Investigating the neural processes underpinning the production and anticipation of stuttering in Adults who Stutter

Dissertation

for the award of the degree

"Doctor rerum naturalium"

of the Georg-August-Universität Göttingen

within the doctoral program

Sensory Motor Neurosciences

of the Georg-August University School of Science (GAUSS)

submitted by

Alexander Sean Whillier

from Sydney, Australia

Göttingen, 2018

Thesis Committee

Prof. Dr. med. Martin Sommer, Klinik für Klinische Neurophysiologie, UMG

Prof. Dr. Julia Fischer, Cognitive Ethology Lab, DPZ

Prof. Dr. Annekathrin Schacht, Affective Neuroscience and Psychophysiology Department, Georg-Elias-Müller-Institute of Psychology

Members of the Examination Board

1st Referee: Prof. Dr. med. Martin Sommer, Klinik für Klinische Neurophysiologie, UMG

2nd Referee: Prof. Dr. Julia Fischer, Cognitive Ethology Lab, DPZ

3rd Referee: Prof. Dr. Annekathrin Schacht, Affective Neuroscience and Psychophysiology Department, Georg-Elias-Müller-Institute of Psychology

Further members of the Examination Board

Prof. Dr. Martin Göpfert, Department of Cellular Neurobiology, Schwann-Schleiden Research Centre

Prof. Dr. Tim Gollisch, Department of Opthalmology, UMG

Prof. Dr. Alexander Gail, Sensorimotor Group, DPZ

Date of submission: 9th January, 2018

Date of oral examination: 9th February, 2018

Date of revision: 04th January, 2019

1.0.0 Thesis Body

1.1.0 Introduction to Stuttering

Stuttering is a disorder of speech production, characterised by physical disturbances that compromise fluency. Diagnosis includes a selection of symptoms, including repetitions of syllables and sounds, strains of sounds and blockages before or within words (DSM 5, 2013). Attempts to terminate a stuttering event, or to avoid it, manifest in accompanying symptoms such as increased effort, associated movements, breathing changes or verbal or even situational avoidance. Anxiety and other psychological comorbidities are believed to be high; however, specific numbers are hard to estimate due to small N samples in reports that examine these comorbidities (Iverach 2014).

Developmental stuttering is generally believed to originate in childhood, with incidence rates estimated between 2-6% (Yairi, 2013). Of these, approximately 80% will respond to therapy or spontaneously enter remission, resulting in an estimated 0.5-1% incidence rate ongoing in the adult population. The gender split in early childhood is under debate, however persistence beyond childhood occurs at an estimated rate of 4:1 males:females. This ongoing condition is termed Persistent Developmental Stuttering in most recent research or persistent childhood onset fluency disorder in the DSM 5 (2013). It should be noted that a second form of stuttering – neurogenic stuttering (Ringo, 1995) – refers to stuttering induced after considerable brain damage or injury; however, this thesis will focus solely on Persistent Developmental Stuttering, hereafter referred to as developmental stuttering or simply stuttering. For this thesis, the term People With Stuttering (PWS) and People with No Stuttering (PNS).

While the symptoms of stuttering have been well known for millennia (Brosch & Pirsig, 2001), the underlying causes remain under contention (for reviews and discussion of causal theories, see Bloodstein & Bernstein Ratner, 2008; Yairi & Seery, 2011). One reason for this contention is the great variety in therapies, targeting many different domains. Early therapies focussed on reducing the stresses in the environment in order to reduce the associated psychological stressors which induce stuttering (Bloodstein & Bernstein Ratner, 2008); additionally, hypnotherapy and various drug therapies have been attempted with limited success (Bloodstein & Bernstein Ratner, 2008; Maguire, Yeh & Ito, 2012). Later therapies focussed on physical interruptions to

speech production by training the movements of the lips and tongue, such as in early Fluency Shaping therapies (Bloodstein & Bernstein Ratner, 2008; Euler, 2014). Such therapies have advanced to integrate psychological factors and awareness in order to reduce anxiety. These therapies, when performed alone, have elicited mixed and, in some cases, only short term results (Euler, 2014; Blomgren, 2005). In combination, however, certain therapies such as Fluency Shaping and Stuttering Modification have been integrated to considerably greater success (Euler, 2014). It has been noted, however, that these techniques are most effective when the individual maintains a strong level of conscious awareness of their stuttering. While awareness had been examined in stuttering going back to the 1930s (e.g., Johnson & Knott, 1937; Milisen, 1938), it remained under contention the extent to which this awareness could benefit the individual – while some argued that greater awareness may facilitate stutter-circumvention strategies, others have shown that distraction techniques (e.g. auditory masking) have the capacity to improve speech fluency. As such, the question was raised as to the extent to which PWS are aware of their stuttering moments and can beneficially utilise this knowledge; this will be addressed in Paper Two (chapter 4).

From a physiological perspective, numerous studies have identified differences in cortical structure between PWS and PNS; however, the structures identified vary greatly between studies. Among the most robust findings, two stand out. The first relates stuttering with a reduction in the white matter integrity of left hemispheric speech motor regions (Sommer et al., 2002; Watkins et al., 2008; Kell et al., 2009; Cai et al., 2014). The second is a connection between stuttering and a deficit in left inferior frontal-premotor functional-connectivity (Chang et al., 2011; Chang & Zhu, 2013; Neef et al., 2015). It should be noted that while these studies imply a correlation and causation from this is generally agreed, to date no studies have adequately identified the direction of causation – that is, whether these structural differences induce stuttering or are a result of stuttering. Neef et al. (2015) identified a large role of cortical excitability in stuttering in single word utterances. However, this did not account for variations in cognitive load – these findings are addressed in detail in Paper Three (chapter 6). Overall, these varied findings suggest that, beyond purely structural differences, stuttering as a disorder is also governed by differences in both functional activity and brain plasticity.

Indeed, the question has been discussed whether stuttering is a single disorder or multiple disorders with similar symptomatology (e.g. Yairi, 2007; Jiang et al., 2012). Differences between patients in efficacy of therapy, triggers, symptoms and more all raise this question. In order to address this question, it is the premise of the current thesis that the neurological basis for stuttering must first be understood. That is, that stuttering must be redefined prescriptively (defined by its causes) not simply descriptively (defined by its symptoms). Only then can it be clear if stuttering is a unified disorder or multiple disorders.

1.2.0 Speech Models

In order to analyse speech deficits, a framework is first required. Speech is both a neurologically and physiologically complex task – it originates with a verbal thought and continues beyond the verbal output, to a twin-stream of feedback monitoring from the auditory and physical (somato-) senses (Lind et al., 2014). This section will discuss two models of speech – the Hierarchical State Feedback Control model (Hickok, 2012; referred to hereafter as the Hickok model), and the DIVA model (Tourville and Guenther, 2011). In addition, this thesis will briefly discuss one model of stuttering – the Packman and Attanasio 3-factor causal model (Packman, 2012; hereafter referred to as the P&A Model) – however its one key and self-identified weakness is the inability to identify cause of the disorder as a whole.

1.2.1 The Hierarchical State Feedback Control Model and the DIVA Model

The Hickok model (Hickok, 2012; see figure 2 below) and the DIVA model (Tourville and Guenther, 2011; see figure 3 below) are two models of speech production that have attempted to integrate the domains of higher level psycholinguistic processing with lower level motor processing. These domains track parallel feedforward paths of auditory and somatosensory signals from the speech centres and similar feedback signals along the same parallel paths. Both models propose that interruption in any of the key components in either the feedforward OR feedback paths can lead to a disruption of fluent speech. The primary difference between the two models is in the

hypothesised relationship of utterance conception relative to the feedback and feedforward mechanisms, as well as their general levels of complexity. While the feedforward and feedback maps are integrated components in the Hickok model, they are discrete elements in the DIVA model.

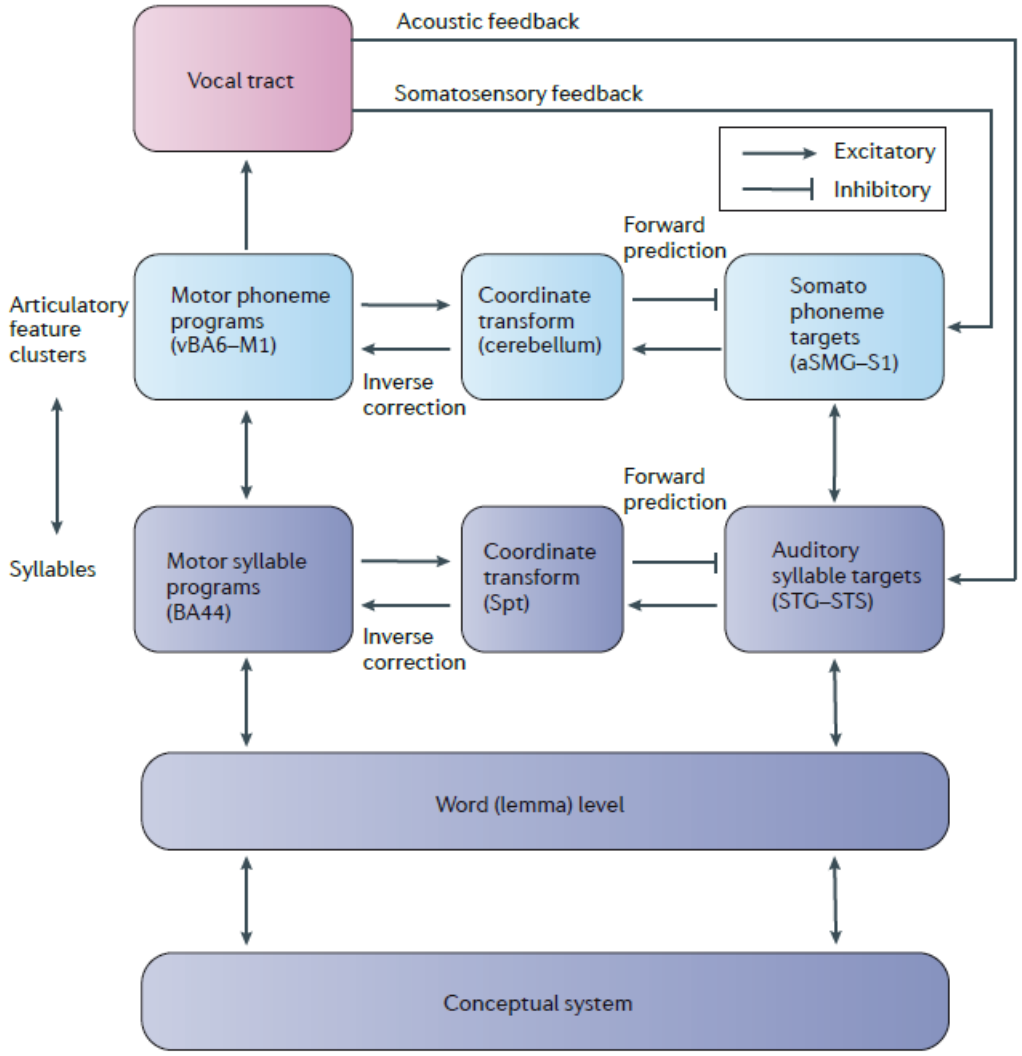

Figure 1. Hierarchical State Feedback Control Model (Hickok, 2012)
Speech begins in the *conceptual system* (bottom) and continues up the left path to the *vocal tract*. Along the way, predictive feedforward prediction signals are sent to the articulators. Two parallel feedback systems then receive the feedback and compare it with the feedforward signals.

These error correction systems in speech are of great importance in understanding stuttering – evidence for their importance comes variously in the form of neuroimaging studies as well as inference from systems research and therapies. These will discussed below.

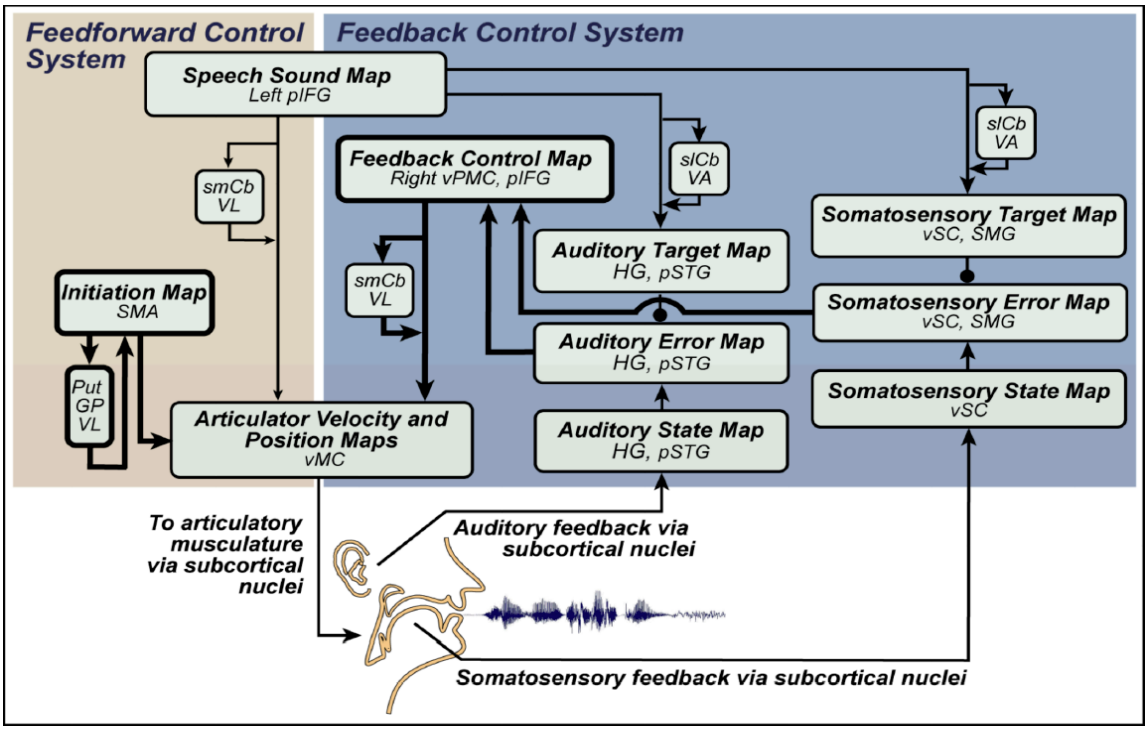

Figure 2. DIVA Model (Tourville and Guenther, 2011).
Speech begins in the *initiation map* (left) and is produced in the *articulatory musculature* (bottom). Concurrently, a *speech sound map* (top left) sends feedforward signals on parallel auditory and somatosensory pathways. Any discrepancy between the *state* and *target maps* are registered by the respective *error maps* and lead to the *feedback control map* for correction. GP = globus pallidus; HG = Heschl's gyrus; pIFg = posterior inferior frontal gyrus; pSTg = posterior superior temporal gyrus; Put = putamen; slCB = superior lateral cerebellum; smCB = superior medial cerebellum; SMA = supplementary motor area; SMG = supramarginal gyrus; VA = ventral anterior nucleus of the cerebellum; VL = ventral lateral nucleus of the thalamus; vMC = ventral motor cortex; vPMC = ventral premotor cortex; vSC = ventral somatosensory cortex.

1.2.2 P&A Model

The P&A Model is a 3-factor method of examining specific stuttering events (herein presented below as figure 3). Specifically, it attempts to explain the necessary and sufficient conditions that presuppose a stuttering moment. The model identifies three factors:

i. a deficit in the neural processing of speech, which affect speech production;
ii. triggers – language features which increase motor demands;
iii. modulating factors, which impact the threshold for a stuttering moment.

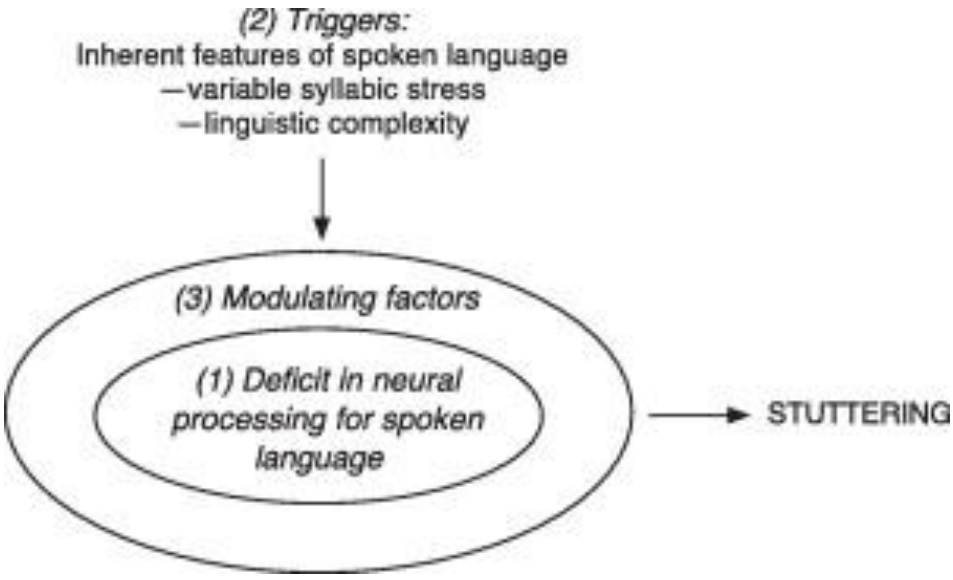

Figure 3. P&A Model
The Packman and Attanasio 3-factor causal model of moments of stuttering (P&A Model); (graphic from Packman 2012).

While the model (figure 3) attempts to explain the individual moments of stuttering, Packman (2012) recognises the limitations of the model in its ability to explain the causes of stuttering and the factors influencing recovery as a whole. The precise mechanisms that induce a stuttering event, which are grouped into the neural deficit factor in the P&A model, appear to have multiple neurological underpinnings; evidence for this can be inferred from functional experiments and therapies.

In order to better understand stuttering, it is necessary to address the role of the feedback mechanisms in dysfluent speech. As the P&A model does not adequately address these low level components, this thesis will focus mainly on the DIVA model.

1.3.0 Delayed Auditory Feedback Evidence

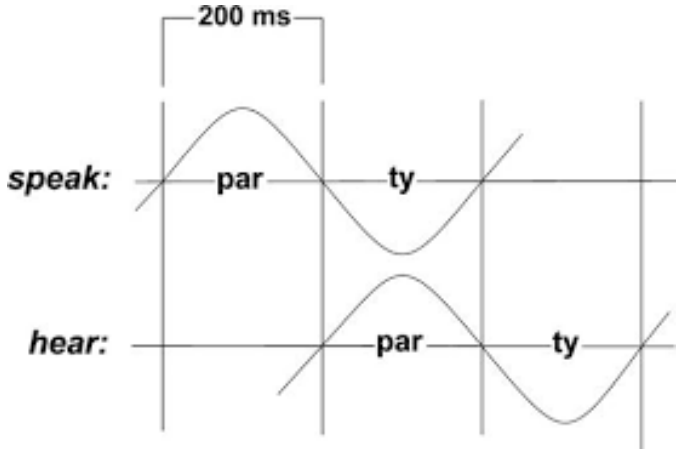

Figure 4. Example of Delayed Auditory Feedback (DAF);
(graphic from Kaspar & Rübeling, 2011)

One key finding, which provides support for the notion of mismatching feedforward and feedback signals suggested by both of the above models of speech, comes from the effects of auditory mismatch research. The phenomenon of auditory masking has been long known to influence speech fluency, not only in PWS but also in PNS (Burke, 1975; Martin et al., 1985; Bloodstein & Bernstein Ratner, 2008). While white noise cancellation and other techniques exist, the primary technique is called delayed auditory feedback (DAF); this involves the speech being recorded in real time and played back into noise cancelling headphones with an auditory delay. DAF in the range of around 150-300ms has long been known to induce strong stuttering symptoms in fluent speakers (Burke, 1975; Chon et al., 2013); conversely, similar DAF applied to PWS can considerably increase speech fluency (Antipova et al., 2008; Ratynska et al., 2012; Unger et al., 2012).

It has been hypothesised that, in fluent speakers, the relative contribution of/reliance on each of the two feedforward/feedback systems (somatosensory and auditory) differs among individuals, thus accounting for individual variance in susceptibility to DAF (Lametti et al., 2012). Comparatively, it can be inferred that DAF removes the possibility of mismatching systems in PWS by forcing them to rely more heavily on just one of the two systems. These findings with PWS are mirrored in other auditory masking techniques such as white noise auditory masking (Martin et al., 1985).

2.0.0 Motivation for the Anticipation Papers

The question then arises, if stuttering were simply a matter of mismatched feedback signals during speech, couldn't PWS simply learn to rely on just one feedback system, much like individual variance in PNS indicates that some speakers are not susceptible to DAF? DAF was the technique which informed the inception and structure of Fluency Shaping and Speech Modification therapies (Bloodstein & Bernstein Ratner, 2008). It has long been understood that PWS experience some awareness of an impending event, accurately predicting and anticipating a majority of events (Johnson & Knott, 1937; Milisen, 1938; van Riper, 1978). However, this also demonstrates that they were not always accurate, sometimes falsely predicting events and sometimes failing to predict (Milisen, 1938). This ability develops over time in PWS, with children exhibiting a reduced ability to predict (Bloodstein, 1960). However, as mentioned above, these techniques assumed both an awareness of and an ability to influence an upcoming stuttering event prior to its occurrence during the stream of speech, which had to date not been precisely examined.

2.1.0 Paper 1 – PAiS Questionnaire

Prior to 2015, there was no method of calculating a PWS's awareness of and ability to anticipate their stuttering. We therefore produced the Premonitory Awareness in Stuttering Scale (PAiS, Cholin, Heiler, Whillier & Sommer, 2016) presented here as the first study (Paper 1). In this paper, we hypothesised that the questionnaire we developed would exhibit positive correlation with the PUTS instrument and would therefore represent an equivalent scale for use with AWS.

2.2.0 PAiS Analyses

To further analyse the data collected in the creation of the PAiS, we then prepared the second paper – a broader analysis and interpretation of the role of anticipation in stuttering (Joana Cholin, Annett Jorschick, Sabrina Heiler, Alexander Whillier, & Martin Sommer, in preparation), presented here as the second study (Paper 2, directly following Paper 1). In this paper, we firstly hypothesised that AWS could better anticipate imminent dysfluencies than ANS could. Secondly, we investigated the relative impact of linguistic factors on the occurrence of dysfluencies; we

hypothesized that all the linguistic factors previously identified (Brown, 1945) would have a significant impact. Thirdly and relatedly, we hypothesized that the linguistic factors implicated in these dysfluencies also significantly impacted anticipation sensations. Finally, we hypothesized that anticipations would be an accurate predictor of upcoming dysfluencies.

3.0.0 Paper 1

Premonitory Awareness in Stuttering Scale (PAiS)

Joana Cholin, Sabrina Heiler, Alexander Whillier, Martin Sommer

Journal of Fluency Disorders 49 (2016) 40–50

http://dx.doi.org/10.1016/j.jfludis.2016.07.001

Primary contributions by doctoral candidate Alexander Whillier:

- Statistics
- Data analysis
- Interpretation
- Writing

Journal of Fluency Disorders 49 (2016) 40–50

Contents lists available at ScienceDirect

Journal of Fluency Disorders

Premonitory Awareness in Stuttering Scale (PAiS)

Joana Cholin[a,*], Sabrina Heiler[b], Alexander Whillier[c], Martin Sommer[c]

[a] Department of Linguistics, Ruhr-University Bochum, Germany
[b] Department of Clinical Linguistics, Bielefeld University, Germany
[c] Department of Clinical Neurophysiology, University Medical Center Göttingen, Germany

ARTICLE INFO

Article history:
Received 5 June 2016
Accepted 12 July 2016
Available online 9 August 2016

Keywords:
Persistent developmental stuttering
Stutter anticipation
Tic disorders
Premonitory urge
Premonitory awareness

ABSTRACT

Anticipation of stuttering events in persistent developmental stuttering is a frequent but inadequately measured phenomenon that is of both theoretical and clinical importance. Here, we describe the development and preliminary testing of a German version of the Premonitory Awareness in Stuttering Scale (PAiS): a 12-item questionnaire assessing immediate and prospective anticipation of stuttering that was translated and adapted from the Premonitory Urge for Tics Scale (PUTS) (Woods, Piacentini, Himle, & Chang, 2005). After refining the preliminary PAiS scale in a pilot study, we administered a revised version to 21 adults who stutter (AWS) and 21 age, gender and education-matched control participants. Results demonstrated that the PAiS had good internal consistency and discriminated the two speaker groups very effectively, with AWS reporting anticipation of speech disruptions significantly more often than adults with typical speech. Correlations between the PAiS total score and both the objective and subjective measures of stuttering severity revealed that AWS with high PAiS scores produced fewer stuttered syllables. This is possibly because these individuals are better able to adaptively use these anticipatory sensations to modulate their speech. These results suggest that, with continued refinement, the PAiS has the potential to provide clinicians and researchers with a practical and psychometrically sound tool that can quantify how a given AWS anticipates upcoming stuttering events.

1. Introduction

Stuttering is an involuntary speech fluency disorder that can disrupt normal communication. In severe cases of stuttering this can lead to avoidance behavior, anxiety and other long term negative outcomes extending well beyond speech itself. Adults with persistent developmental stuttering (AWS) commonly report that they are able to anticipate upcoming stutter events – an AWS can often sense that he or she will stutter during the upcoming utterance. This feeling likely occurs even before a planned utterance is fully encoded internally; that is, before linguistic and motor planning is completed and overt speech articulation begins. The anticipation of stuttering events can prompt a variety of reactions within AWS, with various behavioral consequences (Bloodstein, 1960). As such, the ability to detect these sensations accurately can have a variety of applications in research and therapy.

Two types of anticipation can be distinguished: A prospective anticipation refers to the ability of AWS to consciously predict difficult words that will eventually make them stutter. This may happen in recurring situations; for example, in words that are unavoidable yet difficult such as proper nouns – the names of people or places. Studies have found that

* Corresponding author.
E-mail address: cholin@linguistics.rub.de (J. Cholin).

http://dx.doi.org/10.1016/j.jfludis.2016.07.001
0094-730X/

AWS can reliably predict difficult words or parts of speech (Johnson & Solomon, 1937; Milisen, 1938). In an immediate anticipation, AWS often respond instinctively to the sensation of speech fluency disturbances within the relevant speech utterance, leading some to attempt on-the-fly adjustments to speech in order to avoid the dysfluency.

The study of such anticipations goes back a long time. As early as 80 years ago, it was estimated that approximately 85–94% of all occurring stuttering events can be anticipated and that a stuttering event followed 83-96% of reported anticipations – that is to say, anticipations accurately predicted most events and most events were predicted (Johnson & Knott, 1937; Milisen, 1938; Van Riper, 1978). Equally, however, these numbers also indicate that not every anticipation is followed by a stutter, and not all stuttering events are anticipated (Milisen, 1938). Bloodstein (1960) points out that the ability to anticipate upcoming dysfluencies is a skill that develops over time, and that young children may be unable to consciously predict and apprehend an impending stutter. Indeed, the impact of age on anticipation remains unclear – Silverman and Williams (1972), by comparison, showed a reduced capacity for anticipation within their group of 8–16 year olds, as compared with adults; however, they found no group difference for accuracy of predictions between younger and older children. This inconsistency within the literature likely stems from the difference in types of anticipations as mentioned above – prospective and immediate – and thus, as with any skill that requires training and exposure, the potential for conscious anticipations in AWS develops over time. Nevertheless, it is generally agreed that the capacity of AWS to anticipate their stuttering plays a role in stuttering avoidance as well as in various therapies.

In another recent study, Jackson, Yaruss, Quesal, Terranova, and Whalen (2015) collected and categorized written responses to three qualitative questions regarding stutter anticipation from a group of AWS. The authors report high rates of stutter anticipation (77%) in AWS. Moreover, by dividing AWS' responses into action and non-action responses, various ways of behavioral adjustments to stutter anticipation could be identified. These results emphasize the need to develop diagnostic instruments that capture anticipation characteristics in AWS for the individualized stuttering treatments as well as in research on stutter anticipation.

1.1. Therapy that integrates anticipation

While a lot of research has identified anticipations as a key characteristic of stuttering, only one mainstream therapy focuses on anticipations as one of the core components of interest. *Stuttering modification* or "non-avoidance therapy" (Van Riper, 1978) is one of the most well known and effective stuttering treatments; it stands alone as one which refines a patient's ability to anticipate upcoming stuttering events. Recent treatment studies document the efficacy of stuttering modification therapy: Prüß and Richardt (2015) found that most participants reported improved verbal and personal outcomes. Euler, Lange, Schroeder, and Lange (2014) showed that, of AWS who attended stutter therapy in Germany, those who underwent treatment that combined stuttering modification therapy with a therapy using *Fluency Shaping* profited most (for effectiveness studies on stutter modification treatment, see Blomgren, Roy, Callister, & Merrill, 2005; Breitenfeldt & Girson, 1995). These therapies emphasize that it is especially important in stuttering therapy to identify a patient's capacity, manner and style of anticipation. However, in an examination of the stuttering literature to date, no standardized assessment or scale exists to aid therapists in the examination of premonitory sensations in stuttering patients. In order to find an appropriate basis for a questionnaire on stuttering anticipation, we extended our search to disorders with similar characteristics. This led to the identification of tic disorders as an appropriate point of reference.

1.2. Similarities between tic disorders and stuttering

Tic disorders share many similarities with persistent developmental stuttering. Tic disorders, as stuttering, typically have their onset during childhood and often undergo spontaneous remission later in childhood (Döpfner, Roessner, Woitecki, & Rothenberger, 2010; Yairi & Ambrose, 1999). Within individuals, the symptoms can fluctuate over time in the short and long term, and are also influenced by emotional state (Döpfner et al., 2010). Tic disorders, like stuttering, do not differ by cultural or ethnic background (e.g., Robertson, 2008). Likewise, there is a male to female ratio of approximately 3:1 and a strong genetic factor in tic disorders (e.g., Devinsky & Geller, 1999) and stuttering (e.g., Yairi, Ambrose, & Cox, 1996). When examining tic disorders, Brady (1991) found a significant hypoactivation of the left hemisphere and hyperactivation of the right hemisphere motor areas. The same pattern has been found for stuttering (e.g., Sommer, Koch, Paulus, Weiller, & Büchel, 2002).

Additionally, two key studies have recently examined the similarities between the two disorders: Mulligan, Anderson, Jones, Williams, and Donaldson (2003) found that the movement disturbances in tics share many similarities with those accompanying stuttering events. Similarly, Tavano, Busan, Borelli, and Pelamatti (2011) noted a high prevalence of stuttering in individuals diagnosed with *Tourette's syndrome*; conversely, however, De Nil, Sasisekaran, Van Lieshout, and Sandor (2005) found conflicting evidence. Of greatest interest, during the creation of the PAiS, is that both tic disorders (Döpfner et al., 2010) and stuttering (e.g., Bloodstein & Bernstein Ratner, 2008) typically include a characteristic sensation preceding the movement disturbance; in tic disorders, this is known as a *premonitory urge*. In tic disorders, these sensations can manifest around the age of 10 (Döpfner et al., 2010), and can potentially precede every tic event.

When examining the clinical characteristics that define stuttering events by AWS, there are both similarities and differences that can be drawn between such events and the equivalent sensations of release (e.g., sneezing or itching) experienced by everyone. If we appropriate the framework from Belluscio, Tinaz, and Hallett (2011), which originally compared tic

patients and controls, premonitory sensations prior to an event are described as uncomfortable sensations that build up and may lead to feelings of distress if not released; this is similar in stuttering. However, unlike in normal release sensations, there is no brief period in which the AWS can suppress the forthcoming event while still accomplishing their precise speech goal.

Similarly, when comparing the clinical characteristics of stuttering and tic urges, the premonitory sensations in both disorders do not occur before all events. They are dissimilar, however, in that the sensations in stuttering do not overwhelm the patient's control – that is to say, unlike in tic disorders, AWS can stop a stuttering event by entirely refraining from any speech action. Patients with tic disorders also typically describe an itching sensation before, and subsequent relief after, the release of a tic event (Leckman & Cohen, 2003); by contrast, neither the prerelease itching nor the subsequent relief sensation are considered typical in stuttering (Alm, 2004). Additionally, in Tourette's syndrome, as suggested by the PUTS questionnaire (Crossley & Cavanna, 2013; Eddy & Cavanna, 2014), the occurrence of premonitory urges correlates with disease severity; whether the same holds true for stuttering individuals remains under debate.

It is difficult to make a comparison between the respective pathophysiologies of the premonitory sensations in tic disorders and stuttering, as imaging results and neurophysiological results on movement related cortical potentials are conflicting in tic disorders and scarce in stuttering (Jackson, Parkinson, Kim, Schüermann, & Eickhoff, 2011; Rajagopala, Serib, & Cavanna, 2013; Vanhoutte et al., 2015).

1.3. The premonitory urge in tics scale

Most people affected with Tourette's syndrome report that their tics are often preceded by a premonitory urge, meaning an uneasy sensation inside their body. This unpleasant feeling might influence the execution of the tics themselves (Woods, Piacentini, Himle, & Chang, 2005).

Woods et al. (2005) developed the *Premonitory Urge for Tics Scale* (PUTS) to allow for a standardized test of these anticipatory sensations. This instrument tests for different characteristics of the premonitory urges and was evaluated by Crossley, Seri, Stern, Robertson, and Cavanna (2013). Results showed significant correlations between the overall score of the PUTS and the overall severity score of the Tourette syndrome, for the group of participants older than 10 years of age. Taken together, against the background of the similarities between tic disorders and stuttering, the positive evaluation of the PUTS and the necessity of an instrument to quantify stutter anticipation in AWS, the Premonitory Awareness in Stuttering Scale (PAiS) was developed.

2. Material and methods

2.1. Development of the Premonitory Awareness in Stuttering Scale (PAiS)

A pilot version of the PAiS was derived from the PUTS (Woods et al., 2005) and translated into German. In most items, phrasing from the PUTS was directly translated, and the term *tic* was replaced with *stuttering* throughout the questionnaire. Additionally, certain items were rephrased to better reflect the experience of stuttering.

The pilot PAiS consisted of 9 items ranging on a 4-point Likert scale from *gar nicht* [not at all] to *sehr* [very much]. These items included statements describing the extent to which a premonitory feeling is detected or noticed in different situations. The pilot study was completed during the 40th Congress for Stuttering People which took place in Bielefeld, Germany, in October 2013. The study was approved by the ethics committee of the University Medical Center Göttingen. Written informed consent was obtained from all participants. Fifteen conference attendees who stutter volunteered to participate in this pilot study by completing the PAiS and a feedback questionnaire (e.g., *How suitable is the formulation of items in the PAiS? Would you reformulate one or more items? Which question is missing on the questionnaire? Which items would you label as unnecessary?*). The results and feedback from this pilot study were incorporated into the present 13-item version of the PAiS, by adding, rephrasing and removing items. (See Appendix A for the English version of the final 13-item PAiS Scale). Means and standard deviations for each item for the AWS group are presented in Table 2.

2.2. Psychometric validation

For the formal validation of the PAiS, we selected native speakers of German between 18–60 years of age. Inclusion criteria were as follows:

- a diagnosis of stuttering verified by a speech and language pathologist;
- no comorbid neurological or psychological disorders (e.g., aphasia, tic disorders, depression, epilepsy, bipolar disorder);
- no hearing or vision disorders;
- no speaking or language disturbances other than stuttering;
- adequate reading ability; and,
- no drug addictions including alcohol and prescription medications.

Table 1
Stutter Severity Measurements.

	Subjective Measurement		Objective Measurement									
	Self-report scale Score		SSI-4 score		% of stuttered syllables		Frequency		Durations		Physical Concomitants	
	M	SD	M	SD	M	SD	M	SD	M	SD	M	SD
AWS	4.6	1.5	20.05	8.34	10.34	8.29	8.19	1.01	7.33	2.71	4.95	3.53
ANS	n.a.	n.a.	2	0	0.47	0.032	2	0	2	0	0	0

Note: The self-report scale ranged from 1 = leicht [very mild] to 9 = sehr ausgeprägt [very severe]; M = Mean; SD = standard deviation; AWS = adults who stutter; ANS = adults who do not stutter; SSI-4 scores range from 10–36: scores from 10–17 are severity equivalent to "very mild", from 18–24 to "mild", from 25–31 to "moderate", and from 32–36 to "severe".

Table 2
Means and Standard Deviations for individual items of the PAiS in AWS.

Nr	Item	M	SD
01	Right before I stutter, I can sense that I am about to stutter.	2.10	0.62
02	Right before I stutter, I feel like my insides are itchy and tickly.	0.29	0.56
03	Right before I stutter, I feel pressure inside my brain or body.	1.62	0.97
04	Right before I stutter, I feel tense.	2.19	0.60
05	Right before I stutter, I feel like something is not 'just right'.	1.57	0.98
06	Right before I stutter, I feel like there is energy in my body that needs to get out or that is blocked.	1.14	0.79
07	In rather relaxed situations, I always have anticipatory sensations before I stutter.	1.24	1.00
08	In rather tense situations, I always have anticipatory sensations before I stutter.	1.81	0.81
09	These feelings happen every time before I stutter.	1.38	0.86
10	The anticipatory sensation allows me to avoid the upcoming stutter event by remaining silent.	1.14	1.15
11	The anticipatory sensation allows me to avoid the upcoming stutter event by saying something else.	1.52	0.93
12	After I stutter, the itchiness, pressure, energy, tense feelings or feelings that something isn't "just right" go away, at least for a while.	1.71	1.06
13	I really mind that I stutter.	2.14	.91

Note. On the Premonitory Awareness for Stuttering Scale (PAiS), a score of 0 = "not at all true," 1 = "a little true," 2 = "pretty much true," 3 = "very much true."; M = Mean; SD = standard deviation.

Participants with stuttering were recruited from the Kasseler Stottertherapie (KST) centre and the local self help groups in Bielefeld, Göttingen and Münster. The participants from the therapy centre were tested on the first or second day of their attendance at the KST intensive course, in order to minimize any effect of the treatment on the PAiS. Twenty-one participants, two women and 19 men, provided data for the PAiS validation. The age of participants ranged from 18 to 59 (mean = 31.2, SD = 11.4).

In addition, 21 ANS (two women and 19 men) aged from 18 to 60 (mean = 31.1, SD = 12.0) were recruited and matched for age, sex and highest level of education, with the same inclusion criteria as AWS above, except for the diagnosis of stuttering. We opted to include a group of ANS as control group to examine whether the anticipation of dysfluencies is, in fact, specific to AWS and not a common error predicting mechanism. ANS were recruited from Bielefeld University and the surrounding region of Bielefeld, using the inclusion and exclusion criteria listed above except for stuttering. The ANS group was tested using an adapted version of the final PAiS questionnaire in which all instances of the terms *stutter/stuttering (stottern)* were replaced with *dysfluencies (Unflüssigkeiten)*. The non-stuttering participants were verbally informed that the term *dysfluencies (Unflüssigkeiten)* was meant to include disruptions of speech *(Stockungen im Sprechfluss)*, getting muddled *(Verhaspeln)* and slips of the tongue *(Versprecher)*, but that semantic paraphasia (phonologically accurate but semantically incorrect wording, e.g., *bicycle* in the place of *car*) should not be considered a dysfluency in this context.

3. Results

3.1. Assessment of stuttering severity

3.1.1. Subjective Stutter Severity Measurement

The subjective stuttering severity of AWS was assessed based on a self-report scale (from 1–*sehr leicht* [very mild] to 9–*sehr ausgeprägt* [very severe]). The total scores for the group of AWS ranged from 2-7, the mean total score was 4.2 (severity equivalent to "moderate") see Table 1 for mean and standard deviation.

Table 3
Pearson Correlations.

	SSI-4 score	% of stuttered syllables	PAiS total score
Subjective Severity Score	**0.773****	**0.594****	−0.118
SSI-4 score		**0.775****	−0.207
% of stuttered syllables			−**0.519***

Note. Significance is denoted by asterisks: * = p < 0.05; ** = p < 0.01; *** = p < 0.001.

3.1.2. Stuttering Severity Instrument (SSI-4)

The *Stuttering Severity Instrument* 4 (SSI-4; Riley, 2008) is an objective measurement of stuttering severity that was completed by both speaker groups. The total score of the SSI-4 is derived by adding the scores from the *Frequency*, *Durations*, and *Physical Concomitants subscales.* In addition to SSI-4 total and subscale scores, percent syllables stuttered (%SS) was entered in the analyses as an independent measure of severity.

Speaking samples (sequences of spontaneous speech in response to semi-standardized questions) were recorded on digital video camera and coded by a certified speech therapist (the 2nd author). Descriptive statistics for all speaking measures can be found in Table 1. As expected, AWS had a significantly higher mean score on the SSI-4 (M = 20.05) than ANS (M = 2.00). This difference was highly significant ($t(40) = 8.56$, $p < .001$, Cohen's $d = 3.1$). Again as expected, AWS produced a higher percentage of stuttered syllables (M = 10.34%) compared to ANS (M = 0.47%). This difference was again highly significant ($t(40) = 5.451$, $p < .001$, Cohen's $d = 1.7$), see Appendix B.1 and Appendix B.2 for individual SSI scores for all participants.

3.2. Means and standard deviations of the PAiS

Responses to the 13 items of the PAiS were measured using a 4-point Likert scale ranging from *gar nicht* [not at all] to *sehr* [very much]. Individual items of the PAiS as well as means and SDs for each item are reported in Table 2. Because item 13 was subsequently found to reduce the internal consistency of the PAiS (see internal consistency analysis below) this item was excluded from the subsequent analyses and was not included in the mean of the total scores of the PAiS. For the sample of AWS, the mean PAiS total score was 17.71 (SD = 5.47), with total scores ranging between 9 and 29. For the analogously constructed version of the PAiS for ANS, the mean total score was 3.67 (SD = 4.19) with total scores ranging between 0 and 14. The difference between the two speaker groups, AWS and ANS, was highly significant ($t(40) = 9{,}35$, $p < 0.001$, Cohen's $d = 2.9$).

3.3. Internal consistency of the PAiS

Inter-item correlations (internal consistency) of the PAiS were assessed using Cronbach's alpha. For the entire sample of 21 participants, a standardized Cronbach's alpha level of 0.73 was obtained, indicating good internal consistency. Item 13 was found to reduce the overall reliability of the scale and was removed from the item pool. After exclusion of item 13, the reliability analysis was rerun, yielding a standardized Cronbach's alpha level of 0.76. (See Appendix C & Appendix D respectively for the English and German versions of the final PAiS, with item 13 excluded).

3.4. Correlation analyses

Correlation analyses were performed to examine the relationship between PAiS scores and the speech-related variables: *Self-Report Scale Score, SSI-4 Total Score*, *Percentage of Stuttered Syllables (%SS)*. All inter-correlations between the subjective (*Self-Report Scale Score*) and objective (*SSI-4* and %SS) stuttering measures were significant, with correlations ranging from 0.59 to 0.78. This latter finding indicates that the ability of stutter anticipation is independent of stutter severity. Interestingly, the correlations between the total score of the PAiS and the *Self-Report Scale Score* and between the PAiS total score and the *SSI-4* were non-significant, with correlations of −0.12 and −0.21 respectively. There was, however, a significant negative correlation between the total score on the PAiS and the *% SS*−variable, indicating that AWS with high PAiS scores tended to produce fewer stuttered syllables, see Table 3.

Correlations were performed between all 12 PAiS items and percentage of syllables stuttered in order to determine whether certain questions appeared to be more highly associated with stuttering frequency. Only three items turned out to significantly correlate with the *Percentage of Stuttered Syllables*: item 2 (*Right before I stutter, I feel like my insides are itchy and tickly),* item 5 (*Right before I stutter, I feel like something is not 'just right'*) and item 9 (*These feelings happen every time before I stutter*), see Table 4.

4. Discussion

The final version of the PAiS demonstrates a high internal consistency in the assessment of stuttering individuals. Moreover, the finding of a significant difference between AWS and ANS suggests that stutter anticipation is not a common error predicting mechanism; instead this *premonitory awareness* seems to be a special capacity exclusive to AWS. Stutter antic-

Table 4
Pearson Correlations.

PAiS	% of stuttered syllables
PAiS item1	−0.422
PAiS item 2	**−0.436***
PAiS item 3	−0.316
PAiS item 4	−0.344
PAiS item 5	**−0.480***
PAiS item 6	−0.151
PAiS item 7	−0.170
PAiS item 8	−0.186
PAiS item 9	**-0.463***
PAiS item 10	−1.76
PAiS item 11	0.078
PAiS item 12	−0.354

Note. Significance is denoted by asterisks: * = $p < 0.05$.

ipation, in fact, may be one of the defining characteristics of stuttering, as is argued for premonitory urges in tic disorders (cf. Devinsky & Geller, 1999). As early as 1938, Johnson and Ainsworth argued that, given that the experience of anticipatory feelings is such a common phenomenon amongst AWS, a theory of stuttering that disregards anticipations will not adequately explain stuttering. Recently, Natke and Alpermann (2010) recognized the influence of stutter anticipation on both the occurrence and the characteristics of secondary symptoms (e.g., physical concomitants like distracting sounds, facial grimaces, movements of the head and/or the extremities; for more details see, for example, Van Riper, 1937). To this day, however, despite scientific interest in the causes and consequences of stutter anticipation and despite agreement among AWS and speech therapists that stutter anticipation is a common epiphenomenon of stuttering, there is still no definition of stuttering that explicitly addresses and includes anticipatory sensations.

4.1. Percentage of syllables stuttered

The inverse relationship between the overall PAiS score and the Percentage of Stuttered Syllables is an interesting observation that requires further study. One hypothesis that accounts for this is that AWS who are more fluent have a better command of their speech *because* of their higher anticipation abilities. In other words, the better AWS are at predicting impending stutters, the more likely they may be to adjust their speech planning/motor behaviors to optimize speech fluency. However, even the PAiS items that asked most explicitly for AWS' conscious reaction to a stutter anticipation (i.e., "to remain silent", item 10; or to "reformulate the originally intended utterance", item 11) did not correlate with the *Percentage of Stuttered Syllables;* thus we tentatively conclude that, even for speakers who anticipate impending stutters, this awareness may not necessarily lead to a consciously planned action attempting to prevent this stutter event. Interestingly, the three PAiS items (items 2, 5, and 9, see point 3.4) which did correlate significantly with the fluency parameter (*Percentage of Stuttered Syllables*) all relate to the sensation of *immediate* as opposed to *prospective* anticipation. The primary difference between these two types of anticipation is that immediate anticipation is believed to be less dependent upon specific linguistic items or speaking environments and situations. At present, our knowledge of how accurately AWS detect their stutter events, and the responses or adaptations that are made to premonitory sensations, are not fully understood but may reflect variations in the "introspection" abilities of individual stuttering speakers.

4.2. Limitations of the PAiS

Limitations of the PAiS at the present stage comprise a single validation in a relatively small group of German language speaking adults. It currently lacks age-based norms and a validated translation into English and other languages. It has been argued that the ability to detect upcoming stutter events increases with age (Bloodstein, 1960), though experimental evidence for this claim is lacking. However, the finding that the PUTS only yields internal consistency in older children, but not children below the age of ten, points towards the conclusion that conscious premonitory awareness may, in fact, develop with age as Woods et al. (2005) suggested. Nevertheless, in subsequent research, the utility of the PAiS for children should be explored.

In its current version, the PAiS does not differentiate between prospective and immediate types of anticipation. These more specific characteristics of anticipation should be assessed in a subsequent consultation with the participant to draw a more precise anticipation profile to evaluate the premonitory awareness of AWS in order to inform basic research and apply it to treatment. Moreover, the PAiS does not include information about whether AWS do anything to actively modify their speech when faced with anticipatory sensations. Likewise, there are as of yet no data addressing the relationship between anticipation sensations and actual stuttering; that is, we do not know whether AWS were accurate in identifying their stuttering moments. Whether accuracy of identification is relevant is itself an interesting question that should be addressed in future research.

4.3. Therapy

As a therapy instrument, the PAiS can help to identify a specific profile of response to stuttering anticipations in AWS. As already stated, the degree and manner of anticipation can be indicative of a patient's capacity to respond to the overall stuttering event and thus influence the effectiveness of different therapy techniques. It could identify, for example, whether therapy should focus on the modification approaches that utilize stutter anticipations during treatment through so called *Preparatory Sets* (Van Riper, 1978), i.e., techniques that facilitate speech fluency by applying speech motor adaptations of the utterance that is predicted to induce stuttering (e.g., by reducing speech rate and starting words with a soft voice onset). With practice, adjusting one's speech to anticipated stuttering events will become more and more automated. By focusing speech training on increasing a patient's sensitivity to anticipation events, the patient will likely improve the effectiveness of the stutter modification programs beyond therapy (for discussion of the different programs see Blomgren et al., 2005; Euler et al., 2014).

Another program that incorporates awareness is *Habit Reversal Therapy* (HRT; e.g., Dutta & Cavanna, 2013), which is a form of cognitive behavioral therapy more commonly applied in the treatment of tic disorders. HRT has multiple components that improve self-monitoring of tics, relaxation training, practice of physically competing responses that may help to avoid or disrupt a tic, and motivational techniques (e.g., Himle, Woods, Piacentini, & Walkup, 2006). Stutter therapies could draw on some of these techniques when attempting to improve a patient's awareness training.

One issue that might impede this awareness training is heightened physiological arousal and anxiety during speech. A recent study by Bowers, Saltuklaroglu, and Kalinowski (2012) investigated how anticipatory autonomic arousal and stuttering is interrelated. Skin conductance and heart rate between presentations of previously elicited feared phonemes and the actual occurrence of stuttering were measured. Results showed no direct relationship between anticipatory arousal and stuttering but rather that the omnipresent expectation of stutter creates a generally accelerated level of anticipatory arousal in AWS.

Another study, by Jackson et al. (2015), highlighted the variation in profiles of stuttering. In particular, they identified two main categories differentiated by their response pattern: *non-action* response, which was characterized by mostly negative or passive responses to a stutter event, and *action* response, in which the AWS enacted proactive behavioral strategies in either avoidance or self-management strategies. In this way, the PAiS will allow therapists to draw an individual profile for each patient, incorporating anticipation/awareness and response style, to better tailor therapy to the needs of each patient.

4.4. Future research

The PAiS comes at the forefront of a growing field. It will greatly benefit researchers and therapists alike, but it is not without its limitations. We expect that the limitations of group size will be reduced with ongoing research and broader uptake of the PAiS in both the research and therapy communities. Against the background of more recent studies (e.g., Jackson et al., 2015; Garcia-Barrera & Davidow, 2015), we recommend that future research involving the PAiS should include an additional question; it should appear between the current questions 10 and 11, as follows:

> The anticipatory sensation allows me to avoid the upcoming stutter by changing how I am talking.

This question will help to draw a more complete profile of an individual's stuttering. Therapists can also utilize this question; however, we recommend caution in its interpretation, as the PAiS is not yet statistically validated for this expansion.

Further evaluation should also explore the utility of the PAiS for children. More specifically, in its current version, the PAiS only minimally differentiates between prospective and immediate types of anticipation. These more specific characteristics of anticipation should be assessed more fully using qualitative methods in a subsequent study (such as in Jackson et al., 2015). Correspondingly, the ways in which AWS modify their motor plan during moments of anticipation is interesting and may inform current models of speech production and speech motor control (for an outline of a speech production model that integrates stutter anticipation, see Garcia-Barrera & Davidow, 2015). As a therapy instrument, the PAiS may identify a specific response profile that would help the clinician develop a more targeted and individualized treatment program. Finally, increasing a client's sensitivity and positive response to anticipation sensations may be useful to incorporate into therapy and may promote generalization of treatment gains into outside environments.

Acknowledgements

We are grateful for the assistance of Dr. Alexander Wolff von Gudenberg and his team from the Kasseler Stottertherapie for helping us to recruit adults who stutter. This work has been supported by a grant from the Deutsche Forschungsgemeinschaft DFG SO 429/4-1.

Appendix A.

13-item PAiS Scale.

Nr	Items
(01)	Unmittelbar bevor ich stottere, kann ich spüren, dass ich stottern werde. [Right before I stutter, I can sense that I am about to stutter.]
(02)	Unmittelbar bevor ich stottere, fühlt es sich an, als würde es in mir jucken oder kribbeln. [Right before I stutter, I feel like my insides are itchy and tickly.]
(03)	Unmittelbar bevor ich stottere, fühlt es sich an, als wäre ein Druck in meinem Hirn oder in meinem Körper. [Right before I stutter, I feel pressure inside my brain or body.]
(04)	Unmittelbar bevor ich stottere, fühle ich mich angespannt. [Right before I stutter, I feel tense.]
(05)	Unmittelbar bevor ich stottere, fühlt es sich an, als wäre irgendetwas nicht in Ordnung. [Right before I stutter, I feel like something is not 'just right'.]
(06)	Unmittelbar bevor ich stottere, fühlt es sich an, als sei eine Energie in meinem Körper, die raus muss oder blockiert wird. [Right before I stutter, I feel like there is energy in my body that needs to get out or that is blocked.]
(07)	In eher entspannten Situationen habe ich diese Gefühle fast immer, bevor ich stottere. [In rather relaxed situations, I always have anticipatory sensations before I stutter.]
(08)	In eher angespannten Situationen habe ich diese Gefühle fast immer, bevor ich stottere. [In rather tense situations, I always have anticipatory sensations before I stutter.]
(09)	Diese Gefühle treten vor jedem Stotterereignis auf, das ich habe. [These feelings happen everytime before I stutter.]
(10)	Dieses Vorgefühl erlaubt es mir, das nachfolgende Stotterereignis zu vermeiden, indem ich schweige. [The anticipatory sensation allows me to avoid the upcoming stutter event by remaining silent.]
(11)	Dieses Vorgefühl erlaubt es mir, das nachfolgende Stotterereignis zu vermeiden, indem ich etwas anderes sage. [The anticipatory sensation allows me to avoid the upcoming stutter event by saying something else/different.]
(12)	Wenn ich gestottert habe, verschwinden das Jucken, die Energie, der Druck, die Anspannung oder die Gefühle, oder nicht vollständig wäre – zumindest für eine gewisse Zeit. [After I stutter, the itchiness, energy, pressure, tense feelings or feelings that something isn't "just right" go away, at least for a while.]
(13)	Es stört mich sehr, dass ich stottere. [I really mind that I stutter.]

Appendix B.1.

Stutter Severity Scores for all individual participants in the AWS group.

AWS	Age	Sex	Stutter onset (years of age)	Stutter severity self-estimate	SSI-4 Score	SSI-4 Frequency	SSI-4 Duration	SSI-4 Physical Concomitants	Stuttered syllables
AWS_01	18	m	3	5	19	5	6	8	4,1
AWS_02	23	m	6	7	32	6	12	14	6,6
AWS_03	21	m	3	6	19	6	8	5	6,4
AWS_04	26	m	5	5	26	9	8	9	28
AWS_05	26	f	5	3	5	3	2	9	2,2
AWS_06	33	m	4	5	16	7	8	1	8,3
AWS_07	20	m	5	4	16	8	6	2	13,1
AWS_08	31	m	8	7	25	8	10	7	21,4
AWS_09	24	m	3	4	11	4	6	1	3,6
AWS_10	43	m	3	5	28	8	12	8	20,3
AWS_11	39	m	6	7	37	18	12	7	22,9
AWS_12	23	m	6	3	11	4	6	1	3,7
AWS_13	26	m	4	4	16	4	6	6	2,9
AWS_14	20	m	5	5	18	6	8	4	6,5
AWS_15	21	f	3	4	15	8	6	1	3,8
AWS_16	39	m	4	5	21	1	6	1	11
AWS_17	44	m	4	2	11	4	4	3	1,4
AWS_18	30	m	5	3	24	14	8	2	10,7
AWS_19	38	m	3	6	33	16	10	7	21,7
AWS_20	59	m	5	2	12	4	4	4	1,4
AWS_21	52	m	3	5	26	16	6	4	17,1

Appendix B.2.

Stutter Severity Scores for all individual participants in the ANS group.

ANS	age	sex	Stutter onset (years of age)	Stutter severity self-estimate	SSI-4 Score	SSI-4 Frequency	SSI-4 Duration	SSI-4 Concomitants	Stuttered syllables
ANS_01	25	f	n.a	n.a.	2	n.a.	n.a.	n.a.	,6
ANS_02	23	m	n.a	n.a.	2	n.a.	n.a.	n.a.	,8
ANS_03	25	m	n.a	n.a.	2	n.a.	n.a.	n.a.	,6
ANS_04	33	m	n.a	n.a.	2	n.a.	n.a.	n.a.	,6
ANS_05	29	m	n.a	n.a	2	n.a.	n.a.	n.a.	,0
ANS_06	18	m	n.a	n.a.	2	n.a.	n.a.	n.a.	1,4
ANS_07	38	m	n.a	n.a.	2	n.a.	n.a.	n.a.	,0
ANS_08	20	m	n.a	n.a.	2	n.a.	n.a.	n.a.	,3
ANS_09	23	m	n.a	n.a.	2	n.a.	n.a.	n.a.	,3
ANS_10	27	m	n.a	n.a.	2	n.a.	n.a.	n.a.	,6
ANS_11	32	m	n.a	n.a.	2	n.a.	n.a.	n.a.	,6
ANS_12	19	m	n.a	n.a.	2	n.a.	n.a.	n.a.	,3
ANS_13	26	m	n.a	n.a.	2	n.a.	n.a.	n.a.	,6
ANS_14	54	m	n.a	n.a.	2	n.a.	n.a.	n.a.	,3
ANS_15	46	m	n.a	n.a.	2	n.a.	n.a.	n.a.	,5
ANS_16	44	m	n.a	n.a.	2	n.a.	n.a.	n.a.	,3
ANS_17	41	m	n.a	n.a.	2	n.a.	n.a.	n.a.	,3
ANS_18	20	m	n.a	n.a.	2	n.a.	n.a.	n.a.	,5
ANS_19	18	f	n.a	n.a.	2	n.a.	n.a.	n.a.	,4
ANS_20	60	m	n.a	n.a.	2	n.a.	n.a.	n.a.	,0
ANS_21	31	m	n.a	n.a.	2	n.a.	n.a.	n.a.	,8

Appendix C.

Premonitory Awareness of Stuttering Scale (PAiS).
Name_____.
Age_____.
Date_____.

Nr	How I feel	Not at all	A little	Pretty much	Very much
(01)	Right before I stutter, I can sense that I am about to stutter				
(02)	Right before I stutter, I feel like my insides are itchy and tickly				
(03)	Right before I stutter, I feel pressure inside my brain or body				
(04)	Right before I stutter, I feel tense				
(05)	Right before I stutter, I feel that something is not 'just right'				
(06)	Right before I stutter, I feel like there is energy in my body that needs to get out or that is blocked				
(07)	In rather relaxed situation, I always have anticipatory sensations before I stutter				
(08)	In rather tense situation, I always have anticipatory sensations before I stutter				
(09)	These feelings happen every time before I stutter				
(10)	The anticipatory sensation allows me to avoid the upcoming stutter event by remaining silent				
(11)	The anticipatory sensation allows me to avoid the upcoming stutter event by saying something else				
(12)	After I stutter, the itchiness, energy, pressure, tense feelings or feelings that something isn't "just right" go away, at least for a while				
	Total score (on a scale from 0-3, ranging from *not at all to very much*)				

Appendix D.

German version.
Premonitory Awareness of Stuttering Scale (PAiS).
Name _____.
Alter _____.
Datum _____.

Nr	Wie ich mich fühle	Gar nicht	Ein bisschen	Ziemlich	Sehr
(01)	Unmittelbar bevor ich stottere, kann ich spüren, dass ich stottern werde.				
(02)	Unmittelbar bevor ich stottere, fühlt es sich an, als würde es in mir jucken oder kribbeln.				
(03)	Unmittelbar bevor ich stottere, fühlt es sich an, als wäre ein Druck in meinem Hirn oder in meinem Körper.				
(04)	Unmittelbar bevor ich stottere, fühle ich mich angespannt.				
(05)	Unmittelbar bevor ich stottere, fühlt es sich an, als wäre irgendetwas nicht in Ordnung.				
(06)	Unmittelbar bevor ich stottere, fühlt es sich an, als sei eine Energie in meinem Körper, die raus muss oder blockiert wird.				
(07)	In eher entspannten Situationen habe ich diese Gefühle fast immer, bevor ich stottere.				
(08)	In eher angespannten Situationen habe ich diese Gefühle fast immer, bevor ich stottere.				
(09)	Diese Gefühle treten vor jedem Stotterereignis auf, das ich habe.				
(10)	Dieses Vorgefühl erlaubt es mir, das nachfolgende Stotterereignis zu vermeiden, indem ich schweige.				
(11)	Dieses Vorgefühl erlaubt es mir, das nachfolgende Stotterereignis zu vermeiden, indem ich etwas anderes sage.				
(12)	Wenn ich gestottert habe, verschwinden das Jucken, die Energie, der Druck, die Anspannung oder die Gefühle, oder nicht vollständig wäre – zumindest für eine gewisse Zeit.				
	Gesamtpunktzahl.				
	(auf einer Skala von 0-3, von *gar nicht* bis *sehr*).				

References

Alm, P. A. (2004). Stuttering and the basal ganglia circuits: A critical review of possible relations. *Journal of Communication Disorders*, *37*, 325–369.

Belluscio, B. A., Tinaz, S., & Hallett, M. (2011). Similarities and differences between normal urges and the urge to tic: Commentary in the commentaries section on Jackson SR et al. *Cognition Neuroscience*, *2*, 227–243.

Blomgren, M., Roy, N., Callister, T., & Merrill, R. A. (2005). Intensive stuttering modification therapy: A multidimensional assessment of treatment outcomes. *Journal of Speech, Language, and Hearing Research*, *48*, 509–523.

Bloodstein, O. (1960). The development of stuttering: I. Changes in nine basic features. *Journal of Speech and Hearing Disorders*, *25*, 219–237.

Bloodstein, O., & Bernstein Ratner, N. (2008). *A handbook on stuttering* (6th ed.). Clifton Park, NY: Delmar Learning.

Bowers, A., Saltuklaroglu, T., & Kalinowski, J. (2012). Autonomic arousal in adults who stutter prior to various reading tasks intended to elicit changes in stuttering frequency. *International Journal of Psychophysiology*, *83*, 45–55.

Brady, J. P. (1991). The pharmacology of stuttering: A critical review. *The American Journal of Psychiatry*, *148*, 1309–1316.

Breitenfeldt, D. H., & Girson, J. (1995). Efficacy of the Successful Stuttering Management Program workshops in the United States of America and South Africa. In C. W. Starkweather, & H. F. M. Peters (Eds.), *Proceedings of the First World Congress on Fluency Disorders* (pp. 429–431). Nijmegen, The Netherlands: Nijmegen University Press.

Crossley, E., Seri, S., Stern, J. S., Robertson, M. M., & Cavanna, A. E. (2013). Premonitory urges for tics in adult patients with Tourette Syndrome. *Brain and Development*, *36*, 45–50.

Crossley, E., & Cavanna, A. E. (2013). Sensory phenomena: Clinical correlates and impact on quality of life in adult patients with Tourette syndrome. *Psychiatry Research*, *209*, 705–710.

De Nil, L. F., Sasisekaran, J., Van Lieshout, P. H. H. M., & Sandor, P. (2005). Speech disfluencies in individuals with Tourette Syndrome. *Journal of Psychosomatic Research*, *58*, 97–102.

Devinsky, O., & Geller, B. D. (1999). Gilles de la Tourette's Syndrome. In A. B. Joseph, & R. R. Young (Eds.), *Movement disorders in neurology and neuropsychiatry* (pp. 442–448). Carlton, Australie: Wiley-Blackwell.

Döpfner, M., Roessner, V., Woitecki, K., & Rothenberger, A. (2010). *Tic-Störungen*. Göttingen: Hogrefe.

Dutta, N., & Cavanna, A. E. (2013). The effectiveness of habit reversal therapy in the treatment od Tourette syndrome and other chronic tic disorders: A systematic review. *Functional Neurology*, *28*, 7–12.

Eddy, C. M., & Cavanna, A. E. (2014). Premonitory urges in adults with complicated and uncomplicated tourette syndrome. *Behavior Modification*, *38*, 264–275.

Euler, H. A., Lange, B. P., Schroeder, S., & Neumann, K. (2014). The effectiveness of stuttering treatments in Germany. *Journal of Fluency Disorders*, *39*, 1–11.

Garcia-Barrera, M. A., & Davidow, J. H. (2015). Anticipation in stuttering: A theoretical model of the nature of stutter prediction. *Journal of Fluency Disorders*, *44*, 1–15.

Himle, M. B., Woods, D. W., Piacentini, J. C., & Walkup, J. T. (2006). Brief review of habit reversal for tourette syndrome. *Journal of Child Neurology*, *21*, 719–725.

Jackson, E. S., Yaruss, J. S., Quesal, R. W., Terranova, V., & Whalen, D. H. (2015). Responses of adults who stutter to the anticipation of stuttering. *Journal of Fluency Disorders*, *45*, 38–51.

Jackson, S. R., Parkinson, A., Kim, S. Y., Schüermann, M., & Eickhoff, S. B. (2011). On the functional anatomy of the urge-for-action. *Cognitive Neuroscience*, *2*, 227–257.

Johnson, W., & Knott, J. R. (1937). Studies in the psychology of stuttering I: The distribution of moments of stuttering in successive readings of the same material. *Journal of Speech Disorders*, *2*, 17–19.

Johnson, W., & Solomon, A. (1937). Studies in the psychology of stuttering IV: A quantitative study of expectation of stuttering as a process involving a low degree of consciousness. *Journal of Speech Disorders*, *2*, 95–97.

Leckman, J. F., & Cohen, D. J. (2003). Tic disorders. In M. Rutter, & E. Taylor (Eds.), *Child and adolescent psychiatry* (4th ed., pp. 593–611). Oxford, England: Blackwell.

Milisen, R. (1938). Frequency of stuttering with anticipation of stuttering controlled. *Journal of Speech Disorders*, *3*, 207–214.

Mulligan, H. F., Anderson, T. J., Jones, R. D., Williams, M. J., & Donaldson, I. M. (2003). Tics and developmental stuttering. *Parkinsonism and Related Disorders*, *9*, 281–289.

Natke, U., & Alpermann, A. (2010). Stuttering. Insights, theories, treatment methods) Stottern. *Erkenntnisse, Theorien, Behandlungsmethoden*. Bern, Switzerland: Verlag Hans Huber.

Prüß, H., & Richardt, K. (2015). Bonner Langzeit-Evaluationsskala zur Lebenssituation Stotternder (BLESS) – Ein neues praxisorientiertes Instrument zur Diagnostik, Therapieplanung und Evaluation für stotternde Kinder ab 12 Jahren, Jugendliche und Erwachsene. *Forum Logopädie*, *2*, 14–18.
Rajagopala, S., Serib, S., & Cavanna, A. E. (2013). Premonitory urges and sensorimotor processing in Tourette syndrome. *Behavioural Neurology*, *27*, 65–73.
Riley, G. D. (2008). *Stuttering Severity Instrument (SSI-4): examiner manual and picture plates*. Austin, TX: Pro-Ed.
Robertson, M. M. (2008). The international prevalence, epidemiology and clinical phenomenology of Gilles de la Tourette Syndrome Part 1: The epidemiological and prevalence studies. *Journal of Psychosomatic Research*, *65*, 473–486.
Silverman, F. H., & Williams, D. E. (1972). Prediction of stuttering by school-age stutterers. *Journal of Speech, Language, and Hearing Research*, *15*, 189–193.
Sommer, M., Koch, M. A., Paulus, W., Weiller, C., & Büchel, C. (2002). Disconnection of speech relevant brain areas in persistent developmental stuttering. *The Lancet*, *360*, 380–383.
Tavano, A., Busan, P., Borelli, M., & Pelamatti, G. (2011). Risperidone reduces tic-like motor behaviours and linguistic disfluencies in severe persistent developmental stuttering. *Journal of Clinical Psychopharmacology*, *31*, 131–134.
Vanhoutte, S., Santens, P., Cosyns, M., van Mierlo, P., Batens, K., Corthals, P., De Letter, M., & Van Borsel, J. (2015). Increased motor preparation activity during fluent single word production in DS: A correlate for stuttering frequency and severity. *Neuropsychologia*, *75*, 1–10.
Van Riper, C. (1937). Effect of devices for minimizing stuttering on the creation of symptoms. *Journal of Abnormal Social Psychology*, *32*, 185–192.
Van Riper, C. (1978). *Speech correction: principles and methods* (6th ed.). Englewood Cliffs, NJ: Prentice-Hall.
Woods, D. W., Piacentini, J., Himle, M. B., & Chang, S. (2005). Premonitory Urge for Tic Scale (PUTS): Initial psychometric results and examination of the premonitory urge phenomenon in youths with tic disorders. *Developmental and Behavioral Pediatrics*, *26*, 397–403.
Yairi, E., & Ambrose, N. G. (1999). Early childhood stuttering I: Persistency and recovery rates. *Journal of Speech, Language and Hearing Research*, *42*, 1097–1112.
Yairi, E., Ambrose, N., & Cox, N. (1996). Genetics of stuttering: A critical review. *Journal of Speech and Hearing Research*, *39*, 771–784.

4.0.0 Paper 2

Stuttering and its anticipation in reading

Joana Cholin, Annett Jorschick, Sabrina Heiler, Alexander Whillier, & Martin Sommer

In Preparation (submission anticipated January 2018).

Primary contributions by doctoral candidate Alexander Whillier:

- Statistics
- Data analysis
- Interpretation
- Writing

Keywords: Spoken production planning, dysfluencies, stutter anticipation, persistent developmental stuttering, linguistics factors in stuttering, self-monitoring and control models

Paper 2 – 1.0.0 – Abstract

Adults who stutter (AWS) most commonly report that they can anticipate upcoming stutter events: Even before a planned utterance is fully encoded and overtly articulated, a speaker who persistently stutters can often sense that a certain part of speech will cause a dysfluency. To date, it is not clear whether (i) these anticipatory sensations are in fact specific to speakers who stutter and (ii) what these anticipations are based on. The current study collected anticipation judgements from AWS and adults who do not stutter (ANS) after a silent reading trial of six short stories that were subsequently read aloud. Anticipation judgements were evaluated against the actually occurring stutter events.

We examined a set of linguistic factors that have previously been found to be implicated in stuttering, to test whether speakers' anticipations of stutter occurrences exploit these same linguistic factors. Results revealed that lexical factors (i.e., Word Frequency, Sentence Position) play a role in Stuttering and Anticipation models across AWS while post-lexical factors (i.e., Onset Complexity) and specific combinations of lexical/post-lexical factors seemed to be implicated in AWS' individual models (of Stuttering and Anticipation).

The findings are discussed against the background of current models of spoken production and self-monitoring and control models as well as their implications for treatment approaches.

Paper 2 – 2.0.0 – Introduction

The occurrence and nature of stutter anticipation, i.e., the premonition that a stutter event is imminent, has been the subject of many studies since the 1930s (e.g., Arenas, 2012; Bloodstein & Bernstein Ratner, 2008; Garcia-Barrera & Davidow, 2015; Knott, Johnson, & Webster, 1937; Van Riper, 1936; Wingate, 1975). However, whereas scientific understanding about the nature of stuttering has considerably increased over the last decades (for a comprehensive overview see Bloodstein & Bernstein Ratner, 2008) and prospective studies have detailed the rates of persistence and recovery in childhood and adolescence (e.g., Ambrose, Yairi, Loucks, Seery, & Throneburg, 2015; Spencer & Weber-Fox, 2014; Yairi & Ambrose, 2013), the characteristics of stutter anticipation are still largely unknown. Although most adults who stutter (AWS) report that they can often sense an upcoming stutter event and might have good intuitions about which words and structures are "difficult" for them, it is unclear a) which underlying kinaesthetic, cognitive sensations and/or linguistic factors cause these premonitions and b) how stutter anticipations and stutter occurrences are related. The reported high number of stutter anticipations of approximately 85-94% of all stutter occurrences (e.g., Johnson & Knott, 1937; Milisen, 1938; van Riper, 1978) suggests that AWS can rely on an internal feedback system to identify upcoming stutter events. This capacity can be utilized to circumvent the expected dysfluencies, either by reformulating the utterance that is still under internal construction, by integrating pauses or fillers or by applying other circumvention strategies (e.g., Jackson, Yaruss, Quesal, Terranova, & Whalen, 2015).

P2.2.1.0 – Cognitive models of stuttering and anticipation

In cognitive accounts of stuttering, it has been a long standing assumption that stuttering and its anticipation are in fact disadvantageously intertwined, first suggested by Johnson & Knott (1936) and famously adopted by Bloodstein (e.g., 1959, 1975) in his *Anticipatory Struggle Hypothesis*. According to these accounts, apprehension caused by these anticipations negatively influence the already complex task of speaking fluently, resulting in recurring interruptions of the speech stream. Various other publications have also attributed hyper-critical error correction and/or dysfluency detection that causes persistent interruptions and attempted self-repairs, which, in turn,

lead to repeated speech derailments; such publications include the *Covert Repair Hypothesis* (Postma & Kolk, 1993; Kolk & Postma, 1997), the *Vicious Circle Hypothesis* (Vasić & Wijnen, 2005) and the *Hypervigilant Self-Monitoring* Hypothesis (Lickley, Hartsuiker, Corley, Russell, & Nelson, 2005).

These accounts are embedded into Levelt's production model (1989; Roelofs, Meyer, & Levelt, 1999), which integrates a self-monitoring mechanism that allows speakers to control their inner speech before it is overtly articulated. According to this model, if an error or upcoming dysfluency is detected, a repair can be initiated (see Baars, Motley, & MacKay, 1975; Clark, 1996; Noteboom, 1980; Levelt, 1983; see Levelt, 1989 for suggestions of error repair strategies). There is ample evidence that speakers can quickly and flexibly adapt their speech planning to slight deviations from the intended speech goal, in response to error detection and/or sudden contextual changes (e.g., Levelt, 1983, 1989; Slevc & Ferreira, 2006). However, while this monitoring mechanism might help to smoothen speech output, it may prove detrimental when overly high targets for acceptable speech output are set that hamper the transition from planning to execution. As formulated by the *Vicious Circle Hypothesis* (Vasić & Wijnen, 2005), stuttered speech is caused by the exacerbated correction attempts which are triggered by an overly rigorous monitoring system that sends and even resends already repaired elements into another round of ‘error’ repair. Experiments in which AWS and control groups were asked to judge the fluency of stuttered and non-stuttered speaking samples showed that AWS even judged the speech by fluently speaking controls as partially dysfluent while speakers who do not stutter (ANS) were consistently less critical in their fluency rating (Lickley et al., 2005), supporting the assumption of a 'hypervigilant' self-monitoring system in AWS.

Brocklehurst, Lickley, and Corley (2013) propose the Variable Release Threshold (VRT) hypothesis of stuttering, in which they combine key features of Bloodstein's Anticipatory Struggle Hypothesis and the revised *EXPLAN* model (Howell, 2003; see also Howell, 2002; Howell & Au-Yeung, 2002). The authors present a comprehensive framework that accommodates a large number of stuttering symptoms. For example, in situations that prompt AWS to speak more slowly or accurately as they anticipate not being understood, the release threshold will exceed their own

capability to produce acceptable speech output; this will result in prolongations, pauses or, in the worst case, silent blocks. Another model that incorporates anticipation of stuttering into a model of spoken production is the *Speech and monitoring interaction* (SAMI) framework by Arenas (2012). In this model, stutter anticipation can modulate the monitoring system much like it is formulated by the Error-Likelihood ACC Model proposed by Brown and Braver (2005) – in both models, predictions of error-occurrence prompt the recruitment of cognitive control for response inhibition. Within the SAMI framework, it is assumed that these learned predictions may trigger the monitoring system to over-apply its inhibiting regulator; this will in turn interfere with the speech production system, which will result in temporal derailments and, ultimately, overt stuttering (cf. Arenas, 2012).

Conflict-based monitoring accounts such as the one proposed by Nozari, Dell, and Schwartz, 2011 (see also Riès, Janssen, Dufau, Alario, & Burlau, 2011) assume that error detection is based on conflict that results from competition between alternative representations (e.g., dog vs. cat). However, in stuttering, it is not assumed that such conflict is a result of processes on the lexical level rather on motor programming levels. One model that integrates these lower levels of motor processing is the Hierarchical State Feedback Control (HSFC) model (Hickok, 2012a). During normal speech, parallel feed-forward and feedback pathways are activated – prior to an utterance, forward prediction targets are sent to the auditory syllable target system (in the aSMG-S1) and the somato-phoneme target system (in the STG-STS); after speech, parallel feedback pathways compare the respective signals with the feed-forward prediction targets and allow for near-instant real-time speech modification. Stuttering can result if a signal is temporally mismatched or the threshold for self-monitoring is too high.

The most recent model that integrates a mechanism of stutter anticipation into the process of speech planning is the one by Garcia-Barrera and Davidow (2015). In this model, monitoring procedures check linguistic structures and units on their specific encoding levels – conceptual encoding, grammatical and phonological encoding, and phonetic encoding – against internalized memories of specific grammatical structures, words, morphemes, syllables, phonemes that might

have evoked stutter events in the past. In case of a positive match, the anticipation system triggers a signal through somatic markers that, in turn, can evoke an anticipatory sensation.

All of the reviewed models integrate an error/dysfluency detection process and consider this mechanism as a potential pitfall for fluent speech planning and execution if the margins for acceptable output are set inappropriately high. However, to solely attribute the recurrent derailments in stuttered speech to a hypersensitive monitoring system may only be half the story. Rather, it seems that the monitoring system stumbles over actually deviant encoding procedures, specifically:

- slower phonological encoding procedures as assumed by the Covert Repair Hypothesis (Postma & Kolk, 1993; Kolk & Postma, 1997; but see Brocklehurst, 2008 for a critical review and some counter-evidence) or the feed-forward system (Hickok, 2012b),
- dyscoordination between consecutive linguistic and/or motor planning and execution levels (for a comprehensive overview see Bloodstein & Bernstein Ratner, 2008),
- temporal mismatch in somatosensory and temporal feedback systems (e.g. Hickok, 2012b),
- instable motor representations and/or auditory percepts (e.g., Neef, Sommer, Neef, Paulus, von Gudenberg, Jung, & Wüstenberg, 2012) due to deficient sensory-motor links in the brain (e.g., Cai, Tourville, Beal, Perkell, Guenther, & Ghosh, 2014; Cykowski, Fox, Ingham, Ingham, & Robin, 2010; Sommer, Koch, Paulus, Weiller, & Büchel, 2002), and/or speech motor learning disabilities (Max, Guenther, Gracco, Ghosh & Wallace, 2004; Peters, Hulstjin, & Van Lieshout, 2000 but see Smits-Bandstra & Gracco, 2015).

For fluent speakers, it is assumed that speakers access stored, pre-compiled motor programmes or sequences; the use of these programmes, which are of approximately syllabic size, improves speech planning efficiency relative to a segment-by-segment assembly which would build each motor syllable from scratch (e.g., Levelt, Roelofs, & Meyer, 1999). These motor programs are the first language elements that are learned during early language acquisition through adaptation between production and perception processes, thereby crucially relying on intact connections between these systems.

Speech planning and execution runs smoothest in a highly automated manner. If, however, any of the motor programmes, the auditory percepts or the connection between them are unstable and remain so, the prerequisites for automation may not be given and speech production may remain more resource-costly in speakers who stutter. Attention is then concentrated internally which, as is known from studies on motor performance, negatively influences smooth motor execution, disrupts automation and may lead to failure (e.g., Beilock & Gray, 2012).

However, the fact that even speakers who stutter more severely have islands of undisrupted fluency may suggest that there are circumstances that can help to overcome the inauspicious combination of impaired encoding procedures and /or representations, at least occasionally. Such conditions include speaking under auditory masking/delayed auditory feedback or choral reading/speaking and speaking to external rhythm (e.g., Bloodstein &Bernstein Ratner, 2008; Howell, 2004; 2011; Lee, 1950; Sheehan, 1970; van Riper, 1982).

Taken together, the combination of unstable connections and representations that hamper automation on the one hand and internally directed attention processes attempting to detect and repair fluency deviations on the other hand may render speech planning dysfunctional. However, anticipation procedures may also have positive effects on speech fluency – that is, anticipation may in fact be a tool that can be utilized in order to enhance speech planning processes.

P2.2.2.0 – Experimental studies

The majority of studies that have previously investigated the nature of stutter anticipation are reading or word naming studies (e.g., Arenas, 2012; Brutten & Janssen, 1979; Hendel & Bloodstein, 1973; Johnson, 1959; Martin & Haroldson, 1967; Rappaport & Bloodstein, 1971; Stefankiewicz & Bloodstein, 1974; Wingate, 1979a, 1986a, 1986b). In these studies, participants read lists of words or short texts; they are instructed to indicate when they anticipate an impending stutter event, either by reporting difficult or feared words/phonemes before reading them aloud or, during silent or oral reading, by indicating that they believe they would stutter on specific items. The earliest known study involving a whole series of experiments on stutter anticipation is by Johnson and Knott (1937), for which the authors reported two kinds of effects – the *Consistency Effect* (speakers who stutter tend to stutter consistently on the same words; see Adams & Brutten,

1970) and the *Adaptation Effect* (speakers who stutter tend to stutter less on words that are repeated several times in a row); the latter may, be an effect of motor learning, in some AWS (see Max & Baldwin, 2010). Another effect, the *Adjacency Effect* (Johnson & Millsapps, 1937), describes the finding that even when 'stutter' words (instances on which participants had previously stuttered) are omitted during subsequent reading of the same materials, anticipation will transfer – participants stutter on *adjacent* items (see Rappaport & Bloodstein, 1971; Wingate, 1986a; and Bloodstein, 1975 for critical reviews). In another early study, Knott, Johnson, and Webster (1937) found that participants could predict their upcoming stutter events in 94% of the cases when asked to indicate whether or not they would stutter immediately before reading. Bloodstein (1995) reports that he replicated this finding several times and found that participants were able to anticipate their impending stutter events to no lesser extent than 85%. Johnson and Solomon (1937) instructed a group of AWS to indicate those items on a word list on which they would stutter. Participants were then asked to read the word lists twice – once after a short pause after rating the items and again after 24 hours. On both trials, results showed that AWS were able to predict half of the actual stutter events correctly and they only failed to predict 10% of stutter events which occurred. In a study investigating the relationship between anticipation rates and the Consistency Effect, Martin and Haroldson (1967) asked AWS to rate words in a reading text on a scale from 1-5 with respect to their expected probability of stuttering. When investigating the Consistency Effect, they found that words with the highest expectancy ratings (5 of 5 which amounted to 1,4% of all words) accounted for 43% of all stuttered words. Thus, even though participants also produced a high number of false alarms (57%), AWS were better than chance at predicting their own stuttering.

The reviewed studies suggest that AWS can quite reliably anticipate their imminent stutter events. However, these anticipations appear to be highly individual – a study by Hendel and Bloodstein (1973) demonstrated that only 18% of stuttered words were common between participants, while consistency within participants during a second reading was much higher at 48% (see Stefankiewicz & Bloodstein, 1974 for similar findings on anticipation/stutter consistency within participants). This variability between speakers suggests that stutter anticipation is based on personal experiences and associations with specific items which can be further manipulated by experimental designs and settings. Moreover, and perhaps more importantly, it is not clear whether

the findings of the above reviewed studies are in fact comparable with regard to the nature of the elicited anticipations as there is no clear distinction between more conscious anticipations and more subconscious anticipations. This difference may account for the variability in anticipations and stutter consistency rates across studies.

P2.2.3.0 –Linguistic factors in the occurrence of stuttering

Starting with Brown (1938, 1945), many researchers have investigated the association between linguistic factors and stutter occurrences and found the following factors to be involved in stuttering:

i. *Word Function:* AWS are more likely to stutter on content words (semantically meaningful words such as nouns, verbs, adverbs, and adjectives) than on function words (i.e., shorter closed-class words that do not entail full lexical meanings, such as pronouns, prepositions, conjunctions; Au-Yeung, Howell, & Pilgrim, 1998; Hartsuiker, Kolk, & Lickley, 2005; Howell, Au-Yeung, & Sackin, 1999).
ii. *Word Length:* AWS are more likely to stutter on longer than on shorter words (Brown, 1938, 1945; Logan & Conture, 1995).
iii. *Sentence Position:* Words in early sentence positions are more likely to be stuttered on than words in later sentence positions (Brown, 1938, 1945).
iv. *Onset Complexity:* Words starting with a consonant are more likely to be stuttered on than words starting with a vowel. The more (phonologically/phonetically) complex an onset, the more likely it is for a stutter event to occur. (Brown, 1945; Howell, Au-Yeung, & Sackin, 1998; Neef, Sommer, Neef, Paulus, von Gudenberg, Jung, & Wüstenberg, 2012; Sheehan, 1974).

Importantly, as Brown pointed out and as has been confirmed since his seminal work in 1945, when more than one of these factors coincide on one item, stuttering becomes even more likely. Other factors that have been found to impact the occurrence of stuttering are:

v. *Sentence complexity:* the more complex a given syntactic structure, the more likely a stutter event occurs (Kadi-Hanifi & Howell, 1992; Logan & Conture, 1997; Melnick & Conture, 2000; Bernstein-Ratner & Sih, 1987; Yaruss, 1999).

vi. *Word frequency:* stuttering is more likely to occur on low-frequency words compared to high-frequency words (e.g., Anderson, 2007; Hubbard & Prins, 1994; Newman & Bernstein Ratner, 2007; Palen & Peterson, 1982; Ronson, 1976).

In a growing body of studies, Howell and colleagues (Al-Tamimi, Khamaiseh, & Howell, 2013; Dworzynski, & Howell, 2004; Howell, Au-Yeung, Yaruss, & Eldridge, 2006; Howell, & Au-Yeung, 2007) have shown that the phonetic complexity of a word is linked to higher stuttering rates (see Coalson, Byrd, & Davis, 2012 for counter-evidence). Adapting the Index of Phonetic Complexity Scheme (IPC) originally introduced by Jakielski (1998), the authors measure a word's phonetic complexity by summing up points that are given when words fulfil certain criteria of phonetic intricacy such as dorsal consonants, stops, nasal or glides. This will be relevant in the "Post-hoc Procedures" section of the results, below.

P2.2.4.0 – Hypotheses

Firstly, we hypothesized that AWS can better anticipate imminent dysfluencies in reading, compared with ANS; this was assessed using a word-by-word group difference comparison of silent reading followed by reading aloud. Secondly, we investigated the relative impact of linguistic factors on the occurrence of dysfluencies; we hypothesized that all linguistic factors (as described in Brown, 1945) would have a significant impact. Thirdly and relatedly, we hypothesized that the linguistic factors implicated in these dysfluencies also significantly impacted anticipation sensations. Finally, we hypothesized that anticipations would be an accurate predictor of upcoming dysfluencies (based on Johnson, 1938).

Paper 2 – 3.0.0 – Materials and Methods

The study was approved by the Ethics committee of the University Medical Centre Göttingen. Written informed consent was obtained from all participants.

P2.3.1.0 – Prescreening and Inclusion Criteria

We recruited fluent and stuttering monolingual speakers of German for this study. Exclusion criteria were neurological or internal illnesses, restricted movement ability of fingers and hands or drug use influencing the central nervous system. We employed numerous prescreening tests:

- handedness using the Edinburgh Handedness Inventory (Oldfield, 1971),
- hearing ability using the Whispered voice test (Macphee, Crowther, & McAlpine, 1988)
- visual acuity using a standardized Snellen Chart,
- hand function using the Nine Hole Peg Test (Mathiowetz, Weber, Kashman, & Volland, 1985),
- depression using the Beck Depression Inventory II (Beck, Steer, Brown, Hautzinger, Keller, & Kühner, 2001),
- reading skills using the Salzburg Reading and Spelling Test II (SLRT, Moll & Landerl, 2010).

P2.3.2.0 – Participants

In total, 45 participants (23 AWS and 22 ANS) were recruited to participate in the experiment. All participants in both groups were right handed. We recruited 23 AWS from the Kasseler Stottertherapie (KST) centre and local self help groups in Bielefeld, Göttingen and Münster. All AWS had been diagnosed with developmental stuttering by a speech therapist. Two participants in the AWS group were excluded, one due to a hearing disability in and one due to bilingualism. The age of the remaining 21 participants, two women and 19 men, ranged from 18 to 59 (mean = 31.2, SD = 11.4).

We recruited 22 ANS; each ANS was matched with an individual in the AWS group for age, sex and highest level of education. ANS were recruited from Bielefeld University and the surrounding region of Bielefeld, using the inclusion and exclusion criteria listed above except for stuttering. One control participant was excluded due to a high depression score, leaving 2 women and 19 men, at an average age 31.1 years (range 18 to 60, SD = 12.0).

P2.3.3.0 – Materials and Design

We constructed six short narratives consisting of 3 to 5 sentences. The texts dealt with different topics that readers could easily relate to and bore no semantic relationship with each other. The words were comparable between texts with respect to: initial phoneme class, word-form frequency, word length, word function, accent and onset complexity. Moreover, we matched the length and the complexity of the texts between the narratives.

The order of the six reading texts was counterbalanced using a Latin square Design, resulting in 6 different lists. We kept the order of reading texts constant across the silent and the reading-aloud condition within participants, thereby allowing a maximal time between the two reading cycles of the same stories.

P2.3.4.0 – Procedure

After obtaining consent, all participants took part in the SSI-4. Following this, we administered the vision, hearing and all other screening tests. Pre-testing lasted approximately 45 min. For the experiment, we used the software DMDX (Forster & Forster, 2003). The experiment ran on a Fujitsu Amilo Notebook Pa3553 with a Zoom Handy Recorder H2 microphone. All sessions were audio and video-recorded for further analysis.

All participants were tested individually, seated in front of a laptop in a quiet room. Each participant first read the instructions on the laptop screen, which specified that the task involved reading six different narratives once each for two consecutive conditions: silent reading and overt reading. Analytically, silent reading was associated with ‘prospective anticipations’ and reading

aloud was associated with retrospective anticipations. In the silent reading task, participants were instructed to read the short stories silently while imagining reading aloud. See Figure 1 for an example of one of the reading texts as they were displayed on the screen.

After each narrative, an on-screen prompt asked participants to report if they had experienced any kind of dysfluency anticipation; if they confirmed having anticipatory sensations, they were asked to specify on which words these anticipations occurred. To facilitate reporting of anticipations, the reading text reappeared with a numbered row above the single words (see Figure 1b). Participants then indicated the words that they anticipated to be dysfluent on by typing the numbers above those words using the number row on the laptop keyboard. Multiple numbers were separated by a space. When the participant was finished, the next narrative was displayed and the cycle started anew. This procedure was repeated until participants had read and reported their anticipations on all 6 stories within the prospective anticipation condition. There was a short break at the end of this section.

----------Please insert Figure 1 about here----------

In the second part of the experiment, participants read the same stories out loud and subsequently reported their anticipatory sensations as before. The full silent reading condition always preceded the overt reading condition, with the texts in the same order. In total, the reading experiment lasted between 40-60 minutes.

In order to be able to compare both conditions, participants were informed prior to the second reading stage that they would again be asked to indicate whether they had experienced any form of dysfluency anticipations during the actual reading of each text; however, the retrospective anticipations are inherently contaminated by memory of the actual stuttering outcomes, as it is not possible to gather instant word-by-word feedback from the participants. Therefore, in this analysis, only the prospective anticipations will be evaluated.

Paper 2 – 4.0.0 – Results

P2.4.1.0 – Pretests

P2.4.1.1 – Assessment of stuttering severity and fluency of speech

We used subjective and objective measures to estimate stutter severity and other fluency parameters in our participants. While the objective tests were applied for both speaker groups, AWS and ANS, only the AWS performed the subjective stutter severity tasks.

P2.4.1.2 – Subjective Stutter Severity

The subjective stuttering severity of AWS was evaluated using a self-report scale from 1 (very mild) to 9 (very severe). The total scores for AWS ranged from 2 to 7, with a mean total score of 4.2 (moderate).

P2.4.1.3 –Stuttering Severity Instrument (SSI-4)

The *Stuttering Severity Instrument* 4 (SSI-4; Riley, 2008) is an objective measurement of stuttering severity. It assesses severity using three parameters applied to samples of speech production: *Frequency* of stuttered syllables (i.e., the number of stuttered syllables within 2-3 speaking samples of approximately 300 syllables overall), *Durations* of stuttered syllables (i.e., the mean length of the three longest stuttering), and *Physical Concomitants* (i.e., number of movements of the head and/or the extremities, facial grimaces, distracting sounds). Frequency and duration of stuttered syllables are converted to scale scores with frequency ranging from 4 to 18 and duration from 2 to 18. The four subcategories of the physical concomitants are individually evaluated on scales from 0 = “none” to 5 = “severe”, resulting in a summed scale score from 0-20. The total score of the SSI-4 is derived by adding up the scores from the categories *Frequency*, *Durations*, *Physical Concomitants* ranging from 6 to 56. SSI-4 Scores of the AWS in our study ranged from 10 “very mild” to 36 “severe”, with a mean of 20.05 and a standard deviation of 8.34. No ANS showed any irregularities in the SSI-4. Thus, no ANS scored higher than the minimum possible SSI-4 score of 6.

P2.4.1.4 – Percentage of stuttered syllables within samples of spontaneous speech

Sequences of spontaneous speech in response to semi-standardized questions were recorded on digital video camera and coded by a certified speech therapist (the 3rd author) for both groups (ANS and AWS). AWS showed a much higher percentage of stuttered syllables (*mean* = 10.34%, *sd* = 8.29) compared with ANS (*mean* = 0.47%, *sd* = 0.03). This difference was highly significant ($t(40) = 5.451$, $p < .001$, *Cohen's d* = 1.7).

P2.4.1.5 –Premonitory Awareness in Stuttering Scale

The Premonitory Awareness in Stuttering Scale (PAiS) is a questionnaire assessing stutter anticipation in AWS (Cholin et al., 2016). Participants are asked to indicate whether and to what degree (on a scale from 0-3) they anticipate stuttering. The group of AWS had a mean PAiS total score of 17.71 (*sd* = 5.47), ranging between 9 and 29.

P2.4.1.6 –Reading study

The words in the six narratives were treated as single data points and will be referred to as 'items' throughout the Results section. Due to technical problems, some responses were not recorded and were treated as missing data (107 cases). Additionally, we excluded one item from the analysis as its word frequency could not be obtained from CELEX (42 cases). From the original 14,994 cases (357 items from 42 participants), 14,845 cases were included in the analysis.

In order to evaluate the group difference on our binary response variable Prospective Anticipation, we fitted a log-linear mixed-effects model (Pinheiro & Bates, 2000; Bates, Mächler, Bolker & Walker, 2015) using R (R Core Team, 2016). Repeated measurement was considered using crossed random intercepts for participants and items. The analysis showed a significant effect for Group: AWS anticipated far more often (561 of 7369 = 7.6%) than ANS (49 of 7476 = 0.7%), $\beta = 2.6$, *Wald z* = 5.76, $p < 0.001$. Table 1 displays the absolute numbers and percentages (per Group) of Prospective and Retrospective Anticipations.

----------Please insert Table 1 about here----------

As already discussed under *Methods*, we have focused our analysis on Prospective Anticipations of AWS. Hereafter, the term Anticipation refers to Prospective Anticipations.

P2.4.2.0 – Linguistic Factors in stuttering and anticipation

P2.4.2.1 – Description of the regression models

In order to assess the relative impact of linguistic and psycholinguistic factors on Stuttering and Anticipations, we collected five measures of lexical and phonological complexity:

i. *Word Length*: Number of Phonemes;
ii. *Word Function:* binary measure dividing between content vs. function words;
iii. *log Word Frequency:* number of occurrences of the specific surface form of a word by 1 million words (derived from CELEX word-form frequencies, Baayen et al., 1996). The frequencies were log transformed after adding a constant of 1;
iv. *Sentence Position*: position of a word in a clause or sub-clause;
v. *Onset Complexity:* We determined this predictor as a three-levelled factor dividing between words starting with a vowel, a simple consonant or a complex consonant. This was modelled as two successive difference contrasts comparing a simple consonant vs. vowel (C-V) onset and a simple consonant vs. consonant-cluster onset (C-CC, e.g., /pf/, /tr/).

The obtained linguistic factors were not independent of each other. Table 2 gives the correlations between the linguistic factors for all 356 items in the dataset.

----------Please insert Table 2 about here----------

P2.4.2.2 – Model selection procedure

We fitted log linear mixed-effects models (GLMMs) with *Stuttered Events* and *Anticipation* as binary response variables and our linguistic factors (described above) as predictors. Before being used in the model, all continuous linguistic factors were scaled to a mean of zero and a standard deviation of one. Word Function was converted to a numerical predictor with the values -0.5 for function words and 0.5 for content words. Onset Complexity was dummy coded into two numerical predictors using successive difference contrasts from the MASS package (version 7.3-47, Ripley et al., 2017) – one predictor stood for the simple C-V comparison and the other for the C-CC comparison.

All linguistic factors were treated as within-factors for participants and between-factors for items. Two strands of models were fitted: (1) one using *Stuttered Events* and (2) the other one using *Anticipations* as dependent variables. Modelling the dependent variable started from the full model including all linguistic factors and a fully specified random effects structure, i.e., random intercepts for items and participants and random slopes including their correlation terms for participants. With the full model as a starting point, we used a stepwise procedure to reduce the random effects structure (see Bates, Kliegl, Vasishth, & Baayen, 2015). This procedure aims at reducing the complexity of the models and eliminates random variance components that are not supported by the data. Nested GLMM comparison was based on maximum likelihood estimation. We calculated models that did not contain the correlation parameters of the random effects. With this zero model we tested the contribution of each random slope and random intercept separately. After the removal of superfluous random effects, the contribution of the correlation parameters between the remaining random effects was tested. Finally, we justified whether models with the reduced random effects structure resembled the full models in terms of likelihood ratio tests.

P2.4.2.3 – Stuttered Events

Table 3 summarizes the final model of *Stuttered Events* by linguistic factors along with the maximal random effects structure supported by the data. Word length (i.e., number of phonemes) positively impacted stuttering, that is, stuttering occurred more often in longer words. Moreover, we

found significant negative effects of log Word Frequency, and Sentence Position: Less frequent words were more often stuttered on than high-frequency words. Similarly, words in early sentence position were more frequently stuttered on than words in later positions. Interestingly, neither Onset Complexity nor Word Function correlated with stuttering. As Word Function strongly correlated with word frequency (ρ = -.86, see Table 2) this could be a result of multicollinearity.

----------Please insert Table 3 about here----------

P2.4.2.4 – Anticipations

Assuming that AWS can predict upcoming Stutter Events, we examined whether linguistic factors were also relevant for anticipations. Table 4 displays the model of *Anticipations* by linguistic factors. Four linguistic factors were significantly correlated with Anticipations in AWS:

i. Word Length had a positive correlation – AWS predicted more stuttering events for longer words;
ii. Word Function – AWS predicted more stuttering events on content words than function words;
iii. Word Frequency (log transformation) had a negative correlation – AWS predicted more stuttering events for infrequent words;
iv. Sentence position had a negative correlation – AWS predicted more stuttering events for words in early sentence positions.

Onset Complexity did not significantly impact anticipations; however, this factor significantly correlated with the random effects structure showing that some AWS took Onset Complexity into account. In addition, the random effects component of the anticipations model also reveals high levels of variation between participants for Word Length and Word Function.

The comparison of the Anticipation Model and the Stutter Model showed that the models agree on most linguistic factors, specifically – Word Length, log Word Frequency and Sentence

Position. In contrast with the Stutter Model, Word Function also significantly correlated with the Anticipation model (see Table 2).

P2.4.2.5 – Degree of accuracy of anticipations

In any evaluation of event prediction and accuracy, there is a 2x2 array of possible outcomes – the event can be predicted or not and the prediction can be accurate or not. This results in four categories (see Table 5).

----------Please insert Table 5 about here----------

Most words did not result in stuttering (91.7%); however, even in the small number of stuttered words, only 23.6% of actual stuttering events were preceded by an anticipatory sensation (see Table 6).

----------Please insert Table 6 about here----------

One potential measure to analyse the degree of accuracy of anticipations is the probability of having correctly anticipated a stuttered event plus correctly rejected words that were not stuttered against all counts (i.e., (TP + TN) / all counts). In our study, the mean value for this probability of accuracy is 0.88 (*sd* = 0.12), ranging from 0.53 to 1 between individuals. Thus, 88% percent of all items were correctly anticipated with respect to whether the item will induce a stutter.

Another measure (seen in Knott et al., 1937) involves two separate probability ratios – (a) the ratio of accurate anticipation (i.e., TP / (TP + FP)) and (b) the ratio of inaccurate rejection (i.e. FN / (FN + TN)). Using these measures, we found low accurate anticipation (*mean* = 0.29, *sd* = 0.21, *range* = 0 to .75) and low inaccurate rejection (*mean* = 0.07 (7%), *sd* = 0.11). Of note, two

AWS did not anticipate through the entire experiment; both participants were excluded for this analysis.

P2.4.3.0 – Post-hoc Procedure

P2.4.3.1 – IPC Score

As briefly laid out in the Introduction, the IPC Score (Index of Phonetic Complexity, Jakielski, 1998) is a measure to examine the influence of a word's phonological/phonetic on stuttering. Importantly, the IPC score is derived from the entire word and not just the phonological or phonetic complexity of a word's onset. The IPC score may be the more accurate measure as we did not find an influence from onset complexity alone. The IPC Score is the sum of points calculated from the following list:

- a phoneme of dorsal place of articulation,
- a phoneme of fricative, affricate, or liquid manner of articulation,
- variegated consonants between syllables
- a rhotic consonant,
- three or more syllables,
- a consonant cluster (including affricates), and
- a consonant cluster of different place of articulation.

The IPC Score can sum up to 8 points. Since there are no rhotic consonants in German, the highest possible IPC Score in our study was 7, thus, IPC Scores of a word may range from 0 to 7. For further details on the calculation of the IPC Score, see also Dworzynski and Howell (2004).

As a further post-lexical measure, we included syllable frequency in our post-hoc analyses. Effects of syllable frequency (i.e., high-frequency syllables are produced faster than low-frequency syllables) have been taken as evidence for ready-made syllable motor programs that are retrieved from a mental store (e.g., Cholin et al., 2006, 2011). In ANS, stored syllables are assumed to facilitate spoken production. As these stored programs may be less stable and/or less available in AWS (see Introduction), syllable-frequency effects may be different or lacking in AWS.

P2.4.3.2 – Post-hoc Analyses

We calculated syllable frequency as the cumulative frequency of all German words containing this syllable (Cholin et al., 2006; 2011). For use in the analysis, syllable frequency was log transformed after adding 1 and scaled to a mean of zero and a standard deviation of one.

All predictors relevant for the first model were kept in the model except for Word Length. Word Length was highly correlated with Word Frequency (see Table 2). Moreover, the IPC Score indirectly contains a measure of word length by adding a point for words with three or more syllables. Thus, to avoid multicollinearity, Word Length was not included. Therefore, the following linguistic factors were included in the post-hoc analyses: *Word Function*, *log Word Frequency*, *Sentence Position*, *Onset Complexity* (C-V, C-CC), *IPC Score*, and *log Syllable Frequency*. Table 7 shows the correlations among the linguistic predictors used in the analyses. Analyses were separately conducted for stutter occurrences and anticipations.

----------Please insert Table 7 about here----------

P2.4.3.3 – Stuttered Events

The final model of *Stuttered Events* along with the maximal random effects structure is displayed in Table 8. Both log Word Frequency and Sentence Position correlated negatively with Stuttered Events. There was no significant correlation for any of the newly included linguistic predictors, however log Syllable Frequency only failed to reach significance ($\beta = 0.2$, $p = 0.05088$). Similarly, there was no significant correlation for Onset Complexity. We failed to show a general effect of IPC scores on stuttering. The correlation between IPC Score and log Word Frequency (-0.64, see Table 7) and may thus have obscured the previously reported relationship between IPC Score and stuttering.

Onset Complexity, log Syllable Frequency and Sentence Position added substantially to the random effects structure of the model.

----------Please insert Table 8 about here----------

P2.4.3.4 – Anticipations

Word Function, log Word Frequency, and Sentence Position significantly correlated with Anticipation in the Model, see Table 9. None of Onset Complexity, IPC Score and log Syllable Frequency were significant. Word Function, Onset Complexity, and IPC Scores contributed significantly to the random effects structure of the model.

----------Please insert Table 9 about here----------

Paper 2 – 5.0.0 – Discussion

P2.5.1.0 – Hypotheses Revisited

For this experiment we had four main hypotheses that:

i. AWS could anticipate dysfluencies to a greater extent than ANS;
ii. previously identified linguistic factors would correlate with stuttering occurrences;
iii. linguistic factors would also correlate with anticipation; and
iv. anticipation would be an accurate predictor of upcoming dysfluencies.

P2.5.1.1 – Hypothesis One

Simply put, our first hypothesis was supported – AWS were able to demonstrate an anticipatory sensation prior to dysfluencies that ANS did not reliably report. These findings suggest that anticipation is not simply a subordinate error detection ability that all speakers can employ to enhance fluency of speech; rather it appears to be a reliable factor that can be used to distinguish AWS. However, one can only extrapolate beyond this finding with caution – one cannot not

necessarily conclude from this finding that only AWS can anticipate dysfluencies, as our experiment could not exclude the possibility that greater anticipations are a result of greater familiarity with dysfluency (see Cholin et al., 2016). Nonetheless, what is clear from our study is that AWS do exhibit the capacity for premonitory awareness of an upcoming dysfluency event which we have termed anticipation; this affirms the prerequisite assumptions that permit the interpretation of the rest of this study.

P2.5.1.2 – Hypothesis Two

Regarding the second hypothesis, we were able to identify certain linguistic factors which significantly correlated with actual stuttering occurrences. In particular, AWS stuttered more often on certain lexical factors, such as:

- longer words,
- less frequent/less common words, and
- words in early sentence positions.

These findings corroborate numerous previous studies (e.g., Anderson, 2007; Hubbard & Prins, 1994; Newman & Bernstein Ratner, 2007; Palen & Peterson, 1982; Ronson, 1976).

Unlike in certain previous studies (Newman & Bernstein Ratner, 2007), we were not able to confirm a correlation with Word Function, nor IPC Score, nor with either of the onset complexity terms (vowel-consonant and consonant cluster) on AWS as a group.

That is not to say, however, that these factors were not relevant to AWS. According to our analysis, onset complexity and word function both played a significant role on an individual level. That is to say, these factors greatly differed between the individual participants and were thus still relevant to their stuttering events. They just did not vary uniformly within the group. This finding indicates that AWS have very individualized models of which phonemes, morphemes and/or words are difficult and this agrees with theories of stuttering assuming strong individual variation (Newman & Bernstein Ratner, 2007).

P2.5.1.3 – Hypothesis Three

Regarding hypothesis three, it is unclear the extent to which AWS are consciously aware of the individual characteristics that influence their anticipatory sensations, however they must necessarily be able to at least implicitly or subconsciously identify them in some capacity. Word length and sentence position are both simple factors, which we assume can be easily identified by AWS and thus used to inform anticipation. Comparatively, word frequency is a more subtle measure.

Firstly, the frequency of a word in a language is the result of a complex interplay of various other factors – factors which we also used as predictors in this study. For example (see Table 2), frequency correlates with IPC Score – that is, high frequency words tend to be easier to pronounce resulting in a lower IPC Score. Indeed, word frequency also correlates highly with other psycho-linguistic factors such as shorter word length, word function (grammar terms more than content words), neighbourhood density, age of acquisition and markedness (e.g., Luce, Pisoni, & Goldinger, 1990; Vitevitch, 2002; Greenberg, 1966); consequently, speakers are more likely to be aware of those other factors than 'word frequency' in their predictions.

The IPC score as well as the Onset Complexity (in addition to psycholinguistic factors) made significant contributions to the random effects of our stuttering model. This reflects the high variability between AWS on which words they will stutter on that is not shared between participants. These results are in line with earlier studies on stutter consistency showing that although stuttering is highly consistent within participants there is high variation between participants on words they stutter on (Hendel & Bloodstein, 1973; Stefankiewicz & Bloodstein, 1974). This variation is only partly captured by psycholinguistic factors but also depends on factures that are purely linguistic in nature, such as words starting with a /g/ are difficult for a specific participant.

To our knowledge there is no previous study taking such a wide range of linguistic and psycholinguistic factors as possible causes to stuttering into account. Studies investigating the

influence of linguistic factors on stuttering (Newman & Bernstein Ratner, 2007) have largely not taken psycholinguistic factors into account; similarly, studies examining the influence of word frequency have not included linguistic factors/predictors. To our knowledge, therefore, this is the first study that has combined both.

For anticipation, as in the case of hypothesis two (stuttering) above, we were not able to replicate at the group level all linguistic factors which have previously been identified. At the level of group comparisons, we found that anticipations were significantly correlated with the same three factors (Word Length, Word Frequency and Sentence Position) as for the stuttering events, as well as an additional correlation for Word Function. Similarly, onset complexity was significant at the individual level, as well as IPC Score. This indicates a high level of internal consistency within individual AWS, and has implications in therapy.

P2.5.1.4 – Hypothesis Four

The similarity between the Stuttering and the Anticipation Models supports the assumption that AWS can predict upcoming stutter events. For our final hypothesis, we wanted to further investigate the degree of accuracy with which AWS can anticipate upcoming stutter events. In this context, accuracy is a complicated construct – not only can accuracy be measured by multiple means, but the very act of anticipating implicitly raises the participant's awareness of their speech; this may activate stutter circumvention strategies and, in turn, transform a hypothetical stutter into a "false alarm" for our records.

Regarding the actual measurement of accuracy, a conservative method counts only the TP anticipations. A more liberal approach is to consider both TP and TN as accurate, i.e. all cases in which the anticipations matched the outcome. However, as the goal of anticipation is arguably to reduce stuttering occurrences – especially from the AWS's perspective – a successful anticipation is inherently an anticipation that is *not* followed by a stuttered event. One might therefore argue that TP and FP should be included as anticipations alongside TN, thus only FN responses were 'truly' inaccurate. However, in the current experimental design, we cannot distinguish between

anticipations that resulted in successful prevention and erroneous anticipations (i.e. 'real' False Positives). As such, we have focused on the conservative TP-only method.

Compared with Knott et al. (1937), who found high congruence between anticipations and actual stuttering events (94 – 96%), we found congruence below chance (29%). By extension, we also found a higher percentage of stutter events being 'missed' – in our study, 7% of non-anticipated words still resulted in a stutter, compared with 3% (Knott et al., 1937). One possible explanation for this is the difference in the procedure. Knott and colleagues (1937) prompted their participants to actively decide on a word-by-word basis whether or not they anticipated that they would stutter; by comparison, we also allowed the possibility to report anticipations for every word but the prompts were issued on a text-by-text basis. This method may have resulted in over-reporting response bias in the Knott and colleagues (1937) paper and, potentially under-reporting in our own study. Additionally, as Garcia-Barrera and Johnson (2015) outlined in their model, AWS may only identify words on which they are aware that they have previously stuttered. Had we been able to identify the words that an individual was not consciously aware of in advance, we may have been able to isolate only the true anticipations for each individual in our experiment. We therefore assert that the true value of anticipation accuracy falls somewhere between our 29% and the previously identified 94%.

Paper 2 – 5.2.1 – Overall Interpretations

These procedural differences in the studies (mentioned above) are worth greater consideration. Anticipation cannot meaningfully benefit an AWS if there is no opportunity to use it to prompt dysfluency circumvention. On one extreme, reading from a word list (as in Knott et al., 1937) greatly reduces the context of the speech and this ability to adapt to the anticipations. By presenting short stories/narratives instead of word lists we decided for a high ecological validity while still having a controlled experimental environment. However, a grammatically and linguistically correct text imposes restrictions upon the factors which we compared in this experiment. For example, while IPC scores for words range from 0 to 7, it is not possible to evenly counterbalance a text such that all scores are evenly represented; as such, scores between 2 and 5 (moderately complex) are much more frequent than 0, 1, 6, 7. This may account for the lack of effect identified in IPC Scores in our study (the same holds true for onset complexity manipulations). Nonetheless some assessment of these factors is necessary. In anticipation research, we aim to learn about the manner in which anticipations can enhance speech in daily life. However, in order to experimentally compare between participants, it is not possible to investigate completely unrestricted speech samples. As such, while it is a limitation to restrict speech to predefined texts, it allows us to control for all potential variables.

P2.5.3.1 – Broader Applications of Anticipation in Stuttering

As we outlined in the Introduction, a consensus has not yet been reached in the literature on the precise mechanisms by which anticipation processes help or hinder speech fluency. One reason for this is the contradictory role of attention – on one hand, greater awareness and prediction enables better self-monitoring and activates circumvention strategies; on the other hand, speech fluency has also been shown to improve when attention is diverted from speech monitoring by using either auditory masking (e.g. delayed auditory feedback, see Antipova et al., 2008) or by introducing dual-task conditions (with an additional cognitive task, e.g. Howell, 2011). This may have roots in the different focuses of attention, as lexical factors are more accessible than post-lexical factors for the attention system.

One novel finding from our research is the identification of common factors between anticipation and stuttering occurrence – such overlap has positive implications for both research and therapy. While the extent of an AWS' introspection abilities and their capacity and the manner in which they can employ anticipations to prevent stutter symptoms and enhance fluency remains unclear, what is now clear is that an understanding of the characteristics of an individual's anticipations can provide insight into the same individual's stuttering. To add to these previous findings, it is clear from our study that certain factors are common among AWS (e.g. word length) but other factors vary greatly between individuals (e.g. onset complexity). As such, it behoves both researchers and therapists alike to identify the unique factors for an individual in any assessment of anticipation, otherwise any resultant findings are lacking in validity.

There remains one additional possibility that needs be considered in future anticipation research. In our study, we ran our analyses under the assumption that AWS anticipate dysfluencies and ANS do not; this was a necessary assumption due to the low rate of actual dysfluencies among ANS. It is not clear, however, whether the ability to anticipate a dysfluency is a sensitivity that can be actively trained, such as in Van Riper's "Non-Avoidance" or "Modification" therapy approaches (e.g., Van Riper, 1982). Taken to the extreme, if stuttering is considered from the angle of tic disorders, anticipation could be viewed as simply sensitivity to the early signals of a motor spasm and not a linguistic phenomenon at all. Studies evaluating treatment approaches, such as in *Habit Reversal Therapy* (HRT; e.g., Dutta & Cavanna, 2013), suggest that upcoming tics can be circumvented by training alternative physical responses (e.g. Himle, Woods, Piacentini, & Walkup, 2006).However, in the realm of speech production, articulatory movements are inherently both linguistic and physiological – for example, speech stress and rhythm are concurrently linguistic and physiological processes. As such, from any interpretation of the precursors of stuttering, anticipation can play a role in the solution.

Paper 2 – 6.0.0 – References

Adams, M. R. & Brutten, G. J. (1970). An exploratory study of some learning-based procedures for modifying stuttering. Journal of Communication Disorders, 3, 123-132.

Al-Tamimi, F., Khamaiseh, Z., & Howell, P. (2013). Phonetic complexity and stuttering in Arabic. Clinical Linguistics & Phonetics, 27, 874–887**.**

Ambrose, N. G., Yairi, E. Loucks, T. M. Seery, C.H. & Throneburg, R. (2015). Relation of motor, linguistic and temperament factors in epidemiologic subtypes of persistent and recovered stuttering: Initial findings. Journal of Fluency Disorders, 45, 12-26.

Anderson J. D. (2007). Phonological neighborhood and word frequency effects in the stuttered disfluencies of children who stutter. Journal of Speech, Language, and Hearing Research, 50, 229–247.

Antipova, E.A., Purdy, S.C., Blakeley, M., & Williams, S. (2008). Effects of altered auditory feedback (AAF) on stuttering frequency during monologue speech production. Journal of Fluency Disorders. 33, 274-290.

Arenas, R.M. (2012). The role of anticipation and an adaptive monitoring system in stuttering: A theoretical and experimental investigation. Unpublished Dissertation, University of Iowa, Iowa City.

Au-Yeung, J., Howell, P., & Pilgrim, L. (1998). Phonological words and stuttering on function words. Journal of Speech, Language, and Hearing Research,41, 1019–1030.

Avari, D. N., & Bloodstein, O. (1974). Adjacency and prediction in school-age stutterers. Journal of Speech and Hearing Research, 17, 33–40.

Baars, B. J., Motley, M. T., & MacKay, D. G. (1975). Output editing for lexical status in artificially elicited slips of the tongue. Journal of Verbal Learning and Verbal Behavior, 14, 382-391.

Baayen, R., Piepenbrock, R., & Gulikers, L. (1996). CELEX2 [cd-rom](Linguistic data consortium, Philadelphia, PA).

Bates, D., Kliegl, R., Vasishth, S., & Baayen, H. (2015). Parsimonious mixed models. arXiv Preprint arXiv:1506.04967.

Bates, D., Maechler M., Bolker, B., & Walker, S. (2015). Fitting Linear Mixed-Effects Models Using lme4. Journal of Statistical Software, 67, 1-48.

Beck, A.T., Steer, R.A., Brown, G.K., Hautzinger, M., Keller, F., & Kühner, C. (2001). BDI-II: Beck-Depressions-Inventar: Manual Testhandbuch (2. Aufl.). Frankfurt am Main: Pearson Assessment.

Beilock, S. L., & Gray, R. (2012). From attentional control to attentional spillover: a skill-level investigation of attention, movement, and performance outcomes. Human Movement Science, 31, 1473–1499.

Bernstein Ratner N., & Sih, C. C. (1987). The effects of gradual increases in sentence length and complexity on children's disfluency. Journal of Speech and Hearing Disorders, 52, 278–287.

Bloodstein, O. (1959). Stuttering as an anticipatory struggle reaction. In J. Eisenson (Eds.), Stuttering: A symposium (S.3-69). New York, NY: Harper & Brothers.

Bloodstein, O. (1975). Stuttering as tension and fragmentation. In J. Eisenson (Ed.), Stuttering: A second symposium (pp. 1-96). New York: Harper & Row.

Bloodstein, O. & Bernstein Ratner, N. (2008). A handbook on stuttering (6th ed.). Clifton Park, NY: Delmar Learning.

Bloodstein, O. (1995). A Handbook on Stuttering, (5th ed.). San Diego, CA:Singular Publishing Group.

Brocklehurst, P. H., Lickley, R. J., & Corley, M. (2013). Revisiting Bloodstein's Anticipatory Struggle Hypothesis from a psycholinguistic perspective: A variable release threshold hypothesis of stuttering. Journal of Communication Disorders, 46, 217–237.

Brocklehurst, P.H. (2008). A review of evidence for the Covert Repair Hypothesis of stuttering. Contemporary Issues in Communication Science and Disorders, 35(1), 25-43.

Brown, J.W., Braver, T.S. (2005). Learned predictions of error likelihood in the anterior cingulate cortex. Science, 307, 1118-1121.

Brown, S. F. (1945). The loci of stutterings in the speech sequence. Journal of Speech Disorders, 10(3), 181-192.

Brutten, G.J., & Janssen, P. (1979). An eye-marking investigation of anticipated and observed stuttering. Journal of Speech and Hearing Research, 22(1), 20-28.

Cai, S., Tourville, J. A., Beal, D.S., Perkell, J. S., Guenther, F. H., & Ghosh, S. S. (2014). Diffusion imaging of cerebral white matter in persons who stutter: evidence for network-level anomalies. Frontiers in Human Neuroscience, 8, 54.

Cholin, J., Dell, G. S., & Levelt, W. J. M. (2011). Planning and articulation in incremental word production: Syllable-frequency effects in English. Journal of Experimental Psychology: Learning, Memory and Cognition, 37, 109-122.

Cholin, J., Heiler, S., Whillier, A., & Sommer, M. (2016). Premonitory Awareness in Stuttering Scale (PAiS). Journal of Fluency Disorders. ####.

Clark, H. H. (1996). Using language. Cambridge, MA: University Press.

Cykowski, M. D, Fox, P. T., Ingham, R.J., Ingham J.C., & Robin, D. A. (2010). A study of the reproducibility and etiology of diffusion anisotropy differences in developmental stuttering: a potential role for impaired myelination. Neuroimage, 52, 1495–504.

Dutta, N. & Cavanna, A. E. (2013). The effectiveness of habit reversal therapy in the treatment of Tourette syndrome and other chronic tic disorders: a systematic review. Functional Neurology, 28, 7-12.

Dworzynski, K., & Howell, P. (2004). Predicting stuttering from phonetic complexity in German. Journal of Fluency Disorders, 29, 149–173.

Forster, K. I., & Forster, J. C. (2003). DMDX: A windows display program with millisecond accuracy. Behavior Research Methods, Instruments, & Computers, 35, 116-124.

Garcia-Barrera, M. A. & Davidow, J. H. (2015). Anticipation in stuttering: A theoretical model of the nature of stutter prediction. Journal of Fluency Disorders, 44, 1-15.

Hartsuiker, R. J., Kolk, H. H. J., & Lickley, R. J.(2005). Stuttering on function and content words: A computational test of the covert repair hypothesis. In R. J. Hartsuiker, Y. Bastiaanse, A. Postma, & F. Wijnen (Eds.), Phonological encoding and monitoring in normal and pathological speech (pp. 261–280). Hove, East Sussex Psychology Press.

Hendel, D., & Bloodstein, O. (1973). Consistency in relation to inter-subject congruity in the loci of stutterings. Journal of Communication Disorders, 6, 37-43.

Hickok, G. (2012a). Computational neuroanatomy of speech production. Nature Reviews Neuroscience, 13, 135–145.

Hickok, G. (2012b). The cortical organization of speech processing: Feedback control and predictive coding the context of a dual-stream model. Journal of Communication Disorders, 45, 393–402.

Himle, M. B., Woods, D. W., Piacentini, J. C., & Walkup, J. T. (2006). Brief review of habit reversal for Tourette syndrome. Journal of Child Neurology, 21, 719-725.

Howell, P. (2002). The EXPLAN theory of fluency control applied to the treatment of stuttering. In E. Fava (Ed.), Clinical linguistics: theory and applications in speech pathology and therapy (pp. 95-118). Amsterdam; Philadelphia; : J. Benjamins Pub. Co

Howell, P. (2003). Is a perceptual monitor needed to explain how speech errors are repaired? Gothenburg Papers in Theoretical Linguistics, 90, 31-34.

Howell, P. (2004). Effects of delayed auditory feedback and frequency-shifted feedback on speech control and some potentials for future development of prosthetic aids for stammering. Stammering Research, 1, 31-46.

Howell, P. (2011). Recovery from Stuttering: Psychology Press/Taylor & Francis Group.

Howell, P., & Au-Yeung, J. (2002). The EXPLAN theory of fluency control applied to the diagnosis of stuttering. In E. Fava (Ed.), Clinical linguistics: Theory and applications in speech pathology and therapy (pp. 75–94). Amsterdam; Philadelphia: J. Bechamin's.

Howell, P., & Au-Yeung, J. (2007). Phonetic complexity and stuttering in Spanish. Clinical Linguistics and Phonetics, 21, 111–127.

Howell, P., Au-Yeung, J., & Sackin, S. (1999). Exchange of stuttering from function words to content words with age. Journal of Speech, Language, and Hearing Research 42, 345–354.

Howell, P., Au-Yeung, J., Yaruss, J. S., & Eldridge, K. (2006). Phonetic difficulty and stuttering in English. Clinical Linguistics and Phonetics, 20, 703–716.

Hubbard, C. P. & Prins, D. (1994). Word familiarity, Syllabic Stress Pattern, and Stuttering. Journal of Speech, Language, and Hearing Research, 37, 564-571.

Jackson, E. S., Yaruss, J. S., Quesal, R.W., Terranova, V., & Whalen, D. H. (2015). Responses of adults who stutter to the anticipation of stuttering. Journal of Fluency Disorders, 45, 38-51.

Jakielski, K. (1998). Motor organization in the acquisition of consonant clusters. University of Texas at Austin. Retrieved from https://books.google.de/books?id=_irXpwAACAAJ

Johnson, W. (1959). The onset of stuttering. Minneapolis MI: University of Minnesota press.

Johnson, W., & Knott, J.R. (1936). The factor of attention in relation to the moment of stuttering. Pedagogical Seminary and Journal of Genetic Psychology, 48, 479-180.

Johnson, W. & Knott, J. R. (1937). Studies in the psychology of stuttering I: The distribution of moments of stuttering in successive readings of the same material. Journal of Speech Disorders, 2, 17-19.

Johnson, W., & Millsapps, L. S. (1937). Studies in the Psychology of Stuttering: VI: The Role of Cues Representative of Past Stuttering in the Distribution of Stuttering Moments during Oral Reading. Journal of Speech Disorders, 2, 101-104.

Johnson, W. & Solomon, A. (1937). Studies in the psychology of stuttering IV: A quantitative study of expectation of stuttering as a process involving a low degree of consciousness. Journal of Speech Disorders, 2, 95-97.

Kadi-Hanifi, K. & Howell, P. (1992). Syntactic analysis of the spontaneous speech of normally fluent and stuttering children. Journal of Fluency Disorders, 17, 151–170.

Knott, J.R., Johnson, W., & Webster, M.J. (1937). Studies in the psychology of stuttering II: A quantitative evaluation of expectation of stuttering in relation to the occurrence of stuttering. Journal of Speech Disorders, 2, 20-22.

Kolk, H. H. J., & Postma, A. (1997). Stuttering as a covert repair phenomenon. In R. F. Curlee & G. Siegel (Eds.), Nature and treatment of stuttering: New directions (2 ed., pp. 182-203). Boston; MA: Allyn & Bacon.

Lee, B. S. (1950). Effects of Delayed Speech Feedback. Journal of the Acoustical Society of America, 22,824-826.

Levelt, W.J.M. (1983). Monitoring and self-repair in speech. Cognition, 14, 41–104.

Levelt, W.J.M. (1989). Speaking: From intention to articulation. Cambridge, England: MIT Press.

Levelt, W.J.M., Roelofs, A., & Meyer, A.S. (1999). A theory of lexical access in speech production. Behavioral and Brain Sciences, 22(1), 1-75.

Lickley, R. J., Hartsuiker, R. J., Corley, M., Russell, M., & Nelson, R. (2005). Judgment of Disfluency in People who Stutter and People who do not Stutter: Results from Magnitude Estimation. Language and Speech, 48, 299-312.

Logan, K., & Conture, E. (1995). Length, grammatical complexity, and rate differences in stuttered and fluent conversational utterances of children who stutter. Journal of Fluency Disorders, 20(1), 35-61.

Logan, K. J., & Conture, E. G. (1997). Selected temporal, grammatical, and phonological characteristics of conversational utterances produced by children who stutter. Journal of Speech, Language and Hearing Research, 40(1), 107-120.

Luce, P. A., Pisoni, D. B., & Goldinger, S. D. (1990). Similarity neighborhoods of spoken words. In G. T. M. Altmann (Ed.), *ACL–MIT Press series in natural language processing. Cognitive models of speech processing: Psycholinguistic and computational perspectives* (pp. 122-147). Cambridge, MA: The MIT Press.

MacPhee, G.J.A., Crowther, J.A., & McAlpine, C.H. (1988). A simple screening test for hearing impairment in elderly patients. Age and Ageing, 17(5), 347–351.

Martin, R.R., & Haroldson, S.K. (1967). The relationship between anticipation and consistency of stuttered words. Journal of Speech and Hearing Research, 10(2), 323-327.

Mathiowetz, V., Weber, K. Kashman, N., & Volland, G. (1985). Adult norms for the Nine Hole Peg Test of finger dexterity. The Occupational Therapy Journal of Research, 5, 24-33.

Max, L. & Baldwin, C.J. (2010). The role of motor learning in stuttering adaptation: repeated versus novel utterances in a practice-retention paradigm. Journal of Fluency Disorders, 35, 33–43.

Max, L., Guenther, F. H., Gracco, V. L., Ghosh, S. S., & Wallace, M. E. (2004). Unstable or insufficiently activated internal models and feedback-biased motor control as sources of dysfluency: A theoretical model of stuttering. Contemporary Issues in Communication Science and Disorders, 31, 105-122.

Melnick, K. S., & Conture, E. G. (2000). Relationship of length and grammatical complexity to the systematic and nonsystematic speech errors and stuttering of children who stutter. Journal of Fluency Disorders, 25, 21–45.

Milisen, R. (1938). Frequency of stuttering with anticipation of stuttering controlled. Journal of Speech Disorders, 3, 207-214.

Moll, K. & Landerl, K. (2010). Lese- und Rechtschreibtest (SLRT-II): Weiterentwicklung des Salzburger Lese- und Rechtschreibtests (SLRT). Bern, Schweiz: Verlag Hans Huber.

Neef, N. E., Sommer, M., Neef, A., Paulus, W., von Gudenberg, A. W., Jung, K., & Wüstenberg, T. (2012). Reduced Speech Perceptual Acuity for Stop Consonants in Individuals Who Stutter. Journal of Speech, Language, and Hearing Research, 55, 276-289.

Newman, R. S., & Bernstein Ratner, N. (2007). The role of selected lexical factors on confrontation naming accuracy, speed and fluency in adults who do and do not stutter. Journal of Speech, Language and Hearing Research, 50, 196–213.

Nooteboom, S. (1980). Speaking and unspeaking: Detection and correction of phonological and lexical errors in spontaneous speech. In: V. A. Fromkin (Ed.), Errors in linguistic performance: Slips of the tongue, ear, pen, and hand. New York: Academic Press, 87-96.

Nozari, Dell, & Schwarzt (2011). Conflict based monitoring.

Oldfield, R.C. (1971). The assessment and analysis of handedness: The Edinburgh Inventory. Neuropsychologia, 9, 97-113.

Palen, C., & Peterson, J.M. (1982). Word frequency and children's stuttering: the relationship to sentence structure. Journal of Fluency Disorders, 7(1), 55-62.

Peters, H. M., Hulstijn, W., & van Lieshout, P. H. (2000). Recent developments in speech motor research into stuttering. Folia Phoniatrica et Logopaedica,52, 103–119.

Pinheiro, J. C., & Bates, D. M. (2000). Mixed-effects models in S and S-PLUS. Statistics and Computing. New York: Springer.

Postma, A. & Kolk, H. (1993). The covert repair hypothesis: Prearticulatory repair processes in normal and stuttered disfluencies. Journal of Speech, Language, and Hearing Research, 36, 472-487.

Rappaport, B., & Bloodstein, O. (1971). The Role of Random Blackout Cues in the Distribution of Moments of Stuttering. Journal of Speech Hearing Research, 14(4), 874-879.

Riley, G. D. (2008). Stuttering Severity Instrument (SSI-4): Examiner Manual and Picture Plates. Austin, TX: Pro-Ed.

Ripley, B., Venables, B., Bates, D. M., Hornik, K., Gebhardt, A., Firth, D., & Ripley, M. B. (2017). Package 'MASS'. (URL: https://CRAN.R-project.org/package=MASS, Ver. 7.3-47)

Ronson, I. (1976). Word frequency and stuttering: the relationship to sentence structure. Journal of Speech and Hearing Research, 19, 813-819.

Sheehan, J. G. (1970). Stuttering: Research and Therapy. New York: Harper and Row.

Sheehan, J. G. (1974). Stuttering behavior: A phonetic analysis. Journal of Communication Disorders, 7, 193-212.

Slevc, L. R. & Ferreira V. S. (2006). Halting in single word production: A test of the perceptual loop theory of speech monitoring. Journal of Memory and Language, 54, 515–540.

Smits-Bandstra, S., & Gracco, V. (2015). Retention of implicit sequence learning in persons who stutter and persons with Parkinson's disease. Journal of Motor Behavior, 47, 124–141.

Sommer, M., Koch, M. A., Paulus, W., Weiller, C., & Büchel, C. (2002). Disconnection of speech relevant brain areas in persistent developmental stuttering. The Lancet, 360, 380-383.

Spencer, C. & Weber-Fox, C. (2014). Preschool speech articulation and nonword repetition may predict eventual recovery or persistence of stuttering. Journal of Fluency Disorders, 41, 32-46.

Stefankiewicz, S. P., & Bloodstein, O. (1974). The Effect of a Four-Week Interval on the Consistency of Stuttering. Journal of Speech and Hearing Research, 17(1), 141-145.

Van Riper, C. (1936). Study of thoracic breathing of stutterers during expectancy and occurrence of stuttering spasms. Journal of Speech Disorders, 1,61-72.

Van Riper, C. (1978). Speech correction: Principles and methods (6th ed.). Englewood Cliffs, NJ: Prentice-Hall.

Van Riper, C. (1982). The nature of stuttering (2nd ed.). Englewood Cliffs, NJ: Prentice Hall.

Vasić, N., & Wijnen, F. (2005). Stuttering as a monitoring deficit. In R. J. Hartsuiker, Y. Bastiaanse, A. Postma, & F. Wijnen (Eds.), Phonological encoding and monitoring in normal and pathological speech (pp. 226–247). Hove, East Sussex Psychology Press.

Vitevitch, M. S. (2002). The influence of phonological similarity neighborhoods on speech production. Journal of Experimental Psychology: Learning, Memory, and Cognition, 28(4), 735-747

Wingate, M. E. (1975). Expectancy as basically a short-term process. Journal of Speech, Language, and Hearing Research, 18, 31–42.

Wingate, M.E. (1979a). The first three words. Journal of Speech and Hearing Research, 22, 604–612.

Wingate, M. E. (1979b). The loci of stuttering: Grammar or prosody. Journal of Communication Disorders, 12, 283-290.

Wingate, M. E. (1986a). Adaptation, consistency and beyond: I. Limitations and contradictions. Journal of Fluency Disorders, 11, 1-36.

Wingate, M. E. (1986b). Adaptation, consistency and beyond: II. An integral account. Journal of Fluency Disorders, 11, 37-53.

Yairi, E., Ambrose, N. (2013). Epidemiology of stuttering: 21st century advances. Journal of Fluency Disorders, 38, 66–87

Yaruss, J. S. (1999). Utterance length, syntactic complexity and childhood stuttering. Journal of Speech-Language-Hearing Research, 42, 329–344.

Paper 2 – 7.0.0 – Tables and Figures

Tables

	Prospective Anticipations			Retrospective Anticipations		
Group	Anticipated	Not Anticipated	Sum	Anticipated	Not Anticipated	Sum
AWS	561 (7.6)	6808 (92.4)	7369	536 (7.2)	6873 (92.8)	7409
ANS	49 (0.7)	7427 (99.3)	7476	71 (1)	7390 (99)	7461
Sum	610	14235	14845	607	14263	14870

Table 1: Absolute frequencies
for *Prospective Anticipations* (left) and *Retrospective Anticipations* (right) broken down by *Group*. Percentages per Group are given in parentheses.

	Word Length	Word Function	log Word Frequency	Sentence Position	Onset Complexity: C-V
Word Function	0.64				
log Word Frequency	-0.82	-0.86			
Sentence Position	0.22	0.25	-0.24		
Onset Complexity: C-V	0.14	0.18	-0.24	0.12	
Onset Complexity: C-CC	0.24	0.24	-0.34	0.05	0.4

Table 2: Pair-wise correlation coefficients among linguistic factors
in the dataset (n = 356 items). For continuous variables, the calculations display Spearman correlations, for binary variables (i.e., Word Function), rank biserial correlations were used.

Fixed Effects	β	2.5 %	97.5 %	SE	Wald z	p-value
(Intercept)	-3.90	-4.78	-3.11	0.40	-9.82	0.00
Word Length	0.29	0.13	0.46	0.08	3.62	0.00
Word Function	-0.13	-0.57	0.31	0.21	-0.64	0.52
log Word Frequency	-0.47	-0.68	-0.27	0.10	-4.69	0.00
Sentence Position	-0.33	-0.61	-0.11	0.11	-2.87	0.00
Onset Complexity: C-V	-0.30	-1.00	0.44	0.34	-0.87	0.38
Onset Complexity: C-CC	-0.32	-0.89	0.19	0.25	-1.28	0.20
Random Effects	SD	2.5 %	97.5 %			
Item (Intercept)	0.51	0.32	0.68			
Subject (Intercept)	1.74	1.26	2.54			
Subject (Word Function)	0.50	0.18	0.95			
Subject (Sentence Position)	0.37	0.15	0.68			
Subject (Onset Complexity: C-V)	1.30	0.90	1.97			
Subject (Onset Complexity: C-CC)	0.72	0.40	1.30			
Subject (Correlation: Sentence Position - Word Function)	0.85	0.02	1.00			

Table 3: Summary of the model of Stuttered Events by linguistic predictors for fixed effects (top) and the random effects structure justified by the data (bottom). Note. Likelihood confidence intervals are given for β estimates and explained standard deviation of the random effects. SE refers to standard error, SD to standard deviation.

Table 4. Summary of the model of Anticipations by linguistic predictors for fixed effects (top) and the random effects structure justified by the data (bottom).

Fixed Effects	*β*	*2.5 %*	*97.5 %*	*SE*	*Wald z*	*p-value*
(Intercept)	-4.36	-5.27	-3.60	0.39	-11.30	0.00
Word Length	0.39	0.15	0.61	0.11	3.52	0.00
Word Function	0.75	0.04	Inf	0.32	2.35	0.02
log Word Frequency	-0.72	-0.97	-0.49	0.11	-6.27	0.00
Sentence Position	-0.17	-0.32	-0.03	0.07	-2.46	0.01
Onset Complexity: C-V	-0.24	-1.31	0.83	0.49	-0.48	0.63
Onset Complexity: C-CC	-0.08	-1.03	0.87	0.43	-0.18	0.86
Random Effects	*SD*	*2.5 %*	*97.5 %*			
Item (Intercept)	0.68	0.52	0.85			
Subject (Intercept)	1.63	1.15	2.48			
Subject (Word Length)	0.27	0.12	0.47			
Subject (Word Function)	1.05	0.51	1.75			
Subject (Onset Complexity: C-V)	1.97	1.34	3.06			
Subject (Onset Complexity: C-CC)	1.65	1.04	2.72			
Subject (Correlation: Onset Complexity levels)	-0.45	-0.80	0.10			
Subject (Correlation: Word Function - Onset Complexity: C-V)	0.81					
Subject (Correlation: Word Function - Onset Complexity: C-CC)	-0.68					

Note. Likelihood confidence intervals are given for β estimates and explained standard deviation of the random effects. SE refers to standard error, SD to standard deviation. For two correlations of the random effects the likelihood confidence intervals could not be computed.

	Stuttered	*Not Stuttered*
Anticipated	True Positive (TP)	False Positive (FP)
Not Anticipated	False Negative (FN)	True Negative (TN)

Table 5. Illustration of the relationship between stuttering events and anticipations

	Stuttered	*Not Stuttered*	*Sum*
Anticipated	145 (23.6)	416 (6.2)	561
Not Anticipated	470 (76.4)	6338 (93.8)	6808
Sum	615	6754	7369

Table 6. Absolute number of *Anticipations* for AWS only
for stuttered words and not stuttered words, with percentages (in parentheses) broken down

	Word Function	*log Word Frequency*	*Sentence Position*	*Onset Complexity: C-V*	*Onset Complexity: C-CC*	*IPC score*
Word Function	-					
log Word Frequency	-0.86	-				
Sentence Position	0.25	-0.24	-			
Onset Complexity: C-V	0.18	-0.24	0.12	-		
Onset Complexity: C-CC	0.24	-0.34	0.05	0.4	-	
IPC score	0.72	-0.64	0.14	-0.12	0.47	-
log Syllable Frequency	-0.57	0.56	-0.12	-0.32	-0.73	-0.42

Table 7. Pairwise correlation coefficients among linguistic factors
in the dataset (n = 356 items). For continuous variables the calculation display spearman correlations, for binary variables (i.e., Word Function, Word Onset Complexity) we used rank biserial correlations.

Fixed Effects	*β*	*2.5 %*	*97.5 %*	*SE*	*Wald z*	*p-value*
(Intercept)	-3.91	-4.80	-3.11	0.402	-9.73	0.00
Word Function	0.03	-0.31	0.37	0.166	0.16	0.87
log Word Frequency	-0.71	-0.91	-0.51	0.096	-7.32	0.00
Sentence Position	-0.38	-0.70	-0.13	0.131	-2.92	0.00
Onset Complexity: C-V	-0.29	-1.00	0.46	0.346	-0.82	0.41
Onset Complexity: C-CC	-0.16	-0.72	0.34	0.246	-0.64	0.52
IPC Score	0.08	-0.09	0.26	0.085	0.99	0.32
log Syllable Frequency	0.20	-0.01	0.42	0.103	1.95	0.05
Random Effects	*SD*	*2.5 %*	*97.5 %*			
Item (Intercept)	0.53	0.35	0.70			
Subject (Intercept)	1.75	1.27	2.57			
Subject (Sentence Position)	0.44	0.21	0.78			
Subject (Onset Complexity: C-V)	1.30	0.90	1.97			
Subject (Onset Complexity: C-CC)	0.59	0.23	1.18			
Subject (log Syllable Frequency)	0.27	0.13	0.48			

Table 8. Summary of the post-hoc model of Stuttered Events by linguistic predictors. Note. Likelihood confidence intervals are given for β estimates and explained standard deviation of the random effects. SE refers to standard error, SD to standard deviation.

Fixed Effects	*β*	*2.5 %*	*97.5 %*	*SE*	*Wald z*	*p-value*
(Intercept)	-4.42	-5.29	-3.65	0.40	-11.03	0.00
Word Function	0.83	0.16	1.48	0.31	2.67	0.01
log Word Frequency	-0.89	-1.13	-0.66	0.12	-7.49	0.00
Sentence Position	-0.19	-0.34	-0.04	0.08	-2.53	0.01
Onset Complexity: C-V	-0.25	-1.29	0.79	0.50	-0.50	0.62
Onset Complexity: C-CC	-0.24	-1.20	0.71	0.46	-0.51	0.61
IPC Score	0.18	-0.10	0.44	0.13	1.33	0.18
log Syllable Frequency	-0.06	-0.23	0.10	0.08	-0.72	0.47
Random Effects	*SD*	*2.5 %*	*97.5 %*			
Item (Intercept)	0.74	0.58	0.91			
Subject (Intercept)	1.63	1.14	2.45			
Subject (Word Function)	0.96	0.45	1.76			
Subject (Onset Complexity: C-V)	1.96	1.34	3.00			
Subject (Onset Complexity: C-CC)	1.65	1.03	2.57			
Subject (IPC Score)	0.34	0.15	0.59			
Subject (Correlation: Onset Complexity levels)	-0.46	-0.80	0.10			
Subject (Correlation: Word Function - Onset Complexity: C-V)	0.93	0.41	1.00			
Subject (Correlation: Word Function - Onset Complexity: C-CC)	-0.76	-1.00	-0.08			

Table 9. Summary of the post-hoc model of Anticipations by linguistic predictors.
Note. Likelihood confidence intervals are given for β estimates and explained standard deviation of the random effects. SE refers to standard error, SD to standard deviation.

Figures

Figure 1. Example for the reading text "Reading" during the silent reading trial

Paper 2 – 8.0.0 – Appendix

P2.8.1.0 – Reading texts

(1) Herbst: Wenn die Blätter von den Bäumen fallen und es draußen frisch wird, ist der Herbst gekommen. Der meteorologische Beginn des Herbstes ist jedes Jahr der erste September. Viele Menschen bezeichnen ihn auch als „die goldene Jahreszeit“, weil sich die Blätter in warmen bräunlichen Farben präsentieren. Keine andere Jahreszeit ist so abwechslungsreich und hat so viele Facetten wie der Herbst.

[Autumn: When the leaves fall of the trees and it is getting colder outside, autumn has come/arrived. Every year, the meteorological beginning of autumn is the first of September. Many people coin this time the 'golden season' as the leaves present themselves in warm brownish colours. No other season is as diverse and has so many facets as autumn.]

(2) Finnland: Finnland ist ein Staat Europas, der auf einer mit Deutschland vergleichbar großen Fläche bloß zirka 5 Millionen Einwohner zählt. Wegen der zahlreichen Gewässer wird es auch das Land der 1000 Seen genannt. Es ist ein beliebtes Gebiet für Skifahrer, da der Schnee in der kalten Jahreszeit bei Temperaturen von bis zu -40 Grad garantiert ist.

[Finland: Finland is a European state that has only ca. 5 million inhabitants on an area that is as big as Germany. Because of the many waters it is called the land of the 1000 sees. It is a famous area for skiers as snow is guaranteed by temperatures of -40 degrees.]

(3) Altersvorsorge: Lohnt sich eine private Rentenversicherung? Diese Frage stellen sich in diesen finanziell unsicheren Zeiten viele Menschen. Die geeignete Art der Vorsorge für sich zu ergründen, ist jedoch schwierig. Ob Bausparvertrag oder Fonds, oft fällt es schwer, den Überblick zu behalten. Experten empfehlen, sich von einem neutralen Berater über alle Konditionen aufklären zu lassen und individuell seinen eigenen Bedürfnissen zufolge zu entscheiden.

[Retirement plan: Is a private retirement worthwhile? This question is asked by many people in times of financially uncertain times. However, to find the most suitable financial precaution is difficult. Whether housing-saving or funding, it is often difficult, to keep track. Experts recommend to be advised by a neutral advisor and to take individual following his own needs.]

(4) Pfingsten: Eines von zahlreichen christlichen Festen ist Pfingsten. Warum es eigentlich gefeiert wird, wissen jedoch nur Wenige. Traditionell wird es 50 Tage nach Ostersonntag begangen, da an jenem Tag die Jünger Christi in Jerusalem versammelt waren und die von Christus verkündete Entsendung des Heiligen Geistes erwarteten. So wird gleichzeitig die Fortsetzung des Osterfestes sowie dessen Ende gefeiert. Außerdem wird jener Tag als Gründung der christlichen Kirche angesehen.

[Pentecost: One of many Christian festivities is 'Pentecost'. Why it is actually celebrated, is only known by few. Traditionally, it is celebrated 50 days after Easter Sunday, as it is this day that disciples of Christ in Jerusalem gathered to expect Holy Ghost that was announced by Christ. Therefore, simultaneously, the continuation and the end of the Easter fest is celebrated. Moreover, this day is seen as the inauguration of the Christian church.]

(5) Leseföderung: Lesen ist eines der wichtigsten Güter unserer Gesellschaft. Trotzdem gibt es laut einer Studie der Universität Hamburg zurzeit etwa 7 Millionen Analphabeten in Deutschland, die durch ihre Unfähigkeit zu lesen gesellschaftlich benachteiligt sind. Aus diesem Grund wird das Lesen heutzutage ständig mehr gefördert und viele Kinder lernen bereits vor der Schule die Grundlagen für das spätere Lesen.

[Promoting reading skills: Reading is an important value of our society. Nevertheless, there are more than 7 million illiterates in Germany at the moment who are socially disadvantaged. For this reason, the promotion of reading skills steadily more supported and many children acquire the basic skills for their future reading (skill) prior to school entry.

(6) Urlaub: Einen brillianten Trip verbrachte Frau Stramm in Frankreich. Schließlich ist es ein idealer Fleck zur Glückseligkeit. Es war August und das Hotel hatte einen klassischen, schlichten Stil. Zudem musste sie über die kleine französische Flagge über dem Portal Schmunzeln. Ziemlich grotesk erschien ihnen jedoch zweifelsohne ein Gemälde mit Störchen und Flamingos, die zwischen zwei Grünflächen genüsslich Frösche verspeisten.

[Vacation: A brilliant trip, Mrs Stramm spent in France. Ultimately, this is an ideal spot for happiness. It was August and the hotel had a classic, simple style. Moreover, she had to smile about the small French flag above the portal. Fairly grotesque seemed the portrayal of storks and flamingos that enjoyed eating frogs among two green fields.]

5.0.0 Motivation for the Stimulation Paper

In order to prescriptively redefine stuttering, it is necessary to go beyond a simple understanding of stuttering events within the individual. Numerous structural and neuroimaging studies have identified brain regions associated with stuttering. In a meta-analysis of imaging studies of stuttering, Brown et al. (2005) reported frequent activation abnormalities in numerous cortical structures. Of note, they identified overactivation in PWS in the primary motor (M1) and supplementary motor (SMA) cortices, as well as right hemispheric laterality in PWS in the frontal and Rolandic opercula (at the superior temporal gyrus, STG and the supramarginal gyrus, SMG). According to the Hickok model, the M1 is involved in the initial stages of speech movement; according to the DIVA model, the other regions have been identified as key to the feedforward (SMA) and feedback (posterior STG and SMG) systems respectively. Additionally, Fox et al, (1996) have identified overactivation in the right medial cerebellum, which is responsible for maintaining the acoustic and somatosensory feedforward signals, according to the DIVA model.

Further evidence comes from neurological examination of PWS post therapy. Giraud et al (2008) employed fMRI in a pre-post therapy design to identify brain structures associated with neural repair following successful therapy. In a small sample (9 participants), they were able to demonstrate moderate relateralisation of the left hemisphere around the opercula. Given the post therapy link, this suggests that a mismatch between auditory and somatosensory feedback signals is also responsible in recovery from stuttering. However, they also identified differences in pre-therapy measurements which correlated with post-therapy successes. Specifically, they noted that therapy elicited different effects in the caudate nucleus depending on whether participants had low or high activity there prior to stuttering; caudate nucleus activity is also one of the factors affecting stuttering severity. This lends support to the possibility of stuttering as a multimodal disorder.

As mentioned in the introduction, the most robust findings in structural imaging studies of stuttering are that of a deficit in the left inferior frontal-premotor functional-connectivity (Chang et al., 2011; Chang & Zhu, 2013; Neef et al., 2016) and of a reduction in the white matter integrity of left hemispheric speech motor regions, which has been recently confirmed by an ALE meta-analysis (Neef, Anwander & Friederici, 2015a). In recovered PWS, the findings are reduced but still present

when compared with PNS, both in children (Chang et al., 2008) and in adults (Kell et al., 2009). Most recently on this front, Chow and Chang (2017) identified white-matter recovery as a predictive factor in the persistence of or recovery from stuttering in children. Unfortunately, while the correlation is interesting, a causative link cannot be inferred – even in longitudinal studies. The question remains whether the recovery from stuttering was caused by the white matter growth, or whether both of those factors were a result of a third element, such as individual differences in overall brain plasticity, differences in brain plasticity as a result of training etc. This suggests that, beyond purely structural differences, stuttering needs to be analysed in terms of systematic and individual differences in both functional activity and brain plasticity, an idea further supported by the Giraud et al. (2008) research.

One question which was left open by this research was the role of neural signal lateralisation and imbalanced activation in stuttering, which was previously addressed by Brown and colleagues (2005). This encouraged further examination of speech-motor excitability (Neef et al., 2015a). Excitability regulation of cortical neurons forms the basis of motor action sequences, underlying the planning and execution behind smooth coordinated motion (Stinear et al., 2009). However, the Neef and colleagues (2015a; 2016) studies were the first in a series of studies designed to address this question on the role of signal facilitation in stuttering; we produced the pre-speech facilitation research (Whillier, Hommel, Neef, Wolff von Gudenberg, Paulus & Sommer, in preparation), presented in here as Paper 3.

6.0.0 Paper 3

Adults who stutter lack the specialised

pre-speech facilitation found in non-stutterers

Alexander Whillier, Sina Hommel, Nicole E. Neef,

Alexander Wolff von Gudenberg, Walter Paulus & Martin Sommer

PlosONE (2018) 1-26

https://doi.org/10.1371/journal.pone.0202634

Primary contributions by doctoral candidate Alexander Whillier:

- Statistics
- Data analysis
- Interpretation
- Writing
- Editing

PLOS ONE

RESEARCH ARTICLE

Adults who stutter lack the specialised pre-speech facilitation found in non-stutterers

Alexander Whillier[1☯], Sina Hommel[1☯], Nicole E. Neef[2], Alexander Wolff von Gudenberg[3], Walter Paulus[1], Martin Sommer[1]*

1 Department of Clinical Neurophysiology, University Medical Centre Göttingen, Göttingen, Germany, **2** Department of Neuropsychology, Max Planck Institute for Human Cognitive and Brain Science, Leipzig, Germany, **3** Institut der Kasseler Stottertherapie, Bad Emstal, Germany

☯ These authors contributed equally to this work.
* msommer@gwdg.de

OPEN ACCESS

Citation: Whillier A, Hommel S, Neef NE, Wolff von Gudenberg A, Paulus W, Sommer M (2018) Adults who stutter lack the specialised pre-speech facilitation found in non-stutterers. PLoS ONE 13 (10): e0202634. https://doi.org/10.1371/journal.pone.0202634

Editor: Lutz Jäncke, University of Zurich, SWITZERLAND

Received: July 31, 2017

Accepted: August 7, 2018

Published: October 10, 2018

Data Availability Statement: All relevant data are within the paper and its Supporting Information files.

Funding: This work was funded by the Deutsche Forschungsgemeinschaft (SO 429/4-1) to M.S.

Competing interests: The authors have declared that no competing interests exist.

Abstract

Objectives

Persistent developmental stuttering is a speech fluency disorder defined by its symptoms, where the underlying neurophysiological causes remain uncertain. This study examined the underlying neurophysiological mechanisms of the speech planning process, using facilitation in the motor cortex during speech preparation as an analogue.

Methods

transcranial magnetic stimulation (TMS) pulses induced motor evoked potentials (MEPs), which were recorded from the tongue. Eighteen adults who stutter (AWS) and 17 adults who do not stutter (ANS) completed three experiments, which involved reading a German prefix +verb utterance from a screen. Each experiment involved 120 trials with three distinct levels of speech production: *immediate* speech, *delayed speech without pacing* and *delayed speech with predefined pacing*. TMS was applied shortly before speech onset. Trial MEPs were normalised to average non-speech MEPs. MEP amplitude, MEP facilitation ratio (amplitude: pre-speech offset) and group difference were the outcomes of interest analysed by multiple regression, as well as speech reaction time analysed by correlation.

Results

MEP values were 11·1%-23·4% lower in AWS than ANS (by standardised Beta), across all three experiments. MEP facilitation ratio slopes were also 4·9%-18·3% flatter in AWS than ANS across all three experiments. Reaction times for AWS were only significantly slower than for ANS in *immediate* speech and *predefined pacing* experiments. No stuttering was detected during the trials. The group difference in *immediate* speech was 100% and 101% greater than the other two experiments respectively.

Discussion

While performance of both ANS and AWS worsens under disturbed speech conditions, greater disturbance conditions affected controls worse than AWS. Future research and therapy in stuttering should focus on non-disturbed speech.

1.0.0 –Introduction

Fluent and effortless speech production is one of the most elaborate skills that humans have evolved; it is one of the most common human functions, yet it is often only remarkable when it is disturbed. Stuttering, one of the most common speech disturbances, has two main categories–Childhood-Onset Fluency Disorder [1] and Acquired/Neurogenic stuttering. As the names suggest, the former begins in childhood but persists through to adulthood, while the latter is the result of trauma (e.g. stroke). This study focused on the former, which we refer to hereafter simply as stuttering.

As a speech fluency disorder, stuttering is characterised by intermittent involuntary interruptions of speech motor control. The interruptions can occur in the form of repetitions of speech sounds, prolongations, and tense pauses, among other symptoms (e.g. [1]). This has the potential to affect psychological wellbeing and development, as well as having impacts both academically and culturally. Additionally, stuttering can be influenced by various factors–e.g. increased when stressed/anxious, reduced when planned/rehearsed–and it can even disappear completely during external pacing–e.g. singing [2]. According to the diagnostic criteria, it is estimated that around 5% of children stutter during language development–typically before age 6 [3]. However, ongoing neurological development in these children results in spontaneous recovery in around 80% of such cases. As a result, stuttering in the general population is estimated at around 1% of adults, mostly males, with equivalent levels reported in many countries [4].

To date, stuttering is defined by its symptoms, as the cause remains under debate. While there have been many imaging studies examining the structural neurological differences between Adults Who Stutter (AWS) and Adults who do Not Stutter (ANS), the findings are varied across the cortex. Among the most robust findings are that of a reduction in the white matter integrity of left hemispheric speech motor regions [5–8], recently confirmed by an ALE meta-analysis [9], and a deficit in the left inferior frontal-premotor functional-connectivity [10–12]. In recovered AWS, the findings are reduced but still present as compared with ANS, both in children [13] and in adults [7]. This suggests that, beyond purely structural differences, stuttering as a disorder is also governed by differences in both functional activity and brain plasticity.

Earlier work by Brown and colleagues [14] identified imbalanced activation in the speech-related auditory and motor cortices, which encouraged further examination of the local excitability of the speech-motor areas of the brain. Excitability regulation of cortical neurons forms the basis of motor action sequences, underlying the planning and execution behind smooth coordinated motion [15]. As such, according to this theoretical explanation, a systematic mismatch exists in the primary motor cortex between the facilitation impulse signals and the inhibition of neural populations [16], and it posits that this mismatch causes spontaneous undesired movement, such as stutter symptoms. Recent evidence supports the idea of reduced inhibitory motor control in AWS in non-speech tasks [17] and in speech motor tasks [12]. Busan and colleagues [18] postulated that a lack of left hemisphere dominance in motor

cortical excitability for speech activation was the likely explanation behind their findings of reduced neural activations in AWS.

Immediately before planned movement onset, neural activity spikes; this can be detected in the pre-movement period by Motor Evoked Potentials (MEPs)–potentials recorded by EMG, in the low mV range, following an external stimulation. Transcranial Magnetic Stimulation (TMS) is a non-invasive stimulation technique often employed in the examination of MEPs in stuttering [18–20]. TMS works by generating a focussed electromagnetic pulse, capable of stimulating a small section of cerebral cortex–approximately $1cm^3$ –in a single burst of a few microseconds [21, 22]. In using this technique, most studies examine peripheral MEPs–typically at the hand or wrist–and infer that their findings apply similarly to the speech motor cortex when testing AWS. More recently, however, Neef and colleagues [23, 24] took this examination further by examining the orofacial muscles–the muscles associated with speech–in an examination of speech motor cortex excitability.

In their recent study, Neef and colleagues used TMS to elicit MEPs in the tongue during speech production [24]. They first demonstrated that, although there is equivalent bilateral innervation of the orofacial muscles on both sides, there is significantly greater left hemispheric excitability compared with the right hemisphere in fluent speakers during speech. They [24] then demonstrated that this left hemispheric facilitation was absent in stutterers. Further, they found an inverse correlation between stuttering severity and the facilitation level, implying that this is a possible pathophysiological candidate behind stuttering. Overall, this [24] gave a greater understanding of the role of cortical excitability in stuttering. Nonetheless, the chosen utterance was short (a single verb plus particle), with externally regulated timing and pacing and an equivalent level of planning in every trial. However, as previously mentioned, this can alter stuttering severity [2] and may not reflect normal speech conditions.

Indeed, increased cognitive load has long been identified as a factor in stuttering frequency (e.g. [25]). It has also been suggested that concurrent activity during speech can adversely affect AWS with low working memory capacity (see [26]). While the concurrent coordination of the articulators during spontaneous speech may involve an increased cognitive load, the previous setup [24] of externally regulated speech could be seen as increasing the task complexity. We therefore expanded upon the previous design in order to address these two alternate interpretations of cognitive load in stuttering.

To represent unregulated (spontaneous) and mildly disturbed speech within the confines of the previous experimental setup, we designed two new patterns–*immediate speech* (exp. 1) and *delayed speech without pacing* (exp. 2)–as well as recreating the previous experiment [24] of *delayed speech with pacing* (in exp. 3). In the first two experiments, we planned the variations in the cortical and myogenic states to illustrate the different aspects of disruption that occur during speech preparation. For simplicity, this study considered the differences between these three experimental conditions as representative of differences in working memory complexity.

We first hypothesised that:

1. MEP facilitation would increase before speech–represented by a positive correlation between peak-to-peak MEP facilitation and MEP Time before Speech Onset (MEP-TSO), in all experiments;
2. AWS would exhibit a reduction in overall facilitation in each experiment, compared with ANS;
3. AWS would exhibit reduced facilitation over time–represented by an interaction effect between group and MEP-TSO; and that
4. the between group differences would be greatest when cognitive load intensity is high.

Neef and colleagues [24] also raised the issue that stuttering events would not be accurately detectable with the mouthpiece inserted. Rather, they used reaction time (RT) to represent fluent speech production in the context of this test, as most stuttering occurs at word onset [4]. Neef and colleagues [24] found no difference in RTs, which they interpreted to indicate that their participants did not stutter during the experiment. It has been shown that the insertion of a mouthpiece can improve fluency in AWS [27], which may explain these findings. However, it has also long been known that AWS have slower reaction time (RT) on speech tasks but not on other RT tasks (e.g. [28]). Additionally, we anticipated a level of distraction caused by the TMS pulse as TSO diminishes. We suspected that all of these factors would influence RT. Therefore, we also included reaction time as a variable of interest.

Additionally, as with many developmental disorders, it has been suggested that stuttering exists on a continuum [29], rather than as a categorical diagnosis. Therefore, we ran post-hoc analyses to examine whether speech fluency would better represent the between-groups hypotheses above.

Thus we had two secondary hypotheses:

5. that AWS would respond slower on average than ANS across all three experiments;
6. that 'percentage of stuttered syllables' (%SS), irrespective of group, would better correlate with MEP facilitation than the current method of between-groups analyses.

2.0.0 –Materials and methods

2.1.0 –Participants

For the present study, we recruited 18 stuttering speakers (two females) as well as 17 fluent speaking controls (eight females). All participants were native monolingual or bilingual speakers of German. Stuttering participants were recruited from the local stuttering support group in Göttingen, from the nearby Kassel Stuttering Therapy centre and by advertising on bulletin boards in the university in Göttingen. Fluent speakers were also recruited by advertisement around the university.

Demographic details, including age, sex, handedness, education and relevant family history, as well as stuttering severity and motor threshold, were gathered for all participants at the onset of the testing session. The AWS had a mean age of 26.17 years (SD = 8.36) and the controls had a mean of 24.00 years (SD = 3.31); both groups were predominantly right handed and the groups did not differ by education ranks (see Table 1 for demographic information

Table 1. Demographic data.

Measures	Stuttering	Controls	Significance
Participants, n	18 (16M, 2F)	17 (9M, 8F)	p = ·011 (sig.)
Age in years, mean	27·11 (SD = 9·04)	24 (SD = 3·32)	p = ·185 (n.s.)
Handedness, mean	78·07 (SD = 51·76)	85·96 (SD = 16·99)	p = ·547 (n.s.)
Education, mean rank	2·67 (MR = 14·81)	3·65 (MR = 21·38)	p = ·057 (n.s.)
Motor threshold left hemisphere, mean	45·56 (SD = 7·39)	44·80 (SD = 4·23)	p = ·741 (n.s.)
Percentage of syllables stuttered, mean	10·80 (SD = 11·28)	0·62 (SD = 0·00)	p<·001 (sig.)
SSI-3 Mean Score	23·33 (SD = 11·60)	4·29 (SD = 2·49)	p<·001 (sig.)
Severity Assessment	Moderate	None	-

All group differences were calculated by t-test except for *Education*, which was calculated by Mann-Whitney U test; $U = 95.5$, $z = -1.93$, $p = .057$. Education was assessed on an ordinal scale (1 –high school to year 10; 2 –high school to year 13; 3 –<2 years university; 4–2+ years university; 5–4+ years university and graduated; 6 –completed doctorate); all other variables were scalar. Handedness was assessed with the Edinburgh Handedness Inventory, translated (Schwarz et al., 1995)–handedness is assessed between -100 (completely left handed) and 100 (completely right handed). SD = standard deviation. MR = mean rank.

https://doi.org/10.1371/journal.pone.0202634.t001

and the supplemental file S1 Table for data for each individual). There was a significant difference between the sexes in each group ($\chi 2 = 6{\cdot}429$, $p = {\cdot}011$) due to complications during recruitment, however this was not deemed unlikely to affect the experiment.

Stuttering severity of both fluent and stuttering participants was assessed by a speech language pathologist, using the Stuttering Severity Index 3 or SSI-3 ([30]; German adaption [31]). We collected two video recordings of speech from each participant–reading aloud from a sample text of 500 syllables in length, and spontaneous speech elicited by a standard interview. The SSI-3 uses the frequency and duration of stuttered syllables, as well as physical concomitants of stuttering to score each participant. Despite detecting the small instances of speech pauses and dysfluencies associated with normal speech in all participants, all of the fluent speakers were classified as non-stuttering (SSI-3 overall score <10). Among the AWS participants, two were also classified as non-stuttering; nonetheless, as these participants had past diagnoses of stuttering by qualified speech language pathologists and due to the fact that stuttering severity can vary considerably based on situation and emotional state, we included these two participants in the AWS group to represent low severity stuttering (see supplemental file S1 Table for an individual breakdown).

Seven AWS reported a family history of stuttering. None of the fluent speakers reported having a family history of speech or language disorders. Before commencement of TMS stimulation, all participants were screened for inclusion based on the criteria for standard TMS safety screening [32]–due to the magnetic nature of the device, the questionnaire includes past medical history of the head, surgeries, and work history relevant to metal objects. All participants were deemed fit and able to continue. Besides stuttering in the test group, none of the participants reported a history of neurological disease nor did they show any signs of neurological deficits in a routine neurological examination. Additionally, no participants reported any other medical condition or drug use that would impact the experiment. All participants gave their written informed consent to participate in the study. The protocol used in this study was approved by the Institutional Review Board of the University Medical Centre Göttingen.

2.2.0 –Electromyography

For the EMG recordings, participants sat comfortably relaxed in a reclining chair. We made surface recordings of the lingual muscle bilaterally and simultaneously on both sides of the tongue with two pairs of disposable, pre-gelled, silver/silver chloride (Ag/AgCl) ring electrodes (5mm x 100mm, Viasys Neurocare). The electrodes were mounted in a custom made spoon-shaped silicon mouthpiece produced with dental-laboratory technology. Participants placed the mouthpiece in the mouth, resting on the upper surface of the tongue. They were asked to close their lips and teeth softly around the mouthpiece without additional pressure and, if necessary, to hold the end of the mouthpiece with the left hand and their elbow resting; this ensured that their active hand was ipsilateral to the TMS stimulation site. During the recordings, the participants were asked to raise the tongue against the electrodes (see Fig 1) and their inferior teeth–this procedure was an update of a previous technique [23, 24, 33].

Each recording consisted of two surface EMG signals and one audio signal. The EMG signals were acquired using a Digitimer D360 at a sampling frequency of 5 kHz and amplified (x1000), then filtered (Butterworth bandpass filter 20 Hz to 2kHz) using a 1401 laboratory interface (Cambridge Electronic Design mikro 1401 mk II, UK). Recordings were captured by Signal Software (Cambridge Electronic Design, version 2.16). For the audio signal, we attached a wireless microphone (AKG PT 40) to the mouthpiece and fed the acquired audio signal into a third channel of the CED Mikro 1401, in order to convert the analog signal into a digital one, and in order to ensure that the EMG and audio recordings were temporally matched.

Fig 1. Tongue setup. The electrodes are secured to the underside of the mouthpiece and rest on the tongue. The microphone is also attached to the mouthpiece, visible on the left.

https://doi.org/10.1371/journal.pone.0202634.g001

2.3.0 –Transcranial magnetic stimulation (TMS)

We used a Magstim 200^2 magnetic stimulator with a monophasic current waveform (Magstim company) to apply single-pulse TMS of the primary motor cortex with a standard figure-of-eight coil with mean loop diameter of 7 cm. The coil was positioned tangentially to the skull, laterally at an angle of 45˚ to the sagittal plane (see Fig 2); the handle pointed backwards to generate posterior-anterior direction current flow in the brain [34, 35]. The optimum scalp position was marked when the stimulation elicited the largest motor response. To find the optimal position of the coil, we explored the scalp surface systematically. We defined the 'hot spot' as the position that consistently induced maximal MEPs in the contralateral tongue site, while at lowest stimulus strength; this was marked on the scalp with a pen to ensure accurate coil placement throughout the experiment [23, 36]. The interstimulus interval between single TMS pulses was 6s (+/-10%, ~0.2Hz).

A maximum of 30 pulses was applied before replacing the self-adhesive electrodes–due to salivation, the electrodes had to be regularly optimised. The participants rested during the cleaning process, which took approximately 5 minutes. A maximum of 100 pulses was applied to determine the hotspot and the motor threshold. In each participant, the hotspot of the

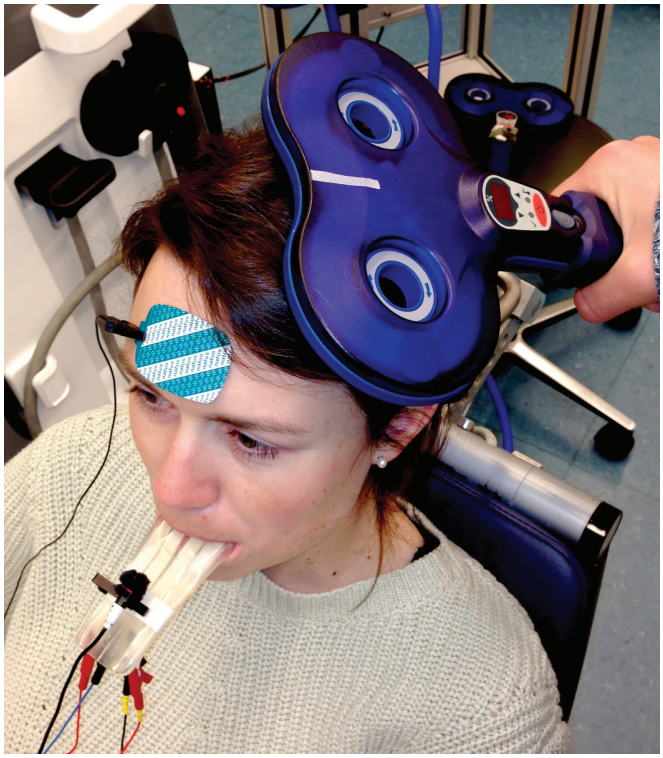

Fig 2. TMS setup. The mouthpiece with electrodes rests on the tongue, with ground electrode on the forehead. The microphone is clipped to the mouthpiece. TMS stimulator is held perpendicular to the scalp over the M1, oriented at 45˚ to the sagittal and frontal planes. The individual depicted has given written informed consent to be depicted here.

https://doi.org/10.1371/journal.pone.0202634.g002

motor tongue area was found approximately 2–3 cm anterior and 1–2 cm lateral to the hand representation, consistent with the literature [37].

To determine the motor threshold, we applied single TMS pulses and found the minimal stimulus intensity (to the nearest 1% of maximum stimulator output) required to produce MEPs *of greater than 100μV* in at least three of six consecutive stimuli. For this experiment, the trials were set to 120% of the motor threshold.

TMS allows a high level of temporal accuracy for a given pulse, but stimulation can only be reliably delivered once every few seconds. As the reaction time of each participant for each trial was unpredictable, one pulse was delivered per trial. Each trial was quasirandomly assigned to one of many pulse timings, balanced within each participant and experiment (see Experiment Setup). This ensured that the resultant data adequately covered the 500ms prior to the moment of speech onset. Additionally, some pulse timings were not set to overlap with speech onset, for use in comparing baseline values. Finally, some trials were assigned as control trials, which had no pulse.

2.4.0 –Verbal stimuli and speech task

The verbal stimuli were randomly drawn from a list of 49 German verbs–each verb selected had a consonant cluster onset, and each verb was preceded by the German initial particle "auf", for example "auf-stehen" (to stand up). The verbs were adapted from the previous paper [24] and were used for all three experiments. In all three experiments, the participant read out the full form of prefix+verb. Each participant completed all three experiments. The experiments were performed in order, on the same day for each participant.

In order to investigate the group differences between unprepared speech and prepared speech, we designed each experiment to maintain equivalent cortical state (neurological excitability) and myogenic state (tongue activity) in both groups. The use of the prefix "auf" was planned in the previous experiment [24]; we maintained this design for comparability. Experiment 3 reproduced the previous design, while experiments 1 and 2 varied the cognitive load from this design in order to represent alternative versions of speech onset disturbance.

Within each experiment, the order of the verbs was randomised between participants; additionally, the order of pulse timings was randomly assigned for each participant. This ensured that participants could not anticipate the timing of each pulse.

2.5.0 –Experiment setup

2.5.1 –First experiment–immediate speech. In the first experiment, the participant had to immediately speak the prefix and verb, as soon as the verb appeared (see Fig 3); this design maximised the cognitive load of motor planning. The participants were instructed that a large white fullstop character would signal "readiness" directly prior to the target verb and that they should respond with the required "auf+verb" utterance for each verb that appeared.

Each trial was 6300ms long; however, the presentation on the screen was continuous for the two blocks of 60 trials, with only a short pause between the two blocks. See Fig 3 for an example trial.

2.5.2 –Second experiment–delayed speech without pacing. The second experiment increased the preparation time, compared with the first experiment, in order to distribute the cognitive load over time. Each trial was 8800ms long. The participants were instructed to silently memorise a verb prior to the speech signal, to allow for preparation (see Fig 4 for an example).

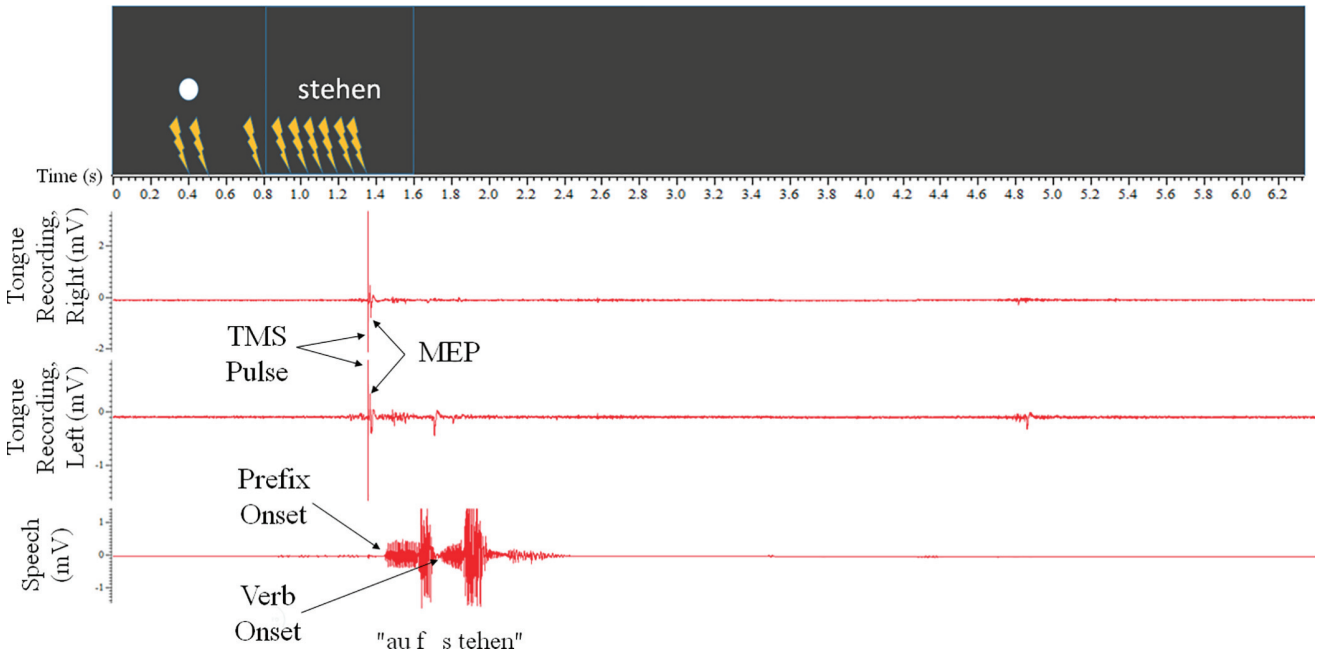

Fig 3. Example trial from Experiment 1. From the participants' perspective, each trial began with the "alertness" signal of the white circle for 800ms. The verb was then presented for 800ms; this was then followed by 4700ms of blank screen, for a total of 6300ms. The participant spoke the prefix+verb utterance when the verb was presented. One TMS pulse would fire during each trial. Within this design, there were nine possible TMS pulse timings– 400ms, 500ms, 800ms, 960ms, 1040ms, 1120ms, 1200ms, 1280ms and 1360ms (each represented by the stimulation symbol)–as well as a null pulse condition.

https://doi.org/10.1371/journal.pone.0202634.g003

2.5.3 –Third experiment–delayed speech with pacing. The third experiment replicated the previous design [24]. As in experiment two, each trial was 8800ms long and began with silent memorisation of the verb (see Fig 5). Participants were instructed to pronounce the "auf" for the full duration of the presentation, prolonging the labio-dental fricative ("auffffff"), before transitioning into the remembered verb (1500ms).

2.6.0 –Experimental design

Each participant was tested in a single session of TMS, with left hemispheric stimulation in all cases. In each session, we began with baseline assessments of the resting motor threshold and input-output curve. This was followed by a familiarisation period, where the participants were asked to perform 5 trials of the speech task with the mouthpiece in the correct position but without delivery of TMS pulses; if the participant was uncertain, we performed another 5 trials. In the first experiment, we conducted 120 trials which were split into four blocks of 30; due to practical laboratory constraints, the second and third experiments consisted of 108 Trials which were split into four blocks of 27 trials. Pauses between blocks lasted 5 minutes. A single TMS pulse was delivered per trial.

2.7.0 –Data analysis

We analysed the data using a custom-written EMG-Browser in Signal (Signal-2.16) and then Matlab (2015b). In Signal, we visually inspected the acoustic speech waveforms and determined the speech onset times of the prefix and verb using script markers which were confirmed by manual precision. Similarly, we visually examined the EMG signals from all recordings, used scripts to mark simple min/max values in the time window 10-30ms after the pulse artefact, then manually corrected for precision. Trials with extreme artefacts of either the

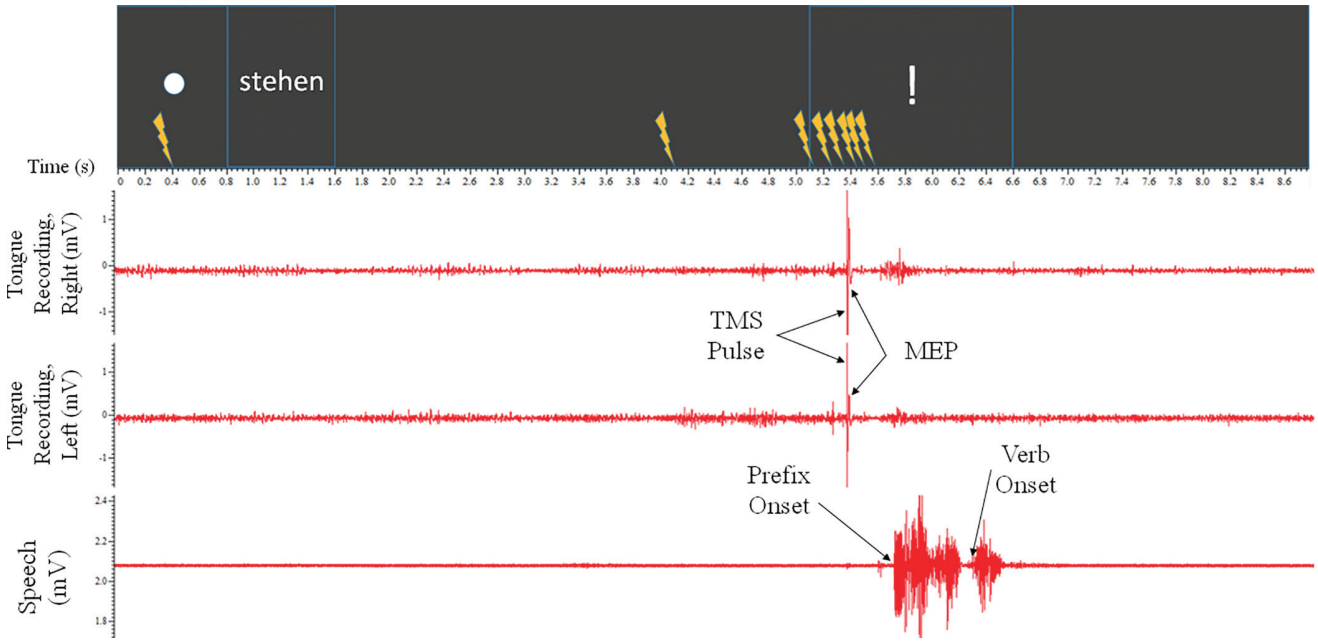

Fig 4. Example trial from Experiment 2. From the participant's perspective, each trial began with the "alertness" signal of the white circle for 800ms. This was followed by a verb for 800ms, then a blank interval of 3500ms. The "go" signal of an exclamation mark was then presented for 1500ms. This was then followed by a blank screen for 2200ms, for a total trial length of 8800ms. Participants spoke the prefix+verb utterance when the "go" signal was presented. One TMS pulse would fire during each trial. This experiment had eight pulse timings– 400ms, 4100ms, 5180ms, 5260ms, 5340ms, 5420ms, 5500ms, 5580ms (each represented by the stimulation symbol)–as well as a null pulse condition.

https://doi.org/10.1371/journal.pone.0202634.g004

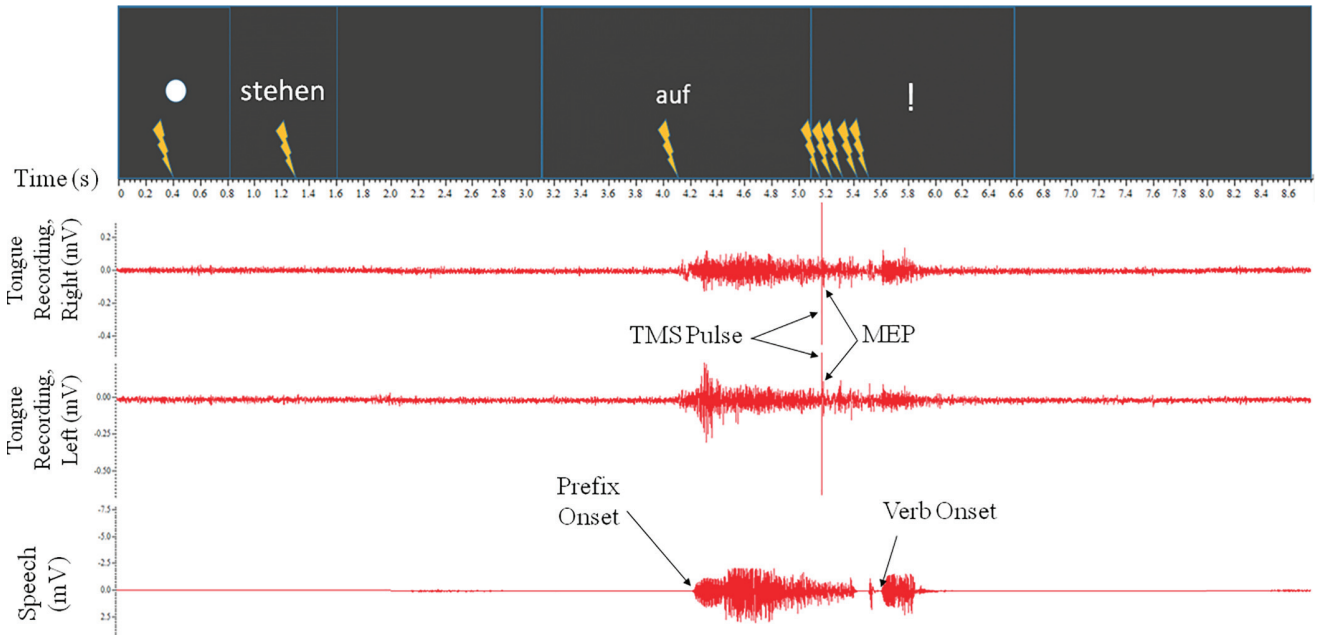

Fig 5. Example trial from Experiment 3. From the participant's perspective, each trial began with the "alertness" signal of the white circle for 800ms. This was followed by a verb for 800ms, then a blank interval of 1500ms. The "auf" signal was then presented for 2000ms, followed by the "go" signal of a white exclamation mark. This was followed by a blank screen for 2200ms, for a total trial length of 8800ms. Participants spoke and held the prefix during the "auf" signal and transitioned into the verb at the "go" signal. One TMS pulse would fire during each trial. This experiment had eight pulse timings– 400ms, 1300ms, 4100ms, 5180ms, 5260ms, 5340ms, 5420ms, 5500ms (each represented by the stimulation symbol)–as well as a null pulse condition.

https://doi.org/10.1371/journal.pone.0202634.g005

EMG or the audio signal were removed. We then stored the millivolt difference in the peak to peak amplitudes in both left and right channels, which were extracted separately for each experiment, for the contralateral and ipsilateral projection in the left hemisphere.

To account for the differences in reaction and hesitation between trials and participants, we cut and re-zeroed all data to the moment of speech onset–to the prefix in experiments 1–2 and to verb onset in experiment 3. Trials were then removed by software analysis based on signal consistency and timing of stimulation–trials were excluded if the recording was too noisy, if there was no pulse artefact or if no pulse could be identified. All invalid recordings were excluded from the respective analyses.

2.8.0 –Statistical analyses

2.8.1 –Statistical analyses–peak-to-peak MEP amplitude. To examine the relationship between pre-speech onset and MEP amplitude, we normalised the speech trials to the mean of non-speech trials then conducted a series of hierarchical multiple regression analyses (HMRAs). To control for individual variation, we first calculated the mean of the MEPs recorded during the non-speech tasks. For each experiment and each individual, we pooled the data from pulses 1 & 2 in order to maximise power (t-tests during the pilot study indicated that the two pulses were not significantly different in each experiment). We then divided each MEP response for pulses 3–9 by that participant's mean baseline score for that experiment. Thus, MEP values represent a ratio score.

As the MEPs were centred on speech, the density of the data reduced rapidly beyond 600ms before speech. To avoid bias from outliers, the data was cut. We used a 500ms window, ending at 40ms after onset of speech. Additionally, extreme MEPs (relative to baseline) were capped at 10x baseline.

To test the primary hypotheses, we conducted HMRAs with the baseline normalised MEPs as the dependent variable and two blocks of predictors:

1. onset of speech–prefix (exp. 1 and exp. 2) or verb (exp. 3), and
2. group (control vs stuttering), side of recording (left/right tongue) and group-TSO interaction (group * MEP-TSO).

In accordance with standard techniques [38], we tested the various statistical assumptions before running the HMRAs for each experiment. For the assumption of normality of distribution, we used stem-and-leaf plots and we observed a small deviation from normality (skewed low), however this was deemed to be within the limits of robustness for the analysis chosen. Upon secondary inspection of the normal probability plot of standardised residuals and the scatterplot of standardised residuals against standardised predicted values, it appeared that the data was more tightly grouped around the mean but that the assumptions of normality, linearity and homoscedasticity of residuals were met. Additionally, all three experiments exhibited high tolerances for all predictors in the final regression model, which indicated that multicollinearity would not be a cause for concern in our HMRA.

As the outcome measures of the HMRAs are ratio data (raw score / mean baseline), the t-statistic of the regression constant was recalculated against a null hypothesis of 1 (no difference between raw score and baseline) instead of the standard null hypothesis of 0. The other variables were not affected.

To test the secondary hypotheses, we used the same HMRA as above, but substituted 'percentage of stuttered syllables' (%SS) in place of 'group' and generated a new interaction term between %SS and MEP-TSO.

To compare between the experiments (hypothesis 4), we conducted unpaired t-test comparisons of the distributions in each experiment. We used an online calculator (GraphPad) to compare the unstandardised coefficients (B), standard errors and sample size (n). All blocks of the regression output were compared (constant, speech onset interval, group/%SS and the interaction effect of group/%SS and MEP-TSO). To control for multiple analyses within each experiment, we used Bonferroni correction (sig. at p = ·0125).

2.8.2 –Statistical analyses–reaction time. In keeping with the previous study [24], we analysed reaction times to all three experiments; we considered group membership, state of stimulation and trial number as factors in the reaction time analysis. Each of these factors were entered stepwise into an HMRA, to test the hypothesis that there would be a difference in response timing as a function of the TMS to Go-signal interval, both overall (Hyp3) and between groups (Hyp4).

As above with MEP analyses, we tested the statistical assumptions in accordance with standard techniques [38]; similarly, the minor deviations from normality were deemed acceptable.

3.0.0 –Results

3.1.1 –Results–peak to peak MEP amplitude. In total, we ran six HMRA regression analyses of MEP amplitude–one 'group' and one with percentage of stuttered syllables (%SS) per experiment–as well as two sets of post-hoc t-test comparisons for the 'group' results from Experiment 1 and each of the other two experiments. All three 'group' level analyses were significant at both steps of each regression (see Tables 2–4), with their respective post-hoc analyses (see Tables 5 & 6), as were the three %SS results (see Tables 7–9).

Our broad findings indicate that AWS exhibit reduced MEPs than ANS, both overall and over time. The difference was most pronounced in the first experiment, where the two groups diverged early (see Fig 6). The second experiment was similar, but with reduced responses by

Table 2.

Model		Unstandardized Coefficients		Standardized Coefficients	t	Sig.	95% CI for B	
		B	Std. Error	Beta			Lower Bound	Upper Bound
1	(Constant)	1·823	0·040		20·575	<0·001	1·744	1·902
	TPO	2·347	0·151	0·241	15·504	<0·001	2·050	2·644
2	(Constant)	2·190	0·083		14·337	<0·001	2·027	2·352
	TPO	3·155	0·216	0·323	14·634	<0·001	2·732	3·578
	Side	-0·034	0·040	-0·013	-0·840	0·401	-0·112	0·045
	Group	-0·607	0·080	-0·234	-7·598	<0·001	-0·764	-0·451
	Group-TPO Interaction	-1·585	0·301	-0·183	-5·274	<0·001	-2·174	-0·996

Hierarchical multiple regression for Experiment 1. B = unstandardized coefficient. TPO = Time before Prefix Onset. Side = Side of tongue recording. Group was binary (0 = control, 1 = AWS). The constant of the regression was tested against an H0 of B = 1, instead of the normal B = 0.

https://doi.org/10.1371/journal.pone.0202634.t002

both groups relative to the first experiment and marginally later divergence (see Fig 7). The third experiment exhibited a reduced peak level, relative to the first, but the overall MEPs maintained a moderately high level relative to baseline throughout the experiment (see Fig 8); this is likely due to the design of the pacing condition. It should be noted that all three experiments characterised a small effect size according to R^2 (see supplementary information).

Our secondary %SS findings supported the primary between-groups findings for the first and third experiments, but the *delayed speech without pacing* experiment 2 did not elicit a significant effect of stuttering. Fig 9A–9C give an overview of these findings, which will be explained in more detail below.

3.1.2 –Results–specific MEP findings by experiment. As noted in the methods, all regression constants were recalculated against a null hypothesis of 1 (no significantly different ratio). All recalculated regression constants were significant for all experiments (see the respective Tables 2–7); this indicates that, on average, the MEPs over the trial window was greater than the MEPs during the non-speech baseline period.

For the first experiment (*immediate* speech), 3916 trials were included in the analysis (see Table 2, with additional model information in the supporting information file under S2 Table). The first block of the regression indicated a positive correlation between pre-speech

Table 3.

Model		Unstandardized Coefficients		Standardized Coefficients	t	Sig.	95% CI for B	
		B	Std. Error	Beta			Lower Bound	Upper Bound
1	(Constant)	1·407	0·040		10·175	<0·001	1·330	1·485
	TPO	1·679	0·150	0·187	11·158	<0·001	1·384	1·974
2	(Constant)	1·479	0·081		5·9136	<0·001	1·321	1·637
	TPO	2·175	0·215	0·242	10·096	<0·001	1·752	2·597
	Side	0·058	0·038	0·026	1·536	0·125	-0·016	0·132
	Group	-0·302	0·079	-0·134	-3·817	<0·001	-0·457	-0·147
	Group-TPO Interaction	-0·943	0·301	-0·121	-3·136	0·002	-1·532	-0·353

Hierarchical multiple regression for Experiment 2. B = unstandardized coefficient. TPO = Time before Prefix Onset. Side = Side of tongue recording. Group was binary (0 = control, 1 = AWS). The constant of the regression was tested against an H0 of B = 1, instead of the normal B = 0.

https://doi.org/10.1371/journal.pone.0202634.t003

Table 4.

Model		Unstandardized Coefficients		Standardized Coefficients	t	Sig.	95% CI for B	
		B	Std. Error	Beta			Lower Bound	Upper Bound
1	(Constant)	1·537	0·049		10·959	<0·001	1·440	1·633
	TVO	0·562	0·210	0·052	2·671	0·008	0·149	0·974
2	(Constant)	1·573	0·106		5·406	<0·001	1·366	1·781
	TVO	0·860	0·292	0·079	2·941	0·003	0·286	1·433
	Side	0·080	0·053	0·029	1·509	0·131	-0·024	0·183
	Group	-0·305	0·098	-0·111	-3·110	0·002	-0·498	-0·113
	Group-TVO Interaction	-0·526	0·420	-0·049	-1·252	0·211	-1·351	0·298

Hierarchical multiple regression for Experiment 3. B = unstandardized coefficient. TVO = Time before Verb Onset. Side = Side of tongue recording. Group was binary (0 = control, 1 = AWS). The constant of the regression was tested against an H0 of B = 1, instead of the normal B = 0.

https://doi.org/10.1371/journal.pone.0202634.t004

interval and MEP response; this effect increased when accounting for all other factors. There were also two negative correlations: one between 'MEP' and 'group' and the other between 'MEP' and the 'group to MEP-TSO' interaction. Due to dummy coding, this negative correlation indicates that AWS exhibited a reduced average MEP and a lesser increase in MEP closer to speech onset compared with controls.

For the second experiment (*delayed without pacing*), 3443 trials were included in the analysis (see Table 3, with additional model information in the supporting information file under S3 Table). As in experiment 1, there was a positive correlation between MEP amplitude and pre-speech interval, as well as negative correlations for both 'group' and the 'group to MEP-TSO' interaction.

For the third experiment (*delayed with pacing*), 2678 trials were included in the analysis (see Table 4, with additional model information in the supporting information file under S4 Table). As before, there was a positive correlation with the regression constant and with the pre-speech interval, as well as a negative correlation with 'group'; however, the 'group to MEP-TSO' interaction effect was not significant.

3.1.3 –Results–post-hoc analyses of the primary regressions. In post-hoc analyses, we compared the regression outputs of the first experiment with the other two experiments. Overall, the second experiment elicited lower MEPs than the first in all comparisons except the 'group to MEP-TSO' interaction (see Table 5 for comparisons and S1 Text Appendix for more information). Similarly, the third experiment elicited lower MEPs than the first–the constant

Table 5.

	Exp1-Exp2	SE of Diff	CI Low	CI High	t	df	Sig.
Constant	0·711	0·117	0·48184	0·94016	6·0959	7357	<0·001
TPO	0·98	0·306	0·37857	1·58143	3·2014	7357	0·0014
Group	-0·305	0·113	-0·52699	-0·08301	2·6994	7357	0·007
Interaction	-0·642	0·427	-1·4818	0·1978	1·502	7357	0·1331

Secondary Data Analysis–Between experiments comparison for Group Difference between experiments 1 and 2. TPO = Time before Prefix Onset. Group was binary, with 0 = controls and 1 = AWS. Interaction represents the Group*TPO interaction.

https://doi.org/10.1371/journal.pone.0202634.t005

Table 6.

	Exp1-Exp3	SE of Diff	CI Low	CI High	t	df	Sig.
Constant	0·617	0·133	0·35519	0·87881	4·6301	6592	<0·001
TPO/TVO	2·295	0·356	1·59612	2·99388	6·4518	6592	<0·001
Group	-0·302	0·126	-0·54995	-0·05405	2·393	6592	0·0167
Interaction	-1·059	0·503	-2·04746	-0·07054	2·1049	6592	0·0353

Secondary Data Analysis–Between experiments comparison for Group Difference between experiments 1 and 3. TPO/TVO = Time before Prefix/Verb Onset. Group was binary, with 0 = controls and 1 = AWS. Interaction represents the Group*TPO/TVO interaction.

https://doi.org/10.1371/journal.pone.0202634.t006

and pre-speech interval were significantly smaller than in the first experiment, while group and the 'group to MEP-TSO' interaction were marginally non-significant after Bonferroni correction (see Table 6 for comparisons and S2 Text Appendix for more information).

3.2.0 –Results–secondary regression analyses. As above, the regressions for %SS had the same participant numbers and the same first blocks in each analysis (see Tables 7–9). The unique contribution of the second block of the regression was significant for all three analyses, as indicated by the significant F Change (see supplementary S5–S7 Tables).

Stuttering was a significant predictor in both the first and third experiments, as was the 'group to MEP-TSO' interaction effect of group and pre-speech MEP time. As both were positively coded, this indicates that better fluency correlates with higher MEPs and this correlation increases faster with greater fluency. In experiment two, the only significant variable in the second block was the MEP-TSO.

3.3.0 –Results–reaction time

In total, we ran four HMRAs: three for *Prefix Reaction Time* (exp. 1–3, Tables 10A–10C) and one for *Verb Reaction Time* (exp. 3, Table 10D). Overall, AWS were slower than ANS in the first and third experiment but not the second. The responses also got faster over the course of experiments 1 and 3 irrespective of group, but not in experiment 2 –this indicated that the participants were learning the precise trial timing. Additionally, responses were slower among all participants when pre-speech pulse intervals were smaller; this implies a level of distraction from the pulse.

Table 7.

		Unstandardized Coefficients		Standardized Coefficients	t	Sig.	95% CI for B	
							Lower Bound	Upper Bound
Model		B	Std. Error	Beta				
1	(Constant)	1·823	0·040		20·575	<0·001	1·744	1·902
	TPO	2·347	0·151	0·241	15·504	<0·001	2·050	2·644
2	(Constant)	1·984	0·077		12·779	<0·001	1·833	2·136
	TPO	2·696	0·179	0·276	15·057	<0·001	2·345	3·047
	Side	-0·033	0·040	-0·013	-0·827	0·408	-0·112	0·045
	%SS	-1·808	0·436	-0·130	-4·147	<0·001	-2·663	-0·953
	%SS-TPO Interaction	-5·873	1·675	-0·114	-3·506	<0·001	-9·158	-2·589

Hierarchical multiple regression for Experiment 1 using Percentage of Stuttered Syllables. B = unstandardized coefficients. TPO = Time before Prefix Onset. Side = Side of tongue recording. %SS = Percentage of Stuttered Syllables. %SS was a continuous variable including all previously included data from both groups. The constant of the regression was tested against an H0 of B = 1, instead of the normal B = 0.

https://doi.org/10.1371/journal.pone.0202634.t007

Table 8.

		Unstandardized Coefficients		Standardized Coefficients	t	Sig.	95% CI for B	
							Lower Bound	Upper Bound
Model		B	Std. Error	Beta				
1	(Constant)	1·407	0·040		10·175	<0·001	1·330	1·485
	TPO	1·679	0·150	0·187	11·158	<0·001	1·384	1·974
2	(Constant)	1·346	0·075		4·613	<0·001	1·199	1·492
	TPO	1·661	0·182	0·185	9·146	<0·001	1·305	2·017
	Side	0·058	0·038	0·026	1·538	0·124	-0·016	0·132
	%SS	-0·385	0·425	-0·032	-0·905	0·365	-1·218	0·448
	%SS-TPO Interaction	0·510	1·582	0·012	0·322	0·747	-2·593	3·612

Hierarchical multiple regression for Experiment 2 using Percentage of Stuttered Syllables. B = unstandardized coefficients. TPO = Time before Prefix Onset. Side = Side of tongue recording. %SS = Percentage of Stuttered Syllables. %SS was a continuous variable including all previously included data from both groups. The constant of the regression was tested against an H0 of B = 1, instead of the normal B = 0.

https://doi.org/10.1371/journal.pone.0202634.t008

4.1.1 –Discussion

Broadly speaking, our results demonstrate that AWS exhibit reduced facilitation compared with ANS prior to speech onset, but this difference is not consistent across conditions. This difference is also not simply a difference in magnitude of facilitation–using between-groups and between-experiments comparisons, our findings indicate that the discrepancy was greatest during our *immediate* condition, but also that the facilitation within both groups diminished under increased speech disturbance. These findings will be discussed in more detail below.

4.1.2 –Note–Facilitation or disinhibition?

It should be noted that changes in MEP response can be due to one of two mechanisms:

1. increased facilitation–up-regulation in cortical positive feedback systems, or

Table 9.

		Unstandardized Coefficients		Standardized Coefficients	t	Sig.	95% CI for B	
							Lower Bound	Upper Bound
Model		B	Std. Error	Beta				
1	(Constant)	1·537	0·049		10·959	<0·001	1·440	1·633
	TVO	0·562	0·210	0·052	2·671	0·008	0·149	0·974
2	(Constant)	1·536	0·099		5·414	<0·001	1·343	1·730
	TVO	1·067	0·244	0·098	4·371	<0·001	0·588	1·546
	Side	0·079	0·053	0·029	1·505	0·132	-0·024	0·183
	%SS	-2·141	0·561	-0·129	-3·813	<0·001	-3·242	-1·040
	%SS-TVO Interaction	-9·291	2·329	-0·141	-3·990	<0·001	-13·858	-4·725

Hierarchical multiple regression for Experiment 3 using Percentage of Stuttered Syllables. B = unstandardized coefficient. TPO = Time before Prefix Onset. Side = Side of tongue recording. %SS = Percentage of Stuttered Syllables. %SS was a continuous variable including all previously included data from both groups. The constant of the regression was tested against an H0 of B = 1, instead of the normal B = 0.

https://doi.org/10.1371/journal.pone.0202634.t009

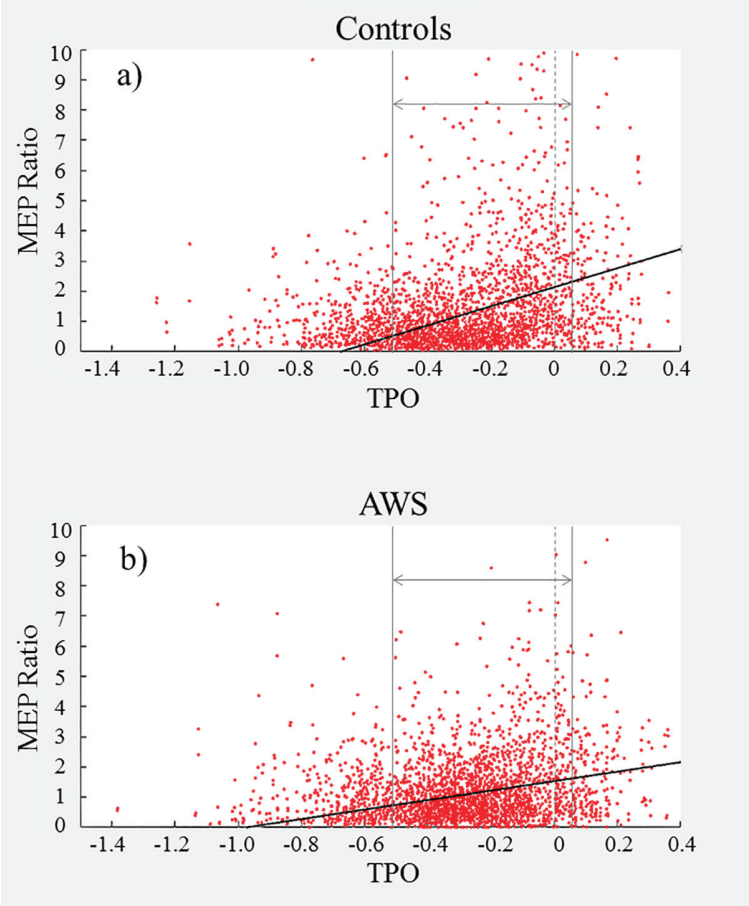

Fig 6. a-b. Experiment 1 Pulse Interval–MEP Peak to Peak Amplitude relative to prefix onset for Controls (a) and AWS (b). Each point represents one trial. Prefix onset for each trial is marked by the dashed vertical bar at TPO = 0. The outer vertical bars denote the 500ms time window chosen for analysis. The diagonal line represents the linear regression predicted by the model applied within the selected window.

https://doi.org/10.1371/journal.pone.0202634.g006

2. reduced inhibition–down-regulation in negative feedback systems.

In our experiments, it is unclear whether increases in MEP are a result of increased facilitation or reduced inhibition. For simplicity, we use 'MEP Facilitation' to refer to our findings; however, it is possible also that the underlying cause is disinhibitory.

4.2.1 –MEP facilitation increases prior to speech

The regulation of cortical excitability forms the basis of motor action sequences, underlying the planning and execution behind smooth coordinated motion–in the moments before movement onset, the neural activity spikes. Our data demonstrates that the same holds true for speech motor activity–supporting our first hypothesis–and the positive 'TPO/TVO' correlation values in each experiment represent the magnitude of this relationship.

4.3.0 –Overall MEP facilitation is reduced in AWS

As stuttering is a speech movement disorder associated with reduced control particularly at movement onset, we hypothesised that AWS would exhibit reduced MEP facilitation,

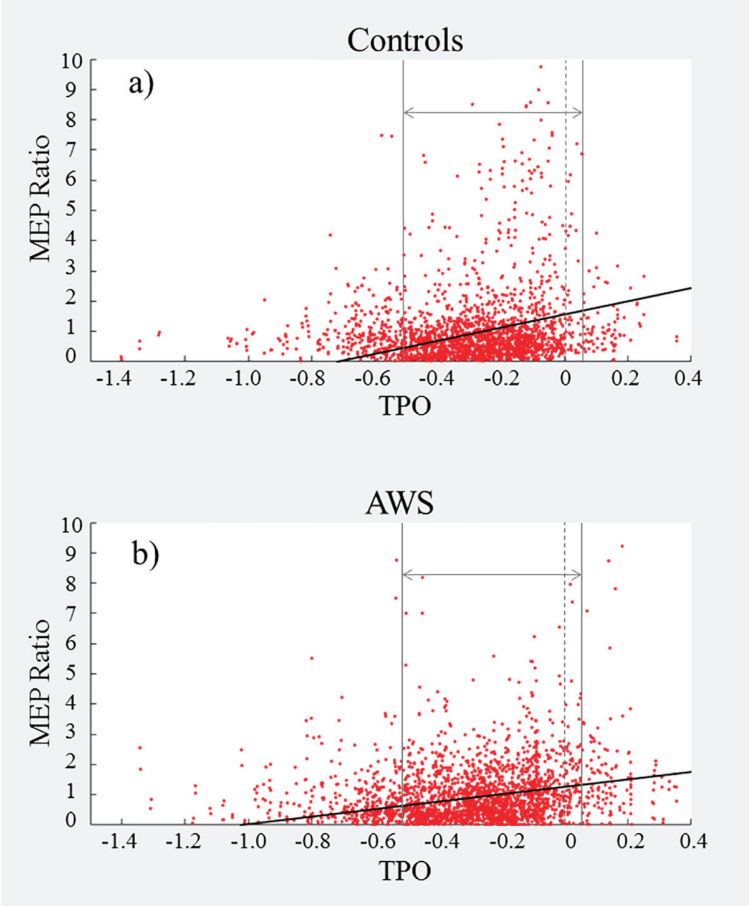

Fig 7. a-b. Experiment 2 Pulse Interval–MEP Peak to Peak Amplitude relative to prefix onset for Controls (a) and AWS (b). Each point represents one trial. Prefix onset for each trial is marked by the dashed vertical bar at TPO = 0. The outer vertical bars denote the 500ms time window chosen for analysis. The diagonal line represents the linear regression predicted by the model applied within the selected window.

https://doi.org/10.1371/journal.pone.0202634.g007

compared with ANS. Again, our results supported this across all three experiments–the significant negative correlation of 'group' suggests that AWS have a significantly diminished overall response than they had at baseline, compared with ANS.

This pattern of increasing MEP Facilitation prior to initiation of motor tasks is analagous to the Bereitschaftspotential (BP). BP research has identified two distinct stages–early (BP1) and late (BP2), beginning around 1200ms and 500ms before movement initiation respectively. It is believed that BP1 originates in the anterior supplementary motor area (SMA) and the pre-SMA, while BP2 probably arises in both the SMA and the contralateral motor cortex (Colebatch, 2007). Many movement disorders are associated with a disturbed BP; for example, the BP is absent in disorders like Parkinson's disease (e.g. [39, 40] and overactive in tic disorders (e.g. [41]) when looking at self-triggered movements. Given our findings of reduced facilitation in AWS, and that of reduced contralateral facilitation in previous research [24], we anticipate a link between MEP and BP in AWS which should be investigated in future research.

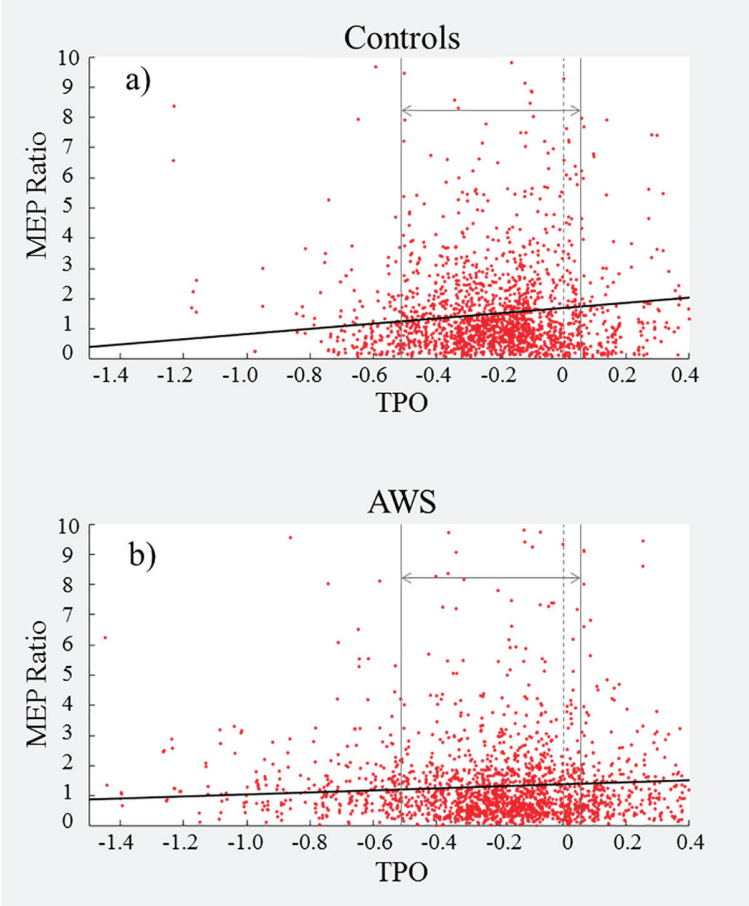

Fig 8. a-b. Experiment 3 Pulse Interval–MEP Peak to Peak Amplitude relative to verb onset for Controls (a) and AWS (b). Each point represents one trial. Verb onset for each trial is marked by the dashed vertical bar at TPO = 0. The outer vertical bars denote the 500ms time window chosen for analysis. The diagonal line represents the linear regression predicted by the model applied within the selected window.

https://doi.org/10.1371/journal.pone.0202634.g008

4.4.0 –AWS exhibit reduced growth in MEPs as a function of time before speech

As demonstrated by the negative 'group to MEP-TSO' interaction effect, AWS exhibited reduced MEP facilitation as a function of time compared with ANS. However, unlike the two findings above, the 'group to MEP-TSO' interaction effect was significant in the *immediate* condition and the *delayed speech without pacing* condition, but not the *delayed with pacing* condition. Note that in the pacing condition, the MEP was recorded during the verb after holding the prolonged prefix. In combination with the significant between-groups finding above, this suggests that AWS have a reduced dynamic range during pre-speech facilitation. As suggested by the Bereitschaftspotential model, one explanation is that AWS lack the late stage rapid facilitation immediately before speech onset in normal speech. However, in highly disrupted speech, the difference disappears. This will be addressed in combination with all three experiments below.

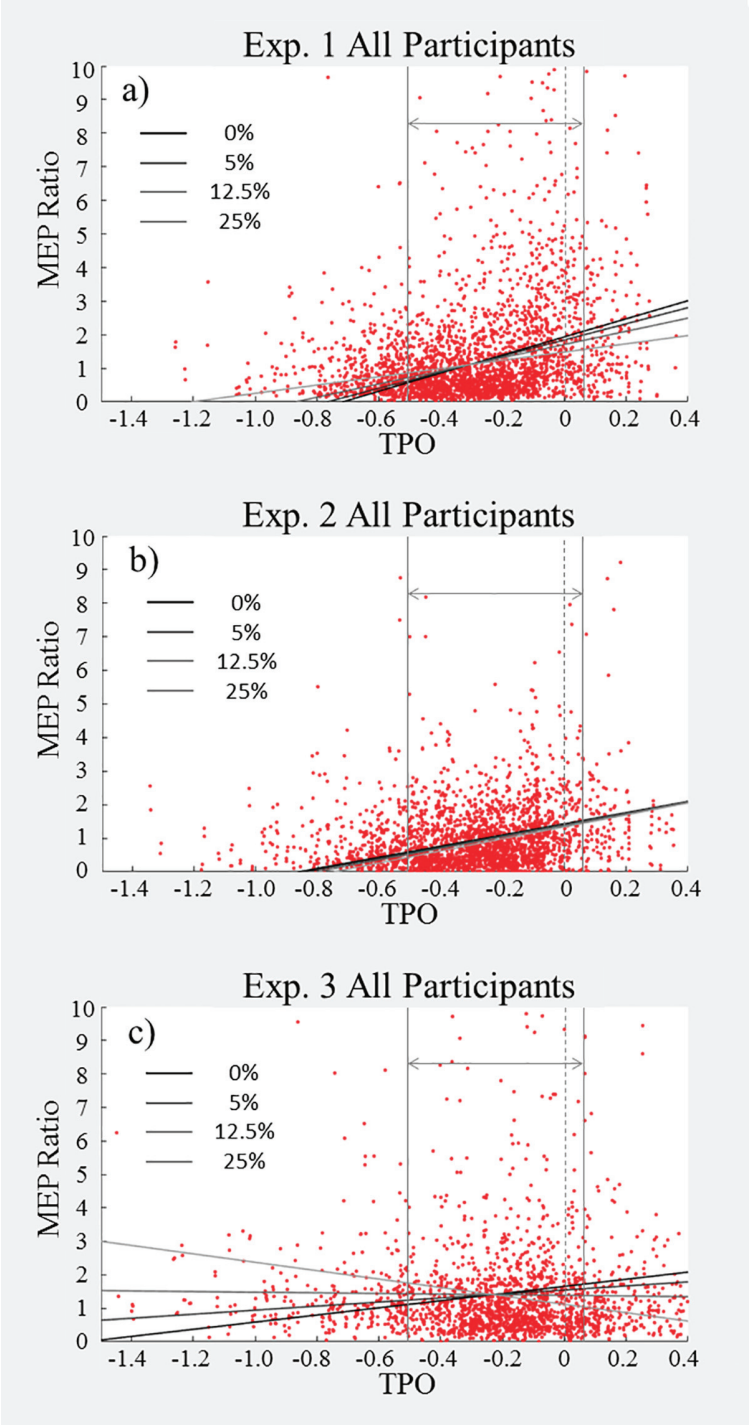

Fig 9. a-c Linear Regression predictions based on stuttering severity (%SS) with respect to time before speech. Each point represents one trial. Each figure includes all data for that experiment, irrespective of group. Prefix onset (Figs 9a & 9b) and verb onset (Fig 9c) for each trial is marked by the dashed vertical bars at TPO = 0. The outer vertical bars denote the 500ms time window chosen for analysis. The diagonal line represents the linear regression predicted by the model applied within the selected window, differentiating between levels of stuttering (none, low, medium and high).

https://doi.org/10.1371/journal.pone.0202634.g009

4.5.0 –Stuttering is not simply derived from a reduction in magnitude of facilitation

It has been previously suggested that there may be a link between stuttering and cognitive load [25] or working memory capacity [26, 42]; however, there is no broader agreement on the nature of the link and its role in AWS. This is likely due to the many different methods used to assess the construct. We examined this controversy by comparing between our three experiments. It can be considered that the spontaneous production of speech in our *immediate* condition represented the highest demand on cognitive load (e.g. [25]); alternatively, it can be interpreted that the drawn out *delayed with pacing* condition placed additional working memory demands from both the planning of the movement and the external disruptions to speech (e.g. [26]).

The technique of artificially drawing out words, as in the third experiment, has been employed in many stuttering therapies to reduce the severity of stuttering. For this paper, we therefore anticipated that such increased speech interference and preparation time, which improve speech fluency in therapy, would manifest in improvements in MEP facilitation. Thus our fourth hypothesis anticipated that the between-groups difference would be smallest in the pacing experiment (exp. 3), as AWS facilitation approached ANS levels, and greatest in the *immediate* experiment (exp. 1).

On the whole, our fourth hypothesis proved correct–the increased timing, which is provided by drawing out the utterance, reduces the concurrent complexity for AWS and results in a trend towards ANS performance. However, our group differences were not linear across the three experiments. Although we did find that the *immediate* experiment (exp. 1) elicited a greater difference in MEPs between groups than either of the other two (see Tables 5A–6A), there was no difference between the second and third experiments. Rather, in combination

Table 10.

n = 3623	Auf RT	Group	Pulse	Trial	n = 3211	Auf RT	Group	Pulse	Trial
Auf RT	-	-0·044**	0·185***	-0·078***	Auf RT	-	-0·018	0·135***	0·022
(Sig.)		0·004	(<0·001)	(<0·001)	(Sig.)		0·156	(<0·001)	0·106
Group		-	-0·01	0·001	Group		-	-0·001	-0·007
(Sig.)			0·275	0·48	(Sig.)			0·478	0·346
State			-	0·052**	State			-	0·016
(Sig.)				(<0·001)	(Sig.)				0·184
Trial				-	Trial				-
10a					**10b**				
n = 3172	Auf RT	Group	Pulse	Trial	n = 3172	Verb RT	Group	Pulse	Trial
Auf RT	-	-0·014	0·002	-0·068***	Verb RT	-	-0·040*	0·030*	-0·032*
(Sig.)		0·221	0·445	(<0·001)	(Sig.)		0·013	0·043	0·036
Group		-	-0·001	-0·015	Group		-	-0·001	-0·015
(Sig.)			0·476	0·192	(Sig.)			0·476	0·192
State			-	-0·012	State			-	-0·012
(Sig.)				0·245	(Sig.)				0·245
Trial				-	Trial				-
10c					**10d**				

Hierarchical multiple regression analyses for reaction time to prefix in each experiment (10a-c) and verb in experiment 3 (10d). Correlation values for each pair, with significances shown in parentheses (* = p < ·05, ** = p < ·01, *** = p < ·001). Negative correlation values represent reductions in reaction time, thereby a faster response by the participant. The significant values of Trial in experiments 1 and 3 indicate that the participants were learning the precise trial timing. The Trial-State interaction in Table 10A is discussed in S3 Text Appendix.

https://doi.org/10.1371/journal.pone.0202634.t010

with the other findings above, it appears that ANS exhibited a reduced facilitation over time, while AWS exhibited average magnitude (the constant) but no change in facilitation over time. In combination with the previous study [24], where they found that ANS have increased left hemispheric facilitation prior to speech but AWS do not, this implies the existence of a speech specialised programme of facilitation in ANS. This additionally supports the suggestion, by Bosshardt [25], of a reduced level of "modularization" in the neural subsystems involved in speech planning in AWS. Further, it suggests that this modularization is speech specific. Specifically, under normal everyday speech conditions, ANS have a specialisation for speech preparation that does not generalise to non-speech mouth movement actions; conversely, AWS do not have this specialisation for speech coordination, and must rely on their general movement preparation sequences for all forms of speech. However, this remains speculative at this stage–further research incorporating undisturbed speech is needed.

4.6.0 –Reduced MEP facilitation in AWS is not simply a result of stutter-like delays

One might argue that these group differences in MEP facilitation may be solely an artefact of experimental design–i.e. as our facilitation data was zeroed to the moment of speech onset, reaction time delays due to stuttering events could reduce the average AWS results. This can be refuted by a few arguments. Firstly, there were no stutter-like events during speech noted by the experimenters and double-checked with the audio recording; this is possibly a result of having a large mouthpiece impeding speech (e.g. [27]. Secondly, a visual inspection of the facilitation graphs (see Figs 6–8) shows that the main bulk of trials in both groups falls in the same time window–if there were a stutter-based delay, we would expect to see a longer, thinner band of data for AWS of at least a few hundred ms.

The third argument addresses the first of our secondary hypotheses–that reaction time would differ between groups, with AWS responding slower across all three experiments, even after accounting for the distraction of pulse timing and learning. As shown in Table 10, AWS responded approximately 40ms slower than ANS in both the first experiment and the verb component of the third experiment, while the second experiment and the prefix component of the third experiment were not significantly different; conversely, the MEP group difference was significant for all three. Although the trend suggested slower reaction times for AWS in all components on average, thus supporting the hypothesis of slower reaction times in AWS, the differences were not uniform. This suggests partial independence between the MEP and reaction time.

The non-uniform reaction times also lend additional support to the possibility of a speech movement specialisation in ANS, which is missing in AWS. While the drawn out speech in the two prepared speech conditions reduces the working memory overload in AWS, it concurrently abstracts away from standard speech for which ANS are specialised.

4.7.0 –Severity of stuttering or group analysis

As with many developmental disorders, stuttering is diagnosed categorically. However, our second secondary hypothesis suggests that stuttering may fall on a continuum, whereby severity of stuttering (and possibly type–e.g. more blockages, fewer elongations) may better illustrate the question of pre-speech preparatory facilitation than a simple binary diagnosis. For simplicity, we used only the total Percentage of Stuttered Syllables (%SS), but not the symptom type–that would deserve a full paper itself. Using this method, we found similar results for both input methods in the *immediate* speech experiment–the simple %SS and the '%SS to

MEP-TSO' interaction effects were both present and stronger than in the between-groups analysis. For the other two experimental conditions, the findings were slightly different.

Firstly, the *delayed speech with pacing* produced better results than in the between-groups analysis–in particular, we found a strong 'group to MEP-TSO' interaction effect that was not demonstrated in the groups analysis. This strong negative effect predicts that in individuals with high severity, MEP facilitation would already be on the decline after the prefix before the verb is actually spoken (see Fig 9C). Whether this holds true in reality requires further investigation.

The *delayed without pacing* condition represented the biggest deviation from our between-groups analysis–in this analysis, the only significant component of the regression was time. Upon visual inspection of the individual data, the likely cause for this was the fact that the very mild and mild AWS had elicited unexpectedly low MEPs. There was the appearance of a linear effect of % SS in the moderate-very severe AWS, but the very mild participants had performed equivalently to the very severe in this experimental condition. This may be due to small *n* effects; however this requires further investigation. As a result, however, we recommend against using %SS in place of group difference unless it is a dedicated examination of this analytical design.

5.0.0 –Conclusion–external speech interference affects AWS and ANS differently

When taken all together, our data suggests that ANS and AWS handle external interference with their speech preparation in functionally distinct manners. It suggests the existence of a speech specific preparation programme in ANS that is lacking in AWS. This is supported by the increase in late stage facilitation in *immediate* speech in ANS, analogous to the late phase Bereitschaftspotential. Additionally, as there were very few stuttering events during the experiment even among participants classified as severe, it supports the idea that stuttering belies a chronic neurophysiological aberration that extends beyond the individual utterance [24].

Our data also suggests the mechanisms underlying the efficacy of moderate external interference in treating stuttering, such as is employed in fluency shaping (e.g. [43–45]–both the reduction in working memory overload and the improvement in preparatory facilitation. Future research to investigate these mechanisms could incorporate active cortical stimulation, such as transcranial direct or alternating current stimulation (tDCS/tACS, see [46]. When employed to up-regulate pre-speech facilitation, it may permit greater preparation in spontaneous speech and improve therapy outcomes, as has been seen in stimulation studies with Parkinson's disease (e.g. [40, 47].

Our data did not allow conclusions with regard to the use of severity as an indicator of the neurophysiological mechanisms. This may be due to a more complex and non-linear relationship between stuttering severity and motor facilitation–for example, it may be that individuals with mild stuttering have a weak specialisation for speech, one that is easily overwhelmed in our interference conditions; alternatively, it may be a quirk of analysis. A dedicated investigation, likely including the non-verbal concomitant symptoms of stuttering, is needed to identify the precise nature of this relationship in the future.

Supporting information

S1 Table. Individual stuttering demographics–Group was used for the main analyses. Percentage of stuttering was used for the supplementary analyses.
(DOCX)

S2 Table. Model Summary for Experiment 1 –Additional statistical information pertaining to Table 2 in the text.
(DOCX)

S3 Table. Model Summary for Experiment 2 –Additional statistical information pertaining to Table 3 in the text.
(DOCX)

S4 Table. Model Summary for Experiment 3 –Additional statistical information pertaining to Table 4 in the text.
(DOCX)

S5 Table. Model Summary for Experiment 1 –Additional statistical information pertaining to Table 7 in the text.
(DOCX)

S6 Table. Model Summary for Experiment 2 –Additional statistical information pertaining to Table 8 in the text.
(DOCX)

S7 Table. Model Summary for Experiment 3 –Additional statistical information pertaining to Table 9 in the text.
(DOCX)

S1 Text. Appendix (to Table 5)–Specific statistical analysis of the comparison between experiments 1 and 2. The constant ($M = 0.711$, $SED = 0.117$, $p < .001$), pre-speech interval ($M = 0.980$, $SED = 0.306$, $p < .01$) and group ($M = -0.305$, $SED = 0.113$, $p < .01$) were all lower than in the *immediate* condition, even after Bonferroni correction (sig. $p < 0.0125$). The interaction did not differ significantly ($M = -0.642$, $SED = 0.427$, $p = .133$).
(DOCX)

S2 Text. Appendix (to Table 6)–Specific statistical analysis of the comparison between experiments 1 and 3. The constant ($M = 0.617$, $SED = 0.133$, $p < .001$) and pre-speech interval ($M = 2.295$, $SED = 0.356$, $p < .001$) were significantly smaller than in the first experiment, while group ($M = -0.302$, $SED = 0.126$, $p = .0167$) and the group-interval interaction ($M = -1.059$, $SED = 0.503$, $p = .035$) were marginally non-significant after Bonferroni correction (sig. $p < 0.0125$)
(DOCX)

S3 Text. Appendix (to Table 10A–10D)–Significance of reaction time with pulse condition and trial. As a side note, one significant value was unexpected–the correlation between State and Trial in the first experiment. This implies that there were more late stimulation states in the later trials, on average. However, due to the random order of presentation and the significant correlations between Reaction Time and both Pulse Condition and Trial, we felt that this did not impact the study adversely.
(DOCX)

Acknowledgments

The authors would like to express thanks to all the participants who attended this study, as well as the staff at Kasseler Stottertherapie.

Author Contributions

Conceptualization: Sina Hommel, Nicole E. Neef, Walter Paulus, Martin Sommer.

Data curation: Alexander Whillier, Sina Hommel.

Formal analysis: Alexander Whillier.

Funding acquisition: Alexander Wolff von Gudenberg, Walter Paulus, Martin Sommer.

Investigation: Alexander Whillier, Sina Hommel.

Methodology: Sina Hommel, Nicole E. Neef, Martin Sommer.

Project administration: Martin Sommer.

Resources: Martin Sommer.

Software: Alexander Whillier.

Supervision: Nicole E. Neef, Alexander Wolff von Gudenberg, Walter Paulus, Martin Sommer.

Validation: Alexander Whillier, Nicole E. Neef, Walter Paulus, Martin Sommer.

Visualization: Alexander Whillier, Sina Hommel.

Writing – original draft: Alexander Whillier, Sina Hommel.

Writing – review & editing: Alexander Whillier, Sina Hommel, Nicole E. Neef, Alexander Wolff von Gudenberg, Walter Paulus, Martin Sommer.

References

1. American Psychiatric Association. Diagnostic and statistical manual of mental disorders. 5th edition ed. Washington, D.C.: American Psychiatric Association; 2013.
2. Gordon N. Stuttering: incidence and causes. Dev Med Child Neurol. 2002; 44(4):278–81. PMID: 11995897
3. Reilly S, Onslow M, Packman A, Cini E, Conway L, Ukoumunne OC, et al. Natural history of stuttering to 4 years of age: a prospective community-based study. Pediatrics. 2013; 132(3):460–7. https://doi.org/10.1542/peds.2012-3067 PMID: 23979093.
4. Bloodstein O, Ratner BN. A Handbook on Stuttering. 6 ed. Canada: Delmar Thomson Learning; 2008.
5. Sommer M, Koch MA, Paulus W, Weiller C, Buchel C. Disconnection of speech-relevant brain areas in persistent developmental stuttering. Lancet. 2002; 360(9330):380–3. https://doi.org/10.1016/S0140-6736(02)09610-1 PMID: 12241779.
6. Watkins KE, Smith SM, Davis S, Howell P. Structural and functional abnormalities of the motor system in developmental stuttering. Brain. 2008; 131(Pt 1):50–9. https://doi.org/10.1093/brain/awm241 PMID: 17928317.
7. Kell CA, Neumann K, von Kriegstein K, Posenenske C, von Gudenberg AW, Euler H, et al. How the brain repairs stuttering. Brain. 2009; 132(Pt 10):2747–60. Epub 2009/08/28. doi: awp185 [pii] https://doi.org/10.1093/brain/awp185 PMID: 19710179.
8. Cai S, Tourville JA, Beal DS, Perkell JS, Guenther FH, Ghosh SS. Diffusion imaging of cerebral white matter in persons who stutter: evidence for network-level anomalies. Front Hum Neurosci. 2014; 8:54. https://doi.org/10.3389/fnhum.2014.00054 PMID: 24611042
9. Neef NE, Anwander A, Friederici AD. The Neurobiological Grounding of Persistent Stuttering: from Structure to Function. Curr Neurol Neurosci Rep. 2015; 15(9):63. https://doi.org/10.1007/s11910-015-0579-4 PMID: 26228377
10. Chang SE, Horwitz B, Ostuni J, Reynolds R, Ludlow CL. Evidence of Left Inferior Frontal-Premotor Structural and Functional Connectivity Deficits in Adults Who Stutter. Cereb Cortex. 2011:18. https://doi.org/10.1093/cercor/bhr028 PMID: 21471556.
11. Chang SE, Zhu DC. Neural network connectivity differences in children who stutter. Brain. 2013; 136(Pt 12):3709–26. https://doi.org/10.1093/brain/awt275 PMID: 24131593.

12. Neef NE, Butfering C, Anwander A, Friederici AD, Paulus W, Sommer M. Left posterior-dorsal area 44 couples with parietal areas to promote speech fluency, while right area 44 activity promotes the stopping of motor responses. Neuroimage. 2016; 142:628–644. https://doi.org/10.1016/j.neuroimage.2016.08.030 Epub Aug 16. PMID: 27542724
13. Chang SE, Erickson KI, Ambrose NG, Hasegawa-Johnson MA, Ludlow CL. Brain anatomy differences in childhood stuttering. NeuroImage. 2008; 39(3):1333–44. https://doi.org/10.1016/j.neuroimage.2007.09.067 PMID: 18023366.
14. Brown S, Ingham RJ, Ingham JC, Laird AR, Fox PT. Stuttered and fluent speech production: an ALE meta-analysis of functional neuroimaging studies. Hum Brain Mapp. 2005; 25(1):105–17. https://doi.org/10.1002/hbm.20140 PMID: 15846815.
15. Stinear CM, Coxon JP, Byblow WD. Primary motor cortex and movement prevention: where Stop meets Go. Neurosci Biobehav Rev. 2009; 33(5):662–73. https://doi.org/10.1016/j.neubiorev.2008.08.013 Epub Aug 26. PMID: 18789963
16. Michelet T, Duncan GH, Cisek P. Response competition in the primary motor cortex: corticospinal excitability reflects response replacement during simple decisions. J Neurophysiol. 2010; 104(1):119–27. https://doi.org/10.1152/jn.00819.2009 Epub 2010 May 5. PMID: 20445034
17. Markett S, Bleek B, Reuter M, Pruss H, Richardt K, Muller T, et al. Impaired motor inhibition in adults who stutter—evidence from speech-free stop-signal reaction time tasks. Neuropsychologia. 2016; 91:444–450. https://doi.org/10.1016/j.neuropsychologia.2016.09.008 Epub Sep 13. PMID: 27619005
18. Busan P, D'Ausilio A, Borelli M, Monti F, Pelamatti G, Pizzolato G, et al. Motor excitability evaluation in developmental stuttering: a transcranial magnetic stimulation study. Cortex. 2013; 49(3):781–92. https://doi.org/10.1016/j.cortex.2011.12.002 PMID: 22225881.
19. Neef NE, Jung K, Rothkegel H, Pollok B, von Gudenberg AW, Paulus W, et al. Right-shift for non-speech motor processing in adults who stutter. Cortex. 2011; 47(8):945–54. Epub Epub 2010 Jun 30. https://doi.org/10.1016/j.cortex.2010.06.007 PMID: 20822768
20. Busan P, Battaglini PP, Sommer M. Transcranial magnetic stimulation in developmental stuttering: Relations with previous neurophysiological research and future perspectives. Clin Neurophysiol. 2017; 128(6):952–64. https://doi.org/10.1016/j.clinph.2017.03.039 Epub Apr 3. PMID: 28431323
21. Sommer M, Alfaro A, Rummel M, Speck S, Lang N, Tings T, et al. Half sine, monophasic and biphasic transcranial magnetic stimulation of the human motor cortex. Clin Neurophysiol. 2006; 117:838–44. https://doi.org/10.1016/j.clinph.2005.10.029 PMID: 16495145
22. Salvador R, Silva S, Basser PJ, Miranda PC. Determining which mechanisms lead to activation in the motor cortex: a modeling study of transcranial magnetic stimulation using realistic stimulus waveforms and sulcal geometry. Clin Neurophysiol. 2011; 122(4):748–58. https://doi.org/10.1016/j.clinph.2010.09.022 PMID: 21035390.
23. Neef NE, Paulus W, Neef A, Wolff von Gudenberg A, Sommer M. Reduced intracortical inhibition and facilitation in the primary motor tongue representation of adults who stutter. Clin Neurophysiol. 2011; 122:1802–11. https://doi.org/10.1016/j.clinph.2011.02.003 PMID: 21377925
24. Neef NE, Hoang TN, Neef A, Paulus W, Sommer M. Speech dynamics are coded in the left motor cortex in fluent speakers but not in adults who stutter. Brain. 2015; 15(138):712–25.
25. Bosshardt HG. Cognitive processing load as a determinant of stuttering: summary of a research programme. Clin Linguist Phon. 2006; 20(5):371–85. https://doi.org/10.1080/02699200500074321 PMID: 16728334
26. Bajaj A. Working memory involvement in stuttering: exploring the evidence and research implications. J Fluency Disord. 2007; 32(3):218–38. https://doi.org/10.1016/j.jfludis.2007.03.002 PMID: 17825670.
27. Buchel C, Sommer M. What causes stuttering? PLoS Biol. 2004; 2(2):159–63.
28. Reich A, Till J, Goldsmith H. Laryngeal and manual reaction times of stuttering and nonstuttering adults. J Speech Hear Res. 1981; 24(2):192–6. PMID: 7265933
29. Maassen B. In: Maassen B, Kent R, Peters H, van Lieshout P, Hulstijn W, editors. Speech motor control in normal and disordered speech. 1 ed. Oxford: University of Oxford Press; 2004.
30. Riley GD. The Stuttering Severity Instrument for Children and Adults- Third Edition (SSI-3). Austin, TX: Pro-Ed.; 1994.
31. Sandrieser P, Schneider P. Stottern im Kindesalter. 3 ed. Stuttgart: Thieme; 2008.
32. Keel JC, Smith MJ, Wassermann EM. A safety screening questionnaire for transcranial magnetic stimulation. Clin Neurophysiol. 2001; 112(4):720. PMID: 11332408.
33. Rodel RM, Laskawi R, Markus H. Tongue representation in the lateral cortical motor region of the human brain as assessed by transcranial magnetic stimulation. Ann Otol Rhinol Laryngol. 2003; 112 (1):71–6. Epub 2003/01/23. https://doi.org/10.1177/000348940311200114 PMID: 12537062.

34. Kaneko K, Kawai S, Fuchigami Y, Morita H, Ofuji A. The effect of current direction induced by transcranial magnetic stimulation on the corticospinal excitability in human brain. Electroencephalogr Clin Neurophysiol. 1996; 101(6):478–82. PMID: 9020819

35. Di Lazzaro V, Oliviero A, Pilato F, Saturno E, Dileone M, Mazzone P, et al. The physiological basis of transcranial motor cortex stimulation in conscious humans. Clin Neurophysiol. 2004; 115(2):255–66. PMID: 14744565

36. Muellbacher W, Boroojerdi B, Ziemann U, Hallett M. Analogous corticocortical inhibition and facilitation in ipsilateral and contralateral human motor cortex representations of the tongue. J Clin Neurophysiol. 2001; 18(6):550–8. Epub 2002/01/10. PMID: 11779968.

37. Svensson P, Miles TS, McKay D, Ridding MC. Suppression of motor evoked potentials in a hand muscle following prolonged painful stimulation. Eur J Pain. 2003; 7(1):55–62. PMID: 12527318

38. Allen P, Bennett K. PASW Statistics by SPSS: A practical guide, version 18. Melbourne: Cengage Learning; 2010.

39. Colebatch JG. Bereitschaftspotential and movement-related potentials: origin, significance, and application in disorders of human movement. Mov Disord. 2007; 22(5):601–10. https://doi.org/10.1002/mds.21323 PMID: 17260337

40. Manenti R, Brambilla M, Benussi A, Rosini S, Cobelli C, Ferrari C, et al. Mild cognitive impairment in Parkinson's disease is improved by transcranial direct current stimulation combined with physical therapy. Mov Disord. 2016; 31(5):715–24. https://doi.org/10.1002/mds.26561 Epub 2016 Feb 16. PMID: 26880536

41. van der Salm SM, Tijssen MA, Koelman JH, van Rootselaar AF. The bereitschaftspotential in jerky movement disorders. J Neurol Neurosurg Psychiatry. 2012; 83(12):1162–7. https://doi.org/10.1136/jnnp-2012-303081 Epub 2012 Sep 5. PMID: 22952323

42. Reilly J, Donaher J. Verbal working memory skills of children who stutter. Contemporary issues in communication science and disorders. 32: National Student Speech Language Hearing Association; 2005. p. 38–42.

43. Blomgren M, Roy N, Callister T, Merrill RM. Intensive stuttering modification therapy: a multidimensional assessment of treatment outcomes. J Speech Lang Hear Res. 2005; 48(3):509–23. https://doi.org/10.1044/1092-4388(2005/035) PMID: 16197269

44. Euler HA, Gudenberg AWv, Jung K, Neumann K. Computergestützte Therapie bei Redeflussstörungen: Die langfristige Wirksamkeit der Kasseler Stottertherapie. Sprache, Stimme, Gehör. 2009; 33(4):193–97.

45. Euler HA, Lange BP, Schroeder S, Neumann K. The effectiveness of stuttering treatments in Germany. J Fluency Disord. 2014; 39:1–11. https://doi.org/10.1016/j.jfludis.2014.01.002 Epub Jan 27. PMID: 24759189

46. Antal A, Paulus W. Transcranial alternating current stimulation (tACS). Front Hum Neurosci. 2013; 7:317. https://doi.org/10.3389/fnhum.2013.00317 Print 2013. PMID: 23825454

47. Wood H. Can tDCS enhance the benefits of physical therapy in patients with PD? Nature Reviews Neurology. 2016; 12:126. https://doi.org/10.1038/nrneurol.2016.24

7.0.0 Discussion of the Papers and the Broader Context

In all studies presented, this thesis identifies characteristics which both unite PWS and also characteristics which differentiate them. The anticipation studies (especially Paper 2) have demonstrated a novel method in PWS by which we can connect their conscious awareness of their stuttering with the stuttering itself. This has broad reaching implications in speech therapy and psycholinguistic research, as well as supporting the notion of stuttering as more than a single disorder. Similarly, the final paper (chapter 6) identifies the existence of a speech preparation programme in PNS that is distinctly lacking in some PWS. This is an ideal place to start in the examination of stuttering as a multimodal disorder.

The second main theme of this thesis is the need for a shift in diagnostic understanding of stuttering – specifically, to a prescriptive, rather than descriptive, understanding of stuttering. As previously identified by our lab (Neef et al., 2016) and supported in the final paper (chapter 6), there is clear evidence that stuttering belies a chronic neurophysiological aberration that extends beyond the individual utterance. To better identify and understand the various forms of stuttering, it is necessary to recognise the neurophyisological underpinnings and be able to categorise them.

One method of active neural exploration that can be effective in this field is non-invasive stimulation. As mentioned at the end of the final paper (chapter 6), noninvasive transcranial brain simulation is a growing area of research being applied in the treatment of neurodegenerative diseases such as Parkinson's Disease (e.g. Manenti et al., 2016; Wood, 2016). Over the past two decades, numerous studies have employed Deep Brain Stimulation (DBS) and Transcranial Magnetic Stimulation (TMS) to investigate pathophysiological processes in the human brain (e.g. Hallett, 2000; Nitsche & Paulus, 2000 & 2001; Siebner & Rothwell, 2003; Kringelbach et al., 2010; Stagg & Nitsche, 2011). This research has paved the way for investigating the potential therapeutic benefit of neurostimulation techniques in various neurological disorders, such as stuttering, Parkinson's disease, stroke and depression (Nitsche et al., 2009, Nitsche and Paulus, 2009). There are two main categories of stimulation techniques employed in these studies – TMS and Transcranial Alternating/Direct Current Simulation (tACS/tDCS). Both categories have applications in stuttering research and both have potentially unrealised benefits when used to

augment stuttering therapy. As standard TMS has already been addressed in the third paper (chapter 6), a variant of TMS called static TMS (sTMS) will be discussed below, as well as tACS and tDCS.

Both tACS and tDCS are stimulation techniques which involve applying a weak electric current across the scalp. In tDCS, a unidirectional current is used – this modulates spontaneous neurological activity by hyperpolarising or depolarising the membrane (Nitsche & Paulus, 2000); in tACS, an alternating current is used which oscillates at a predefined frequency – this induces entrainment by interference and/or resonance across the neural circuit (Paulus, 2014). Both techniques have exhibited varying levels of success in motor learning (e.g. Reis et al, 2008, Cuypers et al., 2013; Fuerra et al., 2013), perception (e.g. Antal & Paulus, 2008; Antal & Paulus, 2013) and other neuromodulation paradigms. In a short and long term motor learning study, Reis et al. (2008) found that anodal tDCS across the motor cortex resulted in improved learning over three months – in the short term, learning speed increased and absolute learning level was higher during the motor task; in the long term, an equivalent rate of forgetting from the higher absolute level resulted in consistently higher retention rates at follow-up, out to three months. They (Reis et al., 2008) suggested that, following traumatic brain injury, their results supported the potential of tDCS to assist in motor rehabilitation. These techniques have similar potential in the speech motor rehabilitation, when employed in combination with traditional stuttering therapies that include motor retraining as a core component.

On a theoretical level, the same may be possible with tACS, albeit via different neurological mechanisms. By applying different oscillating electrical currents, tACS is able to influence cortical excitability (Antal et al., 2008) and improve (alpha frequencies) or inhibit (beta frequencies) motor performance (Antal & Paulus, 2013). In a recent pilot study conducted in our lab (Sommer, unpublished), we found a significant difference between signal latencies in PWS and PNS. Following on the concept of signal mismatch in stuttering suggested by both the DIVA (Tourville & Guenther, 2011) and Hickok (2012) models, it can be hypothesised that tACS could modulate the speech pathways in PWS, resulting in reduced stuttering tendencies during therapy and thereby enhancing the training process during therapy. As such, tACS could also potentially be

applied to enhance the motor learning outcomes in speech rehabilitation. Ethics approval for the application of tACS and tDCS in combination with stuttering therapy has already been sought by the doctoral candidate and the department.

In a study examining the efficacy of sTMS in humans (Oliviero et al., 2011), the authors demonstrated that static magnets can produce lasting after-effects on the human motor cortex. It was shown that sufficiently shown that sufficiently high intensity sTMS could manipulate excitability. Given the potential of stimulation to manipulate pre-speech facilitation, sTMS paired with traditional stuttering therapy has the potential to improve the neurological environment for more efficient and lasting therapeutic outcomes. Additionally, there are numerous potential stimulation sites (Broca's area, Wernicke's area, Supplementary Motor Area (SMA), Motor Cortex) and two poles (positive and negative) that can be manipulated from an experimental perspective. As above, ethics for this research has already been sought by the doctoral candidate and the department.

8.0.0 Conclusion

This thesis demonstrates the need for a shift to a prescriptive, rather than descriptive, understanding of stuttering. The various cortical and peripheral neurological causes influencing stuttering need to be better integrated in experimental examinations of stuttering in the future, as this has the ability to improve both understanding and therapeutic outcomes for patients. Further investigation in the field of concurrent stimulation and traditional stuttering therapy has the potential to both improve stuttering outcomes beyond current levels (estimated around 10-40% relapse rate, e.g. Euler 2014). Additionally, it would enable potential identification and categorisation of stuttering subtypes according to their areas of therapeutic activation. This would help to shift the focus of stuttering research to that of a prescriptive medical disorder.

9.0.0 References

Antal, A., & Paulus, W. (2013). Transcranial alternating current stimulation (tACS). *Frontiers in Human Neuroscience. 7*(317), 1-4. doi:10.3389/fnhum.2013.00317

Antal, A., & Paulus, W. (2008). Transcranial direct current stimulation and visual perception. *Perception. 37,* 367-374. doi:10.1068/p5872

Antipova, E.A., Purdy, S.C., Blakeley, M., & Williams, S. (2008). Effects of altered auditory feedback (AAF) on stuttering frequency during monologue speech production. *Journal of Fluency Disorders. 33*, 274-290.

Bloodstein, O. (1960). The development of stuttering: I. Changes in nine basic features. *Journal of Speech and Hearing Disorders, 25*, 219-237.

Bloodstein, O. & Ratner, N.B. (2008). *A handbook on stuttering. 6th edn*. Clifton Park, NY: Delmar Learning.

Blomgren, M., Roy, N., Callister, T., Merrill, R. M. (2005). Intensive stuttering modification therapy: A multidimensional assessment of treatment outcomes. *Journal of Speech, Language and Hearing. 48*, 509-523.

Brosch, S. & Pirsig, W. (2001). Stuttering in history and culture. *International Journal of Pediatric Otorhinolaryngology, 59(2)*, 81-87. doi:10.1016/S0165-5876(01)00474-8

Brown, S., Ingham, R.J., Ingham, J.C., Laird, A.R., Fox, P.T. (2005). Stuttered and fluent speech production: an ALE meta-analysis of functional neuroimaging studies. *Human Brain Mapping. 25*, 105-117.

Burke, B. D. (1975). Susceptibility to delayed auditory feedback and dependence on auditory or oral sensory feedback. *Journal of Communication Disorders, 8*(1), 75-96. doi: 10.1016/0021-9924(75)90028-3

Cai, S., Tourville, J.A., Beal, D.S., Perkell, J.S., Guenther, F.H. & Ghosh, S.S. (2014). Diffusion imaging of cerebral white matter in persons who stutter: evidence for network-level anomalies. *Frontiers in Human Neurology, 8*, 54. doi: 10.3389/fnhum.2014.00054

Chang, S.E., Erickson, K.I., Ambrose, N.G., Hasegawa-Johnson, M.A. & Ludlow, C.L. (2008). Brain anatomy differences in childhood stuttering. *Neuroimaging, 39*, 1333.

Chang, S.E., Horwitz, B., Ostuni, J., Reynolds, R. & Ludlow, C.L. (2011). Evidence of left inferior frontal–premotor structural and functional connectivity deficits in adults who stutter. *Cerebral Cortex, 21*, 2507–2518. doi: 10.1093/cercor/bhr028.

Chang, S.E. & Zhu, D.C. (2013). Neural network connectivity differences in children who stutter. *Brain, 136*, 3709–3726. doi: 10.1093/brain/awt275

Cholin, J., Heiler, S., Whillier, A., & Sommer, M. (2016). Premonitory Awareness in Stuttering Scale (PAiS). *Journal of Fluency Disorders, 46*, 40-50. doi: 10.1016/j.jfludis.2016.07.001

Chon, H., Kraft, S.J., Zhang, J., Loucks, T., & Ambrose, N.G. (2013). Individual variability in delayed auditory feedback effects on speech fluency and rate in normally fluent adults. *Journal of Speech Language and Hearing Research. 56*, 489-504.

Chow, H. M. & Chang, S. E. (2017). White matter developmental trajectories associated with persistence and recovery of childhood stuttering. *Human Brain Mapping, in press.* doi: 10.1002/hbm.23590

Cuypers, K., Leenus, D. J. F., van den Berg, F. E., Nitsche, M. A., Thijs, H., Wenderoth, N., Meesen, R. L. J. (2013). Is motor learning mediated by tDCS intensity? *PLOS ONE. 8*(6), 1-4. doi:10.1371/journal.pone.0067344

DSM: Diagnostic and Statistical Manual of Mental Disorders, Fifth Edition. (2013). Edited by American Psychiatric Association. doi:10.1176/appi.books.9780890425596

Euler, H. A., Lange, B. P., Schroeder, S., Neumann, K. (2014). The effectiveness of stuttering treatments in Germany. *Journal of Fluency Disorders. 39,* 1-11. doi:10.1016/j.jfludis.2014.01.002

Fox, P.T., Ingham, R.J., Ingham, J.C., Hirsch, T.B., Downs, J.H., & Martin, C. (1996). A PET study of the neural systems of stuttering. *Nature. 382,* 158-161.

Feurra, M., Pasqualetti, P., Bianco, G., Santarnecchi, E., Rossi, A., & Rossi, S. (2013). State-Dependent Effects of Transcranial Oscillatory Currents on the Motor System: What You Think Matters. *The Journal of Neuroscience. 33,* 17483–17489. doi:10.1523/jneurosci.1414-13.2013

Giraud, A.L., Neumann, K., Bachoud-Levi, A.C., von Gudenberg, A.W., Euler, H.A., Lanfermann, H., & Preibisch, C. (2008). Severity of dysfluency correlates with basal ganglia activity in persistent developmental stuttering. *Journal of Brain and Language. 104*, 190-199.

Hallett, M. (2000). Transcranial magnetic stimulation and the human brain. *Nature, 406*(4792), 147-150. doi: 10.1038/35018000

Hickok, G. (2012). Computational neuroanatomy of speech production. *Nature Reviews. 13,* 135-145.

Iverach, L., & Rapee, R. M. (2014). Social anxiety disorder and stuttering: Current status and future directions. *Journal of Fluency Disorders. 40*, 69-82.

Jiang, J., Lu, C., Peng, D., Zhu, C. & Howell, P. (2012). Classification of types of stuttering symptoms based on brain activity. *PlosONE, 7*(6), 1-11. doi: 10.1371/journal.pone.0039747

Johnson, W. & Knott, J. R. (1937). Studies in the psychology of stuttering I: The distribution of moments of stuttering in successive readings of the same material. *Journal of Speech Disorders, 2*, 17-19.

Kaspar, K. & Rübeling, H. (2011). Rhythmic versus phonemic interference in delayed auditory feedback. *Journal of speech, language and hearing research, 54*(3), 932-943. doi: 10.1044/1092-4388(2010/10-0109).

Kell, C.A., Neumann, K., von Kriegstein, K., Posenenske, C., von Gudenberg, A.W., Euler, H. & Giraud, A.I. (2009). How the brain repairs stuttering. *Brain, 132*, 2747-2760. doi: 10.1093/brain/awp185.

Kringelbach, M.L., Green, A.L., Owen, S.L., Schweder, P.M. & Aziz, T.Z. (2010). Sing the mind electric – principles of deep brain stimulation. *European Journal of Neuroscience, 32*, 1070–1079. doi:10.1111/j.1460-9568.2010.07419.x

Lametti, D.R., Nasir, S.M., & Ostry, D.J. (2012). Sensory preference in speech production revealed by simultaneous alteration of auditory and somatosensory feedback. *Journal of Neuroscience, 32*, 9351-9358.

Lind, A., Hall, L., Breidegard, B., Balkenius, C. & Johansson, P. (2014). Auditory feedback of one's own voice is used for high-level semantic monitoring: the "self-comprehension" hypothesis. *Frontiers in Human Neuroscience, 8*, 166. doi: 10.3389/fnhum.2014.00166

Maguire, G. A., Yeh, C. Y., & Ito, B. S. (2012). Overview of the Diagnosis and Treatment of Stuttering. *Journal of Experimental & Clinical Medicine. 4(2),* 92–97.

Manenti, R., Brambilla, M., Benussi, A., Rosini, S., Cobelli, C., Ferrari, C., Petesi, M., Orizio, I., Padovani, A., Borroni, B. & Cotelli, M. (2016). Mild cognitive impairment in Parkinson's Disease is improved by transcranial direct current stimulation combined with physical therapy. *Movement Disorders, 31*(5), 715-724. doi: 10.1002/mds.265 61

Martin, R.R., Johnson, L.J., Siegel, G.M., & Haroldson, S.K. (1985). Auditory stimulation, rhythm, and stuttering. *Journal of Speech and Hearing Research. 28,* 487-95.

Milisen, R. (1938). Frequency of stuttering with anticipation of stuttering controlled. *Journal of Speech Disorders, 3,* 207-214.

Neef, N.E., Anwander, A. & Friederici AD. (2015a). The neurobiological grounding of persistent stuttering: From structure to function. *Current Neurology and Neuroscience Reports, 15*(9), 63. doi:10.1007/s11910-015-0579-4

Neef, N.E., Bütfering, C., Anwander, A., Friederici, A.D., Paulus, W. & Sommer, M. (2016). Left posterior-dorsal area 44 couples with parietal areas to promote speech fluency while right area 44 activity promotes the stopping of motor responses. *Neuroimaging, 142,* 628-644. doi: 10.1016/j.neuroimage.2016.08.030

Neef, N.E., Linh Hoang, T.N., Neef, A., Paulus, W. & Sommer, M. (2015b). Speech dynamics are coded in the left motor cortex in fluent speakers but not in adults who stutter. *Brain, 138*(3), 712-725. doi: 10.1093/brain/awu390

Nitsche, M.A., Kuo, M.F., Karrasch, R., Wachter, B. Liebetanz, D. & Paulus, W. (2009). Serotonin affects transcranial direct current-induced neuroplasticity in humans. *Biological Psychiatry, 66*(5), 503-508. doi: 10.1016/j.biopsych.2009.03.022

Nitsche, M., & Paulus, W. (2000). Excitability changes induced in the human motor cortex by weak transcranial direct current stimulation. *Journal of Physiology, 527*(3), 633-639. doi: 10.1111/j.1469-7793.2000.t01-1-00633.x

Nitsche, M., & Paulus, W. (2001). Sustained excitability elevations induced by transcranial DC motor cortex stimulation in humans. *Neurology, 57*(10), 1899-1901.

Nitsche, M., & Paulus, W. (2009). Noninvasive brain stimulation protocols in the treatment of epilepsy: current state and perspectives. *Neurotherapeutics: the journal of the American Society for Experimental NeuroTherapeutics, 6,* 244-250.

Oliviero, A., Mordillo-Mateos, L., Arias, P., Panyavin, I., Foffani, G. & Aguilar, J. (2011). Transcranial static magnetic field stimulation of the human motor cortex. *Physiology, 589,* 4949-4958.

Packman, A. (2012). Theory and therapy in stuttering: A complex relationship. *Journal of Fluency Disorders, 37*(4), 225-233. doi: 10.1016/j.jfludis.2012.05.004

Paulus, W. (2014). Transcranial brain stimulation: potential and limitations. *e-Neuroforum*.

Ratynska, J., Szkielkowska, A., Markowska, R., Kurkowski, M., Mularzuk, M., & Skarzynski, H. (2012). Immediate speech fluency improvement after application of the digital speech aid in stuttering patients. *Medical Science Monitor, 18,* CR9-12.

Reis, J., Schambral, H. M., Cohen, L. G., Buch, E. R., Fritsch, B., Zarahn, E., Celnik, P. A., & Krakauer, J. W. (2008). Noninvasive cortical stimulation enhances motor skill acquisition over multiple days through an effect on consolidation. *Proceedings of the National Academy of Sciences. 106(5),* 1590-1595.

Ringo, C. C., & Dietrich, S., (1995). Neurogenic stuttering: An analysis of critique. *Journal of Medical Speech-Language Pathology. 2*, 111-122.

Siebner, H.R. & Rothwell, J. (2003). Transcranial magnetic stimulation: New insights into representational cortical plasticity. *Experimental Brain Research, 148,* 1-16.

Sommer, M., Koch, M.A., Paulus, W., Weiller, C. & Büchel, C. (2002). Disconnection of speech-relevant brain areas in persistent developmental stuttering. *Lancet,* 360, 380–383.

Stagg, C.J., Nitsche, M.A. (2011). Physiological basis of transcranial direct current stimulation. *Neuroscientist, 17*, 37-53.

Stinear, C.M., Coxon, J.P. & Byblow, W.D. (2009). Primary motor cortex and movement prevention: Where stop meets go. *Neuroscience and Biobehavioural Reviews, 33,* 662-673.

Tourville, J.A. & Guenther, F.H. (2011). The DIVA model: A neural theory of speech acquisition and production. *Language and Cognitive Processes, 26*(7), 952-981. doi: 10.1080/01690960903498424

Unger, J.P., Gluck, C.W., & Cholewa, J. (2012). Immediate effects of AAF devices on the characteristics of stuttering: a clinical analysis. *Fluency Disorders. 37*, 122-34.

Van Riper, C. (1978). *Speech correction: Principles and methods (6th ed.)*. Englewood Cliffs, NJ: Prentice-Hall.

Watkins, K.E., Smith, S.M., Davis, S. & Howell, P. (2008). Structural and functional abnormalities of the motor system in developmental stuttering. *Brain, 131*, 50-59. doi: 10.1093/brain/awm241

Wood, H.J. (2016). Parkinson disease: Can tDCS enhance the benefits of physical therapy in patients with PD? *Neuroscience, 12*(3) 126. doi: 10.1038/nrneurol.2016.24

Yairi, E. (2007). Subtyping Stuttering I: A review. *Journal of Fluency Disorders, 32*(3), 165-196. doi: 10.1016/j.jfludis.2007.04.001

Yairi, E., & Ambrose, N., (2013). Epidemiology of stuttering: 21st century advances. *Journal of Fluency Disorders. 38*, 66-67.

Yairi, E. & Seery, C.H. (2011). Stuttering: Foundations and clinical applications. *Pearson Education*, Upper Saddle River.

10.0.0 Acknowledgements

First and foremost, I would like to thank my family for supporting and believing in me and giving me the motivation to perservere. In particular, my mother for the focussed and distraction-free environment that ensured success in my final weeks.

I am extremely grateful to Prof. Martin Sommer, for the opportunity to come to Germany and pursue my dream. He facilitated this whole experience, for which I am extremely thankful. By extension, I would like to thank Prof. Walter Paulus for first extending me the invitation to come to Göttingen and for providing the unique environment to complete this degree.

To Annika Primaßin, Sina Hommel, Sabrina Heiler, Giorgi Batsikadze, Ivan Alekseichuk, Zsolt Turi, Gabriel de Lara, Christine Nitsche, Manuel Hewitt, Anna Hackenfort-Leineweber, Nicole Neef, Christina Stier and all the staff members in the Klinische Neurophysiology department of the UMG along the way, whose help was incrementally instrumental in completion. Similarly, I would like to thank the UMG in general for the support provided during this time.

I would like to thank my thesis progress committee members Prof. Julia Fischer and Prof. Annekathrin Schacht for their inspiring presences and poignant insight at key points in my journey.

For her great kindness and personal support in a time of crisis, and her ongoing support over the last three years, I give my heartfelt thanks to Dr. Christina Schütte.

To Kirsten Pöhlker, Mandy Fricke and the whole team at the GGNB, I am extremely thankful for putting up with the dozens upon dozens of calls and emails to reach this point, and the support alongside it.

I would like to thank the Kasseler Stottertherapie (KST) for allowing me numerous opportunities to consult with staff and recruit participants from the ranks of their patients. In particular, I would like to thank Alexander Wolff von Gudenberg for his blessing and Birgit and Charlotte Schröck for assisting me in organising many of these days especially when I lacked the language skills to do so.

Finally I would like to thank the DFG and the UMG for the funding that made this possible.

11.0.0 Supplemental Material – List of Abbreviations

- PWS People with Stuttering
- PNS People with No Stuttering
- AWS Adults with Stuttering
- ANS Adults with No Stuttering
- DAF Delayed Auditory Feedback
- M1 Primary Motor Area
- SMA Supplementary Motor Area
- STG Superior Temporal Gyrus
- SMG SupraMarginal Gyrus
- fMRI functional Magnetic Resonance Imaging
- TMS Transcranial Magnetic Stimulation
- sTMS static Transcranial Magnetic Stimulation
- tACS transcranial Alternating Current Simulation
- tDCS transcranial Direct Current Simulation

Alexander Whillier

Dr. Rer. Nat. in *Neurophysiology*
Address: Lichtenbergstr. 15, 37075 Göttingen
Telephone: +49 157 513 50500
Email: alexanderwhillier@gmail.com
Gender: Male
Date of Birth: 8th May, 1986
Nationality: Australian

Professional Experience

04/2018-current **English Teacher**
Zentrale Einrichtung für Sprachen und Schlüsselqualifikationen (ZESS)
- Teaching intermediate and advanced scientific English classes
- Course preparation

05/2016-12/2016 **Grant Application Consultant**
ProSciencia Beratungs-GmbH (Dr. Christina Schütte)
- Consultation and liaison on large grants (above €5,000,000)
- Managing DFG and Volkswagen application processes
- Document preparation prior to submission

06/2014-03/2018 **Scientific Researcher**
Klinik für Klinische Neurophysiologie, UMG, Göttingen
- Human neurolinguistic research into stuttering
- Initiating research projects and running projects to completion
- Independently conducting research
- Writing ethics and grant applications

08/2013-03/2014 **Research Assistant**
Neuroscience Research Australia (NeuRA) (formerly POWMRI)
- Conduct supervised research on two motor coordination projects
- Manage lab resources and restocking

07/2006-11/2010 **Dance Instructor**
AusLatin Productions
- Salsa dance instruction to beginner and intermediate adult students

Education

08/2014-03/2018 **Dr. rer. nat. in Neurophysiology**
Georg August Universität, Göttingen
Title: Investigating the neural processes underpinning the production and anticipation of stuttering in Adults who Stutter

08/2012-06/2013 **Grad. Dip. Biomedical Engineering (Similar to MSc.)**
University of New South Wales, Australia

03/2011-10/2011 **B.Psych. (Honours)**
Curtin University, Australia

03/2005-10/2009 Combined **B.Sc. (Psychology) & B.A. (Japanese)**
The University of Sydney, Australia

Skills and Competences

Languages and Proficiencies

English	Native
German	Advanced (C1) – 4½ years living in Germany
Japanese	Intermediate (B2)

Software Skills

Office	Word, Excel, Access, Powerpoint (Expert)
Statistics	SPSS (Advanced); MATLAB (Intermediate)
Imaging	Adobe CS (Intermediate); Gimp (Intermediate)

Research Skills

Human testing	Child and adult neurostimulation and psychological studies
Statistics	Database management, research design, statistical analysis and interpretation
Document Prep	Human research ethics application preparation from start to finish
Project management	Defining goals with project partners and coordinating varied departments

Personal Skills

Communication	Excellent written and verbal communication skills, effectively shaping the message to fit the audience
Leadership	Leading a multi-disciplinary, inter-organisational research project
Critical thinking	Strong analytical skills, evaluating competing perspectives
Presentation	Numerous posters and lectures across the 5 years of research assistant work and during the doctorate

Interests

Sports	Acrobatics (12 years), Hockey (5 years)
Theatre	Comedy stage productions (2000-2012), Improvisation (3 years)

Further Experiences

2006-2014	Director (2006), Producer (2008) and various organisational roles for Science Revue, Sydney University and Computer Science Engineering Revue, University of New South Wales