Fine motor timing ability

A study of syllable repetition and finger tapping in persons with developmental stuttering or Parkinson's disease compared with healthy adults

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Cover illustration by the author: oscillogram illustration of finger-tapping and syllable-repetition responses.

"You're braver than you believe,

and stronger than you seem,

and smarter than you think"

- *A. A. Milne*

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ABSTRACT

Aim and methods: The overall aim of this thesis was to explore the fine motor timing ability as manifested by speech motor and fine hand motor activity in persons with developmental stuttering or Parkinson's disease, and in healthy adults. A test method for systematic comparison between speech motor timing and fine hand motor control was developed. The test comprises tasks involving finger tapping and syllable repetition of the syllable /pa/, with and without the support of a metronome in three different tempi and two different rhythms. Additionally, a task of self-initiated maximum rate is included. Three main measures were analyzed: *interval duration* (mean value of the duration between the participants' responses), *interval variability* (coefficient of variation of interval duration), and *asynchrony* (mean value of the difference between the exact time of each participant response and the time of the metronome click closest in time). One hundred healthy adults, 34 adults with developmental stuttering and 27 persons with Parkinson's disease were included in the studies.

Results: The main findings were that for both the adults who stutter (AWS) and the persons with Parkinson's disease (PD), motor timing deviances were found during the synchronization phase, i.e., with the metronome present. The largest deviances for the AWS were found in the fastest tempo, 330 beats per minute (bpm), and in the slowest tempo, 90 bpm, for the persons with Parkinson's disease. Additionally, a previously undocumented phenomenon of abrupt syllable-repetition irregularities was discovered in two of the AWS in tempi of 330–400 bpm.

Conclusion: This thesis adds knowledge about differences and similarities in fine motor timing ability between adults without speech impairment or neurological disorder, adults who stutter, and adults with Parkinson's disease. It is concluded that these differences and similarities between groups could be detected using the specifically developed motor timing test.

Keywords: motor timing, interval duration, interval variability, asynchrony, synchronization, finger tapping, syllable repetition

SAMMANFATTNING PÅ SVENSKA

Begreppet timingförmåga innefattar perception av tidsintervall och produktion av tidsbestämda rörelser. Den motoriska timingförmågan är nödvändig för all sorts rörelse, t.ex. att gå eller att tala. Talet är ett av de mest komplexa motoriska timingbeteenden vi människor utför eftersom varenda rörelse i talapparaten (andning, fonation, artikulation osv) måste ske vid rätt tidpunkt, i rätt ordning och på rätt sätt för att vi ska kunna säga det vi tänkte. Talrytm och tempo är också viktigt för uppfattningen av talet, hur naturligt talet låter och hur förståeligt det är.

Hos personer med Parkinsons sjukdom eller stamning som uppkommit i barndomen så är ett av huvudsymptomen svårigheter att utföra vissa motoriska rörelser. Hos personer med Parkinsons sjukdom påverkas oftast hela rörelseapparaten negativt, och för personer som stammar så har studier visat att, förutom den vedertagna påverkan på talmotoriska rörelser, så kan även förmågan att producera andra rytmiska finmotoriska rörelser, som fingertrumningar, påverkas negativt. För båda dessa diagnoser Parkinson sjukdom och stamning finns kopplingar till dysfunktion dels i hjärnstrukturer som de basala ganglierna och närliggande områden. Dessa områden och strukturer är de samma som vanligtvis kopplas till motorisk timingförmåga. Det saknas studier om dessa två diagnosgrupper som jämför finmotorisk timingförmåga i olika motoriska system (hand och artikulation), och som inkluderar uppgifter som ställer olika höga krav på den inre timingförmågan.

Syftet med denna avhandling var att undersöka finmotorisk timingförmåga hos vuxna som stammar, hos personer med Parkinsons sjukdom och hos friska vuxna. 100 vuxna utan talstörning eller neurologisk sjukdom, 34 vuxna som stammar och 27 personer med Parkinsons sjukdom deltog i föreliggande studier. Ett timingtest utvecklades för att kunna genomföra systematiska jämförelser mellan talmotorik och handmotorik. Testet innehåller bland annat uppgifter med fingertrumningar och stavelse-repetitioner av stavelsen /pa/, synkroniserat med en metronom respektive en fortsättningsfas utan metronom i tre olika tempi, samt en uppgift med maximalt fingertrumnings- eller stavelserepetitionstempo utan metronom. Timingförmågan beskrivs utifrån måtten *intervallduration* (medelvärde av durationen mellan deltagarens responser), *intervallvariabilitet* (variations-koefficienten av intervalldurationen) och *asynkroni* (medelvärde av tidsskillnaden mellan exakt tidpunkt för varje deltagarrespons jämfört med det närmaste metronomslaget).

Resultaten från de fyra delstudierna visade att det gick att upptäcka skillnader mellan de vuxna som stammar, personerna med Parkinsons sjukdom och de vuxna utan talstörning/neurologisk nedsättning genom att använda det specifikt utvecklade timingtestet. Hos de vuxna som stammar visade det sig att synkronisering av fingertrumningsrörelser till det snabba tempot, 330 slag per minut, var extra utmanande, medan det hos personerna med Parkinsons sjukdom var det långsammaste tempot, 90 slag per minut, som innebar störst svårigheter både i fingertrumningsuppgifter och stavelserepetitions-uppgifter. Ett hittills odokumenterat fenomen av plötsliga oregelbundenheter i snabba stavelserepetitionsuppgifter upptäcktes hos två av de vuxna som stammar och beskrivs närmare i en fallstudie, studie **IV**.

Fynden från denna avhandling bidrar med grundläggande kunskap om finmotorisk timingförmåga genom fingertrumningar och stavelse-repetitioner. Fynden ger också kunskap om skillnader och likheter i finmotorisk timingförmåga mellan vuxna med stamning som uppkommit i barndomen, personer med Parkinsons sjukdom och vuxna utan talstörning eller neurologisk nedsättning. Det faktum att vuxna som stammar uppvisade svårigheter med att synkronisera fingertrumningar är ytterligare ett tecken på att det inte är enbart talmotorik som kan vara påverkat hos dessa personer utan även andra motoriska rörelser.

LIST OF PAPERS

This thesis is based on the following studies, referred to in the text by their Roman numerals.

I.   Sundqvist, M., Åsberg Johnels, J., Lindh, J., Laakso, K., & Hartelius, L. (2015). Syllable repetition vs. finger tapping: aspects of motor timing in 100 healthy adults. Journal of Motor Control: accepted for publication.

II. Sundqvist, M., Hartelius, L., & Laakso, K. (2015). Finger tapping in adults with developmental stuttering. Submitted manuscript.

III. Sundqvist, M., Hartelius, L., & Laakso, K. (2015). Syllable repetition vs. finger tapping in persons with Parkinson's disease. Submitted manuscript.

IV. Sundqvist, M., Hartelius, L., & Laakso, K. (2015). Increased syllable repetition variability in specific tempi: A case study of two adults with developmental stuttering. Submitted manuscript.

ABBREVIATIONS

DS   Developmental stuttering

AWS   Adults who stutter

AWNS   Adults who do not stutter

PD   Parkinson's disease

HC   Healthy control persons

SSI-3   Stuttering Severity Index, third edition

UPDRS-III   The Unified Parkinson's Disease Rating Scale, part three

MMSE-SR   Mini Mental State Examination, Swedish revision

bpm   Beats per minute

DDK   Diadochokinesis

AMR   Alternating motion rates

SMR   Sequential motion rates

SYNC   Synchronization

CONT   Continuation

ISO   Tasks with an isochronous pulse (metronome)

MAX   Tasks with maximum self-initiated response rate

SMA   The supplementary motor area

BG   The basal ganglia

fMRI   Functional magnetic resonance imaging

rTMS   Repetitive transcranial magnetic stimulation

CONTENT

1 INTRODUCTION

Human motor timing ability refers to the production and perception of timed movements. It is crucial for, e.g., walking, dancing and speaking. One of the most complex types of human motor timing behavior is speech (e.g., Kent, 2000). The entire speech system – the respiratory system, the laryngeal, the velopharyngeal, and the oral articulatory motor system – needs to be well timed in order to produce the intended speech sounds with precise articulation. Speech motor timing, articulation, and speech intelligibility (the degree to which a spoken message is correctly perceived by the listener) are closely related. For example, a too fast speech rate can contribute to a more imprecise articulation and hence reduce the level of intelligibility of the speech. Speech disorders of neurogenic origin, such as dysarthria and stuttering, often affect the speech rate, articulation, and speech intelligibility negatively (Kent, 2000).

In developmental stuttering and Parkinson's disease (PD), one of the core symptoms is difficulty with motor movements. In persons with PD, both rhythmic fine hand motor movements and rhythmic speech motor activity have been found to be negatively affected (e.g., O'Boyle, Freeman, & Cody, 1996; Konczak, Ackermann, Hertrich, Spieker, & Dichgans, 1997; Elsinger et al., 2003; Yahalom, Simon, Thore, Peretz, & Giladi, 2004; Jones et al., 2011). In persons who stutter, besides the expected speech motor deficits, rhythmic hand motor movements have also been found to be less accurate and more variable compared with persons who do not stutter (Hulstijn, Summers, van Lieshout, & Peters, 1992; Boutsen, Brutten, & Watts, 2000; Neef et al., 2011). The motor deficits in PD are symptoms of basal ganglia dysfunction, and theories of the origin of stuttering point to the basal ganglia and surrounding areas and structures (Alm, 2004; Giraud et al., 2008; Lu et al., 2010; Craig-McQuaide, Akram, Zrinzo & Tripoliti, 2014), i.e., areas and structures also associated with motor timing behavior (e.g., Alm, 2004; Buhusi & Meck, 2005; Bueti, Walsh, Frith, & Rees, 2008). In this thesis, fine motor timing movements, as manifested by syllable repetition and paced finger tapping, are explored in adults with developmental stuttering, persons with PD, and healthy adults. Similarities and differences between adults who stutter (AWS), persons with PD, and adults without a speech disorder or neurological impairment are systematically assessed and described.

1.1 Neural basis and assessment of motor timing ability

The neural basis of human timing behavior has been widely studied. Even though the approaches and theories have taken different paths over the years, results from studies using various neuroimaging techniques have shown that there most likely are multiple timing systems associated with a number of different, yet overlapping, neural mechanisms (Lewis & Miall, 2003b; Buhusi & Meck, 2005; Repp & Su, 2013). An overview article by Buhusi and Meck (2005) describes the timing ability as a three-part system:

- **Circadian timing** – the circadian clock or the 24-hour cycle that controls hunger and the sleep-wake cycle. The suprachiasmatic nuclei in the hypothalamus appear to be the essential area for the circadian timing system
- **Interval timing** – for perception and production of time intervals longer than one second. This part is cognitively controlled and important in decision-making. Essential cortical areas for interval timing is presumed to be the supplementary motor area (SMA), the prefrontal cortex, and the parietal cortex especially the areas related to attention and working memory
- **Millisecond timing** – a largely automatic system controlling intervals shorter than one second primarily used in motor control (such as speaking and playing music). This system is supported by several parts of the motor system: the sensorimotor cortex, the cerebellum, the pre-motor cortex, the thalamus, the basal ganglia (BG), and the superior temporal gyrus

In this thesis there is a focus on exploring the millisecond timing system. The ability to make time estimations in the millisecond-timing range is important for, e.g., speech processing and fine motor coordination, as well as for cognitive processes such as updating the working memory and processing spoken language (Lustig, Matell & Meck, 2005; Schirmer, 2004).

Several theories have been presented regarding the function of our so-called "internal clock", which helps us keep track of time and estimate the duration of time intervals. One established model is the pacemaker–accumulator model based on the scalar–expectancy theory introduced by Gibbon (1977). This model consists of a pacemaker that sends pulses to an accumulator, which functions as a temporary storage of the received pulses.

The accumulator's output becomes stored in our memory, called "the reference memory", and when new durations are perceived they are compared with the previously stored durations. The actual location of our internal clock is not yet determined, but drugs affecting the dopaminergic system have been associated with altered subjective speed of the internal clock (Rammsayer, 1993), indicating involvement of the basal ganglia. The reference memory has been associated with the neurotransmitter acetylcholine in the frontal cortex (Meck, 1993).

All voluntary motor movements are preceded by preparation and motor initiation. The brain activity during this preparation is called Bereitschaftspotential, or readiness potential. The readiness potential has been associated with regions like the BG, the premotor cortex, and the SMA, and the brain activity can be noticed up to two seconds before the actual movement starts (Bortoletto & Cunnington, 2010). The BG, the SMA, and the frontal cortex seems to form a core network that is activated during both the perception and production of timed movements (Rao, Mayer, & Harrington, 2001; Coull, Vidal, Nazarian, & Macar, 2004; Coull, Nazarian, & Vidal, 2008; Merchant, Zarco, & Prado, 2008; Morillon, Kell, & Giraud, 2009); see Figure 1.
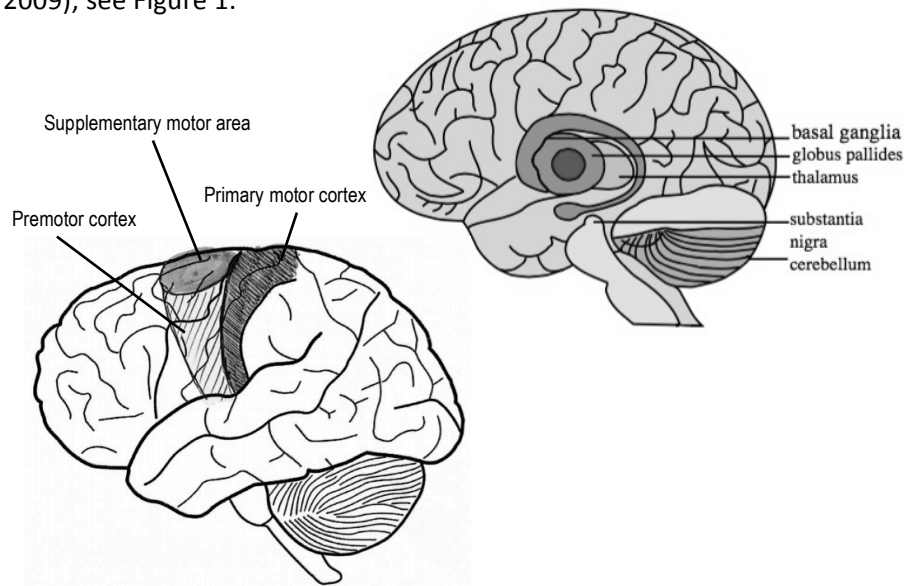

Figure 1. Brain structures commonly associated with motor timing ability: the primary motor cortex, the premotor cortex, and the supplementary motor area (left image), the basal ganglia and the cerebellum (right image).

The BG and SMA are activated both during motor timing tasks that require the production of temporal patterns, such as paced finger tapping or syllable repetition (Rao et al., 1997; Jantzen, Steinberg, & Kelso, 2004; Jahanshahi, Jones, Dirnberger, & Frith, 2006; Bueti et al., 2008), and during perceptual time-estimation tasks (Rao et al., 2001; Coull et al., 2004; Grahn & Brett, 2007; Shih, Kuo, Yeh, Tzeng, & Hsieh, 2009). The cerebellum is activated during both explicit motor timing tasks and perceptual tasks in the sub-second/millisecond range (Lewis & Miall, 2003a; Shih et al., 2009; Morillon et al., 2009). The specific role of the frontal cortex seems to be unclear.

Motor timing ability can be assessed using tasks such as paced finger tapping, in which participants synchronize repetitive finger movements to an external timing cue (e.g., a metronome) and continue with the finger movements for a number of seconds after the timing cue has been turned off. A comparison between the synchronization phase and the continuation phase is then possible, and since the latter phase requires that the participant hold an inner representation of the timing cue, it places higher demands on the millisecond timing system than the synchronization phase (Rao et el., 1997). The first researchers to document this type of synchronization-continuation task with paced finger tapping were Wing and Kristofferson in 1973.

Measures of motor timing accuracy/asynchrony and variability are often used to describe a person's timing ability. The former is based on the mean difference between the participant's rate and the target tempo, and the latter is based on the standard deviation or coefficient of variation (Repp & Su, 2013). The ability to synchronize to an external cue and then keep the same tempo without the external cue requires error correction ability. Without this ability, the asynchrony and variability of participant responses are likely to increase and it should not be possible to keep a steady pulse or rhythm neither with nor without an external timing cue (Pressing, 1998; Repp, 2005; Repp & Su, 2013).

The ability to synchronize motor movements to an external stimulus (e.g. a metronome) typically emerges around the age of four and then continues to develop until the age of 15 (Drake, Jones & Baruch, 2000; Drewing, Aschersleben & Li, 2006). According to Drewing et al., (2006) this ability remains fairly stable after the age of 15. However, musical experience and training can be beneficial in improving the ability to perform motor timing tasks. Persons with musical experience and training generally display less

variable and more accurate motor responses than non-musicians (Repp, 2010; Krause, Pollok & Schnitzler, 2010; Baer, Thibodeau, Gralnick, Li & Penhune, 2013). Moreover, musicians are more skilled in hearing changes in tempo and rhythm than non-musicians (Franek, Mates, Radil, Beck & Poppel, 1991; Ehrlé & Samson, 2005; Repp, 2010).

Motor timing ability is often impaired in persons with neurological deficits or conditions, e.g., PD (O'Boyle et al., 1996; Konczak et al., 1997; Elsinger et al., 2003), Huntington's disease (Rowe et al., 2010), and focal basal ganglia lesion (Coslett, Wiener, & Chatterjee, 2010; Schwartze, Keller, Patel & Kotz, 2011). Difficulties performing motor timing tasks have also been seen in persons with speech and communication disorders such as developmental fluency disorder (Hulstijn et al., 1992; Boutsen et al., 2000; Neef et al., 2011) and apraxia of speech (Ziegler, 2002). Studies of motor timing ability in AWS and in persons with PD are further described below in Sections 1.4 and 1.5.

1.2   Speech motor timing ability

Rate, rhythm, and timing are of critical importance to speech naturalness and intelligibility (e.g., Yorkston, Hammen, Beukelman, & Traynor, 1990). Even small changes in the prosody of speech, e.g., speech rate, loudness or pitch, can alter the perception of the speech rhythm and thus the intelligibility of the speech. Each speech sound and each pause must be correctly timed for the intended message to be perceived correctly (e.g. the review by Kent, 2000 and Schirmer, 2004). Additionally, well-coordinated motor movements are required to produce speech. The speech syllable is an important foundation to the rhythm of speech and the typical mean syllable rate produced is 3-8 syllables per second (180–480 beats per minute) (Greenberg, Carvey, Hitchcock, & Shang, 2003; Poeppel, Idsardi, & Van Wassenhove, 2008; Giraud & Poeppel, 2012). According to Giraud and Poeppel (2012), the 3–8 Hz mean syllable rate is linked to theta-based oscillation/rhythm in the neocortex of the brain, and the intelligibility of the speech (how correctly a listener perceives the spoken words and sentences) is considered optimal when the syllable rhythm is the same as high theta frequencies (Ghiza & Greenberg, 2009).

A person's maximum syllable rate is often assessed by analyzing the verbal diadochokinesis (DDK) (Kent, Kent, & Rosenbek, 1987; Hartelius, Svensson, & Bubach, 1993). Verbal DDK is performed either with alternating motion rates (AMR), where participants repeat a syllable such as /pa/ or /ta/ as fast and as evenly as they can, or with sequential motion rates (SMR), where participants repeat a sequence of syllables such as /pataka/. Maximum rate

and variability can then be assessed (Hartelius et al., 1993). Mean maximum syllable rate in AMR is around 6.4 – 7.6 syllables/second for the syllable /pa/ (Portnoy & Aronson, 1982; Hartelius et al., 1993). The timing of motor speech is often impaired in speech disorders such as dysarthria (Ackermann & Hertrich, 1997; Hartelius, Runmarker, Andersen, & Nord, 2000; Kent, Kent, Weismer, & Duffy, 2000), apraxia of speech (Ziegler, 2002), and developmental fluency disorder (Boutsen et al., 2000).

1.3   Developmental stuttering and motor timing behavior

Developmental stuttering is a fluency disorder that begins in early childhood. Main symptoms of persistent stuttering are involuntary repetitions of sounds, syllables or words, sound prolongations, and blocks (Maguire, Yeh, & Ito, 2012). Associated secondary features of stuttering can be physical, e.g., head movements, facial grimaces and perspiration, or negatively associated behavior and emotions, e.g., fear, frustration, and avoidance (Guitar, 2006; Maguire, 2012). Even though the cause of stuttering has not been fully established, there are well-grounded theories connecting basal ganglia dysfunction to persons who stutter, and also involvement of connected areas such as the SMA and the cerebellum (Alm, 2004; Giraud et al., 2008; Lu et al., 2010; Craig-McQuaide et al., 2014). In a study from 2008 Giraud and colleagues studied reading-related functional magnetic resonance imaging (fMRI) activations in persons who stutter. A significant positive correlation was found between activation of basal ganglia and stuttering severity. Lu et al. (2010) used neural connectivity analysis to explore brain connectivity with magnetic resonance scanning during a picture-naming task performed by persons who stutter and persons who do not stutter. A disturbance in the connection between the basal ganglia, the thalamus, and the cerebral cortex in the left hemisphere was found in persons who stutter – a disturbance also affecting the SMA. In a critical review by Alm from 2004 one of the conclusions were that a possible core deficit of stuttering could be a dysfunction in the basal ganglia resulting in an impaired ability to produce timing cues (Alm, 2004).

Although stuttering is referred to as a speech disorder, the question of whether stuttering is an isolated speech deficit or a more general motor control/motor timing disorder has been asked more than once. Some previous studies that have included non-speech motor tasks, such as finger movements, show that persons who stutter perform differently compared with persons who do not stutter (Smits-Bandstra, De Nil & Rochon, 2006;

Busan, D'Ausilio, Borelli, Monti, Pelamatti, Pizzolato, & Fadiga, 2013; Etchell, Johnson, & Sowman, 2014). In a study from 2006, the ability to automatize sequenced finger-tapping movements was explored in adult males who stutter and adults who do not stutter. The persons who stutter were found to produce finger-tapping sequencing tasks in a slower rate and with higher variability compared with the adults who do not stutter. Additionally, the persons who stutter were not able to automatize movements to the same extent as adults who do not stutter (Smits-Bandstra et al., 2006). Busan et al. (2013) used transcranial magnetic stimulation (TMS) to measure the resting and active motor thresholds of hand-muscle representation and found a hypo-activation in the left hemisphere in the AWS. Etchell et al. (2014) presented the theory that the physical secondary behaviors seen in persons who stutter could indicate that stuttering is a motor control disorder of a general sort, not just affecting speech motor movements.

Previous studies have shown that persons who stutter can have difficulties performing rhythmic timing tasks, such as synchronizing finger taps or syllables to an external pacing signal, e.g., a metronome (Hulstijn et al, 1992; Boutsen et al., 2000; Neef et al., 2011). However, studies of motor timing ability including persons who stutter show diverse results. Externally cued and synchronized speech syllables have been shown to be more variable in AWS than in adults who do not stutter (AWNS) (Boutsen et al., 2000). Max and Yudman (2003) found that AWS did not differ from AWNS in their accuracy or stability when synchronizing finger-tapping movements and syllable-repetition responses separately to a metronome in a steady pulse of 70–133 bpm/1.17–2.22 Hz. Studies on AWS including non-speech motor movements, such as finger tapping, have shown differences between AWS and AWNS. Neef et al. (2011) studied synchronized finger-tapping movements performed both with the left and the right hand, before and after repetitive transcranial magnetic stimulation (rTMS) in AWS and in AWNS. The stimulated brain area/structure was the dorsolateral premotor cortex. According to the results, stimuli over the right dorsolateral premotor cortex increased the asynchrony and variability of left hand finger tapping, while similar results were achieved in AWNS when stimulating the left dorsolateral premotor cortex. In tasks where AWS have been challenged to produce speech sounds and finger tapping simultaneously synchronized with audible tones, the response variability has been found to be higher than in AWNS (Hulstijn et al., 1992).

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1.4 Parkinson's disease and motor timing behavior

Parkinson's disease (PD) is a neurodegenerative disease caused by loss of dopaminergic neurons in the substantia nigra, located in the basal ganglia (Moore, West, Dawson, & Dawson, 2005). The dopamine loss causes a classic symptom triad including tremor, hypokinesia/bradykinesia, and rigidity. Dysarthric speech symptoms, such as monotony of pitch and loudness, reduced stress, variable speech rate, imprecise consonants and a breathy and harsh voice are very common in persons with PD (Adams & Dykstra, 2009). Speech rhythm irregularities are also a well-known feature (Skodda, Flasskamp & Schlegel, 2010). Both speech and non-speech motor timing responses have shown to be more deviant in terms of rate and variability in persons with PD than in healthy controls (e.g., O'Boyle et al., 1996; Konczak et al., 1997; Elsinger et al., 2003; Yahalom et al., 2004; Jones et al, 2011). Jones et al. (2011) tested finger-tapping synchronization ability in persons recently diagnosed with PD who were still medically untreated, in persons with medically treated PD, and in healthy controls. In a finger-tapping task where responses were synchronized with a metronome at 240 bpm, the medically treated persons with PD tapped faster than the metronome, while the recently diagnosed and the healthy controls tapped in a slower tempo than the metronome (Jones et al., 2011). In finger-tapping tasks with self-initiated maximum rate, persons with PD have shown to tap in a slower rate than healthy controls (Yahalom et al., 2004). In contrast, some persons with PD demonstrate a phenomenon called festination or hastening, which is the tendency to speed up the response tempo during quick repetitive movements (Konczak et al., 1997; Moreau et al., 2007). A review of literature on motor timing in persons with PD reveals that another core feature seems to be higher response variability in persons with PD than in healthy adults. In Konczak et al. (1997), the overall response interval variability (finger tapping and syllable repetition) was higher in persons with PD than in healthy controls. Elsinger et al. (2003) performed an fMRI study where higher response variability was found in persons with PD than in healthy controls during a finger-tapping task at 100 bpm. The higher variability in the PD group was found during both the synchronization phase and the continuation phase. The fMRI analysis showed overall brain activity reduction in persons with PD compared with controls, particularly in the SMA and the cerebellum.

In the study by Moreau and colleagues (2007), oral festination was found in 45% of the persons with PD in a task consisting of synchronized syllable-repetition responses. A similar tendency to speed up the syllable-repetition rate was found by Skodda et al. (2010). Here, the task was to choose a comfortable syllable-repetition rate, and in contrast to the healthy controls, the persons with a far progressed PD were not able to maintain a steady syllable rate. Just as in the non-speech motor tasks described above, higher interval variability has been reported in persons with PD than in healthy controls. For example, the interval duration variability was higher in the PD group than in healthy controls during a task involving a self-chosen syllable rate (Flasskamp, Kotz, Schlegel, & Skodda, 2012), and a task with synchronized syllable repetition at 80 bpm (Skodda, Lorenz, & Schlegel, 2013).

An external cue, e.g., a metronome or a visual cue, has been found to facilitate rhythmic motor movements such as gait in persons with PD (Freedland et al., 2002; Howe, Lovgreen, Cody, Ashton, & Oldham, 2003; Lee, Yoo, Ryu, Park, & Chung, 2012). For example, the tempo of a metronome can be helpful in modulating the velocity of gait (Howe et al., 2003), and the presence of an external cue can facilitate motor initiation in persons suffering from so-called "freezing of gait" (Lee et al., 2012).

1.5   Rationale

There is a lack of studies systematically comparing the fine motor timing ability of two different motor systems (hand and speech) including tasks with different levels of effort for the internal timing network in persons who stutter and in persons with PD. Since both developmental stuttering and Parkinson's disease are associated with brain structures connected to the motor timing ability, and since speech motor deficits as well as non-speech motor deficits have been found in persons with these diagnoses, a systematic evaluation of fine hand motor movements and speech motor activity in different tempi, with and without external auditory support is highly motivated.

2 AIM

The overall aim of this thesis was to explore the fine motor timing ability as manifested by speech motor and fine hand motor activity in persons with developmental stuttering and in persons with Parkinson's disease, compared with healthy adults. The aim was further to make a systematic comparison between finger-tapping and syllable-repetition responses to gain insight into the association or dissociation between speech motor timing and fine hand motor control, and to explore the effects of different tempi and the presence and absence of a metronome on fine motor timing ability.

The specific aims of the four studies were:

Study I   To explore the fine motor timing ability (finger tapping and syllable repetition) in a large sample of healthy adults of varying ages, to compare responses with and without the metronome in three different tempi, and to explore individual differences with regard to musical experience and age

Study II   To explore the fine motor timing ability in adults with developmental stuttering compared with adults who do not stutter, using finger-tapping tasks with and without a metronome in three different tempi and at maximum finger-tapping rate

Study III   To explore the fine motor timing ability in persons with Parkinson's disease compared with healthy adults, and to compare finger-tapping movements with syllable repetitions, with and without the support of a metronome, in three different tempi.

Study IV   To explore a previously undocumented phenomenon of abrupt syllable-repetition irregularities observed in two adults who stutter, in tasks consisting of syllable repetition synchronized with a metronome in fast tempi and at maximum syllable-repetition rate.

3 MATERIALS AND METHODS

3.1 Participants

All participants included in this thesis are listed in Table 1. Exclusion criteria for all participants were: (other) known neurological disease or deficit, severely impaired, uncorrected hearing making it impossible to participate in the tasks, non-corrected vision, (other) known speech/language deficit, need for an interpreter when speaking Swedish, and inability to move the dominant hand. For the participants in study III with PD, severe dementia (<25 points on the Mini Mental State Examination - Swedish revision, MMSE-SR) was added as an exclusion criterion. Handedness was reported by the participants.

In study **I,** the participants consisted of 100 healthy adults recruited from, e.g., local universities, retirement homes, and friends and family with a goal to create a sample of individuals aged 20–90 years with an even age distribution and equal proportions of men and women. The mean age was 54.7 (SD 18.4), and there were 50 men and 50 women.

In study **II,** the participants consisted of 34 adults with developmental stuttering (22–71 years of age, mean 39.6, SD 14.9) and 34 non-stuttering controls (from study **I**) closely matched according to musical experience, age, and gender. Seven of the adults who stutter (AWS) were female. All AWS reported a stuttering debut during early childhood. The majority of the AWS were recruited via the local stuttering associations in Gothenburg and Stockholm, Sweden, and the rest via speech and language pathologists in Gothenburg.

In study **III,** 27 persons with Parkinson's disease (PD) (mean age 70.0 years, SD 9.2) and 27 healthy controls (from study **I**) closely matched according to age, musical experience, and gender were included. Persons with PD were recruited in Gothenburg, Sweden via the local Parkinson's disease association and the speech and language pathologist working in the Parkinson team at Sahlgrenska University Hospital. All participants were on a dopaminergic medication regimen that had remained unchanged for at least six months prior to the test study's test session. The test session was scheduled at the time of day when the participants reported to have an optimal effect of their medication.

Study **IV** was designed as an exploratory case study including two AWS from study **II**; participant F (female, age 27) and participant M (male, age 34). Two non-stuttering controls from study **I** were also included. The two AWS were included because of their abrupt syllable-repetition irregularities in certain tempi in the motor timing tasks described in Section 3.2.1.

Table 1. Description of the participants and tests/material included in the four studies

Study	Participants, N	Age, min – max (mean)	Tests/material
I	100 healthy adults	20 – 90 (54.7)	Timing test
II	34 AWS	22 – 71 (38.6)	Timing test, *SSI-3
	34 AWNS	20 – 73 (38.1)	
III	27 PD	47 – 80 (70.0)	Timing test, UPDRS III + *H&Y, MMSE-SR, Swedish dysarthria assessment
	27 HC	42 – 82 (67.5)	
IV	2 AWS	27 – 34 (30.5)	As in study II + two syllable-repetition tasks.
	2 AWNS	25 – 36 (30.5)	

Note: N = number of, AWS = adults who stutter, AWNS = adults who do not stutter, PD = persons with Parkinson's disease, HC = healthy controls. Age is presented in years.
* = assessment performed after the test session, participants not attending.

3.2   Tests and material

Table 1 lists all tests and material included in the four studies. All participants in this thesis were assessed with a specifically developed motor timing test (Sundqvist, Åsberg Johnels, Lindh, Laakso, & Hartelius, 2015a), the Swedish dysarthria assessment (Hartelius, 2015), and a pure-tone audiometry to identify hearing threshold levels. The stuttering severity of adults with developmental stuttering was assessed with the Stuttering Severity Instrument-third edition (SSI-3) (Riley, 1972). For persons with PD, the Unified Parkinson's Disease Rating Scale part III (UPDRS-III) was used to assess current motor function (Fahn & Elton, 1987). The modified Hoehn &

Yahr Staging Scale was used to stage the disease (Fahn & Elton, 1987), and the Mini Mental State Examination, Swedish revision (MMSE-SR) was used for brief screening of cognitive mental state (Folstein, Folstein, & McHugh, 1975). Additionally, all participants reported their level of musical experience on a three-point scale. These tests are further described below.

3.2.1 Motor timing test

A test procedure for assessing motor timing ability of fine hand motor (finger tapping) and verbal motor performance (syllable repetition) was developed. The test comprised a total of 12 tasks: six tasks of synchronization-continuation with an isochronous pulse (ISO), four tasks of synchronization-continuation with a rhythmic pattern (RHYTHM) and two tasks of self-initiated maximum rate (MAX), see Table 2. The tasks were performed with finger tapping, and syllable repetition of the syllable /pa/ separately. The 12 tasks were presented to each participant in random order and each task was repeated in three trials. All trials were used in the data analysis, except the trials that did not fit the set criteria, see Section 3.5.

Table 2. All 12 tasks included in the test procedure.

	Finger tapping	**Syllable repetition**
ISO	90 bpm/ 1.5 Hz	90 bpm/1.5 Hz
	240 bpm/ 4 Hz	240 bpm/ 4 Hz
	330 bpm/ 5.5 Hz	330 bpm/ 5.5 Hz
RHYTHM	Rhythm A	Rhythm A
	Rhythm B	Rhythm B
MAX	Maximum rate	Maximum rate

Note: ISO = tasks with isochronous pulse, RHYTHM = tasks with a different rhythm, MAX = tasks with self-initiated maximum rate, bpm = beats per minute, Hz = hertz.

ISO: Included 3x2 tasks with an isochronous pulse (metronome) in three different tempi: 90 bpm (1.5 Hz), 240 bpm (4 Hz), and 330 bpm (5.5 Hz). The three tempi were chosen based on the following: The middle tempo, 240 bpm (4 Hz), was chosen because 4 Hz is a common speaking rate (e.g. Kent,

2000), and because the syllabic structure of speech normally lies in the 3–8 Hz range (equivalent to 180–480 bpm) (Greenberg et al., 2003; Poeppel et al., 2008), The fast tempo, 330 bpm (5.5 Hz), was chosen based on the maximum rate at which persons both with and without motor impairment have been able to synchronize fine motor movements in previous studies (Konczak et al., 1997; Repp, 2005; Repp & Su, 2013). The slow tempo, 90 bpm (1.5 Hz), was chosen to challenge the two motor systems further, since the asynchrony and variability often increase when the tempo decreases (Repp & Doggett, 2007; Zendel, Ross & Fujioka, 2011).

The subjects were instructed to listen to the metronome for ten seconds and then on a given signal start synchronizing movements to the metronome, and after five seconds, when the metronome stopped, to continue with the movements at the same tempo without the external support for seven seconds (see Figure 2). Participant responses were recorded for the entire 12-second period (synchronization-continuation).
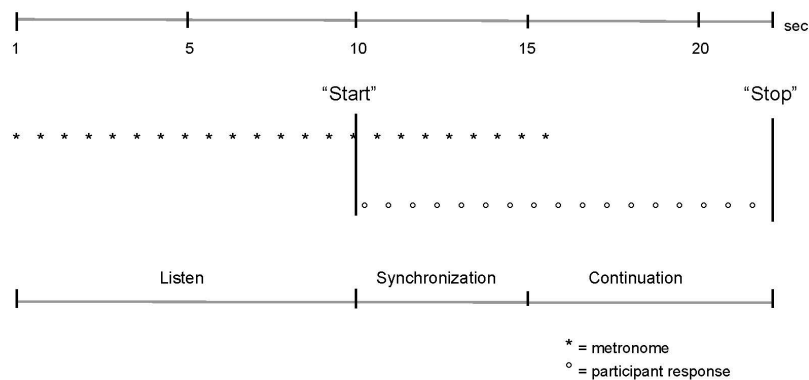

Figure 2. Illustration of the synchronization-continuation procedure used in tasks 1–6.

RHYTHM: Two different rhythms resembling the rhythms of short common spoken phrases were presented in a synchronization-continuation procedure; see Figure 3. The rhythms were presented in the same way as the regular pulses, and participants listened to the rhythm for ten seconds, synchronized for seven seconds and continued on their own for seven seconds. The time for the synchronization phase is extended because rhythms often are more difficult to perceive and follow than a regular pulse. Participant responses were recorded for the entire 14-seconds period

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(synchronization-continuation). These rhythm tasks were performed as part of the motor timing test, but were not included in the data analyses in the four present studies.
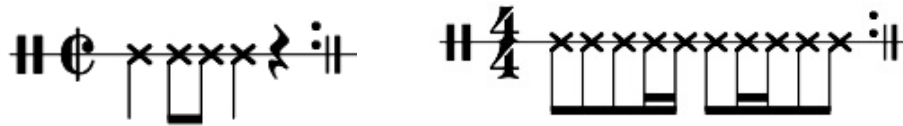

Figure 3. Rhythm A (left), and rhythm B (right).

MAX: Maximum finger-tapping and syllable-repetition rates were tested separately. The instructions were to tap or repeat syllables as fast as possible for seven seconds.

Additional tasks: In study **IV**, two additional synchronization tasks with syllable repetition at 360 bpm (6 Hz) and 400 bpm (6.7 Hz) were included for one of the participants, participant F. The reason for this was that during the original test session this participant showed only a few abrupt irregularities in one of the synchronization-continuation tasks. However, she had severe abrupt rhythm difficulties in the rate of 6–7 syllables per second and reported these difficulties. In these additional tasks, the participant was instructed to listen to the metronome for a few seconds and begin the syllable repetition when she felt ready.

3.2.2   The Swedish Dysarthria Assessment

The Swedish Dysarthria Assessment (Hartelius, 2015) is a revised version of the dysarthria assessment published by Hartelius, Svensson and Bubach (1993). Respiration, phonation, oral motor function, articulation, prosody, and intelligibility are assessed on a four-point scale from 0 (normal function/no or insignificant deviation) to 4 (very severe deviation or no function). A total score between 0 and 4 is obtained corresponding to the degree of speech severity/deviation, where 0 corresponds to "no speech deviation/normal function" and 4 corresponds to "severe speech deviation".

3.2.3   The Stuttering Severity Instrument, third edition

The Stuttering Severity Instrument, third edition (SSI-3) is a revised version of the original Stuttering Severity Instrument (Riley, 1972). It is a tool for assessing and evaluating stuttering severity in children and adults, for both

clinical use and research purposes. It contains behavioral measures of stuttering frequency, duration of the longest stuttered utterances, and physical concomitants. Video recorded speech samples of reading and spontaneous speech should be used in the analyses. The percentage of stuttered syllables is calculated, the duration of the three longest stuttering events is timed, and four types of physical concomitants are rated on a five-point scale. The three rated components are converted into test scores, which are then added to obtain a total test score. The stuttering severity can be derived from the total score on a scale from "very mild" to "very severe". In this thesis, the SSI-3 was used as a report of the current degree or severity of speech dysfluency at the specific day and time for testing.

3.2.4   The Unified Parkinson's Disease Rating Scale, part III

The UPDRS is a clinical rating scale for Parkinson's disease first developed in the 1980's (Fahn & Elton, 1987). It contains four parts covering mentation, behavior, and mood, non-motor and motor aspects of daily life, motor examination, and complications of therapy. Part III, "motor examination", is often used separately to assess current motor function in persons with PD. Aspects of e.g. tremor, rigidity, movement rate, postural stability, and bradykinesia are assessed bilaterally on a four-point scale from "normal" function to "highly affected" or "unable to perform". A total score is obtained, with a maximum of 108 points.

3.2.5   Modified Hoehn and Yahr staging scale

The Hoehn and Yahr staging scale (H&Y) is often used to estimate disease staging in persons diagnosed with Parkinson's disease. The original staging scale was developed in 1967 (Hoehn & Yahr, 1967). Since then, the scale has been somewhat modified (Fahn & Elton, 1987) and now includes a total of seven disease stages: 1) Unilateral involvement only, 1.5) unilateral and axial involvement, 2) bilateral involvements without impairment of balance, 2.5) mild bilateral disease with recovery on pull test, 3) mild to moderate bilateral disease; some postural instability; physically independent, 4) severe disability; still able to stand unassisted, and 5) uses wheel chair or is bedridden unless aided.

3.2.6   The Mini Mental State Examination, Swedish revision

The MMSE is a screening tool designed for brief assessments of cognitive mental state originally developed by Folstein et al., 1975. It is frequently

used to rule out a diagnosis of dementia (Ismail, Rajji, & Shulman, 2010). The assessment contains 20 questions formulated to screen areas such as orientation, memory, and attention. The maximum score is 30 and a total score below 24 could indicate dementia. The Swedish version of MMSE (MMSE-SR) was used in this thesis and the <24 cut-off score was used as exclusion criteria for persons with PD.

3.2.7 Musical experience

Musical experience was assessed in terms of playing a musical instrument, singing, and/or dancing. It was rated on three-point scale (no experience, experience on a hobby level for example singing in a choir or dancing as a leisure activity, and experience on a professional level).

3.3 Equipment

In the motor timing test, the participant responses were recorded on an HP Elite Book laptop using the software Audacity 1.3 Beta and an external Roland Quad-Capture sound card. The metronome click in Audacity was used as external pacing signal. Metronome clicks were presented to participants via closed-ear headphones, Sennheiser HAD 200. Finger tapping responses were recorded using a specially designed wooden board with a CM3 condenser microphone attached to it and a wristband to control for arm movement (see Figure 4). A light metal thimble was placed on the index finger to increase input signal/volume. Syllable repetitions were recorded with a Sennheiser HSP 4 headset microphone with an MZA 900 P phantom power adapter.

Figure 4. The finger-tapping board.

3.4 Ethical considerations

The studies were conducted in accordance with the Declaration of Helsinki and approved by the regional ethics committee. All participants were given

verbal and written information about the study and its purpose. They were also informed that they could decline participation at any time during or after testing without providing a reason why. They all signed a written informed consent.

3.5   Data analysis

The participants' responses in the motor timing task were analyzed using the software Praat, version 5.3.56 (Boersma & Weenink, 2012). Two Praat scripts were created for the analysis. The first script analyzed the audio recordings to discover sound and silence. Sound was defined as being louder than the chosen threshold of -20 dB for both finger tapping and syllables, and longer than a given number of milliseconds defined separately for the two modalities (finger tapping and syllable repetition) and the three tempi (90 bpm, 240 bpm, 330 bpm). The second script extracted three main measures (see Figure 5) from each Praat TextGrid, chosen to describe the motor timing ability: *interval duration, interval variability*, and *asynchrony*. These measures are described in detail below in Sections 3.5.1–3.5.3. The mean values for each modality (finger tapping and syllable repetition) and each tempo (90, 240, 330 bpm) were calculated for the three measures (interval duration, interval variability, asynchrony). Trials that did not fit the set criteria were excluded: start later than second 12, stop earlier than second 20, and/or pauses longer than two seconds at 90 bpm, 0.8 seconds at 240 bpm and 0.6 seconds at 330 bpm (i.e., the times equivalent to three response intervals). In the data analysis of the MAX-tasks, the first response was excluded to avoid onset effects. The number of responses in the first six seconds was then calculated and divided by six to obtain the number of responses per second. Each participant's fastest of three attempts was chosen for analysis. In study **IV** the syllable-repetition tasks ISO and MAX (see Section 3.2.1) were perceptually (visually and auditory) inspected, and trials with syllable irregularities manually analyzed. Table 3 lists the different measures included in the four studies, together with the tasks, modalities, and parameters included in the analyses. In study **I**, the asynchrony was the main measure chosen to describe motor timing ability along with the variability (CoV of asynchrony). Improvements of the analysis and reconsiderations regarding important measures for describing fine motor timing ability led to additions of the measures interval duration and interval variability in studies **II–IV.**
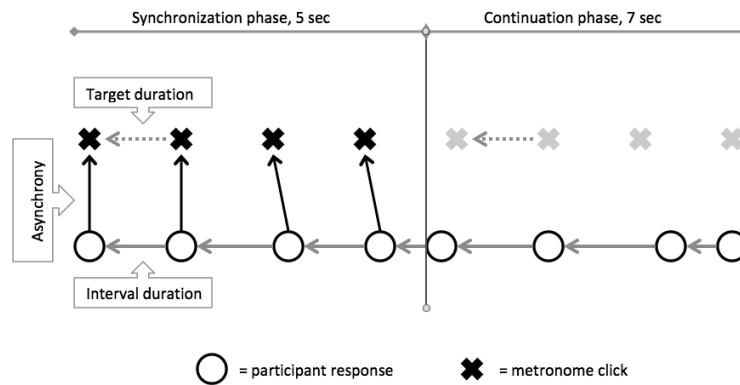
Figure 5. Illustration of the timing measures included in the thesis. The grey arrows illustrate the interval duration of a participant's responses. The interval variability is calculated based on the interval duration but with the coefficient of variation (SD/mean). The grey dotted arrow illustrates the target duration of the metronome. The black arrows illustrate the measure used to calculate asynchrony.

3.5.1   Interval duration

The measure *interval duration* was calculated as the mean length of the intervals between participant responses, measured in seconds. This measure provides information about the relation between the metronome's target interval duration and the duration of the participant's response intervals. The target duration at 90 bpm is 0.667 seconds between each metronome click, at 240 bpm 0.250 seconds, and at 330 bpm 0.182 seconds. If the mean interval duration of the participant's responses is shorter than the target duration, the participant's mean response tempo is faster than the target tempo. Conversely, a longer mean response interval duration than the target duration implies a slower mean response tempo.

3.5.2   Interval variability

The measure *interval variability* was calculated as the coefficient of variation (the standard deviation divided by the mean) of the interval duration, expressed in percent. This is used as a measure of interval and tempo variability. The higher the variability percentage, the higher the variability of interval duration, and thus the more unstable/variable the response tempo. In study **I,** the timing variability was calculated as the coefficient of variation of the asynchrony (see Section 3.5.3). However, in

the subsequent studies **II–IV,** this variability measure was replaced with the measure of interval variability.

3.5.3 Asynchrony

Asynchrony was calculated as the mean value of the difference between the exact time of each participant response and the time of the metronome click closest in time, measured in seconds. The original asynchrony values can be negative or positive, depending on whether the participant response is produced before or after the metronome click. In the data analysis all asynchrony values were transformed to positive to allow calculation of mean values. The asynchrony measure provides information about how well the participant synchronizes the responses to the metronome clicks. A value of 0.0 asynchrony means the responses are totally in sync with the metronome, and the higher the asynchrony, the more the responses deviate from the metronome clicks.

Table 3. Tasks, compared parameters, and timing measures included in the four studies.

Study	Task	Modality	Parameter	Measure
I	ISO	Finger tapping Syllable repetition	Metronome Modality Tempi Age Musical exp.	Asynchrony Variability
II	ISO, MAX	Finger tapping	Metronome Modality Tempi	Interval duration Interval variability Asynchrony
III	ISO	Finger tapping Syllable repetition	Metronome Modality Tempi	Interval duration Interval variability Asynchrony
IV	ISO, MAX	Syllable repetition	Tempi	Interval duration Interval variability

Note: ISO = task with isochronous pulse, MAX = task with maximum self-initiated rate. Musical exp. = musical experience.

3.6 Statistical analysis

In studies **I** and **III,** the repeated measures ANOVA was used to explore differences between *modality* (finger tapping vs. syllable repetition), *tempi* (90 vs. 240 vs. 330 bpm), and *metronome* (synchronization phase vs. continuation phase). In study **III** *group* (Parkinson's disease vs. healthy controls) was added as a between subjects factor. Significant main effects and interaction effects were described. (Bonferroni correction and lower bound were used). Additional t-tests were calculated to explore the source of differences in significant main effects and interaction effects, as well as possible differences depending on musical experience. In study **I,** correlations were explored using Pearson correlation coefficient. All p < .05.

In study **II,** a Kolmogorov-Smirnov test for normality showed that the data distribution was somewhat skewed. The non-parametric Mann-Whitney rank test was therefore used to compare the motor timing responses of the AWS and the AWNS. A level of p ≤ .01 two-tailed significance was chosen to avoid making type I errors.

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4 RESULTS

4.1 Study I: Syllable repetition vs. finger tapping: aspects of motor timing in 100 healthy adults

In this study, syllable-repetition movements and finger-tapping responses of 100 healthy adults were analyzed. Repeated measures ANOVA was calculated to explore possible main and interaction effects of *modality* (finger tapping vs. syllable repetition), *tempi* (90 vs. 240 vs. 330 bpm), and *metronome* (synchronization phase vs. continuation phase). According to the results, the slowest tempo, 90 bpm, posed extra challenges to the participants. The measures of asynchrony (mean) (see Figure 5 in Section 3.5) and variability (coefficient of variation) were measured, and below is a summary of the main findings:

- **Finger tapping vs. syllable repetition:** There was significantly less asynchrony but a higher level of variability in the finger-tapping task than in the syllable repetition task at 90 bpm, and a higher level of variability in the syllable-repetition task than in the finger-tapping task at 330 bpm (see Figures 6 and 7).

- **Synchronization phase vs. continuation phase:** There was significantly less asynchrony during the synchronization phase (SYNC) than during the continuation phase (CONT), especially in the tasks at 90 bpm (see Figure 7). The variability was significantly smaller during SYNC than CONT at 330 bpm (see Figure 7).

- **Musical experience**: Persons with experience playing a musical instrument or singing had significantly less asynchrony than those with no experience. There was no significant difference between those who had dance experience and those who did not.

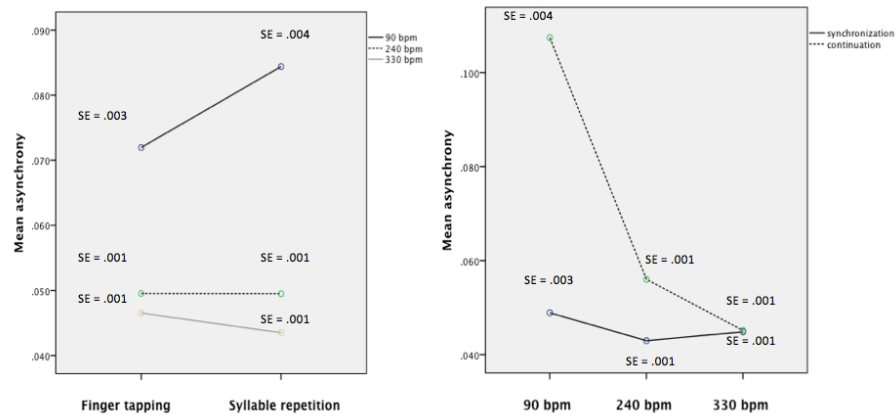- **Age**: The asynchrony increased with age.

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Figure 6. Graphic illustrations of significant interaction effects within the asynchrony measure. The left panel is a demonstration of the interaction effect between modality and tempo; the right panel demonstrates the interaction effect between metronome and tempo. SE = standard error.
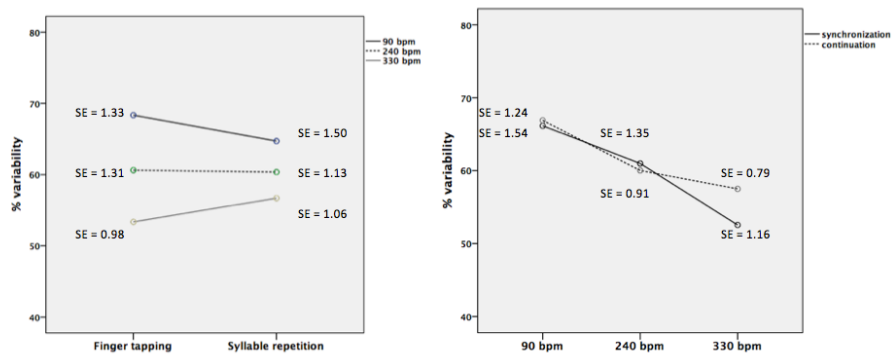

Figure 7. Graphic Illustrations of significant interaction effects of the variability measure. The left panel illustrates the interaction effect between modality and tempo; the right panel illustrates the interaction effect between metronome and tempo. SE = standard error.

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4.2   Study II: Finger tapping in adults with developmental stuttering

In this study, the isochronous finger-tapping tasks were analyzed and possible differences between 34 AWS and 34 closely matched AWNS explored. Overall, the AWS performed quite similarly to the AWNS. However, a few interesting differences appeared:

The AWS had shorter mean interval duration than the metronome and the AWNS group at the fastest tempo 330 bpm during the synchronization phase (SYNC), indicating that the AWS kept a faster mean tempo than 330 bpm; see Figure 8.
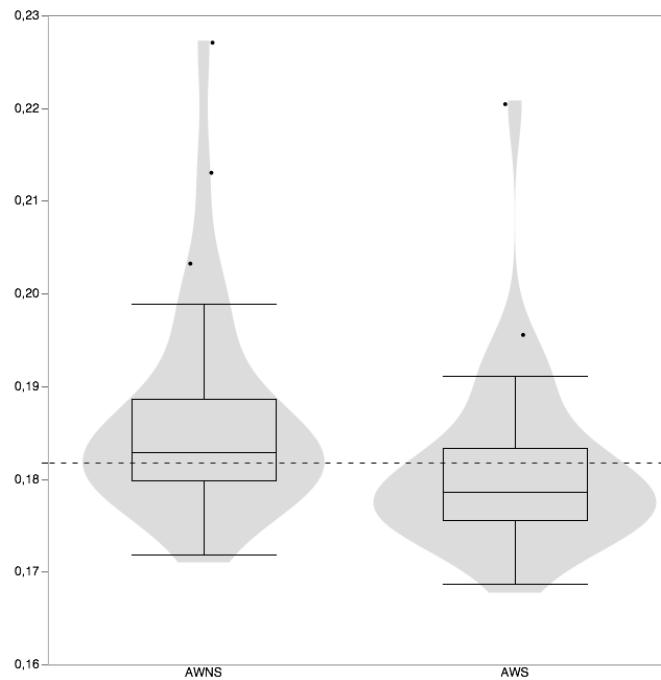

Figure 8. Violin plot showing interval duration in the finger-tapping task at 330 beats per minute during the synchronization phase. The target interval of the metronome (0.182 seconds) is indicated with a dotted reference line. AWNS = adults who do not stutter, AWS = adults who stutter.

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The AWS also had a significantly higher amount of asynchrony than the AWNS at 330bpm, meaning that the AWS had a poorer ability to accurately synchronize finger-tapping movements to the metronome than the AWNS; see Figure 9.

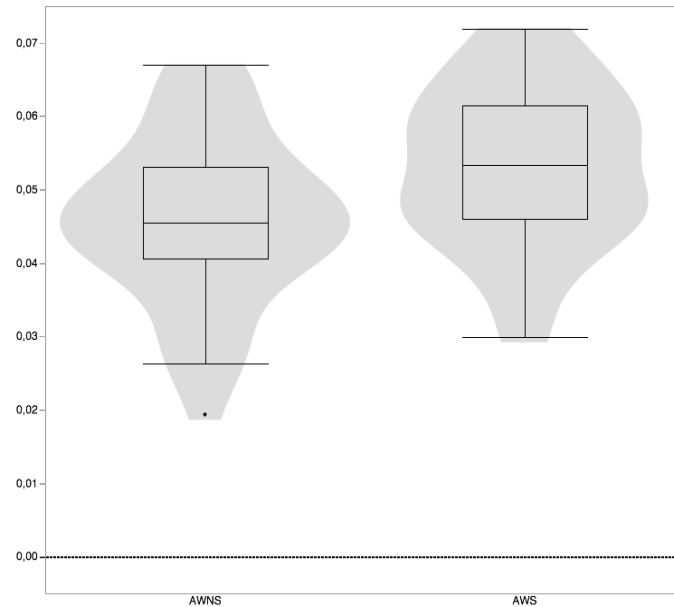There was no significant difference in interval variability between the groups.

Figure 9. Violin-plot showing asynchrony in the finger-tapping task at 330 beats per minute during the synchronization phase. When synchronization is perfect, the value is 0.0 seconds asynchrony, which is indicated in the figure with a reference line. A high asynchrony value indicates large asynchrony. AWNS = adults who do not stutter, AWS = adults who stutter.

4.2.1 Syllable-repetition tasks

The syllable-repetition tasks were not included in the initial analysis reported in the manuscript (study **II**). However, supplementary analysis was performed and significant group differences between AWS and AWNS in the ISO syllable-repetition tasks are reported and illustrated here. The statistically significant differences found occurred during SYNC. There were no significant group differences during the continuation phase (CONT).

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Interval duration: At 90 bpm, the AWS had significantly shorter interval duration than the AWNS (median 0.577sec. vs. 0.641 sec., p < .01, U = 324), which means that AWS were further away from the target duration than AWNS, and kept a faster tempo than both the AWNS and the metronome; see Figure 10.

Figure 10.
Interval duration: Box-plots illustrating the difference between adults who stutter (AWS) and adults who do not stutter (AWNS) in the syllable-repetition task at 90 bpm during the synchronization phase. The dotted line is the target interval duration of the metronome at 0.667 seconds.
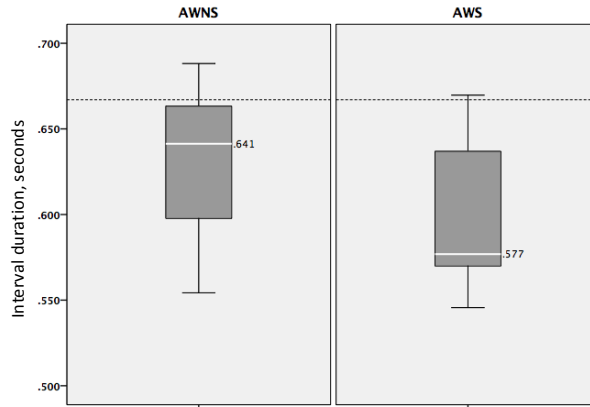
Asynchrony: At 330 bpm, the AWS had a significantly higher asynchrony than the AWNS (median 0.048 sec. vs. 0.044 sec., p < .01, U = 362); see Figure 11.

Figure 11.
Asynchrony: Box-plots illustrating the significant difference between adults who stutter (AWS) and adults who do not stutter (AWNS) in the syllable-repetition task at 330 bpm.

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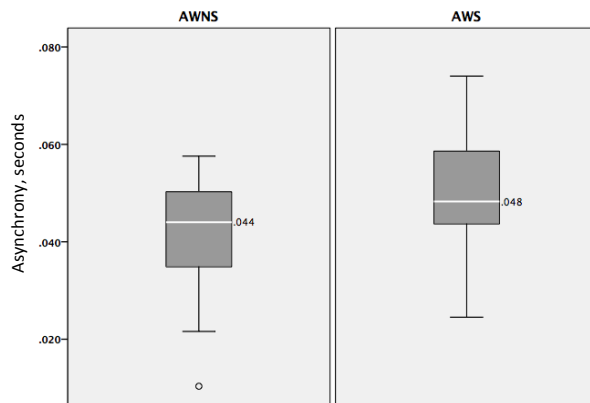
Interval variability: The AWS had significantly higher interval variability than the AWNS at both 90 bpm (median 42% vs. 16%, p < .01, U = 296), and 330 bpm (median 21% vs. 16%, p < .01, U = 303); see Figure 12.
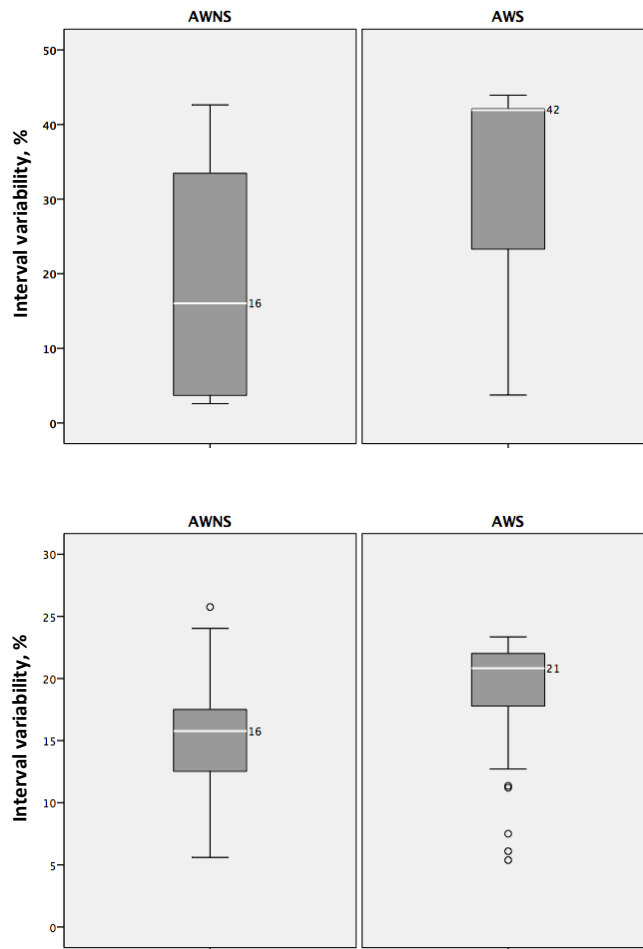

Figure 12. Interval variability: Box-plots illustrating the significant difference between adults who stutter (AWS) and adults who do not stutter (AWNS) in the syllable-repetition tasks during the synchronization phase. The upper panel illustrates the interval variability at 90 bpm, and the lower panel interval variability at 330 bpm. The higher the variability, the more irregular and variable the response tempo. Please note that the scales on the y-axis are not the same in the two panels.

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4.3 Study III: Syllable repetition vs. finger tapping in persons with Parkinson's disease

In the third study, the syllable repetition and finger tapping of persons with PD were analyzed and compared with the responses of closely matched healthy controls (HC). Based on previous studies showing that the ability of persons with PD to produce rhythmic movements can benefit from external support from a metronome, it was hypothesized that the fine motor timing ability would be better during the synchronization phase (SYNC) than during the continuation phase (CONT). However, as opposed to what we hypothesized, the largest tempo deviation and highest amount of variability were found during the synchronization phase. Repeated measures ANOVA was calculated to explore possible main and interaction effects of *modality* (finger tapping vs. syllable repetition), *tempi* (90 vs. 240 vs. 330 bpm), and *metronome* (synchronization phase vs. continuation phase). *Group* (persons with PD vs. healthy controls) was added as a between-subjects factor.

For the measure of **interval duration** (see Figure 4 in Section 3.5) a significant interaction between group (PD vs. HC) and metronome (SYNC vs. CONT) emerged at 90 bpm; see Figure 13. The target duration of the metronome is 0.667 seconds at 90 bpm, indicated with a grey reference line in Figure 13.

Figure 13. Interval duration: Profile plot of a significant interaction effect between group (persons with Parkinson's disease, PD vs. healthy controls, HC) and metronome (synchronization phase vs. continuation phase) at the slowest tempo 90 bpm. The grey reference line at duration 0.667 seconds indicates the target interval duration of the metronome at 90 bpm.
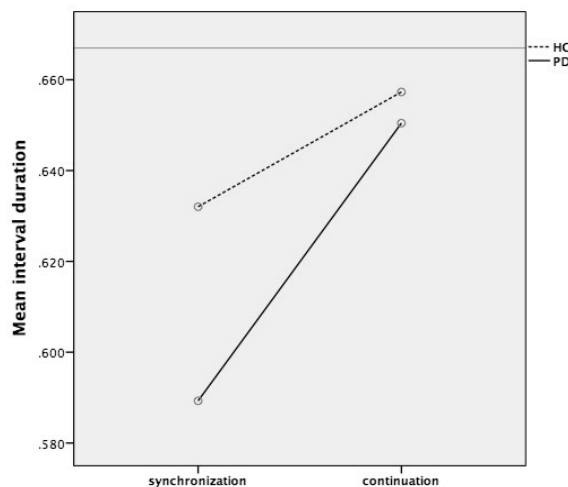
This figure shows that the mean interval duration was shorter and further away from the target duration during SYNC than during CONT in both groups. However, in the persons with PD the responses were further away from the target duration than in the HC during SYNC. The shorter the mean interval duration, the faster the tempo of the participant, indicating that the persons with PD were unable to keep the slow tempo at 90 bpm but kept a faster mean tempo.

For the measure **interval variability**, two significant three-way interactions emerged: one between tempo (90 vs. 240 vs. 330 bpm), metronome (SYNC vs. CONT), and group (PD vs. HC), see Figure 14, and one between modality (finger tapping vs. syllable repetition), metronome, and group. These two interaction effects, together with follow-up t-tests, showed that the mean interval variability was significantly higher in the PD group than in the HC group during both SYNC and CONT, and with both modalities. Within group comparison showed that, in the PD group, the interval variability was higher in the syllable-repetition tasks than in the finger-tapping tasks. Additionally, as illustrated in Figure 14, the mean interval variability was higher at 90 bpm than at 240 and 330 bpm, and higher in the PD group than in the HC group in all tempi during SYNC, and in all tempi but 90 bpm during CONT.

The **asynchrony** was significantly higher in persons with PD than in healthy controls in the finger-tapping tasks, meaning that the persons with PD were less able to accurately synchronize their finger-tapping responses to the metronome than the healthy controls.
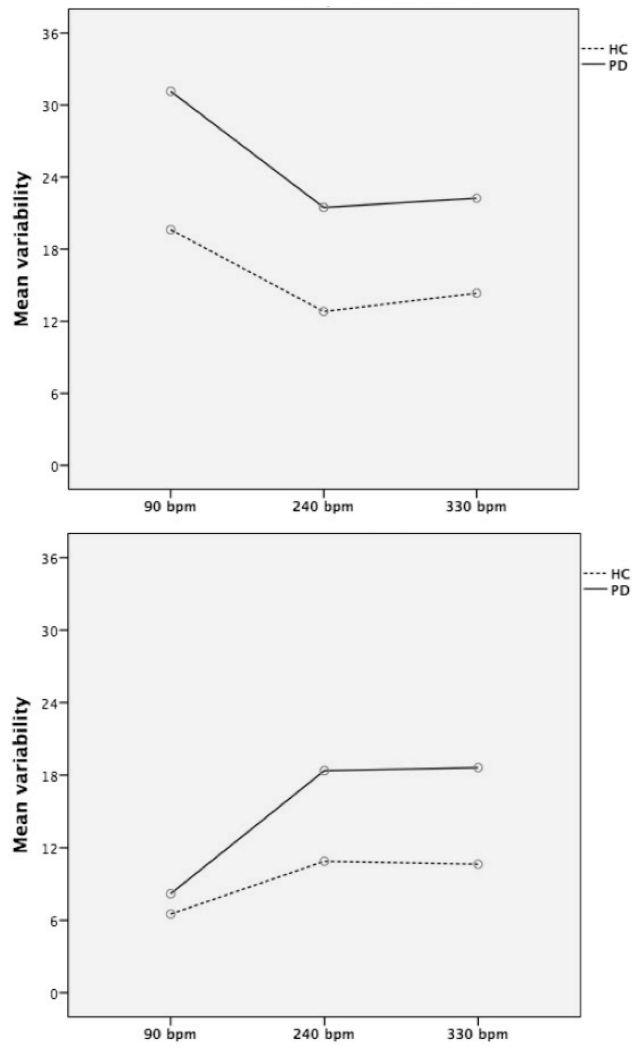
Figure 14. Interval variability: Illustrations of the significant interaction effect between tempi (90 vs. 240 vs. 330 bpm), metronome (synchronization phase, SYNC vs. continuation phase, CONT), and group (persons with PD vs. healthy controls, HC). The upper panel illustrates the mean variability levels during SYNC, and the lower panel illustrates the mean variability levels during CONT.

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4.4 Study IV: Increased syllable repetition variability in specific tempi: A case study of two adults with developmental stuttering

In this study, the purpose was to explore a previously undocumented phenomenon of abruptly occurring syllable repetition variability in specific tempi. Two adults who stutter, participant F and participant M (originally participating in study II), and their two non-stuttering, closely matched controls (CF and CM) were included. The syllable repetition tasks synchronized with a metronome in three tempi were manually measures and analyzed. For both participant F and M, the syllable repetition variability was low in the two slowest tempi, 90 bpm/1.5Hz and 240 bpm/4Hz. In fact, the values were even lower than those for the non-stuttering controls; see Table 4.

Table 4. Levels of variability for the tasks in study IV.

Task	Participant F	Control F	Participant M	Control M
240 bpm	7.5%	8.8%	4.3%	11.7%
330 bpm	6.4%	8.8%	**42.6%**	6.1%
360 bpm	**20.0%**	--	--	--
400 bpm	**40.7%**	--	--	--
MAX	6.5%	8.5%	**39.5%**	8.2%

Note: bpm = Beats per minute, MAX = task with self-initiated maximum syllable repetition rate.

For participant M, the highest variability (42.6%) was found in the syllable repetition task at 330 bpm, where his control CM had only 6.1% variability; see Figure 15. Participant F's responses started to be more irregular at 360 bpm, and the highest variability (40.7%) was found in the task at 400 bpm during her first trial (F 1st); see Figure 16.
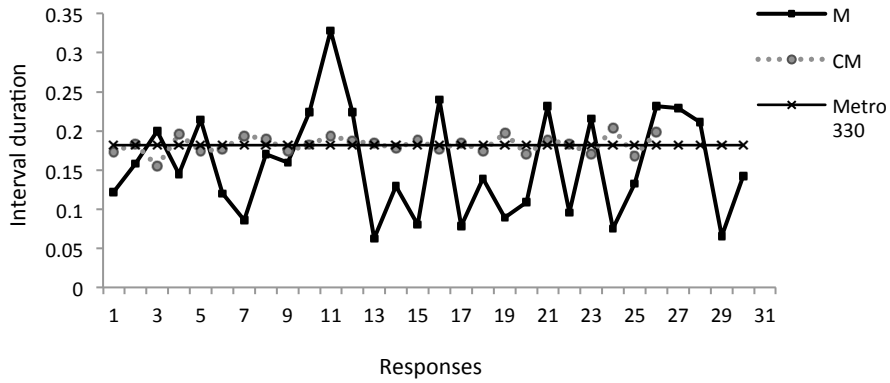
Figure 15. Dotted line chart illustrating the syllable-repetition task at 330 bpm as performed by participant M. M = participant M, CM = control M, Metro 330 = target interval duration of 0.182 seconds at 330 bpm.
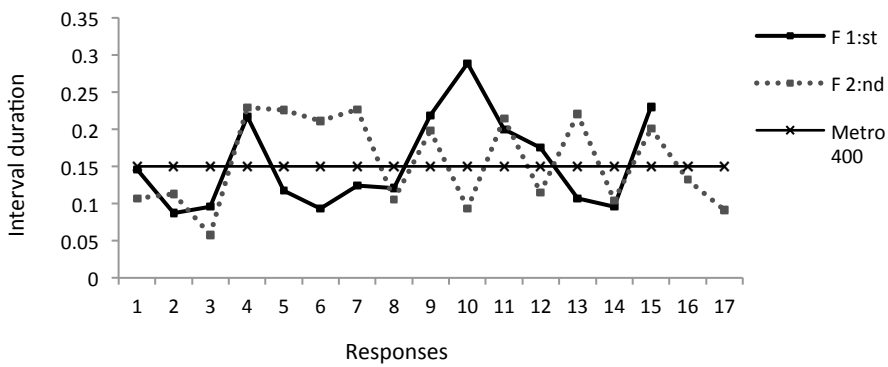

Figure 16. Dotted line chart illustrating the syllable-repetition task at 400 bpm as performed by participant F. F = participant F, 1st and 2nd = the first and second trial, Metro 400 = target interval duration of 0.150 seconds at 400 bpm.

In the task with self-initiated maximum syllable-repetition rate, the results differed between the two AWS. For participant M, the syllable-repetition responses were highly variable at 39.5%, compared with his non-stuttering control's 8.2%. Participant M's syllable rate was around 5.95 syllables/second; for his non-stuttering control, it was around 7.35 syllables/second. Participant F's variability in this task was fairly low, 6.5%, compared with her non-stuttering control's 8.5%. Participant F's maximum syllable rate was rather high, i.e., around 9.175 syllables/second, compared with 6.28 syllables/second for her non-stuttering control.

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4.5   Summary of results

Table 5 (page 35) presents a summary of results from study **II** with AWS and study **III** including persons with PD. The supplementary results of the syllable-repetition tasks for adults who stutter (see Section 4.2.1) are included to present a visual overview of the differences and similarities between the two groups. The grey areas in the table are the parameters were the responses of AWS and the persons with PD were significantly different from their closely matched controls. As described above in Section 4.2 the overall performance of AWS was comparable to the adults who do not stutter (AWNS). The two significant differences noted in the originally included finger-tapping tasks, were shorter interval duration and the higher asynchrony during the synchronization phase (SYNC) at 330 bpm. In the additional analysis of the syllable-repetition tasks significant differences were found for the interval variability, which was significantly higher in the AWS compared with the AWNS at both 90 bpm and 330 bpm. For the persons with PD a significantly higher interval variability than their healthy controls was what covers most of the grey areas in the table, together with higher finger-tapping asynchrony at all tempi, and shorter interval duration at 90 bpm.

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Table 5. Summary of results for adults who stutter (study II) and persons with Parkinson's disease (study III).

			AWS (study II + syllables)			PD (study III)		
Modality	Task	Metro	Int. duration	Int. variability	Async.	Int. duration	Int. variability	Async.
Finger tapping	ISO 90 bpm	SYNC	-	-	-	*** ↑	** ↓	* ↓
		CONT	-	-	/	-	-	/
	ISO 240 bpm	SYNC	-	-	-	-	*** ↓	* ↓
		CONT	-	-	/	-	*** ↓	/
	ISO 330 bpm	SYNC	** ↑	-	** ↓	-	*** ↓	* ↓
		CONT	-	-	/	-	*** ↓	/
Syllable repetition	ISO 90 bpm	SYNC	** ↑	** ↓	-	*** ↑	** ↓	-
		CONT	-	-	/	-	-	/
	ISO 240 bpm	SYNC	-	-	-	-	*** ↓	-
		CONT	-	-	/	-	*** ↓	/
	ISO 330 bpm	SYNC	-	** ↓	** ↓	-	*** ↓	-
		CONT	-	-	/	-	*** ↓	/

Note: * = significant difference compared with healthy controls (for the persons with Parkinson's disease, study III) or adults who do not stutter (for adults who stutter, study II) at the alpha level $p \leq .05$, ** = significant difference compared with healthy controls or adults who do not stutter at the alpha level $p \leq .01$, *** = significant difference compared with healthy controls or adults who do not stutter at the alpha level $p \leq .001$. ↑ = shorter interval duration than controls, ↓ = higher interval variability or larger asynchrony than controls, - = no difference compared with controls. ISO = tasks with an isochronous pulse, bpm = beats per minute, SYNC = synchronization phase, CONT = continuation phase, AWS = adults who stutter, PD = persons with Parkinson's disease. Int. = interval, Async. = asynchrony.

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5 DISCUSSION

In this thesis, fine motor timing responses in healthy adults and adults with developmental stuttering or Parkinson's disease were explored and analyzed. The overall aim was to assess hand and speech motor movements, and to compare and explore possible differences in performance between different tempi and between the presence or absence of the external support of a metronome. The results of the four studies varied depending on the measures used to describe the timing ability, the tempi included, whether movements were synchronized to a metronome or not, and the participant group included. Differences in the fine motor timing ability between the adults who stutter (AWS), the persons with Parkinson's disease (PD), and the healthy adults could be detected using the motor timing test. Synchronizing finger-tapping movements to the fastest tempo, 330 bpm, was particularly challenging for the AWS, while synchronizing movements to the slowest tempo, 90 bpm, was the most challenging for the persons with PD. Both the AWS and the persons with PD had difficulties accurately synchronizing syllable-repetition responses to the slow tempo, 90 bpm, and the syllable-repetition variability was higher in both groups compared with the closely matched controls.

In the 100 healthy adults in study **I**, the highest asynchrony and variability levels were noticed at the slowest tempo, 90 bpm, during the continuation phase (without the metronome). In study **II** there were significant differences between the AWS and the AWNS. Interestingly, the significant differences were noticed solely during the synchronization phase. In the finger-tapping task at 330 bpm the AWS kept a faster mean tempo than both the AWNS and the metronome, and the AWS deviated more than the AWNS in their ability to accurately synchronize finger-tapping responses to the metronome. In the additional syllable-repetition tasks, the supplementary results indicated that, at 90 bpm, the AWS kept a faster mean tempo than both the AWNS and the metronome and that the faster mean tempo also was significantly more variable in the AWS (42%) than in the AWNS (16%). At 330 bpm, the syllable-repetition interval variability in AWS (21%) was also higher than in the AWNS (16%), but the group difference was smaller here than in the slower tempo. At 330 bpm, the AWS also had significantly higher asynchrony indicating difficulties synchronizing syllables to the metronome at the fastest tempo. High syllable-repetition variability was also found in study **IV** for two AWS, as their syllable-repetition variability was abruptly increased in high tempi (330–400 bpm).

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For the persons with Parkinson's disease (PD) in study **III** the largest differences compared with the healthy controls appeared during the synchronization phase, at 90 bpm. Here, the interval duration of the persons with PD was shorter than for both the healthy controls and the metronome, indicating a faster mean tempo than the metronome, and their variability in both syllable repetition and finger tapping was higher than that of the healthy controls at the slowest tempi. Additionally, the results of the asynchrony measure revealed that the persons with PD had higher finger-tapping asynchrony and thus greater difficulty synchronizing their finger-tapping responses accurately to the metronome than the healthy controls.

5.1 Finger tapping vs. syllable repetition

In this thesis, possible differences between finger-tapping movements and syllable-repetition responses were explored in studies **I** and **III**. In study **I**, which included adults without speech impairment or a neurological condition, the asynchrony was higher in the syllable-repetition task than in the finger-tapping task at 90 bpm. However, the finger-tapping variability was higher than the syllable variability. This means that at the slowest tempo, the syllable-repetition accuracy was deviant on a higher, more stable level than the finger-tapping accuracy. This is an interesting, and somewhat unexpected finding given that the participants were adults without speech impairment or disorder. One hypothesis is that this is connected to the normal syllable rate in speech of 3–8 Hz (Greenberg et al., 2003; Poeppel et al., 2008; Giraud & Poeppel, 2012), which is associated with the natural theta frequencies of the brain (Giraud & Poeppel, 2012). The slowest tempo included in the timing test, 90 bpm/1.5 Hz, is the only assessed tempo below 3 Hz, which is the lowest syllable rate even in persons with dysarthria (Ackermann & Hertrich, 2000).

In study **III,** there was no significant difference in interval duration between finger tapping and syllable repetition, but the interval variability calculations showed that the PD group displayed a more variable tempo in the syllable-repetition tasks than in the finger-tapping tasks. However, persons with PD displayed higher asynchrony in the finger-tapping tasks than in the syllable-repetition tasks. To our knowledge, only one previous study has systematically has compared fine motor timing ability in syllable-repetition and finger-tapping tasks. Konczak et al. (1997) had persons with PD and healthy controls perform both types of tasks synchronized with a metronome separately and simultaneously in different tempi. A maximum-rate task was also included. As for the results, the PD group displayed a

significant temporal increase in syllable-repetition variability during the max task, as well as an overall higher amount of response variability (syllables and tapping) compared with healthy controls. Several other studies confirm the pattern of overall higher response variability in persons with PD compared with healthy controls, during both speech and non-speech motor movements (Elsinger et al., 2003; Flasskamp et al., 2012; Skodda et al., 2013).

Study **II** involved AWS and AWNS and only the finger-tapping tasks were included. However, supplementary analyses and results showed that there were some differences between the finger-tapping tasks and the syllable-repetition tasks. For example, in the finger-tapping tasks there was no significant difference between the groups (AWS vs. AWNS) for the measure of interval variability. In the syllable-repetition tasks, however, the syllable variability was higher in the AWS than in the AWNS at both 90 and 330 bpm. The fact that there were significant differences between AWS and AWNS, where the AWS had significantly more deviating finger-tapping responses than the AWNS, confirms that AWS can have difficulties performing non-speech motor movements, and that there is a possibility that other motor systems than speech are affected in persons who stutter. Another difference between finger tapping and syllable repetition in AWS was noticed regarding the measure of interval duration; in the syllable-repetition tasks the group difference was found at 90 bpm and not at 330 bpm as was the case in the finger-tapping tasks. At 90 bpm, the mean syllable-repetition tempo was significantly faster than both the AWNS and the metronome. The fact that differences between the AWS and the AWNS could be detected using fine-tapping movements supports previous findings of difficulties also with non-speech motor movement in persons who stutter (Hulstijn et al., 1992; Boutsen et al., 2000; Neef et al., 2011; Busan et al., 2013).

In summary, differences between syllable repetition and finger tapping were found in the first three studies, including the supplementary analysis of the syllable-repetition tasks for the AWS. For the AWS, differences in finger-tapping performance compared with the AWNS were found at 330 bpm. For the syllable-repetition tasks, differences were also found at 90 bpm. The persons with PD displayed higher syllable-repetition variability than finger-tapping variability, but their asynchrony was higher in the finger-tapping tasks. For the 100 healthy adults, the syllable-repetition asynchrony was higher than the finger-tapping asynchrony at 90 bpm.

5.2 Synchronization vs. continuation

Possible differences in performance between the synchronization phase and the continuation phase were explored in studies **I**, **II**, and **III**. In study **I** with healthy adults, the presence of a metronome seemed to have the largest impact in the slowest tempo, 90 bpm, since the asynchrony was significantly higher during the continuation phase than in the synchronization phase. The continuation phase is considered more demanding to the internal timing system than the synchronization phase since it requires an inner representation of the stimulus interval (Rao et al., 1997). Additionally, the continuation phase involves a higher degree of neural processing (Serrien, 2008). Thus, it was quite expected to find higher asynchrony during the continuation phase. In contrast, in study **II**, significant differences between AWS and AWNS were only found during the synchronization phase. This can not be explained by the higher demands on the timing system during the continuation phase, as established by Rao et al. (1997) and Serrien (2008). Yet, the results from study II are in line with Hulstijn et al. (1992), who found higher response variability in AWS than in AWNS during the synchronization phase. The same pattern was identified in study **III,** where the largest group differences were found during the synchronization phase, even though there were differences between the persons with PD and the healthy controls also during the continuation phase. In study **III**, we hypothesized that in persons with PD, the timing difficulties and thus differences compared with the healthy controls, would appear during the continuation phase when no metronome support is present. This hypothesis was partly grounded in previous results showing that the presence of external support in the form of a metronome or a visual cue can facilitate the ability to initiate and maintain rhythmic movements, like gait (Freedland et al., 2002; Howe et al., 2003; Lee et al., 2012). In study **III**, the mean tempo kept by the PD group at 90 bpm was significantly faster and further away from the target tempo during the synchronization phase than the continuation phase. This could be an indication of a hastening phenomenon occurring in persons with PD. As we do not know this for certain it would be interesting to take a closer look and analyze the response duration and variability at a more detailed level to see whether the tempo is increased within during the synchronization phase of a task.

In addition to the shorter interval duration during the synchronization phase in the persons with PD, this group's interval variability in both the syllable-repetition tasks and the finger-tapping tasks was significantly higher during the synchronization phase than during the continuation phase. The metronome seems to have a more disturbing effect than supporting the

production of a steady pulse. This was seen in the AWS group during the fastest and the slowest tempi and in the PD group during the slowest tempi. In persons with PD, previous research comparing the fine motor timing ability during the synchronization phase and the continuation phase has reported diverse results. In Jones et al. (2011), the finger-tapping response variability was higher and the response timing less accurate during the continuation phase than the synchronization phase at slow tempi (30–60 bpm). In contrast, in a study by Cerasa et al. (2006), the finger-tapping variability was significantly higher in the PD group than in the healthy controls during the synchronization phase at 80 bpm.

The external support of a metronome has previously been found to change the speech rate and facilitate speech fluency in persons who stutter (Brady, 1969; Davidow, Bothe, Andreatta, & Ye, 2009; Toyomura, Fujii, & Kuriki, 2011). However, this is not in line with the findings of study **II**, in which the deviances were found only during the synchronization phase. The question is, why did the differences between the AWS and the AWNS appear in the phase when the metronome was present? Perhaps studies of the auditory perception in persons who stutter can give us a clue. A different functional organization of the auditory cortex in AWS compared with AWNS was concluded by Salmelin et al. (1998). A whole head magneto-encephalography was used to study the auditory cortical function, and differences between AWS and AWNS were found, especially in the left hemisphere (Salmelin, Schnitzler, Schmitz, Jäncke, Witte & Freund, 1998). This indicates that the auditory perception could differ between AWS and AWNS. Such a difference is supported by studies and clinical implications of the benefits of altered auditory feedback for persons who stutter. Altered or delayed auditory feedback is a portable device than can be used by persons who stutter. The idea with the device is that the auditory feedback is altered, facilitating more fluent speech for some persons who stutter (Stuart, Kalinowski, Rastatter, Saltuklaroglu, & Dayalu, 2004; Van Borsel, Drummond, & Pereira, 2010). For persons who do not stutter the effect is the opposite. The possible deviations of the auditory system in AWS could be a reason why the synchronization phase is particularly challenging in this group.

5.3   Motor timing ability at different tempi

In this thesis, tempo turned out to be a determinant of motor timing performance in all participant groups included. In study **II,** the deviating timing pattern in the AWS appeared in the fastest tempo included in the

timing test, 330 bpm/5.5 Hz. No significant difference was found between the AWS and the AWNS in the task with self-initiated maximum tapping rate, however. The median maximum finger-tapping rate produced by the AWS was 6.6 responses per second, which is a higher mean tempo than the fastest tempo of 330 bpm/5.5 responses per second in the isochronous tasks (ISO, see Section 3.2.1 Motor timing task). This indicates that in the AWS, the difficulty is not to tap the finger in a fast tempo in general, but to accurately synchronize the responses to an external auditory stimulus (the metronome). However, for participant M included in study **IV,** the abrupt irregularities occurred during both the syllable-repetition task where responses were synchronized with an isochronous pulse of 330–400 bpm/5.5–6.7 Hz and the maximum syllable-rate task without a metronome. Participant F on the other hand, was able to produce stable syllable-repetition responses in the maximum syllable-rate task at a high rate (around 9 syllables per second). The two included AWS were well able to maintain a steady syllable rate in slower tempi, like 90 and 240 bpm. Participant M's syllable-repetition responses became abruptly irregular at 330 bpm. For participant F, the abrupt syllable-repetition irregularities appeared at a somewhat higher tempo and her highest variability was noticed at 400 bpm. For participant F, the low syllable variability and the steady syllable rate were regained at even higher syllable rates around 9 Hz/540 bpm during the self-initiated max task. So, it seems as if we located some critical tempi where syllable-repetition responses became abruptly irregular for these two participants: For participant M the critical tempo was 330 bpm, and for participant F it was somewhere around 360–400 bpm. Furthermore, it seems as if the actual tempo per se is the determinant, and not the presence or absence of a metronome.

In study **II**, the supplementary results from the syllable-repetition tasks showed that the slowest tempo caused some difficulties. Max and Yudman (2003) did not find any significant differences between AWS and AWNS when performing syllable repetition and finger tapping at tempi between 70 and 133 bpm. In Hulstijn et al. (1992), however, the response variability of speech sounds produced simultaneously with finger tapping at 150 bpm was higher in AWS than in AWNS.

In contrast, in study **III** on persons with Parkinson's disease, the timing difficulties appeared in the slowest tempo, i.e., 90 bpm/1.5 Hz. Considering the fact that slow movements is one core symptom in PD, it was somewhat surprising that no significant difference was found between persons with PD and the healthy controls for interval duration in the fastest tempo. Another surprising finding was the low variability at 90 bpm during the continuation

phase, which in fact was equivalent to the variability level of the healthy controls. According to previous results, higher response variability at a slow tempo was to be expected in the PD group. The finger-tapping response variability has been reported to be higher in persons with PD than in healthy controls in synchronization tasks at 100 bpm (Elsinger et al., 2003) and at slow tempi around 30–60 bpm (Jones et al., 2011). Similarly, syllable-repetition variability has been found to be higher in persons with PD than in healthy adults in a synchronization task at 80 bpm (Skodda et al., 2013).

5.4   The motor timing test

The purpose of the specifically designed motor timing test was to facilitate a systematic comparison of hand motor movements and speech motor responses, produced in synchronization with a metronome and a subsequent phase without the metronome support, in three different tempi, from slow to fast, in simple rhythms, plus self-initiated maximum tempo. When constructing test methods aimed to assess abilities or assets in persons with motor difficulties or disorders, a lot of aspects need to be considered. Here, for example, the test could not be too time consuming since the possibility of fatigue had to be considered. At the same time, it had to cover the whole range of tasks needed to gather the information necessary for the four studies. The test should be relatively easy to administer and participate in, yet it should contain tasks putting different load on the perception as well as the movement production, and the inner timing representation. Finding the optimal measures of timing ability is another challenge.

To achieve sufficient consistency, and to allow for comparison with findings in previous literature, the test method developed was not completely new. Instead, motor timing tasks that have been found to be important and useful in previous studies, such as paced finger tapping movements and syllable repetition responses, were used. Inspecting the results from study **I**, the utility of the test method was considered confirmed since there were expected results of higher asynchrony during the continuation phase than during the synchronization phase (Rao et al., 1997; Serrien, 2008). However, in study **I**, it was stated that to optimize the test method more tempi in the range of 90–240 bpm/1.5–4 Hz should be included. The reason for this was that the largest discrepancies in this study were found at 90 bpm/1.5 Hz which is the only tempo included that has a lower frequency than the normal mean syllable rate and the theta-based frequencies of 3–8 Hz found in the neocortex (Giraud & Poeppel, 2012). By including tempi in this lower

frequency range, one could perhaps determine whether the lower limit of 3 Hz is applicable to this test method as well. Then, in studies **II** and **IV**, the largest differences between the AWS and the AWNS appeared at fast tempi, i.e., 330–400 bpm/5.5–6.7 Hz. The fastest tempo originally included in the motor timing test was 330 bpm (see Table 2). In study **IV** only one of the AWS, participant M, displayed the phenomenon of abrupt syllable-repetition variability/ irregularities to a large extent in the syllable-repetition task at 330 bpm and the maximum syllable-rate task. For the other participant included in study **IV**, participant F, only a few occasional irregularities appeared in the first test session. Fortunately, this participant was aware of her inability to produce a steady syllable-repetition rate at even faster tempi like 6–7 Hz/360–420 bpm, and hence a second test session comprising additional syllable repetition tasks at 360 bpm and 400 bpm was conducted with this participant. Since the highest tempo included in the test was 330 bpm, we do not know whether other participants would have demonstrated abrupt syllable repetition irregularities had higher tempi been included. This phenomenon needs to be further explored preferably in larger participant groups with a timing test including higher tempi than 330 bpm, in order to identify each participant's possible critical tempo.

The middle tempo included in the timing test, 240 bpm/4 Hz, caused few obvious timing difficulties in the included participants groups. In study **III**, persons with PD had higher interval variability in all tempi compared with the healthy controls. This tempo, 240 bpm, was originally included in the timing test because it is equivalent to the normal speech syllable rate in many languages. Since this tempo was not as decisive of motor timing difficulties as the other two tempi, it could be excluded from the timing test in future studies and replaced with a slower or faster tempi, as discussed above.

When assessing and evaluating the fine motor timing ability, the results will vary depending on the measures chosen, tasks included, and methods used to calculate and describe motor timing as evident in previous literature. The main reason for the large variation is most likely that the aims and purposes vary across studies. The main measures chosen to describe motor timing ability in this thesis were interval duration, interval variability, and asynchrony. In study **I,** it was decided that asynchrony (the mean value of the difference between the exact time of each participant response and the time of the metronome click closest in time) and variability (the coefficient of variation of the asynchrony) were the most important measures to use. These two measures provide information about how well participants can

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synchronize their responses to each of the metronome clicks, and how variable that ability is throughout the trial. The asynchrony measure was also used in studies **II** and **III**, yet in a somewhat modified form: In study I asynchrony was calculated and analyzed during both the synchronization phase and the continuation phase, but since no actual metronome clicks are present during the continuation phase the comparison was made between the exact time of the participant response and the exact time of the metronome clicks had they continued. Although the measure of asynchrony provides important information about how well participant responses are synchronized to the metronome clicks, it does not say anything about for example how steady or variable the response tempo is. Many other studies in the field of motor timing have analyzed the "inter-response interval" or "inter-tap interval" which is based on the duration from each participant response to the next (O´Boyle et al., 1996; Bolbecker et al., 2011; Schwartze et al., 2011). A comparison between the target interval of the metronome and the interval duration of the participant can be performed, providing information about the mean tempo kept by the participant. By looking at the standard deviation, or more preferably, the coefficient of variation of the interval duration, a measure of tempo variability is achieved. By using these three different measures, i.e., interval duration, interval variability, and asynchrony, included in studies **II** and **III**, many aspects of a person's fine motor timing ability can be expressed.

5.5   Participants and individual differences

In study **II,** the majority of the participants included in the AWS group had a "very mild" to "mild" stutter. This could be considered a limitation of the study. In this study the AWS and the AWNS performed quite similarly on the finger-tapping tasks, with a few exceptions. One reason for this could be the high percentage of participants with mild overt stuttering. In future research, a more evenly distributed range of stuttering severity in a group of AWS could yield other results. It could also facilitate an exploration of a possible correlation between stuttering severity and the different timing parameters.

In study **II,** a couple of the participants reported to previously have experienced occasional cluttering tendencies, as was also was noted during the test session. Cluttering is a speech-fluency diagnosis characterized by dysrhythmic, fast speech resulting in poor articulatory precision (St.Louis, Myers, Bakker, & Raphael, 2007; Alm et al., 2011). The cluttering diagnosis is

separate from the stuttering diagnosis, yet the conditions can co-occur (St.Louis et al., 2007). Whether cluttering and stuttering affect the motor timing ability differently is not yet known. However, since both conditions are associated with similar neural mechanisms as those associated with motor timing behavior, cluttering could also have a negative effect on fine motor timing. This should be studied further to find out what possible similarities and differences can be found between persons who stutter and persons with cluttering.

Difficulties starting a movement, "motor initiation" is a core symptom of Parkinson's disease. In study **III,** many of the participants with PD showed difficulties initiating the movements, resulting in a delayed response start. In the motor timing test used in this thesis, the participants first listened to the metronome for ten seconds in each trial (see Figure 2). The subsequent synchronization phase was limited to five seconds and then the metronome clicks stopped. One reason for keeping the synchronization phase, and the whole trial, to a minimum number of seconds was to facilitate syllable-repetition trains produced in one single breath. The drawback of a short synchronization phase, however, is that for persons with movement initiation difficulties five seconds could be too short to both initiate the movement and then have time left to actually synchronize the movement before the metronome stops. A repeated phase of synchronization-continuation per task, where the first continuation phase is followed by a second synchronization phase, could be one way to get around the motor initiation problem. Furthermore, a more detailed analysis of the duration and variability of the motor timing responses during the synchronization phase could be performed to assess the possible impact of motor initiation difficulties and the potential presence of a hastening phenomenon.

In study **III,** the participants were 47–80 years old with a mean age of 70. In the first study, timing asynchrony increased with age. Additionally, higher cognitive functions of attention and working memory tend to decrease as we get older (Li & Lindenberger, 2002; Yordanova, Kolev, Hohnsbein & Falkenstein, 2004). Although the mental state of the participants with PD in study **III** was assessed, a normal decrease of cognitive and motor function with rising age is to be expected, which could have affected the results. However, closely matching the healthy controls in terms of musical experience, age, and gender, at least gave us comparable participant groups.

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In the literature of AWS there have been discussions about possible subgroups and important variables. For example the type of dysfluency, diadochokinetic rate, gender and handedness have occurred as plausible important variables (Yairi, 2007; Seery, Watkins, Mangelsdorf, & Shigeto, 2007). The phenomenon of specific syllable-repetition irregularities that was explored in study **IV** was found in only two of the AWS, suggesting that there could be possible subgroups among AWS based on the occurrence of this phenomenon. This needs to be further explored to find out whether abrupt syllable-repetition irregularities can be detected in a larger group of individuals, and to explore the similarities and/or differences between the individuals with these difficulties.

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6 CONCLUSIONS

- Healthy adults 20–90 years old are better able to accurately synchronize fine motor timing movements in the presence of a metronome than without, especially in a slow tempo like 90 beats per minute (bpm). However, their accuracy in finger tapping is significantly better than their syllable-repetition accuracy.

- Persons with experience playing a musical instrument or singing at a hobby or professional level are better able to accurately synchronize fine motor timing movements to a metronome than those without such experience.

- The ability to accurately synchronize fine motor movements to a metronome and then continue without the support of a metronome decreases with age.

- When adults with persistent developmental stuttering (AWS) synchronize finger-tapping movements to a metronome at a fast tempo such as 330 bpm they keep a mean tempo that is faster than both the mean tempo of adults who do not stutter (AWNS) and the metronome. Their finger-tapping responses of AWS are also less accurately synchronized to the metronome at 330 bpm than those of AWNS.

- When persons with Parkinson's disease (PD) synchronize their fine motor movements to a metronome at 90 bpm, the mean tempo is faster than the metronome and further away from the target tempo than the responses of healthy adults. Additionally, this group displays a more variable tempo than the healthy adults in all tempi tested, in particular in the syllable-repetition tasks.

- A tendency to speed up the tempo, or to produce responses in a faster tempo than the target tempo was seen in both the AWS and the persons with PD. Higher syllable-repetition variability compared with closely matched controls was also seen in both AWS and the persons with PD.

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- A previously undocumented phenomenon of abrupt syllable-repetition irregularities was discovered in two adults with persistent developmental stuttering. Their syllable-repetition interval variability was abruptly high at fast tempi between 330 and 400 bpm.

These findings add knowledge about the basic foundations of fine motor timing ability as manifested by syllable repetition and finger tapping. They also add knowledge about the differences and similarities in fine motor timing behavior between adults who stutter, persons with Parkinson's disease, and adults without a speech disorder or neurological impairment. By systematically exploring the fine motor timing ability using a specifically developed motor timing test, knowledge is gained regarding the impact of different tempi, the presence or absence of the metronome, whether movements are performed with finger tapping or syllable repetition, and the different measures used to describe the fine motor timing ability.

The awareness that persons who stutter can show motor timing difficulties, not only in speech motor movements but also in non-speech motor behavior (such as finger-tapping), can perhaps gradate the view of stuttering as an isolated speech disorder.

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7 FUTURE RESEARCH

This thesis reports some interesting findings about differences and similarities between adults who stutter, persons with Parkinson's disease, and healthy adults without a speech disorder or neurological impairment. Based on the findings of the studies included further exploration of the fine motor timing ability in other participant groups should be performed. The motor timing test used in the thesis is easily administrated and non-invasive. Since it was possible to detect differences between the participant groups by using this motor timing test, further studies including this test should be performed and it's area of application further explored. For example, the possibility of detecting other neurological impairment, such as Huntington's disease, or other diagnoses affecting speech rhythm and perception, such as specific language impairment and dyslexia, should be further evaluated.

One concrete suggestion for improvement of the test method is to exclude the originally included tempo of 240 bpm and replace it with a somewhat slower rate between 90 and 180 bpm. This slower tempo could be used to assess whether the lower threshold of 3 Hz associated with a normal speech syllable rate as well as the theta-based oscillations in neocortex also can be detected with this motor timing test. In addition, to allow for a scanning of possible critical tempi where abrupt syllable-repetition irregularities can occur in persons who stutter, tempi faster than 330 bpm should be included. To avoid possible problems with movement initiation difficulties, a repetition of the synchronization-continuation phases could be used.

The motor timing test originally also included tasks with two simple rhythmic patterns. These tasks were not analyzed in the studies included in this thesis. However, it would be very interesting to assess whether the ability to synchronize with a simple rhythmic pattern differs from the ability to synchronize with an isochronous pulse.

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