analysis

14 Martin Koch
Measurement of the Self-Diffusion Tensor of Water in the Human Brain

15 Axel Hutt
Methoden zur Untersuchung der Dynamik raumzeitlicher Signale

16 Frithjof Kruggel
Detektion und Quantifizierung von Hirnaktivität mit der funktionellen Magnetresonanztomographie

17 Anja Dove
Lokalisierung an internen Kontrollprozessen beteiligter Hirngebiete mithilfe des Aufgabenwechselparadigmas und der ereigniskorrelierten funktionellen Magnetresonanztomographie

18 Karsten Steinhauer
Hirnphysiologische Korrelate prosodischer Satzverarbeitung bei gesprochener und geschriebener Sprache

19 Silke Urban
Verbinformationen im Satzverstehen

20 Katja Werheid
Implizites Sequenzlernen bei Morbus Parkinson

21 Doreen Nessler
Is it Memory or Illusion? Electrophysiological Characteristics of True and False Recognition

22 Christoph Herrmann
Die Bedeutung von 40-Hz-Oszillationen für kognitive Prozesse

23 Christian Fiebach
Working Memory and Syntax during Sentence Processing.
A neurocognitive investigation with event-related brain potentials and functional magnetic resonance imaging

24 Grit Hein
Lokalisation von Doppelaufgabendefiziten bei gesunden älteren Personen und neurologischen Patienten

25 Monica de Filippis
Die visuelle Verarbeitung unbeachteter Wörter. Ein elektrophysiologischer Ansatz

26 Ulrich Müller
Die katecholaminerge Modulation präfrontaler kognitiver Funktionen beim Menschen

27 Kristina Uhl
Kontrollfunktion des Arbeitsgedächtnisses über interferierende Information

28 Ina Bornkessel
The Argument Dependency Model: A Neurocognitive Approach to Incremental Interpretation

29 Sonja Lattner
Neurophysiologische Untersuchungen zur auditorischen Verarbeitung von Stimminformationen

30 Christin Grünewald
Die Rolle motorischer Schemata bei der Objektrepräsentation: Untersuchungen mit funktioneller Magnetresonanztomographie

31 Annett Schirmer
Emotional Speech Perception: Electrophysiological Insights into the Processing of Emotional Prosody and Word Valence in Men and Women

32 André J. Szameitat
Die Funktionalität des lateral-präfrontalen Cortex für die Verarbeitung von Doppelaufgaben

33 Susanne Wagner
Verbales Arbeitsgedächtnis und die Verarbeitung ambiger Wörter in Wort- und Satzkontexten

34 Sophie Manthey
Hirn und Handlung: Untersuchung der Handlungsrepräsentation im ventralen prämotorischen Cortex mit Hilfe der funktionellen Magnet-Resonanz-Tomographie

35 Stefan Heim
Towards a Common Neural Network Model of Language Production and Comprehension: fMRI Evidence for the Processing of Phonological and Syntactic Information in Single Words

36 Claudia Friedrich
Prosody and spoken word recognition: Behavioral and ERP correlates

37 Ulrike Lex
Sprachlateralisierung bei Rechts- und Linkshändern mit funktioneller Magnetresonanztomographie

38 Thomas Arnold
Computergestützte Befundung klinischer Elektroenzephalogramme

39 Carsten H. Wolters
Influence of Tissue Conductivity Inhomogeneity and Anisotropy on EEG/ MEG based Source Localization in the Human Brain

40 Ansgar Hantsch
Fisch oder Karpfen? Lexikale Aktivierung von Benennungsalternative bei der Objektbenennung

41 Peggy Bungert
Zentralnervöse Verarbeitung akustischer Informationen Signalidentifikation, Signallateralisation und zeitgebundene Informationsverarbeitung bei Patienten mit erworbenen Hirnschädigungen

42 Daniel Senkowski
Neuronal correlates of selective attention: An investigation of electro-physiological brain responses in the EEG and MEG

43 Gert Wollny
Analysis of Changes in Temporal Series of Medical Images

44 Angelika Wolf
Sprachverstehen mit Cochlea-Implantat: EKP-Studien mit postlingual ertaubten erwachsenen CI-Trägern

45 Kirsten G. Volz
Brain correlates of uncertain decisions: Types and degrees of uncertainty

46 Hagen Huttner
Magnetresonanztomographische Untersuchungen über die anatomische Variabilität des Frontallappens des menschlichen Großhirns

47 Dirk Köster
Morphology and Spoken Word Comprehension: Electrophysiological Investigations of Internal Compound Structure

48 Claudia A. Hruska
Einflüsse kontextueller und prosodischer Informationen in der auditorischen Satzverarbeitung: Untersuchungen mit ereigniskorrelierten Hirnpotentialen

49 Hannes Ruge
Eine Analyse des raum-zeitlichen Musters neuronaler Aktivierung im Aufgabenwechselparadigma zur Untersuchung handlungssteuernder Prozesse

50 Ricarda I. Schubotz
Human premotor cortex: Beyond motor performance

51 Clemens von Zerssen
Bewusstes Erinnern und falsches Wiedererkennen: Eine funktionelle MRT Studie neuroanatomischer Gedächtniskorrelate

52 Christiane Weber
Rhythm is gonna get you.
Electrophysiological markers of rhythmic processing in infants with and without risk for Specific Language Impairment (SLI)

53 Marc Schönwiesner
Functional Mapping of Basic Acoustic Parameters in the Human Central Auditory System

54 Katja Fiehler
Temporospatial characteristics of error correction

55 Britta Stolterfoht
Processing Word Order Variations and Ellipses: The Interplay of Syntax and Information Structure during Sentence Comprehension

56 Claudia Danielmeier
Neuronale Grundlagen der Interferenz zwischen Handlung und visueller Wahrnehmung

57 Margret Hund-Georgiadis
Die Organisation von Sprache und ihre Reorganisation bei ausgewählten, neurologischen Erkrankungen gemessen mit funktioneller Magnetresonanztomographie – Einflüsse von Händigkeit, Läsion, Performanz und Perfusion

58 Jutta L. Mueller
Mechanisms of auditory sentence comprehension in first and second language: An electrophysiological miniature grammar study

59 Franziska Biedermann
Auditorische Diskriminationsleistungen nach unilateralen Läsionen im Di- und Telenzephalon

60 Shirley-Ann Rüschemeyer
The Processing of Lexical Semantic and Syntactic Information in Spoken Sentences: Neuroimaging and Behavioral Studies of Native and Non-Native Speakers

61 Kerstin Leuckefeld
The Development of Argument Processing Mechanisms in German. An Electrophysiological Investigation with School-Aged Children and Adults

62 Axel Christian Kühn
Bestimmung der Lateralisierung von Sprachprozessen unter besondere Berücksichtigung des temporalen Cortex, gemessen mit fMRT

63 Ann Pannekamp
Prosodische Informationsverarbeitung bei normalsprachlichem und deviantem Satzmaterial: Untersuchungen mit ereigniskorrelierten Hirnpotentialen

64 Jan Derrfuß
Functional specialization in the lateral frontal cortex: The role of the inferior frontal junction in cognitive control

65 Andrea Mona Philipp
The cognitive representation of tasks – Exploring the role of response modalities using the task-switching paradigm

66 Ulrike Toepel
Contrastive Topic and Focus Information in Discourse – Prosodic Realisation and Electrophysiological Brain Correlates

67 Karsten Müller
Die Anwendung von Spektral- und Waveletanalyse zur Untersuchung der Dynamik von BOLD-Zeitreihen verschiedener Hirnareale

68 Sonja A.Kotz
The role of the basal ganglia in auditory language processing: Evidence from ERP lesion studies and functional neuroimaging

69 Sonja Rossi
The role of proficiency in syntactic second language processing: Evidence from event-related brain potentials in German and Italian

70 Birte U. Forstmann
Behavioral and neural correlates of endogenous control processes in task switching

71 Silke Paulmann
Electrophysiological Evidence on the Processing of Emotional Prosody: Insights from Healthy and Patient Populations

72 Matthias L. Schroeter
Enlightening the Brain – Optical Imaging in Cognitive Neuroscience

73 Julia Reinholz
Interhemispheric interaction in object- and word-related visual areas

74 Evelyn C. Ferstl
The Functional Neuroanatomy of Text Comprehension

75 Miriam Gade
Aufgabeninhibition als Mechanismus der Konfliktreduktion zwischen Aufgabenrepräsentationen

76 Juliane Hofmann
Phonological, Morphological, and Semantic Aspects of Grammatical Gender Processing in German

77 Petra Augurzky
Attaching Relative Clauses in German – The Role of Implicit and Explicit Prosody in Sentence Processing

78 Uta Wolfensteller
Habituelle und arbiträre sensomotorische Verknüpfungen im lateralen prämotorischen Kortex des Menschen

79 Päivi Sivonen
Event-related brain activation in speech perception: From sensory to cognitive processes

80 Yun Nan
Music phrase structure perception: the neural basis, the effects of acculturation and musical training

81 Katrin Schulze
Neural Correlates of Working Memory for Verbal and Tonal Stimuli in Nonmusicians and Musicians With and Without Absolute Pitch

82 Korinna Eckstein
Interaktion von Syntax und Prosodie beim Sprachverstehen: Untersuchungen anhand ereigniskorrelierter Hirnpotentiale

83 Florian Th. Siebörger
Funktionelle Neuroanatomie des Textverstehens: Kohärenzbildung bei Witzen und anderen ungewöhnlichen Texten

84 Diana Böttger
Aktivität im Gamma-Frequenzbereich des EEG: Einfluss demographischer Faktoren und kognitiver Korrelate

85 Jörg Bahlmann
Neural correlates of the processing of linear and hierarchical artificial grammar rules: Electrophysiological and neuroimaging studies

86 Jan Zwickel
Specific Interference Effects Between Temporally Overlapping Action and Perception

87 Markus Ullsperger
Functional Neuroanatomy of Performance Monitoring: fMRI, ERP, and Patient Studies

88 Susanne Dietrich
Vom Brüllen zum Wort – MRT-Studien zur kognitiven Verarbeitung emotionaler Vokalisationen

89 Maren Schmidt-Kassow
What's Beat got to do with ist? The Influence of Meter on Syntactic Processing: ERP Evidence from Healthy and Patient populations

90 Monika Lück
Die Verarbeitung morphologisch komplexer Wörter bei Kindern im Schulalter: Neurophysiologische Korrelate der Entwicklung

91 Diana P. Szameitat
Perzeption und akustische Eigenschaften von Emotionen in menschlichem Lachen

92 Beate Sabisch
Mechanisms of auditory sentence comprehension in children with specific language impairment and children with developmental dyslexia: A neurophysiological investigation

93 Regine Oberecker
Grammatikverarbeitung im Kindesalter: EKP-Studien zum auditorischen Satzverstehen

94 Şükrü Barış Demiral
Incremental Argument Interpretation in Turkish Sentence Comprehension

95 Henning Holle
The Comprehension of Co-Speech Iconic Gestures: Behavioral, Electrophysiological and Neuroimaging Studies

96 Marcel Braß
Das inferior frontale Kreuzungsareal und seine Rolle bei der kognitiven Kontrolle unseres Verhaltens

97 Anna S. Hasting
Syntax in a blink: Early and automatic processing of syntactic rules as revealed by event-related brain potentials

98 Sebastian Jentschke
Neural Correlates of Processing Syntax in Music and Language – Influences of Development, Musical Training and Language Impairment

99 Amelie Mahlstedt
The Acquisition of Case marking Information as a Cue to Argument Interpretation in German
An Electrophysiological Investigation with Pre-school Children

100 Nikolaus Steinbeis
Investigating the meaning of music using EEG and fMRI

101 Tilmann A. Klein
Learning from errors: Genetic evidence for a central role of dopamine in human performance monitoring

102 Franziska Maria Korb
Die funktionelle Spezialisierung des lateralen präfrontalen Cortex: Untersuchungen mittels funktioneller Magnetresonanztomographie

103 Sonja Fleischhauer
Neuronale Verarbeitung emotionaler Prosodie und Syntax: die Rolle des verbalen Arbeitsgedächtnisses

104 Friederike Sophie Haupt
The component mapping problem: An investigation of grammatical function reanalysis in differing experimental contexts using eventrelated brain potentials

105 Jens Brauer
Functional development and structural maturation in the brain's neural network underlying language comprehension

106 Philipp Kanske
Exploring executive attention in emotion: ERP and fMRI evidence

107 Julia Grieser Painter
Music, meaning, and a semantic space for musical sounds

108 Daniela Sammler
The Neuroanatomical Overlap of Syntax Processing in Music and Language - Evidence from Lesion and Intracranial ERP Studies

109 Norbert Zmyj
Selective Imitation in One-Year-Olds: How a Model's Characteristics Influence Imitation

110 Thomas Fritz
Emotion investigated with music of variable valence – neurophysiology and cultural influence

111 Stefanie Regel
The comprehension of figurative language: Electrophysiological evidence on the processing of irony

112 Miriam Beisert
Transformation Rules in Tool Use

113 Veronika Krieghoff
Neural correlates of Intentional Actions

114 Andreja Bubić
Violation of expectations in sequence processing

115 Claudia Männel
Prosodic processing during language acquisition: Electrophysiological studies on intonational phrase processing

116 Konstanze Albrecht
Brain correlates of cognitive processes underlying intertemporal choice for self and other

117 Katrin Sakreida
Nicht-motorische Funktionen des prämotorischen Kortex: Patientenstudien und funktionelle Bildgebung

118 Susann Wolff
The interplay of free word order and pro-drop in incremental sentence processing: Neurophysiological evidence from Japanese

119 Tim Raettig
The Cortical Infrastructure of Language Processing: Evidence from Functional and Anatomical Neuroimaging

120 Maria Golde
Premotor cortex contributions to abstract and action-related relational processing

121 Daniel S. Margulies
Resting-State Functional Connectivity fMRI: A new approach for assessing functional neuroanatomy in humans with applications to neuroanatomical, developmental and clinical questions

122 Franziska Süß
The interplay between attention and syntactic processes in the adult and developing brain: ERP evidences

123 Stefan Bode
From stimuli to motor responses: Decoding rules and decision mechanisms in the human brain

124 Christiane Diefenbach
Interactions between sentence comprehension and concurrent action: The role of movement effects and timing

125 Moritz M. Daum
Mechanismen der frühkindlichen Entwicklung des Handlungsverständnisses

126 Jürgen Dukart
Contribution of FDG-PET and MRI to improve Understanding, Detection and Differentiation of Dementia

127 Kamal Kumar Choudhary
Incremental Argument Interpretation in a Split Ergative Language: Neurophysiological Evidence from Hindi

128 Peggy Sparenberg
Filling the Gap: Temporal and Motor Aspects of the Mental Simulation of Occluded Actions

129 Luming Wang
The Influence of Animacy and Context on Word Order Processing: Neurophysiological Evidence from Mandarin Chinese

130 Barbara Ettrich
Beeinträchtigung frontomedianer Funktionen bei Schädel-Hirn-Trauma

131 Sandra Dietrich
Coordination of Unimanual Continuous Movements with External Events

132 R. Muralikrishnan
An Electrophysiological Investigation Of Tamil Dative-Subject Constructions

133 Christian Obermeier
Exploring the significance of task, timing and background noise on gesture-speech integration

134 Björn Herrmann
Grammar and perception: Dissociation of early auditory processes in the brain

135 Eugenia Solano-Castiella
In vivo anatomical segmentation of the human amygdala and parcellation of emotional processing

136 Marco Taubert
Plastizität im sensomotorischen System – Lerninduzierte Veränderungen in der Struktur und Funktion des menschlichen Gehirns

137 Patricia Garrido Vásquez
Emotion Processing in Parkinson's Disease: The Role of Motor Symptom Asymmetry

138 Michael Schwartze
Adaptation to temporal structure

139 Christine S. Schipke
Processing Mechanisms of Argument Structure and Case-marking in Child Development: Neural Correlates and Behavioral Evidence

140 Sarah Jessen
Emotion Perception in the Multisensory Brain

141 Jane Neumann
Beyond activation detection: Advancing computational techniques for the analysis of functional MRI data

142 Franziska Knolle
Knowing what's next: The role of the cerebellum in generating predictions

143 Michael Skeide
Syntax and semantics networks in the developing brain

144 Sarah M. E. Gierhan
Brain networks for language
Anatomy and functional roles of neural pathways supporting language comprehension and repetition

145 Lars Meyer
The Working Memory of Argument-Verb Dependencies
Spatiotemporal Brain Dynamics during Sentence Processing

146 Benjamin Stahl
Treatment of Non-Fluent Aphasia through
Melody, Rhythm and Formulaic Language

147 Kathrin Rothermich
The rhythm's gonna get you: ERP and fMRI evidence on the interaction of metric and semantic processing

148 Julia Merrill
Song and Speech Perception – Evidence from fMRI, Lesion Studies and Musical Disorder

149 Klaus-Martin Krönke
Learning by Doing?
Gesture-Based Word-Learning and its Neural Correlates in Healthy Volunteers and Patients with Residual Aphasia

150 Lisa Joana Knoll
When the hedgehog kisses the frog
A functional and structural investigation of syntactic processing in the developing brain

151 Nadine Diersch
Action prediction in the aging mind

152 Thomas Dolk
A Referential Coding Account for the Social Simon Effect

153 Mareike Bacha-Trams
Neurotransmitter receptor distribution in Broca's area and the posterior superior temporal gyrus

154 Andrea Michaela Walter
The role of goal representations in action control

155 Anne Keitel
Action perception in development: The role of experience

156 Iris Nikola Knierim
Rules don't come easy: Investigating feedback-based learning of phonotactic rules in language.

157 Jan Schreiber
Plausibility Tracking: A method to evaluate anatomical connectivity and microstructural properties along fiber pathways

158 Katja Macher
Die Beteiligung des Cerebellums am verbalen Arbeitsgedächtnis

159 Julia Erb
The neural dynamics of perceptual adaptation to degraded speech

160 Philipp Kanske
Neural bases of emotional processing in affective disorders

161 David Moreno-Dominguez
Whole-brain cortical parcellation: A hierarchical method based on dMRI tractography