MOTOR PREPARATION PRECEDING STUTTERED AND NONSTUTTERED SPEECH

by

RYAN DANIEL POLLARD

B.A., University of Northern Colorado, 2001

A dissertation submitted to the

Faculty of the Graduate School of the

University of Colorado in partial fulfillment

of the requirements for the degree of

Doctor of Philosophy

Departments of Speech, Language & Hearing Sciences and Neuroscience

2010

ProQuest LLC
789 East Eisenhower Parkway
P.O. Box 1346
Ann Arbor, MI 48106-1346

This dissertation entitled:
Motor Preparation Preceding Stuttered and Nonstuttered Speech
written by Ryan Daniel Pollard
has been approved for the Departments of Speech, Language & Hearing Sciences and Neuroscience

_____
(Phillip Gilley, Chair)

_____
(Peter Ramig)

_____
(Donald Finan)

_____
(Gail Ramsberger)

_____
(Albert Kim)

Date__04/09/10__

The final copy of this thesis has been examined by the signatories, and we find that both the content and the form meet acceptable presentation standards of scholarly work in the above mentioned disciplines.

HRC protocol # _____0508.2_____

Pollard, Ryan Daniel (Ph.D., Speech, Language & Hearing Sciences; Neuroscience)

Motor Preparation Preceding Stuttered and Nonstuttered Speech

Dissertation directed by Assistant Professor Phillip Gilley

Purpose: This dissertation examined the Bereitschaftspotential (BP), a movement-related cortical potential and robust electrophysiological correlate of motor behavior, just prior to stuttered and fluent speech production. The objective was to investigate whether stuttering is linked to atypical speech motor preparation.

Method: BP was recorded with a 64-channel electroencephalograph (EEG) in persons who stutter (PWS) and nonstuttering controls while they performed an oral reading task. Fluent and disfluent trials from each cohort were grouped together and independent component analysis (ICA) was used to remove unwanted components in the EEG related to speech and other artifact.

Results: Visual inspection of scalp topography and statistical measures of BP morphology revealed that motor preparation preceding stuttered and fluent speech differed between PWS and controls and within PWS based on fluency status.

Discussion: This investigation demonstrated the feasibility of utilizing EEG to directly examine the neurophysiological correlates of stuttered speech. Differences on measures of BP latency, slope, amplitude, and scalp location suggest that PWS may differentially recruit motor systems when preparing to speak. Results indicate that stuttered speech is prepared and/or executed less efficiently than fluent speech within PWS. More research is needed to elucidate whether PWS engage involuntary motor systems before moments of stuttering, and how the atypicality of BP preceding

disfluencies might be viewed in the light of recent etiological theories postulating distinct premotor systems for stuttered and fluent speech.

Keywords: stuttering, Bereitschaftspotential, electroencephalography, event-related potentials, neuroimaging, speech production, independent component analysis

Acknowledgements

I have never been known for pithiness (which is ironic for a stutterer, incidentally), but I'll try to keep this short. For the completion of this dissertation, I would like to thank my three, very helpful and accommodating advisors during different periods of my doctoral program: Peter Ramig, Don Finan, and Phillip Gilley. For the completion of the clinical portion of my graduate studies—a feat possibly even more hard-won than this dissertation—I am indebted to Barb Miller, Graduate Program Assistant extraordinaire, and gratefully acknowledge my excellent clinical supervisors during my time at CU. For the sustainment of my equanimity and, often, my sanity over the past several years as I have worked toward this point, I have been lucky to receive the love and support of the best girlfriend and then wife that a man could hope for. Thank you, Erin, for being there at the beginning and for still standing now at the end of all this.

I would also like to extend my gratitude to Anu Sharma for use of her Brain and Behavior laboratory, as well as the quite knowledgeable lab members, particularly Amy Nash and Julia Campbell, who never failed to give generously of their time and expertise when I came knocking with a hangdog look. My thanks as well to the two other members of my dissertation committee, Gail Ramsberger and Al Kim. Finally, I gratefully acknowledge the Stuttering Foundation for providing financial support during the first four years of my doctoral program through the Malcolm Fraser Foundation fellowship.

Table of Contents

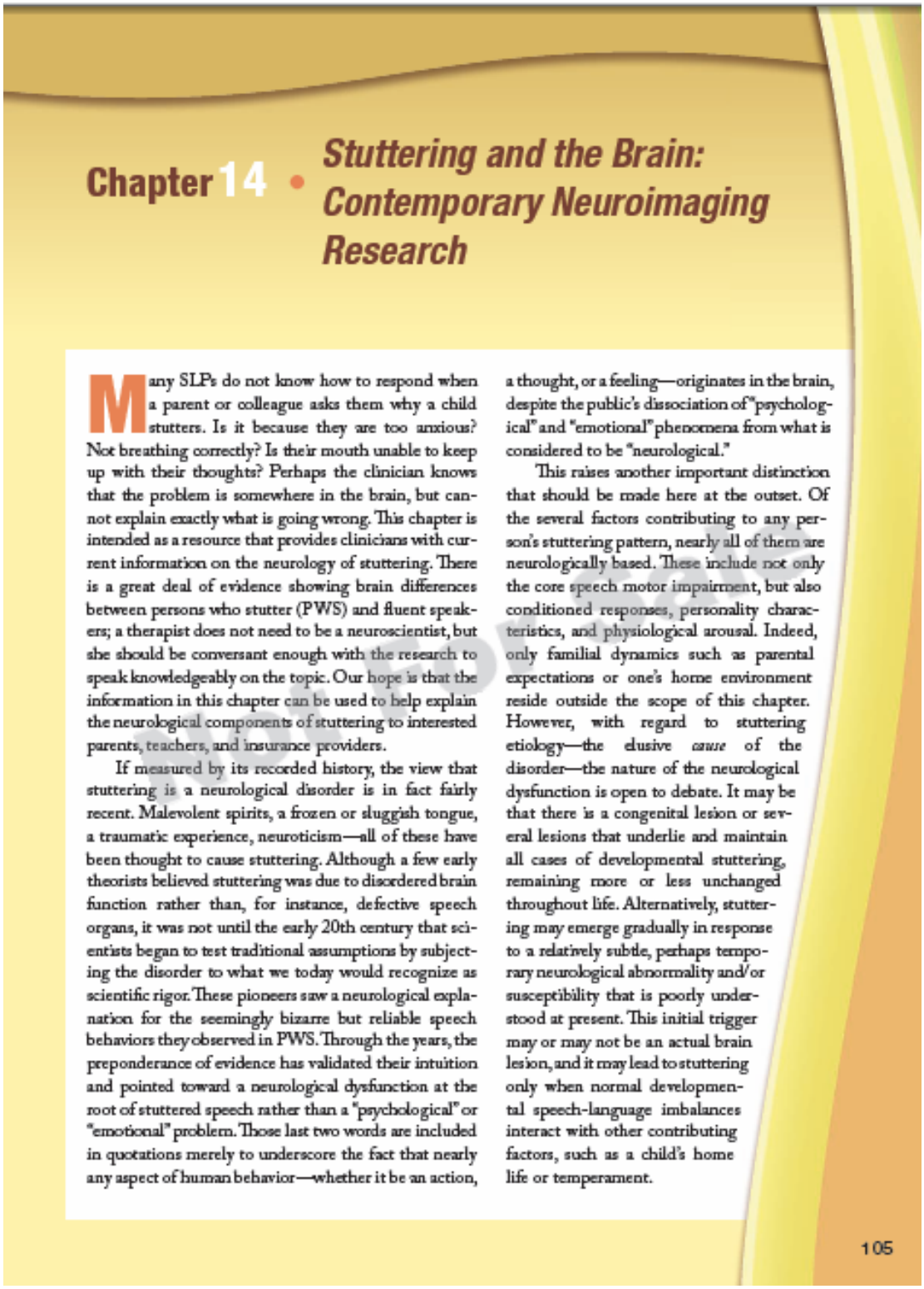
List of Tables

List of Figures

INTRODUCTION

This dissertation examines neurophysiological correlates of stuttering through various lenses. Chapter one is an extensive review and synthesis of the neuroimaging literature on stuttering. It appeared in an applied book about stuttering therapy and was intended as a resource for clinicians and graduate students who wish to better understand the neurological components of stuttering and explain them to interested clients, parents, teachers, or insurance providers. Chapter two describes a research project that examined electrophysiological correlates of motor preparation before stuttered and fluent speech. The purpose of the experiment was to investigate whether stuttering is associated with atypical activity in cortical motor preparation areas just prior to onset of speech.

CHAPTER ONE



Chapter 14 • Stuttering and the Brain: Contemporary Neuroimaging Research

Many SLPs do not know how to respond when a parent or colleague asks them why a child stutters. Is it because they are too anxious? Not breathing correctly? Is their mouth unable to keep up with their thoughts? Perhaps the clinician knows that the problem is somewhere in the brain, but cannot explain exactly what is going wrong. This chapter is intended as a resource that provides clinicians with current information on the neurology of stuttering. There is a great deal of evidence showing brain differences between persons who stutter (PWS) and fluent speakers; a therapist does not need to be a neuroscientist, but she should be conversant enough with the research to speak knowledgeably on the topic. Our hope is that the information in this chapter can be used to help explain the neurological components of stuttering to interested parents, teachers, and insurance providers.

If measured by its recorded history, the view that stuttering is a neurological disorder is in fact fairly recent. Malevolent spirits, a frozen or sluggish tongue, a traumatic experience, neuroticism—all of these have been thought to cause stuttering. Although a few early theorists believed stuttering was due to disordered brain function rather than, for instance, defective speech organs, it was not until the early 20th century that scientists began to test traditional assumptions by subjecting the disorder to what we today would recognize as scientific rigor. These pioneers saw a neurological explanation for the seemingly bizarre but reliable speech behaviors they observed in PWS. Through the years, the preponderance of evidence has validated their intuition and pointed toward a neurological dysfunction at the root of stuttered speech rather than a "psychological" or "emotional" problem. Those last two words are included in quotations merely to underscore the fact that nearly any aspect of human behavior—whether it be an action, a thought, or a feeling—originates in the brain, despite the public's dissociation of "psychological" and "emotional" phenomena from what is considered to be "neurological."

This raises another important distinction that should be made here at the outset. Of the several factors contributing to any person's stuttering pattern, nearly all of them are neurologically based. These include not only the core speech motor impairment, but also conditioned responses, personality characteristics, and physiological arousal. Indeed, only familial dynamics such as parental expectations or one's home environment reside outside the scope of this chapter. However, with regard to stuttering etiology—the elusive *cause* of the disorder—the nature of the neurological dysfunction is open to debate. It may be that there is a congenital lesion or several lesions that underlie and maintain all cases of developmental stuttering, remaining more or less unchanged throughout life. Alternatively, stuttering may emerge gradually in response to a relatively subtle, perhaps temporary neurological abnormality and/or susceptibility that is poorly understood at present. This initial trigger may or may not be an actual brain lesion, and it may lead to stuttering only when normal developmental speech-language imbalances interact with other contributing factors, such as a child's home life or temperament.

105

Important Caveat on the Child Versus Adult Brain

It is important to bear in mind that nearly all of the experiments covered in this chapter focused on adult subjects rather than children. This is the norm because, although neurological research on children who stutter is sorely needed, it is a relatively difficult undertaking fraught with obstacles. Some older children become uneasy in the brain scanning setting or cannot be kept still long enough to obtain clean data, while imaging younger, preschool-age children can be challenging without sedation, which introduces its own problems. It can also be difficult to locate enough child subjects who pass stringent inclusion criteria, such as the absence of co-occurring speech or behavioral deficits besides stuttering. In addition, larger sample sizes are typically required for studies involving children because their brain structures are more variable than adults' due to ongoing brain development during childhood.

Because little neuroimaging work has examined children, researchers remain uncertain whether their results can be applied to that population or whether the brains of children who stutter are fundamentally different from their adult counterparts. We know that the brain has a remarkable ability to change and adapt over time through experience and learning, a process called **neuroplasticity**. This term refers to both short-term changes (lasting hours) that alter the effectiveness of a synapse, and long-term effects (lasting days) that may eventually result in permanent anatomical changes. These lasting changes often involve pruning existing connections or growing new connections between neurons. Neuroplasticity can be adaptive, for instance when one area of the brain takes over for another area that has been

damaged, but it can also be maladaptive, as with certain types of synaptic alterations that result from prolonged drug addiction. To date, it is still unclear if neurological differences measured in stuttering adults are present at onset or are the result of maladaptive neuroplasticity caused by years of coping with the disorder.

NEUROIMAGING AND STUTTERING

Over roughly the past two decades, advances in neuroimaging and genetic marking techniques have finally allowed scientists to delve into the underpinnings of stuttering by studying the nervous system at the molecular, cellular, and systems levels. Along with using improved DNA analysis methods to pinpoint candidate genes for stuttering, scientists can now probe speech-relevant areas in detail using powerful technologies previously unavailable to them.

This chapter will focus mainly on contemporary neuroimaging research. **Neuroimaging** is a collective term for a family of techniques that either (a) record brain activity by exploiting changes in blood flow, cellular metabolism, or electrical activity accompanying neural processing, or (b) provide high-resolution images of the brain. This is exciting research, as it establishes a strong base of physiological evidence against which to test past and present theories of stuttering. It also helps to further legitimize stuttering (at least the form we treat in this book) as a true neurodevelopmental disorder and combat long-held social stigmas that, even today, stereotype PWS as being constitutionally nervous, feebleminded, or socially inept.

Many neuroimaging technologies have been used to examine stuttering. These approaches broadly fall into the two categories of functional and structural imaging (See Figure 1).

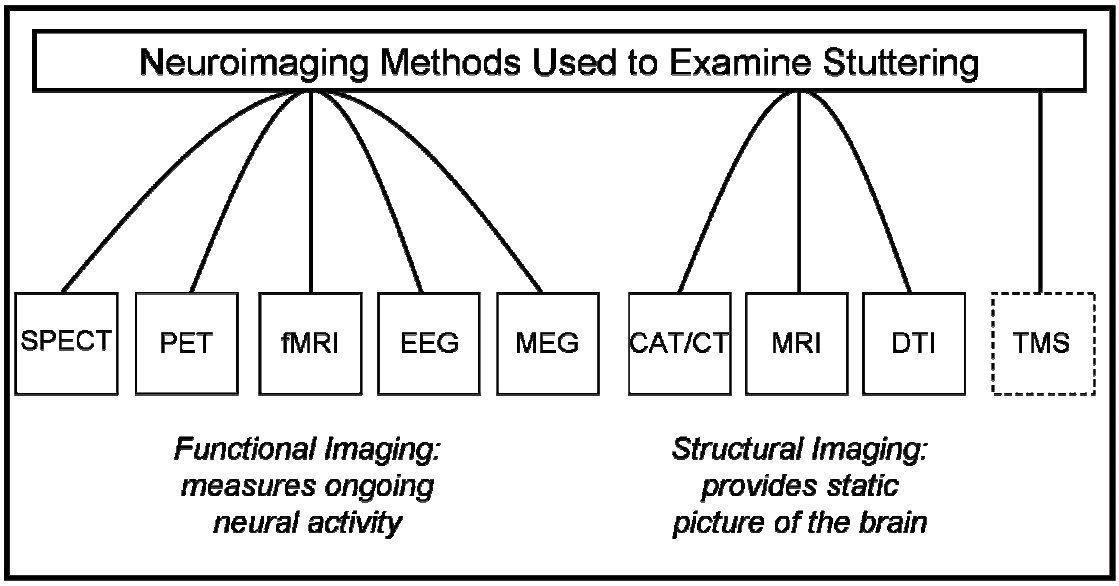


Figure 1 caption: Neuroimaging methods that have been used to examine stuttering. From RAMIG/DODGE. *The Child and Adolescent Stuttering Treatment & Activity Resource Guide*, 2E. © 2010 Delmar Learning, a part of Cengage Learning, Inc. Reproduced by permission. www.cengage.com/permissions

Functional imaging measures neural activity in the brain while it is performing a task, responding to some kind of stimuli, or at rest. The entire brain is always processing information, but when certain regions are doing more processing than others we say that those areas are activated or "light up." Examples of functional neuroimaging methods include single photon emission computed tomography (SPECT), positron emission tomography (PET), functional magnetic resonance imaging (fMRI), electroencephalography (EEG), and magnetoencephalography (MEG).

Structural imaging provides a static picture of the brain. It allows us to see the size, shape, or integrity of certain regions and compare that image to what we would expect from a normal, healthy brain. Scientists basically take pictures of the brain's gray and white matter and look for abnormalities. **Gray matter** refers to the cell bodies of neurons, while **white matter** is made up of fiber tracts that extend out from cell bodies to carry signals to other neurons. Some examples of structural imaging methods include computed axial tomography (CAT or CT), magnetic resonance imaging (MRI), and diffusion tensor imaging (DTI).

A relatively novel tool called transcranial magnetic stimulation (TMS) is not, strictly speaking, a neuroimaging technique, but deserves mention here because it has been used in stuttering research (e.g., Sommer, Wischer, Tergau, & Paulus, 2003). With TMS, neurons in the brain are excited by applying brief magnetic pulses through a metal coil placed over the scalp.

Pouring over the neuroimaging articles on stuttering published in recent years can be a daunting task, particularly to clinicians who lack the necessary expertise to

extract anything meaningful from the reports. Typically, the results sections of these articles read like a laundry list of unfamiliar, hyphenated brain regions that clinicians may have learned about once during a neuroanatomy lecture. These areas are either activated, lateralized, atypical, anomalous, or described with some other adjective in relation to other areas. Lines like, "anterior-temporal extra primary auditory cortex was more activated," "post-rolandic sensory and paleocortical paralimbic regions were activated bilaterally," and "planum temporale exhibited atypical rightward asymmetry" can mean little to those outside a small group of initiates. How is one to decipher all of that neurospeak and get to the gist of the paper? This problem is unfortunately compounded by the fact that, with functional imaging studies, research labs around the world have seldom used the same experimental tasks as their peers. It is therefore difficult to directly compare results between studies. To quote the sobering conclusion reached by Grabowski and Damasio (2000), "When two functional imaging studies attempt to isolate a specific language-processing component using different tasks, the results usually differ" (p. 445). This sentiment is echoed by other experts, who state that, "It has been shown repeatedly that even subtle variations in task parameters may result in significant changes in the observed neural activation patterns" (De Nil, Kroll, Kapur, & Houle, 2000, p. 1040).

To the question "What has recent neuroimaging research shown us?," the short answer is that, despite several carefully designed and well executed studies, no firm consensus has been reached on the casual mechanism(s) of stuttering. There are several candidates, each supported by varying degrees of evidence. However, one must remember the caution already put forth regarding the lack of neuroimaging data

on childhood stuttering, as well as the likelihood that for each individual, stuttering results from an amalgam of causative factors. As one researcher noted, "One possible explanation for these somewhat conflicting reports is that no single type of brain anomaly underlies all cases of developmental stuttering" (Ingham, 2003, p. 416). The available evidence indicates that this may be the case. Other theorists go a step further to speculate that neurological findings "suggest that there may be several 'forms of stuttering' that are differentiated by the specific locus of the disruption in the process of fluency generation" (Watson et al., 1994, p. 1227). This also seems plausible. Both of these possibilities may account for why The Cause of Stuttering, whether it be a permanent lesion(s) or a more indefinite neural predisposition leading to persistence for some and remission for others, has yet to be determined.

RESEARCH FINDINGS

In the following sections we will look at proposed neurological explanations for stuttering and review some of the recent neuroimaging findings that bear on these theories, which are summarized in Table 1.

Table 1 title: Neuroimaging Data Supporting Theories of Stuttering Causality

Etiological Theory	Recent Neuroimaging Studies	Current Consensus of Findings
Impaired auditory processing and/or speech self-monitoring	Beal et al. (2007) Biermann et al. (2005) Braun et al. (1997) Foundas et al. (2001, 2004) Fox et al. (1996, 2000) Ingham et al. (2000) Jacke et al. (2004) Pool et al. (1991) Salmelin et al. (1998)	~ Compared to controls, PWS reliably show differences in structure and function of brain regions that process auditory input. ~ Although many studies point toward an overactive right auditory cortex and underactive left, others suggest this may not be universal (e.g., Fox et al., 2000; Ingham et al., 2000)
Lateralization phenomena	Biermann et al. (2005) Braun et al. (1997) De Nil et al. (2000) Fox et al. (1996, 2000) Ingham et al. (1996) Jancke et al. (2004) Neumann et al. (2005) Pool et al. (1991) Watson et al. (1992, 1994)	~ Many reports indicate PWS may have atypical lateralization for speech and language processes, relying more heavily on right-sided areas than controls.
Anatomic disconnections or abnormalities	Beal et al. (2007) Braun et al. (1997) Foundas et al. (2001, 2004) Fox et al. (1996) Jancke et al. (2004) Neumann et al. (2003, 2005) Sommer et al. (2002) Stager et al. (2003)	~ PWS appear to have impaired communication between speech-relevant brain regions. ~ PWS appear to have abnormal brain anatomy in important speech-language areas.
Impaired speech motor preparation and/or execution	Braun et al. (1997) De Nil et al. (2001, 2003) Pool et al. (1991) Salmelin et al. (2000) Watson et al. (1992)	~ Abnormalities have been consistently found in regions controlling speech movements. This corroborates historical evidence of speech motor control deficits in phonation, breathing, articulation, etc. ~ Cerebellum may be involved in the inability of PWS to accurately and effortlessly coordinate speech musculature.
Subtle language processing deficits	Biermann et al. (2005) Blomgren et al. (2003)	~ Evidence indicates that brain regions controlling certain

	Cuadrado & Weber-Fox (2003) Watson et al. (1994) Weber-Fox (2001) Weber-Fox et al. (2004)	aspects of language (e.g., sentence processing, lexical access) may function differently in adult PWS compared to controls.

This will not be a completely exhaustive review, but we will try to cover the bulk of contemporary literature on the subject and cite direct quotations whenever possible. It is important to remember that theories of stuttering causality may overlap each other and are not mutuality exclusive; a particular neuroimaging finding could be applied to one theory or to several. This highlights what many researchers in the field have come to understand: stuttering is a multifactoral disorder, caused by an undefined combination of interrelated motor and linguistic deficits.

Impaired Auditory Processing and/or Speech Self-monitoring

Several well-documented conditions that can dramatically enhance fluency for PWS, including choral speech and altered auditory feedback. Since many of these methods change the input to the auditory system, it seems reasonable to speculate that "there may be a defect at the level of auditory processing that is at least partially reversed with these procedures" (Foundas et al., 2004, p. 1640). Many imaging studies of PWS have revealed abnormalities in the function or structure of brain regions that process speech sounds.

Pool, Devous, Freeman, Watson, and Finitzo (1991) examined subjects at rest and found PWS to have less blood flow in the left temporal lobe, which houses the auditory cortex. They concluded that their finding implicates a central auditory system dysfunction in at least some PWS. Fox et al. (1996) found that "left superior temporal activations, observed in the controls and attributed to self-monitoring, were virtually absent during stuttering" (p. 161), and that left posterior temporal cortex also was not activated while subjects stuttered. Similarly, Braun et al. (1997) showed that

two areas of temporal cortex (Brodmann areas 22 and 39)—both of which are part of Wernicke's area and help process auditory input—were not effectively activated during stuttering. They concluded that "decreased activation of this network of regions would be consistent with the notion that a disturbance of central auditory function may underlie symptom production in developmental stutterers" (p. 776). One MEG study found that, at least in some PWS, the balance of auditory processing between hemispheres was more unstable and more easily disturbed when language demands increased (Salmelin et al., 1998). Interestingly, they also reported that "the right auditory cortex of stutterers… responded both in silent and spoken conditions as if it were constantly loaded with auditory feedback" (p. 2229). This finding of an overactive right auditory cortex was not confirmed by subsequent reports, however. Ingham, Fox, Ingham, and Zamarripa (2000) reported the opposite pattern (i.e., less activation) during stuttered speech, while Fox et al. (2000) demonstrated that as stuttering increased, activity in right-sided auditory regions decreased.

Regarding the structure of the auditory system in PWS, Foundas and colleagues have reported anatomical differences in several recent papers. Their group has mainly looked at symmetry patterns in the gray matter of brain regions involved in monitoring one's own speech. The general premise is that certain regions are supposed to be larger in one hemisphere than the other, and symmetry of an area that is usually disproportional might be disruptive to the system. For most people, a structure called the **planum temporale** is larger in the left hemisphere than the right. The left-sided planum temporale (made up of auditory cortex) is important for higher order processing of linguistic information and is part of Wernicke's area. Many

experts believe it to be one of the brain's key language structures. In 2001, Foundas, Bollich, and Corey found that the planum temporale was larger on both sides and more symmetric in PWS. In a later study, this group demonstrated that when PWS have a larger planum temporale on the right side, they tend to respond better to delayed auditory feedback than those for whom this structure is larger on the left (Foundas et al., 2004). This finding led them to speculate that there may be at least two subgroups of PWS: one in which the planum temporale is bigger on the left (as is typical for fluent speakers) and one in which it is abnormally large on the right (see Figure 2).

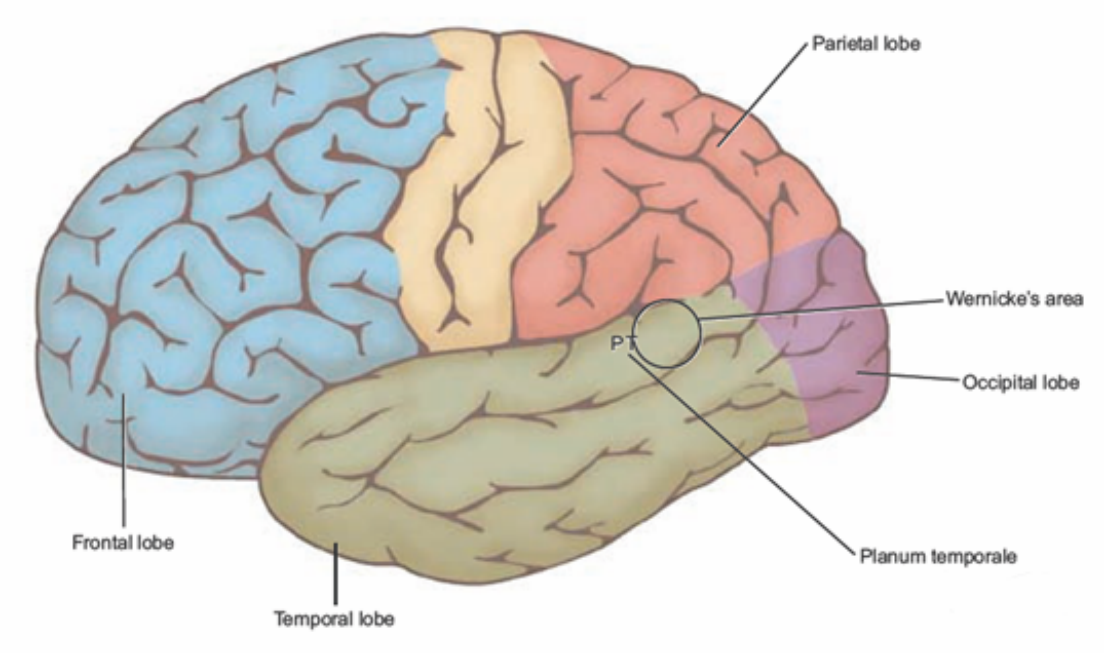


Figure 2 caption: The planum temporale (PT) is a portion of the auditory cortex and is part of Wernicke's area. In most people, this area is larger in the left hemisphere than the right. Researchers have found that when people who stutter have a larger PT on the right side, they tend to respond better to delayed auditory feedback than those who have a larger left-sided PT. This suggests that a subgroup of people who stutter may rely more on auditory feedback when they speak, as opposed to, for instance, relying on internal feedback from their speech muscles. From RAMIG/DODGE. *The Child and Adolescent Stuttering Treatment & Activity Resource Guide*, 2E. © 2010 Delmar Learning, a part of Cengage Learning, Inc. Reproduced by permission. www.cengage.com/permissions

Researchers in Europe have supplied another piece to the puzzle by demonstrating increased white matter in these auditory areas. Jäncke, Hänggi, and Steinmetz (2004) found that "stutterers do not reveal the typical leftward asymmetry, they rather show symmetry with an atypically enlarged white matter volume in the right auditory cortex" (p. 4). Given these gray and white matter findings, there appears to be some consensus growing that important brain areas for processing speech sounds may be abnormally formed in PWS. These anatomical differences could cause problems in two ways. First, PWS might have trouble processing slowly changing auditory cues needed to control suprasegmental features of speech, such as intonation and pitch. Secondly, it may be more difficult for them to segregate quickly changing acoustic cues, such as the individual phonemes of speech.

Lateralization Phenomena

Since the birth of speech-language pathology at the University of Iowa in the 1920's, many researchers have suspected that the cause of stuttering lies in miscommunication between the hemispheres. A popular early formulation of this idea was the cerebral dominance theory. This theory stated that to produce the precise synchronization necessary for fluent speech, one hemisphere must impose its timing patterns on the other to regulate neural signals to the paired, midline speech structures. PWS were thought to have improper cerebral dominance for speech movements. A variety of factors eventually caused the influence of this theory to wane, not least of which were technological limitations that allowed the theory to be tested only through behavioral measures such as handedness and articulatory control.

Recent advances in neuroimaging have allowed investigators to probe laterality effects at their origin in the brain, and some reliable differences are beginning to emerge. It seems that there may be some credence after all to the notion that many PWS have atypical lateralization (i.e., incomplete or abnormal dominance) for speech and language processes.

In 1991, Pool et al. measured **regional cerebral blood flow (rCBF)** in subjects at rest. The brain requires a certain amount of blood to meet its metabolic needs; rCBF is a measure of that blood supply. Pool et al. found that PWS showed significantly reduced blood flow in left-sided temporal areas, as well as deeper brain regions involved in the emotionality of speech and controlling the body's emotional responses. Shortly after, this group published two papers attempting to link rCBF abnormalities to behavioral phenomena such as speech motor control and linguistic deficits. They found that disrupted speech motor control for PWS was related to abnormal rCBF in the left superior and middle temporal gyrus (Watson, Pool, Devous, Freeman, & Finitzo, 1992). They also demonstrated that a subgroup of PWS had poorer linguistic performance that co-occurred with lower blood flow in regions involved in language processing (Watson et al., 1994). The main region showing reduced blood flow in these linguistically impaired subjects was, again, the middle temporal area of the left hemisphere.

A still unresolved issue is whether PWS preferentially use their non-dominant speech and language systems while they are talking. This was most prominently reported by Fox et al. (1996) in a letter to the journal *Nature*. They found that when people stuttered, much more activity took place in the motor system as compared to

normal speakers, and much of this occurred in the right hemisphere motor regions. This group later argued that their findings "support long-held theories that the brain correlates of stuttering are located in speech-motor regions, especially of the non-dominant (right) cerebral hemisphere" (Fox et al., 2000, p. 1992). Another group found that during oral reading, "stuttering speakers may have relied proportionally more on right hemisphere processing resources for the cognitive formulation and planning of word production… They engaged comparatively more right hemisphere processes than did the nonstuttering control speakers" (De Nil et al., 2000, p. 1050). Neumann et al. (2005) showed that, after treatment, the brain was more active in left-sided frontal speech and language regions and temporal areas, whereas prior to treatment the right hemisphere was more active.

These laterality differences have also been reported structurally and during tasks in which no speech was produced. Jäncke et al. (2004) examined MRI images and claimed that their findings "show again that stutterers reveal atypical anatomical lateralization in the speech-language areas" (p. 5). In three separate frontal motor areas involved in controlling the speech articulators, the stuttering group had more white matter on the right side than on the left. This study also found increased white matter in the right auditory areas of PWS. Another European group used MEG to look at brain activation during speech perception. They found that PWS had additional activity in a right-sided sensorimotor area that was not present in fluent speakers. They interpreted this "as one piece of evidence for an altered cerebral dominance in stutterers, which becomes obvious in speech perception, well before overt speech production… The group differences in activation of the sensorimotor

(rolandic) area may be interpreted in terms of weaker left hemisphere lateralization of speech sensorimotor functions in stutterers" (Biermann-Ruben, Salmelin, & Schnitzler, 2005, p. 800).

Some reports, however, have not supported the view that stuttering is caused by using nondominant speech-language systems. For example, the results of Braun et al. (1997) actually suggest left hemisphere dysfunction in the disorder. They concluded that stuttering was associated with activation of anterior regions located almost exclusively within the left hemisphere. While activity in these areas increased as speech became more disfluent, speech-language areas in the right hemisphere were activated as subjects became more fluent. Although they tested subjects at rest rather than while they were talking, Ingham et al. (1996) found no consistent evidence for abnormal function between hemispheres. Instead, "inconsistent laterality differences were noted, with three of the five areas more left lateralized in the men who stutter" (p. 1221).

A few years ago, the collective results of neuroimaging research were summarized as follows: "The emerging pattern of activation observed during a variety of speaking tasks in these studies points to a general overactivation of the sensorimotor and higher association cortices associated with language formulation and speech production. While this overactivation appears to exist bilaterally, a right-hemisphere bias can be detected" (De Nil, Kroll, Lafaille, & Houle, 2003, p. 358). This remains a fairly accurate summarization of modern neuroimaging research findings, particularly as they relate to laterality effects. When speaking, people who stutter seem to use the right sides of their brains in ways that normal speakers do not.

It appears that the old, largely discarded cerebral dominance theory may have been on to something after all. Although it is unlikely that recent evidence will lead to a wholesale reemergence of the theory, at the least, a reworking of it may be in order.

Anatomic Disconnections or Abnormalities

When one observes the breaks and disruptions in the steady flow of speech that characterize stuttering, it is easy to draw a parallel with faulty wiring in an electrical circuit. That is, in essence, what some stuttering researchers have done. Through this lens, fluency breakdowns are viewed as the outward signs of impaired fiber tracts connecting speech-language regions of the brain. But bad connections between brain regions might not be the only problem; the regions themselves that are generating the signals could also be disordered in some way, possessing what is called "anomalous anatomy." Both of these hypotheses have been supported by recent work.

Fox et al. (1996) showed that stuttering coincided with lower activation in a "verbal fluency circuit" between left frontal (BA 47) and left temporal (BA 22) cortex. This malfunctioning circuit between inferior frontal cortex and posterior temporal cortex is close to the well known Broca's area–Wernicke's area loop. Similarly, Sommer et al. (2002) found a disconnection just beneath a brain region that controls the face and mouth. This region is called the **rolandic operculum**, located in the left sensorimotor cortex (see Figure 3A).

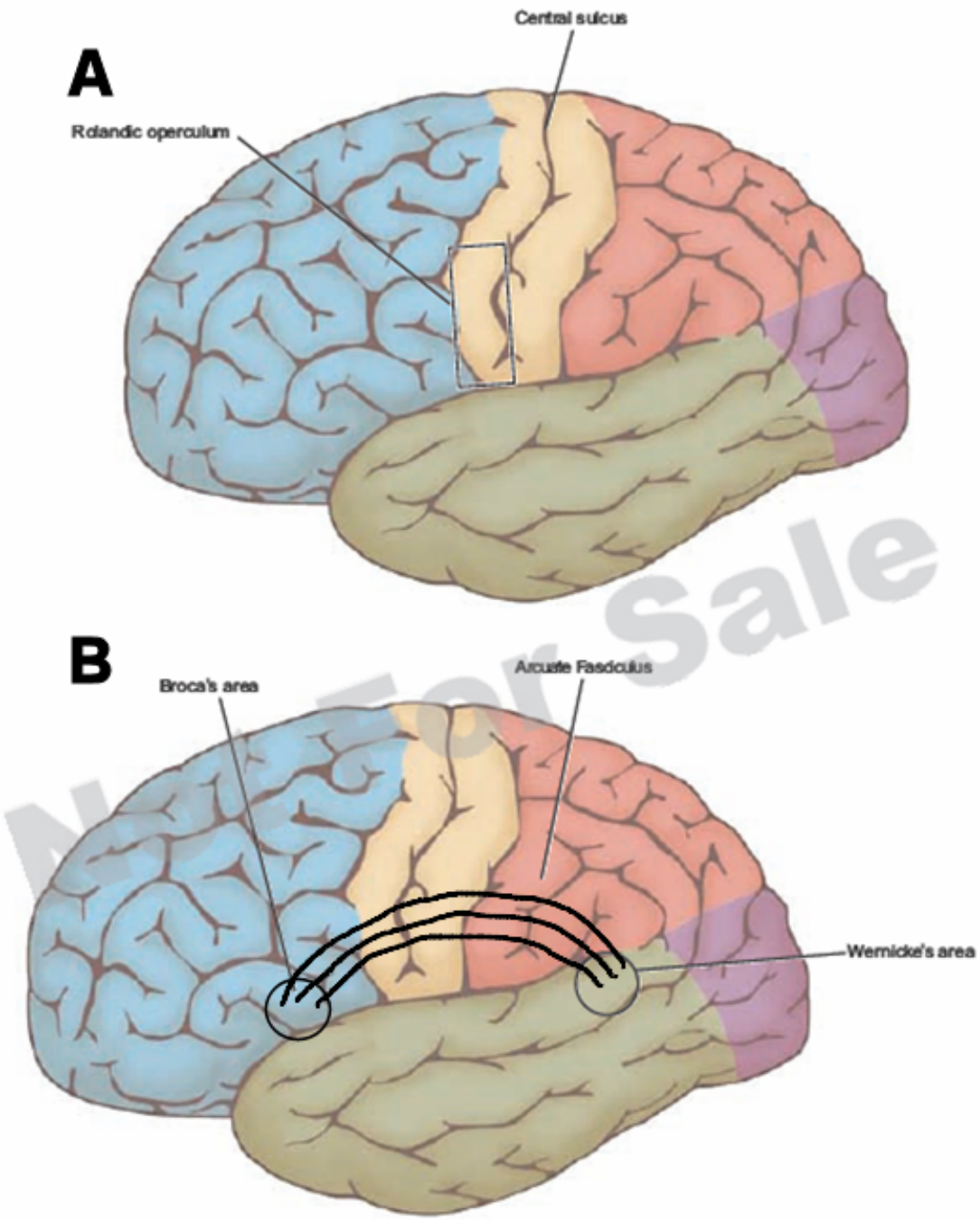


Figure 3 caption: Researchers have found structural weakness just beneath a brain area that controls the face and mouth. This area is called the rolandic operculum and is located in the left sensorimotor cortex (A). Fiber tracts extend from here to connect speech muscles with frontal motor areas controlling articulation and planning of speech movements. The region immediately surrounding the rolandic operculum includes the arcuate fasciculus, a bundle of neurons that links Wernicke's area and Broca's area (B). From RAMIG/DODGE. *The Child and Adolescent Stuttering Treatment & Activity Resource Guide*, 2E. © 2010 Delmar Learning, a part of Cengage Learning, Inc. Reproduced by permission. www.cengage.com/permissions

Fiber tracts extend from here to connect many muscles needed for speech with frontal motor areas controlling articulation and planning of speech movements. The area immediately surrounding the rolandic operculum includes the **arcuate fasciculus**, a bundle of neurons that links posterior (i.e., Wernicke's) and frontal (i.e., Broca's) language areas (see Figure 3B).

These findings by Sommer's group were later corroborated by Neumann et al. (2003), whose data pointed to a region in the right frontal operculum that was consistently implicated in stuttering. Since the right frontal operculum can be considered the right-sided counterpart to Broca's area, "it seems plausible that it compensates for deficient signal transmissions between Broca's area and left-sided articulatory motor representations, as suggested by Sommer et al. (2002), or for a dysfunctional Broca's area, by automatically taking over its disturbed functions, as occurs during recovery from aphasia after frontal injury" (p. 384).

Furthering this story of possible impaired communication between speech-relevant areas are the findings of Braun et al. (1997). These researchers concluded that stuttering may result from an imbalance between frontal areas that control motor activity and posterior areas involved in the reception and decoding of auditory signals. They state, "It is possible that the posterior regions fail to provide the integrated sensory input upon which anterior regions depend for accurate regulation of motor function. Such a dissociation may underlie the production of stuttering symptoms" (p. 776). Essentially, they argue that there is a communication problem between anterior and posterior brain regions: too much activation in anterior regions

controlling speech movements, too little activation in posterior regions that process what is spoken. Stager, Jeffries, and Braun (2003) present similar findings, although their study looked more closely at the relationship between motor activity and auditory feedback by having PWS sing and use paced speech with a metronome. They found that areas associated with increased fluency under these conditions "included auditory association areas that process speech and voice and motor regions related to control of the larynx and oral articulators. This suggests that a common fluency-evoking mechanism might relate to more effective coupling of auditory and motor systems—that is, more efficient self-monitoring, allowing motor areas to more effectively modify speech" (p. 319). The implication is that auditory areas responding to speech and the motor areas creating it are not communicating well when stuttering occurs.

A few other groups have investigated whether PWS have abnormally formed brains, hypothesizing that atypical structure of an area can cause it to function in a disordered manner. Foundas et al. (2001) used MRI to examine whether PWS have abnormal folds in the cortex in speech-related areas. They found this to be the case and speculated that the presence of anatomic anomalies may disrupt the flow of information within posterior and frontal speech–language areas. Interestingly, Sommer et al. (2002) also found abnormal structure in a region that is very close to the unusual folds reported in the 2001 Foundas et al. study. Remember, too, the previously covered work by Foundas et al. (2004) that showed a subgroup of PWS to have larger planum temporale on the right side, which might lead to a deficit in auditory perception. Researchers have also shown PWS to have abnormal increases in

white matter within a right hemisphere network that includes speech and language regions (Jancke et al., 2004). They concluded that their findings may point toward poor communication via nerve fibers within the right hemisphere; this could lead to different processing strategies in that hemisphere.

These possibilities are quite intriguing: firstly, with regard to the concept of neuroplasticity touched upon at the beginning of this chapter, and second, when considered alongside the theory that right-sided regions may compensate for impaired left-sided areas that typically control speech and language. For adults, it may be that a lifetime of coping with stuttering causes permanent changes in brain anatomy and function. What sort of effects might intensive therapy have on those altered brains, then? A study by Neumann et al. (2005) investigated this question. Their experiment involved scanning the brains of PWS before and after they underwent intensive fluency shaping treatment. After treatment, the group showed increased left hemisphere activation in the rolandic operculum, among other areas. Recall that the rolandic operculum hosts brain regions controlling the oral articulators and is near the same region where PWS have been shown to have impaired fiber tracts. Neumann et al. interpreted their data as "suggesting that fluency shaping techniques reorganize neuronal communication between left-sided speech motor planning, motor execution, and temporal areas" (p. 23–24). The key word here is "reorganize," implying that impaired brain networks are repaired in some way. They contend that intensive therapy may remodel brain circuitry near the source of the dysfunction, rather than increase compensation by similar brain networks in the opposite hemisphere. This is a very important distinction. It implies that the right hemisphere differences found by

several laboratories (e.g., Jancke et al., 2004; Neumann et al., 2003) are likely the result of years of living with the disorder and attempting to compensate for defective left hemisphere networks. We will revisit this issue of the cause versus effect of stuttering at the conclusion of the chapter. For now, it is enough to state that the right hemisphere story—whether signifying compensation or reorganization—has yet to be fully told and warrants further exploration.

Impaired Speech Motor Preparation and/or Execution

Some who have studied the disorder of stuttering see it primarily as an impairment in the coordination of speech musculature. This seems to be a sensible hypothesis. After all, movement parameters such as velocity, displacement, positioning, and timing of speech structures must be precisely sequenced and executed to yield fluent speech; this motor cascade is obviously interrupted at some point during stuttered speech. Studies in this area have traditionally focused on measuring aspects of articulatory control, such as the speed and regularity of articulatory movements, delays in voicing onset, airflow characteristics, and so on. In recent years, neuroimaging has become another way to explore the impairments in speech-motor control that have been reliably demonstrated in the surface features of speech just mentioned.

The same group who demonstrated lateralization effects in brain blood flow also found evidence for impaired control of speech structures. Knowing that motor planning for speech has been localized to the left inferior frontal cortex, Pool et al. (1991) made the link between their finding of reduced levels of blood flow in that

region and impaired motor output. They argued that "an association between disfluency in stuttering and cortical dysfunction in the left cingulate and left inferior frontal gyrus is consistent with classic anatomoclinical principles of speech-motor control" (p. 512). As adverted to previously, these researchers also linked brain blood flow abnormalities to deficits in speech motor control. They found that slower laryngeal reaction times in stuttering subjects were strongly correlated with abnormal blood flow in left temporal regions. They speculated that stuttering subgroups might be distinguished by the presence, location, and relative magnitude of abnormalities in regions controlling speech production (Watson et al., 1992). Another group that tied temporal lobe deficits to impaired speech motor control was Braun et al. (1997). As mentioned in the section on anatomic disconnections, they found posterior temporal regions that process speech sounds to be poorly activated when someone stutters. They claimed that "The posterior regions may somehow fail to provide the integrated sensory feedback upon which the anterior regions depend for efficient coordination of speech output" (p. 780).

If the coordination of speech movements is impaired in PWS, one possibility is that the synchronization of those movements—the precise ordering of neural events—is somehow disturbed. This in fact has been demonstrated in an oft-cited MEG study (Salmelin, Schnitzler, Schmitz, & Freund, 2000). While subjects read single words aloud, Salmelin et al. found that PWS inverted the sequence of speech production steps, initiating motor commands *before* activating phonological output codes. In fluent speakers, brain processing advanced from front-to-back so that articulatory programming occurred before motor preparation and execution. This

normal sequence was reversed in the stuttering group, who showed a back-to-front pattern with early motor cortex activation followed by a delayed inferior frontal signal. They concluded that "Stutterers thus appeared to initiate motor programmes before preparation of the articulatory code" (p. 1184). It seems that the brains of PWS may jump the gun, so to speak, and this reordering of speech production steps could lead to disfluencies.

Finally, another line of research probing impaired coordination of speech musculature involves the **cerebellum**. The cerebellum, located at the base of the brain, is a powerful space-time computer that compares the motor plan (i.e., what you intended to do) with the sensory feedback (i.e., what you actually did). It makes rapid adjustments when errors are detected and helps us learn by making long-term adjustments to future motor plans. De Nil and colleagues have found that PWS may rely on their cerebellums more than normal speakers. They believe this is due to a lack of **automaticity** in the speech movements of those who stutter. Automaticity is the ability to perform complex actions effortlessly and mechanically, with very little conscious thought. A good example is learning to drive a car. At first, you had to concentrate on every detail, but after a while you could do many other things simultaneously because driving required minimal thought. Applying this concept to speech, in one study these researchers followed a group of PWS who received intensive fluency shaping treatment (De Nil, Kroll, & Houle, 2001). They found high activation in the cerebellum immediately before and after treatment, but normalized activation after one year of practicing fluency enhancing techniques. Heavy reliance on the cerebellum pre- and post-therapy "suggests the presence of increased sensory

or motor monitoring of the ongoing or planned movements associated with lower levels of automaticity during the execution of such movements" (p. 79). In a later study they concluded that generally high activation in the motor cortex, combined with greater involvement of the cerebellum, supports the idea that speech control in stuttering speakers lacks the automaticity usually seen in fluent speakers (De Nil et al., 2003). Essentially, PWS may have to use more neural resources when speaking because it has never become an automatic and effortless skill for them.

Subtle Language Processing Deficits

There is still controversy as to whether the language skills of stuttering children are equivalent to those of their fluent peers (see Andrews et al., 1983; Yairi, Watkins, Ambrose, & Paden, 2001). The overall language abilities of adults who stutter is also a debatable topic, although it is generally agreed that adult PWS do, as a group, have certain, subtle language processing deficits (Bloodstein & Bernstein Ratner, 2008). It is therefore unsurprising that some differences in well established language processing areas of the brain have been found for this population.

Using tasks involving high-level discourse production and comprehension abilities (i.e., story retelling), Watson et al. (1994) found that "linguistic performance deficits in a subgroup of persons who stutter co-occur with cortical blood flow asymmetries in regions classically related to language processing. Subgroups of persons who stutter and who differ by the presence of a linguistic performance deficit demonstrated different patterns of rCBF asymmetry" (p. 1225). They found that PWS with high-level linguistic impairment also had unusual blood flow (left < right) in

middle temporal and inferior frontal regions compared to controls, and only in middle temporal regions when compared to linguistically normal PWS.

There is also some evidence to suggest that the defect(s) causing stuttering may exist at linguistic levels prior to the stages of motor preparation and execution. It has been proposed that the problem "may exist at pre-speech levels as early as morphological encoding, lexical selection (access), and perhaps even during lexical conceptualization" (Blomgren, Nagarajan, Lee, Li, & Alvord, 2003, p. 341). Due to high variability within groups, Blomgren et al.'s conclusions were based on visual comparison of brain scans rather than statistically significant differences; however, they remain thought provoking and deserve mention here. These authors concluded that fluent and disfluent speakers produced different patterns of activation during lexical access (i.e., while attempting to find a word). By and large, the classic left hemisphere language activation pattern was observed in the controls, while a more bilateral activation pattern was seen in the PWS. They maintained that their results "appear to provide support for numerous earlier findings indicating unusual laterality of speech and language in stuttering speakers" (Blomgren et al., 2003, p. 352). These differences occurred in a language task during which subjects did not speak but only had to silently retrieve the word being described.

A European group examined neural activation in PWS during speech perception and production. They reported no differences compared to a control group for early neural responses to tones (i.e., auditory processing), but found differences in more complex language tasks (Biermann-Ruben et al., 2005). In addition to finding abnormalities in areas controlling speech production, their data also suggested that

left inferior frontal regions in stutterers respond differently during speech perception. Recall that the left inferior frontal cortex is part of Broca's area and primary motor cortex, regions that mainly control aspects of speech production. Since this region was highly active as PWS processed sentences prior to repeating them aloud, the researchers "interpreted the obtained group difference in the left inferior frontal region in terms of anticipation of enlarged load of articulatory planning in stutterers dealing with sentences" (p. 799). This is consistent with behavioral studies showing that when language becomes more complex—for instance, when phrase length is longer or phonologic encoding demands increase—more stuttering usually results.

FINAL THOUGHTS

Neurological research on stuttering in recent years has focused mainly on brain activation patterns and structural abnormalities. Broadly speaking, researchers have demonstrated two important phenomena concerning those who stutter. First, during certain tasks the brains of PWS do not function like a fluent speaker's brain. Second, certain areas in the brains of PWS do not look like what we would expect from a fluent speaker's brain. What remains unclear, however, is whether these differences are what caused stuttering initially or whether they are the result of years of living with the disorder. This is the old problem of causal mechanisms versus compensatory mechanisms that exists for many developmental disorders. Regarding commonly reported laterality differences among PWS, to take one example, "it has never been clear whether increased activity in the right hemisphere might be interfering with normal left hemisphere processing or compensating for left

hemisphere dysfunction" (Braun et al., 1997, p. 778). This statement illustrates the difficulty faced by researchers: when recording neurological differences between PWS and fluent controls, what is measured in the chronic stage of the disorder is probably a combination of the primary pathology and secondary neural reorganization. It can be quite difficult to disentangle the two.

As alluded to at the beginning of the chapter, an obvious way to resolve this chicken-and-egg issue would be to investigate the brains of young children as close to stuttering onset as possible. Thankfully, some laboratories have begun to do so.

A study published recently by Watkins, Smith, Davis, and Howell (2008) employed a group of PWS aged 14 to 27 with an average age of 18 years. While their findings apply more directly to adolescents than to children who stutter, they nonetheless offer a much needed glimpse into the disorder closer to its inception. A primary finding was that the stuttering group had significantly more activity in midbrain regions relative to fluent controls. The overactive areas deep in the brain included the **substantia nigra** and several clusters of neurons involved in the **basal ganglia** circuitry. These brain structures are critical for the initiation and fluid execution of movements and become less active in patients with Parkinson's disease, a disease in which **dopamine** levels plummet in deeper, midbrain motor areas. Dopamine is a chemical messenger that helps motor neurons and other types of cells communicate with each other. There has long been a so-called "dopamine hypothesis" for stuttering, basically arguing that PWS may have excessive levels of dopamine in areas controlling verbalization. According to Watkins et al., their results

"revive the debate about the involvement of the basal ganglia in normal and abnormal speech production" (p. 57).

A groundbreaking study by Chang, Erickson, Ambrose, Hasegawa-Johnson, and Ludlow (2008) examined the brain structures of three groups of boys aged 9 to 12, with an average age of roughly 11 years. To date, this is the youngest sample of PWS to be examined through neuroimaging procedures. The groups consisted of children who persisted in stuttering, children who had recovered from stuttering, and fluent peers.

The first important finding from this experiment was that the stuttering children, regardless of whether they recovered or persisted, showed similar white matter deficiencies in the arcuate fasciculus previously found in adults who stutter (Sommer et al., 2002). Recall that the arcuate fasciculus is a bundle of neurons connecting Wernicke's and Broca's area, making it a main conduit between regions involved in the understanding and generation of language. This fiber tract lies beneath the rolandic operculum, which, you may recall, hosts the brain regions controlling the oral articulators (Figure 4).

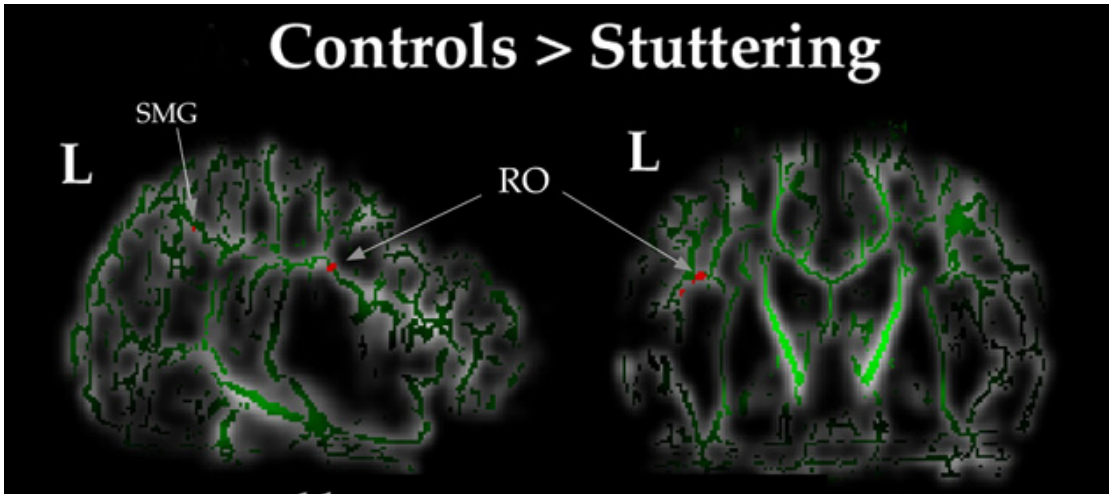


Figure 4 caption: This image shows a skeleton of the brain's white matter tracts (green). These can be thought of as bundles of wires through which different areas of the brain communicate with each other. Chang et al. found that the arcuate fasciculus—the fiber tract in the left hemisphere connecting Wernicke's area and Broca's area—was impaired in children who stutter. The arcuate fasciculus is located very close to the rolandic operculum (RO in the figure), an area that controls key speech-related structures. From RAMIG/DODGE. *The Child and Adolescent Stuttering Treatment & Activity Resource Guide*, 2E. © 2010 Delmar Learning, a part of Cengage Learning, Inc. Reproduced by permission. www.cengage.com/permissions

Because white matter fibers here seem to be damaged in both adults and children who stutter or had stuttered, the authors concluded that this may be a key causal factor in the disorder.

A second major finding was that the combined group of stuttering children had less gray matter compared to their fluent peers in important speech-language regions such as Broca's area and the planum temporale. These gray matter results in childhood differ from Foundas et al.'s (2001) report of larger planum temporale overall, and particularly on the right side in adults who stutter. Since their child subjects did not show the differences in this area that were previously found in adults, Chang et al. argued that "perhaps both the anatomical and functional increases in right hemisphere speech related areas in adults are the result of compensatory mechanisms used over a lifetime of stuttering" (p. 1342).

This is where the results of this study become so intriguing and illustrate the need for further characterization of the brains of stuttering children. Chang et al.'s findings suggest that at least some of the neurological differences seen in adult PWS may be due to years of employing right hemisphere mechanisms to compensate for left hemisphere dysfunction. In other words, differences in adults may represent maladaptive neuroplasticity, as mentioned at the beginning of this chapter. By struggling to talk fluently for so long, adults may have fundamentally changed the way their brains process speech and language. That this plasticity can occur soon after stuttering onset is supported by another exciting finding from the study: the persistent stuttering children had more gray matter than the recovered children in the upper part of the left and right temporal lobe. These gray matter differences in the persistent

group concur with Foundas et al.'s (2001) results from adults who stutter, indicating that such changes can occur only 6 to 9 years after one begins to show symptoms of the disorder.

Stuttering Therapy and the Plastic Brain

What significance does all of this hold for parents who are considering stuttering therapy for their child or the clinician who may be providing treatment? After all, it has long been known from behavioral studies that early childhood is the crucial window of opportunity for halting the progression of stuttering before it develops into a potentially lifelong, debilitating disorder. It would seem that recent findings provide even more support for early intervention, this time at the level of the nervous system itself.

It is reasonable to infer that if unchecked stuttering eventually leads to compensatory processes resulting in many of the neurological differences seen in adulthood, then early treatment may foster more adaptive changes in the brain that lead to recovery. Speech therapy activities may very well stimulate growth and/or interconnections of neurons in the arcuate fasciculus, for example, and perhaps in other, integral speech-language areas as well. Therapy might also work by shifting control of speech from dysfunctional or inhibited motor systems to more stable networks that reliably produce fluency. Moreover, successful intervention does not necessarily have to involve the usual neurological procedures. This is suggested by data showing that even children who had recovered their fluency still had several regions with less gray matter compared to their peers who had never stuttered (Chang

et al., 2008). There may be many ways for the developing brain to generate fluent speech! This can be comforting news to parents who are understandably dismayed by their child's stuttering problem.

Regardless of the precise mechanisms through which early stuttering therapy operates, it is almost certainly effective at the neurological level. In other words, early treatment can facilitate the adaptive neuroplasticity needed to permanently alter a child's disfluent speech patterns. To be sure, these lasting changes in the brain can be effected through natural developmental courses, as with spontaneous recovery from stuttering that occurs with many children. But such changes can also be fostered through therapy activities that minimize speech disruptions caused by fear and frustration, alter parents' responses to their child's stuttering, and enable the child to speak in a more fluent manner—all of which can be achieved under the guidance of an adept and caring clinician.

BIBLIOGRAPHY

Andrews, G., Graig, A., Feyer, A., Hoddinott, S., Howie, P., & Neilson, M. (1983). Stuttering: a review of research findings and theories circa 1982. *Journal of Speech and Hearing Disorders, 48*, 226–246.

Biermann-Ruben, K., Salmelin, R., & Schnitzler, A. (2005). Right rolandic activation during speech perception in stutterers: a MEG study. *NeuroImage, 25*, 793–801

Blomgren, M., Nagarajan, S. S., Lee, J. N., Li, T., & Alvord, L. (2003). Preliminary results of a functional MRI study of brain activation patterns in stuttering and nonstuttering speakers during a lexical access task. *Journal of Fluency Disorders, 28(4)*, 337–355.

Bloodstein, O. & Bernstein Ratner, N. (2007). *A handbook on stuttering* (6th ed.). San Diego, CA: Singular.

Braun, A. R., Varga, M., Stager, S., Schulz, G., Selbie, S., Maisog, J. M., et al. (1997). Altered patterns of cerebral activity during speech and language production in developmental stuttering. An H215O positron emission tomography study. *Brain, 120*, 761–784.

Chang, S.-E., Erickson, K. I., Ambrose, N. G., Hasegawa-Johnson, M. A., & Ludlow, C. L. (2008). Brain anatomy differences in childhood stuttering. *NeuroImage, 39*, 1333–1344.

De Nil, L. F., Kroll, R. M., & Houle, S. (2001). Functional neuroimaging of cerebellar activation during single word reading and verb generation in stuttering and nonstuttering adults. *Neuroscience Letters, 302*, 77–80.

De Nil, L. F., Kroll, R. M., Kapur, S. & Houle, S. (2000). A positron emission tomography study of silent and oral single word reading in stuttering and nonstuttering adults. *Journal of Speech, Language, and Hearing Research, 43*, 1038–1053.

De Nil, L. F., Kroll, R. M., Lafaille, S. J., & Houle, S. (2003). A positron emission tomography study of short- and long-term treatment effects on functional brain activation in adults who stutter. *Journal of Fluency Disorders, 28(4),* 357–379.

Foundas, A. L., Bollich, A. M., & Corey, D. M. (2001). Anomalous anatomy of speech-language areas in adults with persistent developmental stuttering. *Neurology, 57*, 207–215.

Foundas, A. L., Bollich, A. M., Feldman, J., Corey, D. M., Hurley, M., Lemen, L. C.,

et al. (2004). Aberrant auditory processing and atypical planum temporale in developmental stuttering. *Neurology, 63*, 1640–1646.

Fox, P. T., Ingham, R. J., Ingham, J. C., Hirsch, T., Downs, J. H., Martin, C., et al. (1996). A PET study of the neural systems of stuttering. *Nature, 382*, 158–162.

Fox, P. T., Ingham, R. J., Ingham, J. C., Zamarripa, F., Xiong, J.-H. & Lancaster, J. L. (2000). Brain correlates of stuttering and syllable production: a PET performance-correlation analysis. *Brain, 123*, 1985–2004.

Grabowski, T. J., & Damasio, A. R. (2000). Investigating language with functional neuroimaging. In A. W. Toga & J. C. Mazziotta (Eds.), *Brain mapping: The systems* (pp. 425–461). San Diego, CA: Academic Press.

Ingham, R. J. (2003). Brain imaging and stuttering: Some reflections on current and future developments. *Journal of Fluency Disorders, 28*, 411-420.

Ingham, R. J., Fox, P. T., Ingham, J. C. & Zamarripa, F. (2000). Is overt stuttered speech a prerequisite for the neural activations associated with chronic developmental stuttering? *Brain and Language, 75*, 163–194.

Ingham, R. J., Fox, P. T., Ingham, J. C., Zamarripa, F., Jerabek, P. & Cotton, J. (1996). Functional-lesion investigation of developmental stuttering with positron emission tomography. *Journal of Speech and Hearing Research, 39*, 1208–1227.

Jäncke, L., Hänggi, J., & Steinmetz, H. (2004). Morphological brain differences between adult stutterers and non-stutterers. *BMC Neurology, 4(1)*, 23.

Neumann, K., Euler, H. A., Wolff von Gudenberg, A., Giraud, A.-L., Lanfermann, H., Gall, V., et al. (2003). The nature and treatment of stuttering as revealed by fMRI: a within- and between-group comparison. *Journal of Fluency Disorders, 28*, 381–410.

Neumann, K., Preibisch, C., Euler, H. A., Wolff von Gudenberg, A., Lanfermann, H., Gall, V., et al. (2005). Cortical plasticity associated with stuttering therapy. *Journal of Fluency Disorders, 30*, 23–39.

Pool, K. D., Devous, M. D., Freeman, F. J., Watson, B. C., & Finitzo, T. (1991). Regional cerebral blood flow in developmental stutterers. *Archives of Neurology, 48,* 509–512.

Salmelin, R., Schnitzler, A., Schmitz, F. & Freund, H. J. (2000). Single word reading in developmental stutterers and fluent speakers. *Brain, 123,* 1184–1202.

Salmelin, R., Schnitzler, A., Schmitz, F., Jäncke, L., Witte, O. W. & Freund, H. J. (1998). Functional organization of the auditory cortex is different in stutterers and fluent speakers. *NeuroReport, 9*, 2225–2229.

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

Sommer, M., Wischer, S., Tergau, F., Paulus, W. (2003). Normal intracoritcal excitability in developmental stuttering. *Movement Disorders, 18(7)*, 826–830.

Stager, S. V., Jeffries, K. J., & Braun, A. R. (2003). Common features of fluency-evoking conditions studied in stuttering subjects and controls: An $H_2{}^{15}O$ PET study. *Journal of Fluency Disorders, 28*, 319–336.

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.

Watson, B. C., Freeman, F. J., Devous, M. D., Chapman, S. B., Finitzo, T., & Pool, K. D. (1994). Linguistic performance and regional cerebral blood flow in persons who stutter. *Journal of Speech and Hearing Research, 37*, 1221–1228.

Watson, B. C., Pool, K. D., Devous, M. D., Freeman, F. J., & Finitzo, T. (1992). Brain blood flow related to acoustic laryngeal reaction time in adult developmental stutterers. *Journal of Speech and Hearing Research, 35,* 555–561.

Yairi, E., Watkins, R., Ambrose, N., & Paden, E. (2001). What is stuttering? *Journal of Speech, Language, and Hearing Research, 44*, 585–592.

CHAPTER TWO

INTRODUCTION

Stuttering has been characterized as a disorder of speech motor control (Van Riper, 1982; Zimmermann, 1980). The lineage of this idea is extended, reaching back at least to the Persian physician Avicenna, who hypothesized that brain lesions were responsible for the epiglottic spasms which supposedly caused stuttered speech. In the early 20th century, the cerebral dominance theory of stuttering gained prominence as an explanation for how speech motor control might be disrupted in persons who stutter (PWS) (Orton, 1927; Travis, 1931). The hypothesis centered on the fact that speech muscles are paired, midline structures, each side innervated by descending pathways originating in the contralateral cerebral hemisphere. It was theorized that, to produce the precise synchronization necessary for fluent speech, one hemisphere must impose its timing patterns on the other to regulate the neural input to the speech structures. PWS were thought to have reduced or ambilateral cerebral dominance for speech movements, resulting in dysynchronies that could be exacerbated by factors such as environmental stress or physiological arousal. The theory spurred a great deal of research into behavioral issues such as handedness (e.g., Bryngelson, 1935; Johnson & King, 1942) and articulatory control (e.g., Blackburn, 1931; Travis, 1934). Ultimately, however, several factors, including equivocal findings, the existence of ipsilateral motor tracts, and the frequency of left-sided speech and language laterality in PWS relegated the theory to obsolescence (Van Riper, 1982). Its waning influence was also due to technological limitations of the time that allowed the theory to be tested only through distal measures. With recent advances in neuroimaging

techniques, laterality differences between PWS and fluent controls can now be probed at their origins within the central nervous system. Some reliable differences have recently been reported (De Nil, Kroll, Kapur, & Houle, 2000; Fox et al., 1996; Neumann et al., 2005), suggesting that the theory, or more likely a reworking of it, may again find credence with contemporary researchers.

As mentioned above, the view of stuttering as an impairment in the coordination of speech musculature has yielded a line of research examining articulatory control in this population. It seems an intuitive supposition. Movement parameters such as velocity, displacement, positioning, and timing of speech structures must be precisely sequenced and executed to produce fluent speech; this motor cascade is obviously interrupted at some point during stuttered speech. Studies in this area have traditionally focused on peripheral phenomena such as the speed, precision, and regularity of articulatory movements, delays in voicing onset, airflow characteristics, etc. Williams and Brutten (1994) observed atypical timing relationships between respiratory and laryngeal movements before and during speech production in PWS. Zimmerman (1980) found evidence of articulatory slowness and impaired coordination between lip and jaw movements during fluent utterances of CVC syllables. Other investigators have probed diadochokinetic rates and other temporal patterning abilities and found that PWS were significantly poorer at rapid and rhythmic sequencing tasks than fluent controls (Rickenberg, 1956; Zaleski, 1965). PWS have demonstrated increased disfluency the more often phonation must be initiated (Adams & Reis, 1971), as well as aerodynamic abnormalities during both fluent and disfluent speech (Adams, 1974). Delays in voice onset time—the time

between a supra-laryngeal articulatory gesture and the onset of phonation—relative to fluent speakers have also been reported during the perceptually stutter-free speech of PWS (Healey & Gutkin, 1984; Healey & Ramig, 1986). Another index of motor coordination abilities is laryngeal reaction time: a measure of how quickly the speaker begins phonating after presentation of a cue stimulus. Even when analyzing only fluent utterances so as to prevent contamination by the presence of stuttering, studies have consistently demonstrated delayed laryngeal reaction times among PWS, further suggesting that speech motor deficits may be inherent to this population (Peters & Hulstijn, 1987; Starkweather, Hirschman, & Tannenbaum, 1976; Watson & Alfonso, 1983). In the aggregate, the results of these investigations have indicated general "slowness or limitation of movement, lateness of response, or incoordination of the articulators and larynx" (Bloodstein & Bernstein Ratner, 2008, p. 165).

Although much evidence exists to suggest that PWS have peripheral deficiencies in the timing and control of various speech movements, the results have not been entirely uniform. Differences in the speed and/or stability of jaw, tongue, or lip movements have not been found during several experiments (Chworowski, 1952; Healy & Adams, 1981; Robb & Blomgren, 1997; Strother & Kriegman, 1943; Zebrowski, Conture, & Cudahy, 1985). Smith and colleagues (Smith, Denny, Shaffer, Kelly, & Hirano, 1996) found no differences between PWS and fluent controls on electromyographic (EMG) measures of intrinsic laryngeal muscle tension during speaking. Additionally, some studies have failed to show an overall deficit in voice onset time for the fluent utterances of PWS (Borden, Baer, & Kenney, 1985; Jancke, 1994).

The precise mechanisms underlying the occasional inability of PWS to produce fluent speech remain unknown. Many reports, however, have shown neurological differences between PWS and nonstuttering controls. These presumed neural correlates of stuttering have been demonstrated in structural as well as functional abnormalities. Regarding the former, Foundas, Bollich, Corey, Hurley, and Heilman (2001) reported anomalous anatomy in perisylvian speech-language areas and later found that response to delayed auditory feedback correlated with asymmetry patterns in the planum temporale: a key language structure important for higher-order processing of linguistic information (Foundas et al., 2004). A more recent report similarly demonstrated atypical morphology in the superior temporal gyri of PWS that extended beyond the planum temporale to include primary auditory cortices and other speech-related sites (Beal, Gracco, Lafaille, & De Nil, 2007). Employing diffusion tensor imaging to measure the diffusion of water in white matter tracts, Sommer and colleagues reported decreased fractional anisotropy in speech-relevant areas in left sensorimotor cortex, including the rolandic operculum: a region directly controlling many oral articulators (Sommer, Koch, Paulus, Weiller, & Buechel, 2002). This evidence of reduced fiber coherence or myelination defects in PWS indicates that poorer connectivity and signal transmission in this area may impair sensorimotor integration needed for fluent speech.

In respect to functional correlates, response patterns of the auditory cortices of PWS appear to differ in significant ways from fluent controls, often showing incomplete or reversed patterns of hemispheric dominance for speech production and perception (Braun et al., 1997; Fox et al, 1996; Salmelin et al., 1998). Relatedly,

defects in auditory self-monitoring of speech have been implied from findings of decreased temporal activation while stuttering (Braun et al., 1997; Fox et al., 1996, 2000; Ingham, Fox, Ingham, & Zamarripa, 2000; Salmelin et al., 1998). Lateralization phenomena seen in PWS also include a shift to the right hemisphere motor and premotor cortices during speech tasks that is not observed in normally fluent speakers (Fox et al., 1996; Braun et al., 1997). Additionally, impaired oral motor control for speech movements (De Nil, 1999) and synchronization deficits in left hemisphere speech preparation and execution regions (Salmelin, Schnitzler, Schmitz, & Freund, 2000) have also been described. This last report is of particular relevance to this dissertation in that it suggests the possibility of premotor dysfunction related to speech in PWS.

Motor Preparation in PWS

Salmelin et al. (2000) used magnetoencephalography (MEG) and a classical contingent negative variation (CNV) paradigm to examine neural correlates of single-word reading. The CNV task involves providing a warning stimulus that alerts subjects to an upcoming imperative stimulus to which they must quickly respond (Brunia, 2003). For this study, the warning stimulus was a word and the imperative stimulus was a question mark. The investigators found that, while behavioral measures were similar between the stuttering and nonstuttering groups, cortical responses differed significantly in the left inferior frontal cortex and the motor and dorsal premotor cortices bilaterally. The left inferior frontal cortex is assumed to subserve high-level articulatory encoding and the premotor and motor cortices

prepare movement parameters and execute motor tasks, respectively. For the fluent speakers, activation proceeded from left inferior frontal cortex to premotor and motor cortices, as would be expected. This sequence was reversed in the stuttering group, however, as they had an early left motor/premotor response (i.e., motor preparation and execution) followed by delayed left inferior frontal activation (i.e., articulatory programming). The authors interpreted this as, "suggesting that motor programmes were initiated before preparation of the articulatory code, which could certainly result in disrupted speech and even stuttering" (p. 1198).

Three other groups have utilized evoked potentials and a CNV design to investigate preparation of speech movements in this population. Motivated by the cerebral dominance theory, Zimmermann and Knott (1974) placed electrodes over inferior frontal sites and at vertex to test for lateral asymmetries in PWS and nonstuttering controls. They reported no differences between groups at vertex preceding nonverbal or verbal conditions, but found that at inferior frontal sites PWS failed to show the typical left lateralized anticipatory slow potential shift preceding speech. This effect occurred regardless of whether the motor aspect of speech was performed (i.e., subjects spoke aloud) or not (i.e., subjects imagined speaking). They concluded that, "When processing verbal stimuli, stutterers appear to show more variable interhemispheric relationships and do not show a shift that is consistently larger in the left hemisphere than in the right" (p. 604). Interestingly, this group provides the only extant report of premovement potentials prior to stuttered speech, albeit in the form of an abstract in which the topic is only treated briefly (Zimmermann & Knott, 1973). The abstract states that, just before fluent responses,

PWS showed the usual premotor negativity at vertex but not at either inferior frontal location. Stuttered responses, on the other hand, were prefaced by the following neural mélange: no potential at vertex, a negative shift over left inferior frontal cortex, and "a discernable positive shift" over right inferior frontal cortex. This finding of premotor components with opposite polarities over each hemisphere is intriguing but difficult to interpret given the study's parameters and instrumentation. Furthermore, the authors did not pursue its implications and it has not been replicated.

Using the same three-electrode placement as the foregoing Zimmermann and Knott studies, Prescott (1988) had subjects vocalize during a series of single-word and letter conditions. He found electrophysiological differences between groups prior to speaking but not during the act of speaking. Specifically, he reported increased premovement negativity for the stuttering group compared to the nonstuttering group for most conditions. These differences were interpreted as evidence that PWS have difficulty establishing efficient motor programs prior to the onset of speech. He concluded that stuttering may result from an inability to effectively set up the parameters of speech rather than a problem with the ongoing control of speech once initiated.

More recently, Walla and colleagues employed MEG to explore a concept they called "focused verbal anticipation" (Walla, Mayer, Deecke, & Thurner, 2004). They used a single-word reading CNV task, with a plus sign as the warning stimulus and a word as the imperative stimulus. Cortical activity was seen prior to the onset of word presentation in the control group but not in the stuttering group. The authors argued that this activity was reflective of the Bereitschaftsfield2, which is roughly

analogous to the late phase of the Bereitshaftspotential and has been localized to primary motor cortex (M1) (Deecke & Kornhuber, 2003). However, close inspection of their methodology reveals that their findings probably relate more to early premovement processes associated with anticipation and expectancy, rather than later, strictly motor activity just prior to movement execution. At any rate, focused verbal anticipation was conceptualized as reflecting the function of *what to speak*. *What to speak*, in their model, is presumably the main parameter the brain is anticipating but is unknown in the interval between the warning stimulus and the imperative stimulus. While the subject waits for the word to appear on screen so that he/she can execute speech movements, premotor regions are activated preparatory to visual presentation of the word. The authors called this motor preparation for speech by the term focused verbal anticipation. In their own words, "Our idea is that the speech motor system anticipates verbal information to come in order to be translated into various distinct motor events to produce speaking" (p. 1326). Thus, this preparatory process—a supposed prerequisite for fluent speech—is suggested to be the crucial function that is defective in those who stutter.

The Bereitschaftspotential

While CNV protocols have been used to investigate preparatory neural activity related to speech in PWS, there are other cortical potentials that might be applied to the task as well. One such component will now be described in detail, followed by an explanation of its unique assets as a tool for investigating certain aspects of motor behavior.

The Bereitschaftspotential (BP), also called the readiness potential, is a negative cortical potential that begins roughly 1.5 sec before self-initiated movements (Jahanshahi & Hallett, 2003). A well-established tool for measuring the electrophysiological correlates of motor behaviors, it is part of a larger group of movement-related cortical potentials (MRCP) occurring just before and after volitional movement. Eight components of MRCP have been identified, four occurring before and four occurring after movement onset. Although some inconsistencies in nomenclature exist in the literature, the terminology for the components is usually derived from the surface polarity and time interval between each component's peak and the averaged, rectified EMG. The component names are as follows: early BP, late BP or NS', pre-motion positivity (PMP or P-50), motor potential (MP or N-10), N+50, P+90, N+160, and P+300 (Shibasaki & Hallett, 2006). Although both segments of the BP will be described, this dissertation will focus on the late component of the BP that occurs just before movement initiation. An idealized representation of the entire BP is shown in Figure 5.

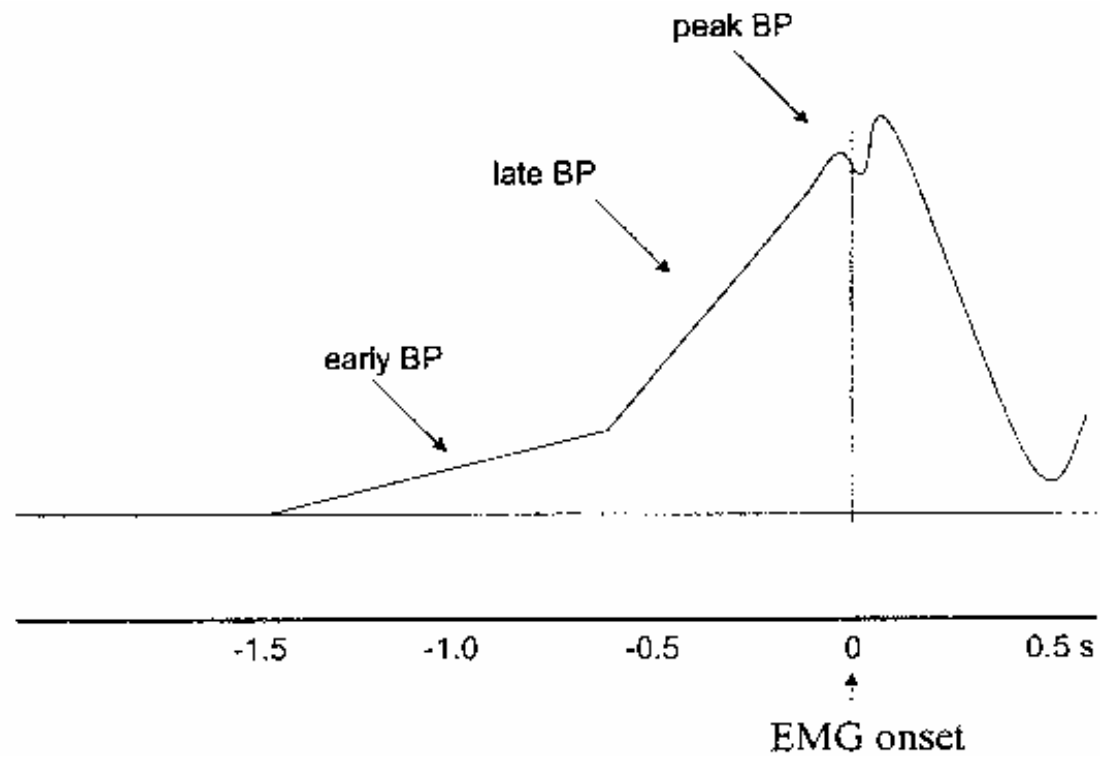


Figure 5 caption: Schematic representation of the time course and components of the BP prior to movement onset (from Jahanshahi & Hallett, 2003).

Early BP is the initial slow negative segment of BP. It is a gently rising negativity beginning approximately 1.5 sec prior to movement onset with a symmetrical, widespread scalp distribution. The cortical generators of BP in humans have been studied through EEG source analysis, MEG, and invasive subdural recordings in patients with intractable epilepsy. These investigations indicate that early BP begins bilaterally in pre-SMA, continues to SMA proper with some somatotopy, and then to lateral premotor cortices (area 6: crown of precentral gyrus) with some somatotopy (Shibasaki & Hallett, 2006). Early BP is maximal over the midline centro-parietal area (Cz) and widely distributed over the scalp regardless of the site of movement. The potential was originally assumed to index general preparation for the forthcoming movement due to its midline maximal, symmetric distribution. However, it is now believed to be at least partially movement site specific and its diffuse distribution may be due to, "summation of electrical fields generated from homologous areas of both hemispheres via volume conduction" (Shibasaki & Hallett, 2006, p. 2343). Late BP, or NS', is the steeper negative slope of BP that occurs when the signal abruptly increases its gradient about 400 ms before movement onset. It originates in contralateral central motor areas, specifically M1 (area 4: anterior bank of central sulcus) and lateral premotor cortex, both with precise somatotopy (Shibasaki & Hallett, 2006; Toma & Hallett, 2003). Late BP is thought to index the preparatory activity of neurons in M1 and adjacent areas just prior to a willed movement.

It is worth noting that the exact natures of the processes underlying each component of BP are still unresolved. Although early BP, "is believed to reflect

intention and motor planning, and the NS' [late BP] probably reflects more intense activity in preparation for movement" (Karp, Porter, Toro, & Hallett, 1996, p. 105), as yet there is no firm consensus on the issue. Nevertheless, "it is certain that both components are related to preparation and/or execution of voluntary movement" (Shibasaki & Hallett, 2006, p. 2353), and it is within that framework that we will labor.

A further caveat also pertains to this notion of what BP is actually measuring. Lang (2003) rightly raises the question of intentionality when he notes that subjects participating in a study of simple, repetitive single movements (e.g., finger taps) already have the decisions of *what to do* and *how to do it* resolved in advance. They are primarily focused on *when to do it*. Therefore, since the motor programs needed for performance are already available, Lang assumes that BP, "at least in the simple paradigm, does not reflect aspects of 'programming' but the transitional process of the intention to act into action at a certain time. The involvement of this transitional process is assumed to reflect volition" (p. 20). From this view, the decision to act is contingent upon the necessary motor areas being already in a general preparatory state and the transduction of intention into action may or may not be present with each single movement. While this interpretation of BP is relevant for simple acts such as finger tapping, it may be less so for more complex motor behaviors such as speech—an act in which a different set of articulatory programs must be retrieved, planned and executed for each new utterance.

The classical BP paradigm involves self-paced finger movements separated by five or more seconds. BP has also been elicited from several other tasks involving

movements of the toes, eyes, elbow, leg, and prior to speech, vocalization and deglutition (Shibasaki & Hallett, 2006). By and large, the similarities among these conditions are far more striking than their differences. Also, the morphology of the component remains consistent regardless of the body part performing the movement (Lang, 2003). These features attest to the robustness of BP as a general index of motor preparation.

While mode of movement appears to minimally affect the signal's latency and morphology, the effects of movement parameters and internal factors are more striking. The magnitude and time course of BP have been shown to be influenced by factors such as: movement complexity; speed, precision and force of movement; level of subjective involvement; and learning and skill acquisition. Concerning the act of speech, it is noteworthy that increased complexity of movement causes enhanced amplitude of late BP, faster movement execution causes BP to begin closer to movement onset, and BP amplitude decreases when subjects become bored with the task and perform movements in an automatic fashion (Lang, 2003).

BP associated with speech production in normally fluent speakers has been studied extensively. The results have been somewhat conflicting, likely due to differences in location of recording sites, potential EMG contamination, and variable linguistic processing demands. Several earlier studies found no evidence for hemispheric lateralization of BP prior to speech (e.g., Brooker & Donald, 1980; Wohlert, 1993). Wohlert's findings failing to show laterality for speech were obtained from a sample of females, in whom speech lateralization may be less marked (Rippon, 1990). Some recent efforts, by contrast, have supported the theory that

motor control for spoken language is a lateralized function of the dominant hemisphere. For instance, Tarkka (2001) reported a lateralized dipole in the left precentral gyrus region that was found for vocalization but not for a nonspeech oral motor task. McArdle et al. (2009) showed that increasing the articulatory complexity of an utterance caused a stronger BP at the frontocentral midline, while a simpler speech task resulted in a weaker, more posterior BP located over the vertex. They concluded that "under certain conditions the speech-related BP is markedly left lateralized over the mid-frontal region" (p. 283). Interestingly, the manner in which subjects move their articulators during speech may also play a role in BP topography. This is supported by a study of mandibular movements. Yoshida et al. (2000) found symmetrical distribution of BP for routine mouth opening and closing, but lateral movements of the mandible produced EEG activity predominating over the hemisphere ipsilateral to the direction of movement.

The cortical generators of BP are at present far better characterized than the subcortical generators. This imbalance owes partly to the difficulty of obtaining reliable surface recordings from the tangentially oriented neurons of many subcortical regions. Consequently, most of what is known about premovement potentials arising from these areas has come from animal studies and a few invasive recordings in humans. With respect to the cerebellum, intracortical recordings in monkeys have shown that unilateral cerebellar ablation completely suppresses BP as measured from the contralateral motor cortex (Sasaki, Gemba, Hashimoto, & Mizuno, 1979). Scalp recorded early and late BP were also found to be absent from patients with cerebellar efferent lesions (Shibasaki, Barrett, Nechige, Hirata, & Tomoda, 1986). Such findings

support a model of cerebro-cerebellar interaction in voluntary movements. This model holds that BP is generated from the motor cortices only with the presence of feedforward activation from the cerebellum via the thalamo-cortical projection (Ikeda et al. 1997; Ikeda & Shibasaki, 2003). Interestingly, late CNV is preserved after unilateral cerebellar ablation or cerebellar efferent lesions (Ikeda et al., 1997), suggesting a different generator mechanism for that component.

Basal ganglia also mediate motor control and have been implicated in the generation of BP. It is well established that activity in basal ganglia begins slightly later than in motor cortex or cerebellum relative to movement onset (Ikeda et al., 1997; Rektor, 2003). This has led some to speculate that basal ganglia likely play a lesser role in the generation of BP than the latter regions (Ikeda et al., 1997). However, BP has been measured in humans through invasive recordings in putamen, caudate head, and pallidum (Rektor, 2003). Additionally, scalp recorded BP was found to be disturbed in patients with basal ganglia lesions, including those with Parkinson's disease (Deecke, 1985; Dick et al., 1989). This has led others to claim that, "the cortico-basal ganglia-thalamo-cortical circuitry seems to be involved not only in movement execution, but also in its preparation" (Rektor, 2003, p. 69). Whatever the true extent of subcortical involvement in the preparation of spontaneous movement, it is certain that such generators play an important, albeit currently undetermined, role.

Subcortical structures are also pertinent to this discussion inasmuch as they have been implicated in a recent neurological model of stuttering (Alm, 2004, 2005). This model stems from Goldberg's (1985, 1991) dual premotor systems hypothesis

which argues that the human brain has two parallel systems for the planning and execution of movement. The lateral system (e.g., lateral premotor cortex, cerebellum) is thought to be active when movement is controlled relative to external sensory input, for instance when speaking with a metronome. The medial system (e.g., SMA, basal ganglia) relies on automatized, internally-generated programs in the absence of external feedback, for instance during spontaneous speech. In this model, stuttering is caused primarily by disturbed functioning of the medial system, particularly the basal ganglia. More specifically, the model describes speech as a motor sequence and suggests that the basal ganglia send impaired "go-signals" to trigger the next motor segment in the sequence. Well known fluency-evoking conditions such as choral speech and altered auditory feedback are effective because they presumably allow control of speech output to momentarily bypass the impaired medial system in favor of the intact lateral system.

As it happens, late BP is sensitive to dysfunctions in the lateral system (particularly cerebellum), while early BP is sensitive to SMA and basal ganglia lesions in the medial system (Gerloff, 2003). It of course follows that BP might be applied to study the putative subcortical sources of stuttering. Contiguous with that potential utilization of BP, however, are several unknowns. For instance, it is still unclear if basal ganglia and their projections are causatively involved in the pathophysiology of stuttering, and researchers have cautioned that, "it is not 'safe' to interpret any of these [MRCP] components as specific markers for the integrity of distinct brain regions" (Gerloff, 2003, p. 187). Suffice it that Alm's theory has ample heuristic value and is amenable to empirical testing. Such testing could be performed,

for example, with neuroimaging techniques that exploit the brain's hemodynamic and metabolic responses. The use of EEG source localization procedures to examine the medial system's role in stuttered speech also seems an obvious avenue of inquiry.

Since previous work using motor potentials with this population has employed only CNV designs, it is crucial to distinguish CNV from BP. Broadly conceived, the CNV paradigm is associated with re-actions, while the BP paradigm is associated with actions. More specifically, CNV is elicited by a response performed during a forewarned reaction time task. It is thought to be an index of expectancy, reflecting processes involved in the preparation of signaled movements, and is therefore also known as the "expectancy wave" (Deecke & Kornhuber, 2003). BP, by contrast, is elicited by a response performed without external cues indicating when to act. It stems from self-paced, voluntary movements, rather than signaled movements. CNV is a slow negative wave developing in the interval between the warning stimulus and imperative stimulus, therefore it reflects several related processes: anticipation for a forthcoming signal; preparation for the execution of a response; and other factors such as time estimation and uncertainty. This arguably makes CNV a more intricate and potentially challenging signal to work with than BP. While the two potentials are similar, CNV is "confounded by activity related to anticipatory attention for the imperative stimulus. This causes serious difficulty for the interpretation of the CNV" (Brunia, 2003, p. 207).

Applying BP to the Disorder of Stuttering

Due to its relative simplicity and long history as a versatile indicator of motor preparation, BP seems ideally suited to address questions related to speech preparation. Furthermore, BP has been used to study disorders of pathological movement, of which stuttering surely is. Ikeda and Shibasaki (2003) state that, "BP is considered to provide an important clue to the understanding of preparatory cortical functions in association with voluntary movements in normal subjects, pathogenesis of movement disorders like dystonia and parkinsonism, and psychogenic movement disorders" (p. 45). Stuttering shares similarities with movement disorders like Tourette syndrome, myoclonus, and motor tics, all of which have been investigated using premovement potentials (Karp et al., 1996; Obeso, Rothwell, & Marsden, 1981; Shibasaki & Kuroiwa, 1975; Terada et al., 1995; Trenkwalder et al., 1993). The possibility clearly exists for BP to be applied to the abnormal speech behaviors associated with stuttering as well.

Fortunately, BP lends itself readily to a procedure commonly used to study the pathological movements of the disorders mentioned above, as well as other types of nonpathological movements. By time-locking the EEG to the EMG onset (i.e., using the EMG signal as the fiducial point for back averaging the EEG signal), one can detect the cortical spike preceding the movement of interest (Barrett, Shibasaki, & Neshige, 1985). This procedure of back averaging is thought to detect BP when movements are mediated by voluntary mechanisms, but not before movements that are involuntary or passive (Terada et al., 1995). An important caveat to this assumption, however, is mentioned by several researchers: voluntary movements do not always produce a premotor potential, therefore one cannot necessarily call a

movement involuntary if premotor negativity is missing (Karp et al., 1996; Terada et al., 1995). This qualification must be borne in mind when interpreting the presence or absence of BP preceding a moment of stuttering.

Back averaging appears to be a ready means for examining neural processing that precedes stuttering moments. That the technique has not previously been applied to this end is unsurprising, given the inherent methodological difficulties. For instance, the EEG signal is quite susceptible to artifactual contamination, particularly from the eye blinks, tensing of speech muscles, and head movements that often accompany instances of stuttering (Tran, Craig, Boord, & Graig, 2004). These obstacles are not insurmountable, however, and can be managed with the proper preventive measures. By carefully devising experimental tasks and giving precautionary instructions aimed at minimizing the occurrence of artifacts preceding speech output, one can be confident that much of data collected during an experiment will be useable. Additionally, the application of independent component analysis (ICA) to remove artifact in concatenated single trial data can help overcome these obstacles (Makeig, Debener, Onton, & Delorme, 2004; Tran et al., 2004).

ICA is a technique for extracting information of interest from large data sets. It is a family of algorithms for performing blind source separation, a process that extracts unknown, independent source signals (e.g., EEG artifact components) that are mixed into and essentially buried within a larger set of known signals (e.g., the entire EEG) (Stone, 2004). ICA can be applied to EEG data due to the reasonable assumption that different physiological sources—for instance speech musculature and neuronal firing—generate source signals that are statistically independent of each

other. This supposition is satisfied because the neuronal activity that produces scalp recorded EEG is typically not time-locked to artifact components associated with muscular noise. In addition to the assumption of statistical independence, other assumptions must also be met for the outcomes of ICA algorithms to be valid. First, the mixing medium must be linear and any propagation delays as signals travel through that medium to the electrodes must be negligible relative to the inverse bandwidth of the EEG signal (Jung et al., 2000). With multichannel EEG, activity originating in cortex and muscles mixes linearly at the scalp; also, propagation delays from these different sources are minute compared with the wavelength of EEG signals. The signals can therefore be treated as arriving immediately. Secondly, the number of independent signal generators must be less than or equal to the number of EEG sensors on the scalp (Jung et al., 2000). Using a 64-channel electrode array makes it highly probable that the number of source signals will not exceed the number of components measured on the scalp. Since each independent component generated from ICA theoretically represents the activity of a single contributing source to the average evoked potential, it is possible to linearly subtract artifactual components from the ICA output.

Purpose of this Experiment

The purpose of this experiment is to examine whether there is atypical activity in cortical motor preparation areas prior to stuttered speech. Specifically, this experiment will help clarify if stuttering is linked to dysfunction in motor preparation just prior to speech onset. By comparing activity within stuttering subjects, I will

investigate whether stuttered and fluent speech show different patterns of premotor activity. As the neural time course of motor preparation prior to speech output is on the order of hundreds of milliseconds, and since the technique has precedence for this type of research (e.g., Prescott, 1988; Walla et al., 2004), BP seems an appropriate tool for our purposes. Corollary questions will be addressed pertaining to the recruitment of involuntary mechanisms during stuttering moments, and how the presence or absence of BP preceding stuttering moments might be viewed in the light of recent etiological theories postulating distinct premotor systems for stuttered and fluent speech. Finally, this dissertation aims to extend the findings of Walla et al. (2004), who used a slightly different protocol and found the analogue of early BP to be absent in PWS well before speech onset, despite their subjects producing no stuttered speech.

METHODS

Participants

This study was approved by the University of Colorado Human Research Committee and informed consent was obtained from all participants prior to the recordings. Nine PWS and nine normal speaking adults (16 male, 2 female) matched for age, gender, and handedness were recruited from the Colorado Front Range region. All participants but one were dextral. The mean age for the stuttering group was 29.6 years (SD = 14.6 years), and the mean age for the control group was 30.6 years (SD = 11.1 years). An independent samples t-test reveled no significant differences in ages between the groups ($t = .16$, $df = 16$, $p > .05$). All subjects had normal or corrected to normal vision and were not taking dopaminergic drugs at the

time of testing, as such agents may affect BP amplitude (Trenkwalder et al., 1993). The stuttering participants ranged in severity from Mild to Severe, as measured by the *Stuttering Severity Instrument for Children and Adults, 3rd Ed.* (SSI-3) (Riley, 1994).

Stimuli

Sixty English words beginning with the phoneme /b/ and 60 English words beginning with /p/ were compiled from an online search of the Brown Corpus, with the most frequently appearing 3- or 4-syllable words chosen for inclusion (see Appendix). Familiar words were selected so that speech production would not be confounded by difficult or uncertain pronunciation. Bilabial plosives were selected for word-initial phonemes because it is relatively easy to visually detect stuttering on those sounds. Words were presented at the beginning of the carrier phrase, *"___ is the word I say."* These stimuli were chosen to increase the likelihood of educing stuttering from the PWS group, as stuttering is more likely to occur with production of sentences rather than single words, multi-syllabic rather than monosyllabic words, and usually occurs at the beginning of a sentence (Bloodstein & Bernstein Ratner, 2008). Stimuli were presented using E-Prime (Psychology Software Tools, Pittsburgh, PA) on a screen roughly 1.5 m from the viewer in black type on a white background.

Experimental Paradigm

Prior to beginning the EEG recording session, all participants in the stuttering group were videotaped in the laboratory room outside of the recording booth while

giving speech samples for the SSI-3 (Riley, 1994). During recording, participants sat in a comfortable chair in a dimly lit, sound-treated booth with a computer screen directly in front of them. Participants performed a self-paced sentence reading task. Each trial consisted of a target sentence that appeared at the top of the screen and slowly moved toward the bottom in a vertical line. The duration for the sentence to move across the screen was 7 sec. After the sentence disappeared, the screen was blank for 3 sec. Before the presentation of each sentence, a plus sign (+) was shown for 3 sec as a fixation point. Different initial words were used on each trail so as to require the continual generation of different motor programs. Participants were instructed to say the sentence aloud at any time they wished before it reached the bottom of the screen. This ensured that participants were initiating speech movements voluntarily (i.e., generating BP) rather than in immediate response to an external signal (i.e., generating CNV). Post hoc analysis of participants' response times from stimulus onset to voice onset revealed no significant differences between groups (control group mean = 1.87 sec; PWS mean = 1.85 sec; $t = .12$, $df = 16$, $p > .05$).

To minimize muscle and eye artifact, participants were asked to avoid blinking and extraneous head (e.g., licking lips, turning head, swallowing) and body (e.g., tapping hand, moving feet) movements just before they began speaking. Participants in the stuttering group were instructed to allow their disfluencies to occur spontaneously and not attempt to use previously learned motoric techniques to suppress or control them. All participants were instructed to keep their articulators relaxed just prior to speaking. This was modeled by the experimenter and then practiced by the participants. A video camera was placed next to the computer screen

to record trials for later analysis and to potentially heighten communicative pressure, thereby increasing the occurrence of disfluencies in the stuttering group. Additionally, a confederate was placed in the room during testing to further heighten communicative pressure for the stuttering group. The confederate remained silent during testing, sat cater-cornered from the participant while making markings on a clipboard, and made no eye contact with the participant during recording.

Sessions were recorded in two 13-minute blocks, consisting of 60 sentences per block, with a 5-miute break in between. Initial words were randomized across recording blocks and subjects. After the session was completed and the participants exited the recording booth, they answered two 7-point Likert style questions (e.g., 1 = strongly disagree, 4 = neutral, 7 = strongly agree) regarding perceptions about the presence of the confederate during testing. The questions were: 1) “Having an observer in the booth caused me to feel more pressure than I would have felt if I were alone” and 2) “Having an observer in the booth caused my speech to be more disfluent than it would have been if I were alone.”

Recordings

Continuous EEG was collected with a 64-channel scalp electrode array (sintered Ag/AgCl, Neuroscan QuickCap) placed on the scalp according to the extended International 10–20 System for electrode placement. During recording, the nasion was used as reference, but following artifact rejection and filtering the data were re-referenced to the average reference (Lehmann & Skrandies, 1980). Electrodes were also placed supra-orbitally and over the outer canthus of the left eye to record

the electrooculogram (EOG). Auditory activity associated with verbalization was recorded on a separate bipolar channel with a lavalier microphone attached to participants' shirt collars. The EEG was recorded using a 68-channel Synamps amplifier system (Compumedics-Neuroscan, Charlotte, NC) with two separate bipolar channels for monitoring eye movements. An online analog bandpass of DC – 200 Hz was used, at a sampling rate of 2000 Hz, and an amplifier gain of 1000. Electrode impedances were kept below 25 kΩ.

Data Analysis

Analysis of the data was performed using Matlab 7.01 (Math-Works, Natick, MA), EEGLAB 7.2.9 (Delorme and Makeig, 2004), and SCAN 4.4 (Compumedics-NeuroScan, Charlotte, NC). Each participant's EEG was filtered offline with a band pass of .1 Hz – 30 Hz. The low end of the filtering was set to .1 Hz to preserve the low frequencies that show SMA activity (Walla et al., 2004).

The EEG was divided into individual epochs around speech onset, with a 400 ms pre-stimulus interval and a 100 ms post-stimulus interval, resulting in 120 trials with 1001 sample points per trial for each recording. Epochs were baseline corrected to the average amplitude across the entire epoch inclusive of any artifact occurring within the record. Epochs containing eye blink activity of +/- 75 μV on the EOG channel were rejected from further analysis.

For the stuttering group, trials on which unambiguous stuttering occurred on the initial syllable (as confirmed through offline video and audio analysis) were grouped as "disfluent" (stuttering-disfluent: SD). Trials on which the initial syllable

was articulated fluently (using the same confirmation criteria) were grouped as "fluent" (stuttering-fluent: SF). All other trials were classified as "ambiguous". These included: 1) trials containing indeterminable stuttering or nonstuttering on the initial syllable; 2) trials in which the participant made an extraneous movement within the analysis window prior to speech onset (e.g., licking lips, yawning); and 3) trials in which the participant employed a fluency-enhancing technique during articulation of the initial syllable. Ambiguous trials were rejected from further analysis. For the control group, all trials were classified as "fluent" (control-fluent: CF) except those in which the initial syllable was not articulated fluently or an extraneous movement was made within the analysis window prior to speech onset. Such trials were rejected from further analysis.

Triggers marking speech onset were manually entered offline into the continuous EEG by examining digitized audio activity from the lavalier microphone and were confirmed by video analysis. Originally, speech onset was determined by monitoring lips movements involved in articulation of bilabial plosives, similar to Walla et al. (2004). A pair of bipolar EMG electrodes were applied over the superior and inferior obicularis oris and EEG was analyzed relative to EMG onset. Unexpectedly, I was unable to measure a BP signal using this method. I was then successful in locating BP after using voice onset as the fiducial time point. A similar method for marking speech onset has been employed in previous premovement research with PWS (e.g., Prescott, 1988).

Baseline for measuring late BP amplitude was defined as the mean EEG amplitude during the interval from 400 ms – 350 ms sec prior to speech onset.

Latency of the late BP was defined as a visually abrupt and steep rise in negativity occurring roughly 350 ms – 250 ms before speech onset (Shibasaki & Hallett, 2006). After ICA analysis removed unwanted components in the EEG (described below), an average waveform for each participant was computed, resulting in two conditions for the stuttering group (fluent: SF, disfluent: SD) and one condition for the nonstuttering group (fluent: CF). These conditions were treated as separate groups for the purposes of statistical analyses.

EEG files were imported into the Matlab environment using the EEGLAB Toolbox (EEGLAB, San Diego, CA) under the public GNU license (Delorme & Makeig, 2004). ICA was performed first on the individual and then the group level EEG recordings using the Infomax approach (Bell & Sejnowski, 1995). Weighted components were clustered on the two activity measures of 'scalp map' and 'ERP.' I estimated that these two measures contained equally relevant information, so they were given equal weights and an equal number of dimensions. The total number of dimensions in the component distance measure used for clustering was 10. This was done because clustering algorithms may work poorly with measures having more than 10 to 20 dimensions (Delorme & Makeig, 2010). Using the kmeans clustering algorithm, eight clusters were returned. The backprojected scalp distributions of each component within the clusters were visually inspected. Components were linearly subtracted from the mixing matrix that showed eye activity over frontal electrode sites, noise from predominantly one or several channels, or inconsistent inter-trial activity within the expected time range of the BP. Eighty-two components were

ultimately retained at the group level to produce a filtered EEG dataset. That dataset was used to compute final average waveforms for the three groups.

As the study design was unbalanced and partially nested, the assumption of independence did not hold (i.e., the SF and SD groups contained data from the same participants and so were not drawn from independent samples). Due to this confound, interpretations of any differences between the controls and the stuttering groups must be made with caution (Delorme, 2006). A Kruskal-Wallis nonparametric one-way ANOVA was used to test for differences between the three groups on measures of onset latency, peak latency, peak amplitude, and slope. A non-parametric test was chosen because the Kolmogorov–Smirnov normality test (Chakravart, Laha, & Roy, 1967) revealed non-normality in the group distributions. A Friedman nonparametric ANOVA assuming repeated measures was performed on the SF and SD groups to test for differences within the stuttering participants based on fluency status. To conform with the traditional BP literature, comparisons for the standard latency, amplitude, and slope measures were made from activity recorded at vertex (i.e., electrode CZ).

RESULTS

Answers to Post-test Questions

An independent samples t-test did not reveal significant differences between the PWS and control groups on answers to the first post-test question: “Having an observer in the booth caused me to feel more pressure than I would have felt if I were alone.” For the second question, “Having an observer in the booth caused my speech to be more disfluent than it would have been if I were alone,” the responses from the

stuttering group were significantly different from the controls ($t = 2.21$, $df = 16$, $p = .04$). PWS were more likely to agree that the presence of an observer in the recording room caused them to be more disfluent.

Traditional BP Measures at Vertex

Figure 5 shows grand average ERPs from the vertex electrode CZ in each of the three groups.

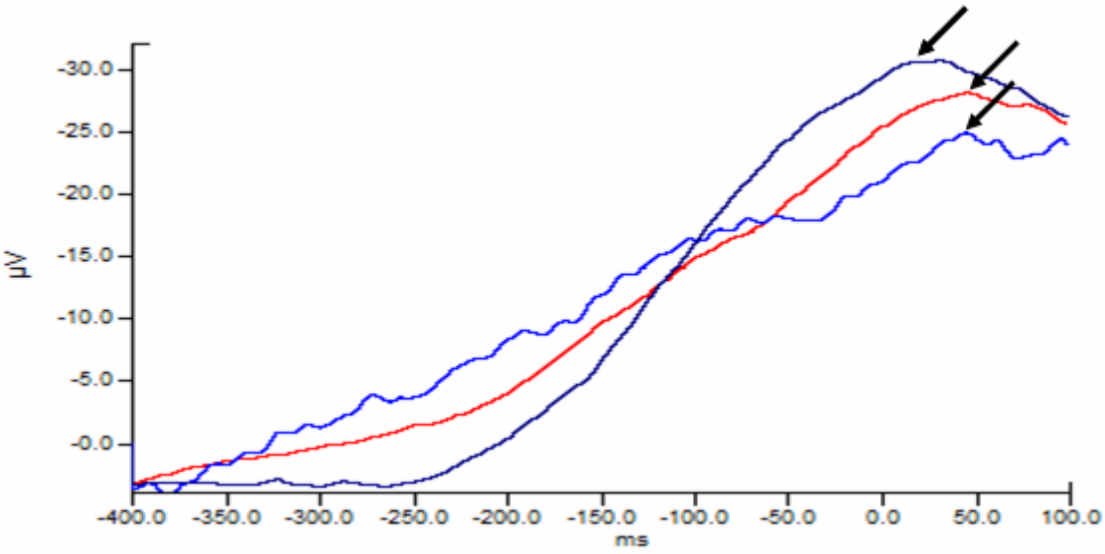


Figure 5 caption: Grand average ERPs for all groups at electrode CZ. Dark blue waveform = CF group; red waveform = SF group; light blue waveform = SD group; black arrows indicate peak ampltiude; negative polarity is up.

The general morphology of the late BP waveform was similar across groups, with a marked increase in gradient occurring just prior to speech onset. However, the CF group showed a more pronounced and abrupt slope increase compared to the stuttering groups (see Figures 6 and 7).

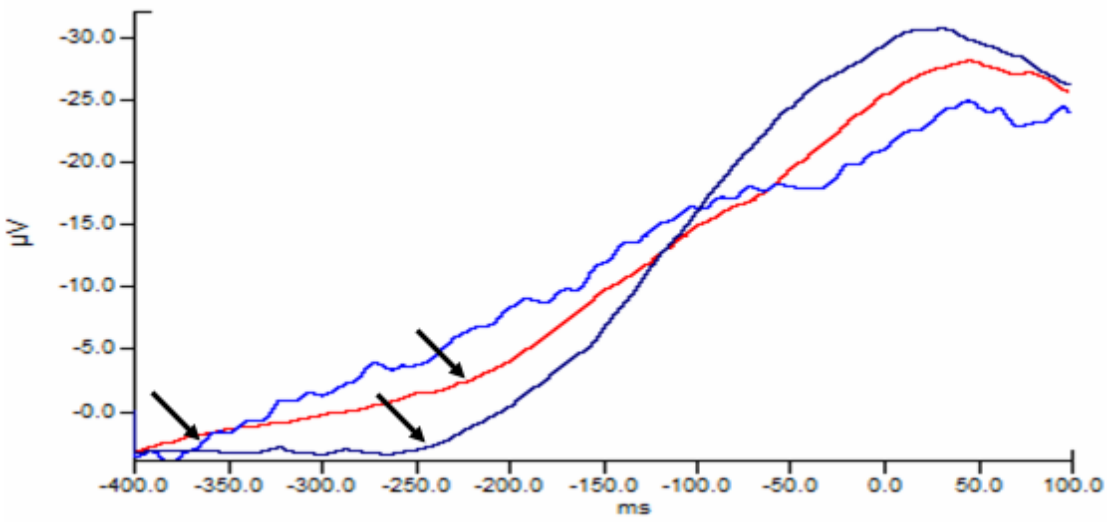


Figure 6 caption: Grand average ERPs for all groups at electrode CZ. Dark blue waveform = CF group; red waveform = SF group; light blue waveform = SD group; black arrows indicate BP onset; negative polarity is up.

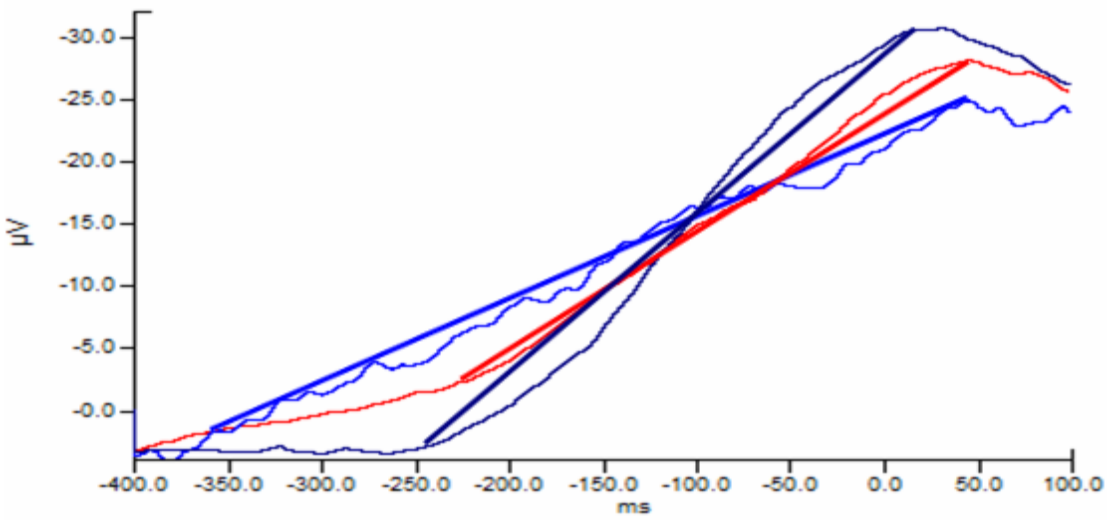


Figure 7 caption: Grand average ERPs for all groups at electrode CZ. Dark blue waveform = CF group; red waveform = SF group; light blue waveform = SD group; straight lines visually describe slope from BP onset to peak amplitude; negative polarity is up.

For BP onset latency, the Kruskal-Wallis test showed a significant difference between groups (df = 26, Chi-square = 13.07, p = .002). There was a significant difference between the CF (mean = -248.6 ms, SD = 56.4 ms) and SD (mean = -357.2 ms, SD = 46.1 ms) groups, and between the SF (mean = -230.8 ms, SD = 63.8 ms) and SD groups. Friedman's test revealed a significant difference between the SF and SD groups (df = 17, Chi-square = 5.44, p = .019), indicating that the SD group began their BP response earlier than the SF group. For BP peak latency, the Kruskal-Wallis test showed a significant difference between groups (df = 26, Chi-square = 8.85, p = .012). There was a significant difference between the CF (mean = 20.5 ms, SD = 21.1 ms) and SF (mean = 53.9 ms, SD = 20.0 ms) groups, and between the CF and SD (mean = 45.7 ms, SD = 19.1 ms) groups. Friedman's test revealed no significant difference between the SF and SD groups. For measures of slope, the Kruskal-Wallis test showed a significant difference between groups (df = 26, Chi-square = 5.98, p = .050). The CF group (mean = -.14, SD = .08) differed significantly from the SD group (mean = -.07, SD = .05), but did not differ from the SF group (mean = -.09, SD = .04). Friedman's test comparing the SD and SF groups nearly reached significance (df = 17, Chi-square = 5.0, p = .082). These results indicate that the BP response for the SD group had a flatter gradient than the controls' and had a trend toward a flatter gradient compared to the SF group. No significant differences were found between groups on measures of BP peak amplitude.

Table 2 contains individual data for peak amplitude, peak latency, and onset latency (slope was computed from the formula $m = (y_2 - y_1)/(x_2 - x_1)$).

Table 2 title: Individual Data for Peak Amplitude, Peak Latency, and Onset Latency

Control-Fluent (CF) Group

Participant	Peak Amplitude (μV)	Peak Latency (msec)	Onset Latency (msec)
1	-47.1	24.5	-250
2	-43.3	-22.0	-241
3	-40.7	53.0	-263
4	-43.7	20.5	-228
5	-47.9	16.5	-241
6	2.7	32.0	-251
7	-17.0	1.0	-157
8	1.7	29.5	-375
9	-50.7	29.5	-231

Stuttering-Fluent (SF) Group

Participant	Peak Amplitude (μV)	Peak Latency (msec)	Onset Latency (msec)
1	-58.2	82.5	-270
2	-29.9	44.5	-207
3	-26.4	80.5	-241
4	-15.7	38.0	-175
5	-28.5	23.5	-258
6	-35.6	65.0	-223
7	-10.4	39.0	-166
8	-4.3	51.5	-170
9	-54.4	60.5	-367

Stuttering-Disfluent (SD) Group

Participant	Peak Amplitude (μV)	Peak Latency (msec)	Onset Latency (msec)
1	-70.5	54.0	-312
2	-21.6	41.5	-347
3	-20.0	48.5	-382
4	-19.6	61.5	-372
5	-14.7	21.5	-395
6	-28.5	65.5	-258
7	-20.9	11.5	-400
8	-4.5	41.0	-387
9	-46.6	66.0	-362

Scalp Maps

Visual inspection of the scalp maps of the averaged activity from the evoked potential recordings (Figure 8) indicated that the CF group had a stronger BP response than both of the stuttering groups at peak.

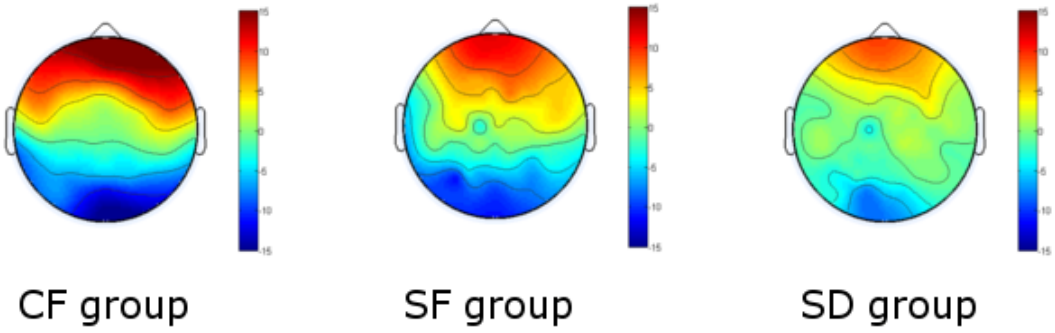


Figure 8 caption: Scalp maps of average evoked activity for all groups at peak amplitude as measured at electrode CZ. Color bar scale is in μV; CF group = 21 ms after speech onset, SF group = 54 ms after speech onset, SD group = 46 ms after speech onset.

Despite clear differences in amplitude, the scalp topography for all three groups was quite similar at peak amplitude of BP. All groups revealed positive, bilateral frontal activation and negative, bilateral occipital activation. This symmetric distribution suggests bilateral dipole activation at motor cortex or close to motor cortex.

Comparison of the scalp maps at BP onset revealed more striking differences in scalp topography among groups (Figure 9).

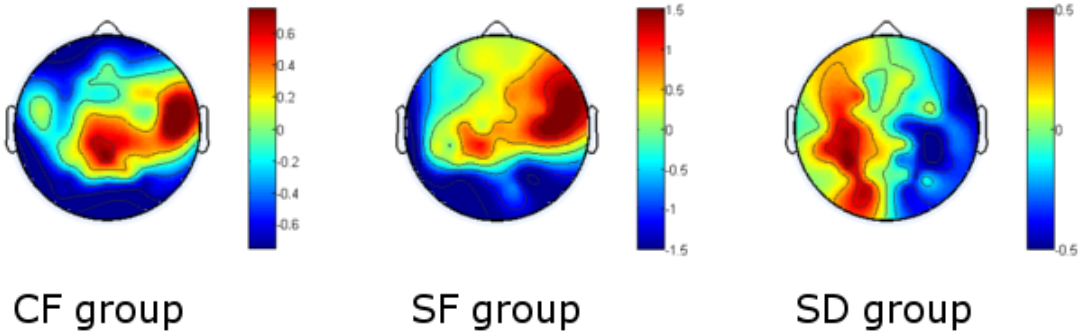


Figure 9 caption: Scalp maps of average evoked activity for all groups at BP onset as measured at electrode CZ. Color bar scale is in µV; CF group = -249 ms before speech onset, SF group = -231 ms before speech onset, SD group = -357 ms before speech onset.

The CF and SF groups showed similar patterns of activity while initiating their BP responses. Both groups showed positive right temporal and central activation near vertex, along with bilateral parieto-occipital and left temporal negative activation. Within the stuttering subjects, there were markedly different scalp distributions at onset of the BP based on fluency status. While scalp maps for fluent trials revealed the topographies just mentioned, stuttered trials were associated with a nearly symmetric distribution of differently valenced activity: right negativity and left positivity covering mostly central and posterior regions, both peaking over lateral centro-parietal areas.

ICA Results

ICA was used to examine the possibility of multiple underlying generators for the BP. Figure 10 shows group evoked potentials at different scalp sites.

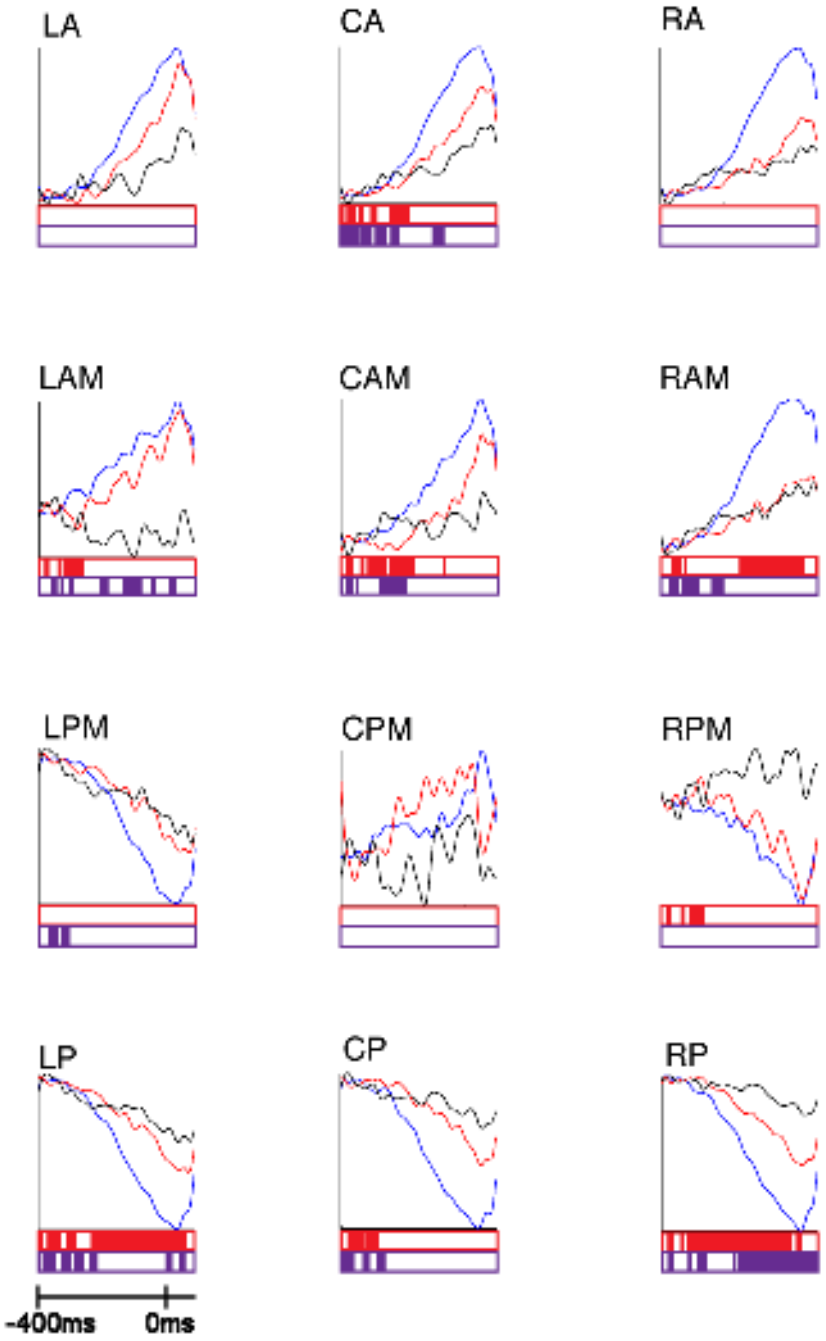


Figure 10 caption: Group ERPs at different scalp locations. Blue waveforms = CF group; red waveforms = SF group; black waveforms = SD group; bars represent planned comparisons between groups; red bars = CF vs. SF groups; purple bars = SF vs. SD groups; filled areas represent significant differences at $p < .01$.

Each graph corresponds to a location on the map in Figure 11 (Gilley, unpublished).

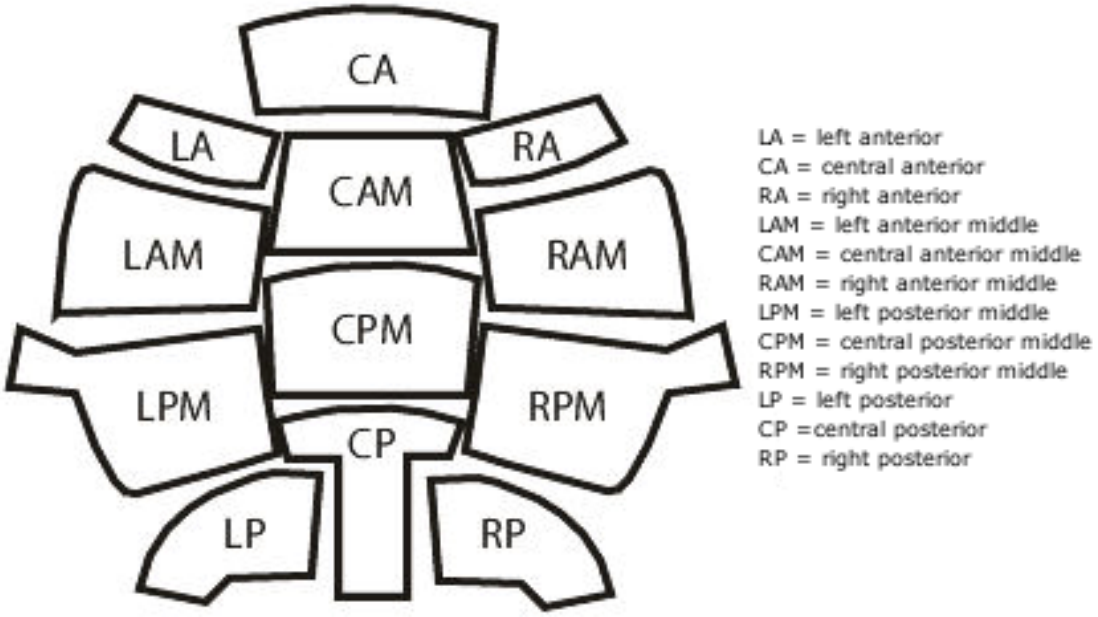


Figure 11 caption: Map of twelve scalp regions corresponding to group waveforms in Figure 10.

The map organizes electrodes into twelve regions of interest, each region composed of several electrodes. There were significant amplitude differences at multiple scalp sites and latencies at an alpha level of .01. The CF vs. SF comparisons revealed late (i.e., closer to speech onset) differences over the right anterior middle area, early differences over central anterior areas, and differences in posterior areas bilaterally throughout the epoch. For those comparisons, the waveforms for the CF group always showed stronger activation than the SF waveforms. SF vs. SD comparisons revealed amplitude differences at numerous scalp sites and latencies as well. The central anterior area differed at earlier latencies (SF < SD). The posterior areas appeared to show a laterality effect, with the fluent and disfluent waveforms diverging close to speech onset on the right and diverging earlier on the left. There was also an apparent laterality effect over the anterior middle areas, with the fluent and disfluent waveforms diverging near onset on the left but remaining similar on the right.

DISCUSSION

Using BP as an index of motor preparation, I found evidence for atypical cortical activity before stuttered speech as compared to fluent speech within PWS. Differences in peak onset latency and slope were found at vertex, where the late phase of BP is presumed to be most robust (Shibasaki & Hallett, 2006). When subjects stuttered, their BP responses began much earlier and had a trend toward a flatter gradient compared to when they were fluent. Additionally, potential laterality effects were found over the left anterior middle and right posterior areas close to speech onset. In both areas, preparatory activity associated with disfluent speech was

heavily depressed or absent. Comparisons of the scalp distributions between PWS and controls and within PWS based on fluency status revealed clear differences in strength and scalp location of the BP. Not surprisingly, the controls showed much stronger activation overall than PWS, particularly at peak. This complements Walla et al.'s (2004) findings of reduced activity for PWS prior to speech onset. I found that the fluent speech of PWS showed a pattern similar to controls at BP onset. However, the same subjects' disfluent speech revealed a very different scalp topography for BP onset: symmetrical right negativity and left positivity over mainly central and posterior regions, both peaking over centro-parietal areas. Taken together, these findings signify that stuttered speech in PWS may be prepared and/or executed less efficiently than fluent speech.

Implications

Applying EEG to disfluencies. The results of this research have several implications. First, this design demonstrated that EEG can be applied to disfluencies in situ. In other words, the neurophysiology of stuttered speech can be studied directly. Commonly, research protocols using neuroimaging techniques to examine PWS have either 1) failed to obtain a sufficient number of stuttered trials to compute a robust average signal associated with that behavior, or 2) have discarded stuttered trials due to contamination from artifact. I found that manipulating linguistic, contextual and instructional variables allowed for a sufficient number of authentic disfluencies to be gathered from most subjects. Also, by applying ICA to the data, extraneous noise caused by speech and other artifact could be removed from the EEG.

Possible laterality effects for disfluent speech. These results indicate that the neural correlates of fluent and disfluent speech may be different within PWS. This is suggested by findings demonstrating that fluency status produced dissociable effects on BP morphology and topography. Regarding the former, there was a trend toward a flatter gradient and a longer time course of the BP at vertex for disfluent as compared to fluent speech. With respect to the latter, there were visual differences in scalp topography at onset of BP, as well as apparent laterality effects over anterior middle and posterior areas.

These laterality effects are intriguing, as they occurred over brain regions that have been implicated in a recent etiological theory of stuttering (Alm, 2004, 2005). Alm's dual premotor systems model implicates the medial and lateral premotor systems in the generation of stuttered and fluent speech, respectively. The left anterior middle area overlies the lateral premotor cortex, an area thought to be involved in the putatively intact lateral system. It was over this site that premovement activity in PWS was found to be virtually absent prior to stuttered speech, while activity before fluent speech in PWS was robust and nearly identical to that seen before the fluent speech of controls. This concurs with results in normal speakers showing a dipole unique to vocalization located in the left precentral gyrus very near lateral premotor cortex (Tarkka, 2001). Perhaps uncoincidentally, within PWS I also found premovement activation associated with stuttered speech to be heavily reduced over right posterior sites compared to when they were fluent. These posterior sites overlie the cerebellum, the other generator implicated in the lateral premotor system.

While these laterality findings are compelling, they are also preliminary. Further work is needed before any conclusions can be drawn regarding neurophysiological mechanisms involved in the production of fluent or disfluent speech. Without the use of source reconstruction techniques and dipole source analyses to estimate generators of the BP, one can only speculate as to the regions responsible for the scalp differences observed in this study. If indeed it was regions of the lateral system that contributed to BP for fluent but not for disfluent speech, it is unclear why those areas were activated for an automatized task under internal control (i.e., sentence reading) when the dual premotor systems model would predict that such a task would preferentially activate medial system regions. It also remains an open question as to whether the same preparatory systems are being used in a less efficient/atypical manner during disfluency, or if altogether different neural substrates are involved in the preparation and production of disfluent speech.

Potential recruitment of involuntary mechanisms. Since BP is thought to be involved in only voluntary movements (Lang, 2003; Shibasaki & Hallett, 2006), a reduced or atypical BP response preceding a moment of stuttering may implicate involuntary, or at least not fully volitional, motor systems in stuttered speech. If true, this would provide more proximal evidence for stuttering as a movement disorder that shares common features with disorders such as Tourette syndrome, motor tics, and myoclonus. Several commonalities exist between stuttering and Tourette syndrome, for instance. These include: onset in childhood; high male-to-female ratio; involvement of involuntary movements; definite genetic contribution; symptoms that are exacerbated by anxiety and stress (including social stress); and following a

waxing and waning course (Van Borsel & Tetnowski, 2007). These similarities suggest that "a possible relationship between developmental stuttering and Tourette syndrome and perhaps a shared underlying pathogenesis" (Van Borsel & Tetnowski, 2007, p. 287) is at least plausible.

There are also reports of BP accompanying voluntarily initiated movements while spontaneous motor tics are not preceded by BP within the same patients (Karp, 1996; Obeso et al., 1981). A comparable pattern of differential premotor responses for stuttered compared to nonstuttered speech was found within the PWS cohort examined in this study. Whether such parallels imply common generator mechanisms for stuttered speech and motor tics remains a subject for further exploration. Likewise, further inquiries will need to address the potential suitability of pharmacological interventions for tic and other movement disorders for treating stuttering. If stuttered speech is indeed prepared by motor systems similar to those responsible for known involuntary movements, it stands to reason that similar pharmacological means of mitigating such movements might be applied to managing stuttering symptoms as well.

Directions for Future Research

The research paradigm employed in this experiment and similar methods offer a host of possible extensions. It would be worthwhile to test the feasibility of using this protocol or a modified version to examine a pediatric population of PWS. Very little is currently known about the neurophysiology of children and adolescents who stutter. Better characterization of not just motor and sensory systems, but also limbic,

attentional, and other neurological systems closer to the age of stuttering onset is needed. As nearly all findings in adults are likely confounded by secondary reorganization, the primary pathology(ies) subserving stuttered speech is poorly understood at present.

The functional implications of these findings vis-à-vis possible therapeutic or behavioral correlates are difficult to ascertain, given the difficulty of interpreting neurological differences seen in adults. As mentioned above, differences in preparatory activity that distinguished disfluent from fluent speech in this study may indicate learned, compensatory processes rather than true causal factors. This is why pediatric imaging research is vital. Such efforts might be more easily extended into the domain of treatment. For instance, it is well documented that stuttering often co-occurs with fine motor impairments during childhood, including articulation and writing difficulties (Bloodstein & Bernstein Ratner, 2008). Devising integrated treatment programs informed by neurophysiological data on childhood stuttering and related disorders might provide more efficient remediation than targeting each domain separately.

Similar to neurological findings in children, evidence of how or whether PWS differentially employ speech-language systems when using motoric techniques learned during therapy is exiguous. Some data suggest that PWS may preferentially employ cerebellar pathways when speaking. This may be due to "increased sensory or motor monitoring of ongoing or planned movements associated with lower levels of automaticity during the execution of such movements" (De Nil, Kroll, & Houle, 2001, p. 79). De Nil and colleagues posit that PWS overactivate motor feedback and

execution systems to control speech because speaking has never become an automatic and effortless act for them (De Nil et al., 2001, 2003). This suggests that employment of fluency-enhancing skills would likewise recruit motor systems in an abnormal fashion. Neural activation associated with the purposeful use of motoric skills has rarely been studied directly but would be illuminating.

Another salient question pertains to better differentiation between premotor stages. A great deal of processing must occur before one begins to speak. To describe this processing, terms such as motor "programming", "planning", and "preparation" are often used synonymously in the literature. This imprecise language is unfortunate because the slow waves preceding movement onset are composed of several elements and such activation is most likely a composite phenomenon (Deecke & Kornhuber, 2003). These premotor processes can and ought to be better delineated in PWS. The excellent temporal resolution of EEG makes it an ideal tool for that purpose. While the present experiment did not address these issues, BP and CVN paradigms are well suited for such explorations.

An obvious caveat is that the motor system does not operate in such a straightforward manner. Parallel distributed networks and modulatory processes operate before and after movement onset, consequently speech production is not merely a linear series of discreet stages; there is much overlap between them. However, a simplified model can serve as a useful heuristic.

Such a model might be conceptualized as containing the functions of *what to speak*, *how to speak*, and *when to speak*. *What to speak* mainly involves programming of articulatory gestures for sequential speech movements. Electrophysiologically, it

begins as a slow potential two or more seconds before speech onset, and likely constitutes a great deal of early BP. *How to speak* can be conceived as an intermediate stage during which movement parameters such as velocity, displacement and positioning of articulators are prepared. It at least partly coincides with the preceding and subsequent processes, but contributes uniquely to the utterance as well. *When to speak* involves processing that finally executes the motor commands to produce speech. Activity associated with this phase is observed as rapidly increasing cortical excitability in speech motor areas (Jananshahi & Hallet, 2003). This activation likely constitutes much of the late BP.

Through the lens of this model, the findings of Walla et al. (2004) relate most closely to the relatively early function *what to speak*. Their concept of "focused verbal anticipation" can be viewed as a ramping up of the motor system to a general preparatory state before *what to speak* is engaged. The system is waiting for, anticipating, visual word presentation (which supplies the input for *what to speak*) so that the motor sequence leading to speech output can commence. The present study examined a different but related time point in that motor sequence. The time window I analyzed was nearer to speech onset and likely included aspects of both *how to speak* and *when to speak*.

Since the PWS cohort reported that the presence of an observer in the recording room caused them to be more disfluent than they otherwise would have been, one might speculate about the effects on BP of cognitive factors such as anticipation of stuttering and perceived communicative stress. More to the point, did such factors operating prior to stuttered speech contribute to the longer time course

and flatter gradient of BP for the SD group? This explanation appears unlikely because those factors, if present, existed prior to fluent speech as well, as the presence of the confederate remained constant throughout testing. Moreover, anticipation was likely present in the earlier time period of CNV (i.e., the "expectancy wave"), which was analyzed in the Walla et al. (2004) study but not in this experiment. Since I focused on the late phase of BP—a time period during which cortical activation for movement is mainly confined to motor areas— any dissociable effects of cognitive factors related to stuttering were likely negligible. However, the present study could not rule out the possibility of such effects and future investigations of BP in PWS would do well to minimize such confounds.

Conclusions

This study demonstrated preliminary evidence that motor preparation preceding stuttered and nonstuttered speech may differ. Brain activation associated with the fluent speech of PWS revealed certain similarities in overall scalp topography and BP slope at vertex compared to controls. By contrast, activity associated with the disfluent speech of PWS did not resemble that of controls on nearly any measure that was assessed. Importantly, premovement activity within PWS showed clear visual differences in scalp topography and significant or nearly significant differences in BP latency, amplitude, and slope based on fluency status. This suggests that PWS may employ premotor systems differently for fluent versus disfluent speech when preparing movements for the forthcoming utterance. As this

was primarily an exploratory study, further testing is necessary to better elucidate and extend the results reported herein.

BIBLIOGRAPHY

Adams, M. (1974). A physiologic and aerodynamic interpretation of fluent and stuttered speech. *Journal of Fleuncy Disorders, 1*, 35-47.

Adams, M., & Reis, R. (1971). The influence of the onset of phonation on the frequency of stuttering. *Journal of Speech and Hearing Research, 14*, 639-644.

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

Alm, P. A. (2005). On the causal mechanims of stuttering (Doctoral dissertation, Lund University, 2005).

Barrett, G., Shibasaki, H., & Neshige, R. (1985). A computer-assisted method for averaging movement-related cortical potentials with respect to EMG onset. *Electroencephalography and Clinical Neurophysiology, 60*, 276-281.

Beal, D. S., Gracco, V. L., Lafaille, S. J., & De Nil, L. F. (2007). Voxel-based morphometry of auditory and speech-related cortex in stutterers. *NeuroReport, 18(12),* 1257-60.

Bell, A. J., & Sejnowski, T. J. (1995). An information-maximization approach to blind separation and blind deconvolution. *Neural Computation, 7(6)*, 1129-59.

Blackburn, B. (1931). Voluntary movements of the organs of speech in stutterers and non-stutterers. *Psychological Monographs, 41(4)*, 1-13.

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

Borden, G. J., Baer, T., & Kenney, M. K. (1985). Onset of voicing in stuttered and fluent utterances. *Journal of Speech & Hearing Research, 28(3)*, 363-372.

Braun, A. R., Varga, M., Stager, S., Schulz, G., Selbie, S., Maisog, J. M., et al. (1997). Altered patterns of cerebral activity during speech and language production in developmental stuttering. An H215O positron emission tomography study. *Brain, 120*, 761–784.

Brooker, B. H., & Donald, M. W. (1980). Contribution of the speech musculature to apparent human EEG asymmetries prior to vocalization. *Brain and Language, 9,* 226-245.

Brunia, C. H. M. (2003). CNV and SPN: Indices of anticipatory behavior. In M.

Jahanshahi & M. Hallett (Eds.), *The Bereitschaftspotential: Movement related cortical potentials* (pp. 201-227). New York: Kluwer Academic/Plenum Publishers.

Bryngelson, B. (1935). Sidedness as an etiological factor in stuttering. *Journal of Genetic Psychology, 47*, 204-217.

Chakravarti, I. M., Laha, R. G., & Roy, J. (1967). *Handbook of methods of applied statistics, volume I*. New York: John Wiley and Sons.

Chworowski, C. R. (1952). A comparative study of the diadochokinetic rates of stutterers and nonstutterers in speech related and non-speech related movements. [Abstract]. *Speech Monographs, 19*, 192.

Cross, H. M. (1936). The motor capacities of stutterers. *Archives of Speech, 1*, 112-132.

Deecke, L. (1985). Cerebral potentials related to voluntary actions: Parkinsonian and normal subjects. In Delwaide & Agnoli (Eds.), *Clinical Neurophysiology in Parkinsonism* (pp. 91-105). Amsterdam: Elsevier.

Deecke, L., & Kornhuber, H. H. (2003). Human freedom, reasoned will, and the brain: The Bereitschaftspotential story. In M. Jahanshahi & M. Hallett (Eds.), *The Bereitschaftspotential: Movement related cortical potentials* (pp. 283-320). New York: Kluwer Academic/Plenum Publishers.

Delorme, A. (2006). Statistical methods. *Encyclopedia of Medical Device and Instrumentation*, 6, 240-264.

Delorme, A., & Makeig, S. (2004). EEGLAB: an open source toolbox for analysis of single-trial EEG dynamics including independent component analysis. *Journal of Neuroscience Methods, 134(1),* 9-21.

Delorme, A., & Makeig, S. (2010). *EEGLAB tutorial: Chapter 04: Independent component clustering*. Retrieved from http://sccn.ucsd.edu/wiki/Chapter_04:_Independent_Component_Clustering.

De Nil, L. F. (1999). Stuttering: A neurophysiological perspective. In N. Bernstein Ratner & E. C. Healey (Eds.), *Stuttering research and practice: Bridging the gap between theory and practice* (pp. 85-102). Mahwah, NJ: Lawrence Erlbaum.

De Nil, L. F., Kroll, R. M., & Houle, S. (2001). Functional neuroimaging of cerebellar activation during single word reading and verb generation in stuttering and nonstuttering adults. *Neuroscience Letters, 302*, 77–80.

De Nil, L. F., Kroll, R. M., Kapur, S., & Houle, S. (2000). A positron emission tomography study of silent and oral single word reading in stuttering and nonstuttering adults. *Journal of Speech, Language, and Hearing Research, 43*, 1038-54.

De Nil, L. F., Kroll, R. M., Lafaille, S. J., & Houle, S. (2003). A positron emission tomography study of short- and long-term treatment effects on functional brain activation in adults who stutter. *Journal of Fluency Disorders, 28(4),* 357–379.

Dick, J. P. R., Rothwell, J. C., Day, B. L., Cantello, R., Buruma, O., Gioux, M., et al. (1989). The Bereitschaftspotential is abnormal in Parkinson's disease. *Brain, 112*, 233-244.

Foundas, A. L., Bollich, A. M., Corey, D. M., Hurley, M., & Heilman, K. M. (2001). Anomalous anatomy of speech-language areas in adults with persistent developmental stuttering. *Neurology, 57*, 207-215.

Foundas, A. L., Bollich, A. M., Feldman, J., Corey, D. M., Hurley, M., Lemen, L. C., et al. (2004). Aberrant auditory processing and atypical planum temporale in developmental stuttering. *Neurology, 63*, 1640-1646.

Fox, P. T., Ingham, R. J., Ingham, J. C., Hirsch, T., Downs, J. H., Martin, C., et al. (1996). A PET study of the neural systems of stuttering. *Nature, 382*, 158–162.

Fox, P. T., Ingham, R. J., Ingham, J. C., Zamarripa, F., Xiong, J. H., & Lancaster, J. L. (2000). Brain correlates of stuttering and syllable production: a PET performance-correlation analysis. *Brain, 123*, 1985–2004.

Gerloff, C. (2003). Movement-related cortical potentials in patients with focal brain lesions. In M. Jahanshahi & M. Hallett (Eds.), *The Bereitschaftspotential: Movement related cortical potentials* (pp. 45-59). New York: Kluwer Academic/Plenum Publishers.

Goldberg, G. (1985). Supplementary motor area structure and function: review and hypotheses. *The Behavioral and Brain Sciences, 8*, 567-616.

Goldberg, G. (1991). Microgenetic theory and the duel premotor systems hypothesis: Implications for rehabilitation of the brain-damaged subject. In R. E. Hanlon (Ed.), *Cognitive microgenesis: A neurophysiological perspective* (pp. 32-52). New York: Springer.

Healey, E. C., & Adams, M. R. (1981). Speech timing skills of normally fluent and stuttering children and adults. *Journal of Fluency Disorders, 6*, 233-246.

Healey, E. C., & Gutkin, B. (1984). Analysis of stutterers' voice onset times and fundamental frequency contours during fluency. *Journal of Speech and Hearing Research, 27(2)*, 219-225.

Healey, E. C., & Ramig, P. R. (1986). Acoustic measures of stutterers' and nonstutterers' fluency in two speech contexts. *Journal of Speech and Hearing Research, 29*, 325-331.

Hunsley, Y. L. (1937). Disintegration in the speech musculature of stutterers during the production of a nonvocal temporal pattern. *Psychological Monographs, 49*, 32-49.

Ikeda, A., Shibasaki, H. (2003). Generator mechanisms of the Bereitschaftspotential as studied by epicortical recording in patients with intractable partial epilepsy. In M. Jahanshahi & M. Hallett (Eds.), *The Bereitschaftspotential: Movement related cortical potentials* (pp. 45-59). New York: Kluwer Academic/Plenum Publishers.

Ikeda, A., Shibasaki, H., Kaji, R., Terada, K., Nagamine, T., Honda, M., et al. (1997). Dissociation between contingent negative variation (CNV) and Bereitschaftspotential (BP) in patients with parkinsonism. *Electroencephalography and clinical Neurophysiology, 102*, 142-151.

Ingham, R. J., Fox, P. T., Ingham, J. C., & Zamarripa, F. (2000). Is overt stuttered speech a prerequisite for the neural activations associated with chronic developmental stuttering? *Brain and Language, 75*, 163–194.

Jancke, L. (1994). Variability and duration of voice onset time and phonation in stuttering and nonstuttering adults. *Journal of Fluency Disorders, 19*, 21-37.

Jahanshahi, M., & Hallett, M. (2003). The Bereitschaftspotential: What does it measure and where does it come from? In M. Jahanshahi & M. Hallett (Eds.), *The Bereitschaftspotential: Movement related cortical potentials* (pp. 1-17). New York: Kluwer Academic/Plenum Publishers.

Johnson, W., & King, A. (1942). An angle board and hand usage study of stutterers and nonstutterers. *Journal of Experimental Psychology, 31*, 293-311.

Jung, T-P., Makeig, S., Westerfield, M., Townsend, J., Courchesne, E., & Sejnowski, T. J. (2000). Removal of eye activity from visual event-related potentials in normal and clinical subjects. *Clinical Neurophysiology, 111(10),* 1745-58.

Karp, B. I., Porter, S., Toro, C., & Hallett, M. (1996). Simple motor tics may be preceded by a premotor potential. *Journal of Neurology, Neurosurgery, and Psychiatry, 61*, 103-106.

Lang, W. (2003). Surface recordings of the Bereitschaftspotential in normals. In M. Jahanshahi & M. Hallett (Eds.), *The Bereitschaftspotential: Movement related cortical potentials* (pp. 19-34). New York: Kluwer Academic/Plenum Publishers.

Lehmann, D., & Skrandies, W. (1980). Reference-free identification of components of checkerboard-evoked multi-channels potential fields. *Electroencephalography and Clinical Neurophysiology, 48,* 609–621.

Makeig, S., Debener, S., Onton, J., & Delorme, A. (2004). Mining event-related brain dynamics. *Trends in Cognitive Sciences, 8(5),* 204-210.

McArdle, J. J., Mari, Z., Pursley, R. H., Schulz, G. M., & Braun, A. R. (2009). Electrophysiological evidence of functional integration between the language and motor systems in the brain: a study of the speech Bereitschaftspotential. *Clinical Neurophysiology, 120*, 275-284.

Neumann, K., Preibisch, C., Euler, H. A., von Gudenberg, A. W., Lanfermann, H., Gall, V., et al. (2005). Cortical plasticity associated with stuttering therapy. *Journal of Fluency Disorders, 30*, 23-39.

Obeso, J. A., Rothwell, J. C., & Marsden, C. D. (1981). Simple tics in Gilles de la Tourette's syndrome are not prefaced by a normal premovement EEG potential. *Journal of Neurology, Neurosurgery, and Psychiatry, 44*, 735-738.

Orton, S. T. (1927). Studies in stuttering. *Archives of Neurology and Psychiatry, 18*, 671-672.

Peters, H. F. M., & Hulstijn, W. (1987). Programming and initiation of speech utterances in stuttering. In H. F. M. Peters & W. Hulstijn (Eds.), *Speech motor dynamics in stuttering* (pp. 185-195). New York: Springer-Verlag.

Prescott, J. (1988). Event-related potential indices of speech motor programming in stutterers and non-stutterers. *Biological Psychology, 27*, 259-273.

Rektor, I. (2003). Intracerebral recordings of the Bereitschaftspotential and related potentials in cortical and subcortical structures in human subjects. In M. Jahanshahi & M. Hallett (Eds.), *The Bereitschaftspotential: Movement related cortical potentials* (pp. 61-77). New York: Kluwer Academic/Plenum Publishers.

Rickenberg, H. E. (1956). Diadochokinesis in stutterers and nonstutterers. *Journal of Medical Society of New Jersey, 53*, 324-326.

Riley, G. D. (1994). *Stuttering Severity Instrument for Children and Adults* (3rd ed.). Austin: Pro-Ed.

Rippon, G. (1990). Individual differences in electrodermal and electroencephalographic asymmetries. *International Journal of Psychophysiology, 8,* 309-320.

Robb, M., & Blomgren, M. (1997). Analysis of F2 transitions in the speech of stutterers and nonstutterers. *Journal of Fluency Disorders, 22*, 1-16.

Salmelin, R., Schnitzler, A., Schmitz, F., & Freund, H. J. (2000). Single word reading in developmental stutterers and fluent speakers. *Brain, 123,* 1184–1202.

Salmelin, R., Schnitzler, A., Schmitz, F., Jäncke, L., Witte, O. W., & Freund, H. J. (1998). Functional organization of the auditory cortex is different in stutterers and fluent speakers. *NeuroReport, 9*, 2225–29.

Sasaki, K., Gemba, H., Hashimoto, S., & Mizuno, N. (1979). Influences of cerebellar hemispherectomy on slow potentials in the motor cortex preceding self-paced hand movement in monkeys. *Neuroscience Letters, 15*, 23-28.

Seth, G. (1934). An experimental study of the control of the mechanism of speech and in particular that of respiration in the stutterer. *British Journal of Psychology, 24*, 375-388.

Shibasaki, K., Barrett, G., Nechige, R., Hirata, I., & Tomoda, H. (1986). Volitional movements are not preceded by cortical slow negativity in cerebellar dentate lesion in man. *Brain Research, 368*, 361-365.

Shibasaki, H., & Hallett, M. (2006). What is the Bereitschaftspotential? *Clinical Neurophysiology, 117*, 2341-56.

Shibasaki, K., & Kuroiwa, Y. (1975). Electroencephalographic correlates of myoclonus. *Electroencephalography and Clinical Neurophysiology, 39*, 455-463.

Smith, A., Denny, M., Shaffer, L. A., Kelly, E. M., & Hirano, M. (1996). Activity of intrinsic laryngeal muscles in fluent and disfluent speech. *Journal of Speech and Hearing Research, 39*, 329-348.

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

Starkweather, C. W., Hirschman, P., & Tannenbaum, R. S. (1976). Latency of vocalization onset: stutterers versus nonstutterers. *Journal of Speech and Hearing Research, 19*, 481-492.

Stone, J. V. (2004). *Independent component analysis: A tutorial introduction*. Cambridge, MA: The MIT Press.

Strother, C. R., & Kriegman, L. S. (1943). Diadochokinesis in stutterers and nonstutterers. *Journal of Speech Disorders, 8*, 325-335.

Tarkka, I. M. (2001). Cerebral sources of electrical potentials related to human vocalization and mouth movement. *Neuroscience Letters, 298*, 203-206.

Terada, K., Ikeda, A., Van Ness, P. C., Nagamine, T., Kaji, R., Kimura, J., et al. (1995). Presence of Bereitschaftspotential preceding psychogenic myoclonus: clinical application of jerk-locked back averaging. *Journal of Neurology, Neurosurgery, and Psychiatry, 58*, 745-747

Toma K., & Hallett, M. (2003). Generators of the movement-related cortical potentials and dipole source analysis. In M. Jahanshahi & M. Hallett (Eds.), *The Bereitschaftspotential: Movement related cortical potentials* (pp. 113-130). New York: Kluwer Academic/Plenum Publishers.

Tran, Y., Craig, A., Boord, P., & Craig, D. (2004). Using independent component analysis to remove artifact from electroencephalographic measured during stuttered speech. *Medical & Biological Engineering & Computing, 42*, 627-633.

Travis, L. E. (1931). *Speech pathology*. New York: Appleton-Century.

Travis, L. E. (1934). Dissociation of homologous muscle function in stuttering. *Archives of Neurology and Psychiatry, 31*, 127-133.

Trenkwalder, C., Bucher, S. F., Oertel, W. H., Proeckl, D., Plendl, H., & Paulus, W. (1993). Bereitschaftspotential in idiopathic and symptomatic restless leg syndrome. *Electroencephalography and Clinical Neurophysiology, 89*, 95-103.

Van Borsel, J., & Tetnowski, J. A. (2007). Fluency disorders in genetic syndromes. *Journal of Fluency Disorders, 32*, 279-296.

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

Walla, P., Mayer, D., Deecke, L., & Thurner, S. (2004). The lack of focused verbal anticipation in stutterers: a magnetoencephalographic study. *NeuroImage, 22*, 1321-27.

Watson, B. C., & Alfonso, P. J. (1983). Foreperiod and stuttering severity effects on acoustic laryngeal reaction time. *Journal of Fluency Disorders, 8*, 183-205.

Williams, D. F., & Brutten, G. J. (1994). Physiologic and aerodynamic events prior to the speech of stutterers and nonstutterers. *Journal of Fluency Disorders, 19*, 83-111.

Wohlert, A.B. (1993). Event-related brain potentials preceding speech and nonspeech oral movements of varying complexity. *Journal of Speech and Hearing Research, 36*, 897-905.

Yoshida, K., Kaji, R., Hamano, T., Kohara, N., Kimura, J., Shibasaki, H., et al. (2000). Cortical potentials associated with voluntary mandibular movements. *Journal of Dental Research, 79(7)*, 1514-18.

Zaleski, T. (1965). Rhythmic skills in stuttering children. *De Therapia Vocis et Loquellae, 1*, 371-372.

Zebrowski, P. M., Conture, E. G., & Cudahy, E. A. (1985). Acoustic analysis of young stutterers' fluency: preliminary observations. *Journal of Fluency Disorders, 10*, 173-192.

Zimmermann, G. (1980). Stuttering: a disorder of movement. *Journal of Speech and Hearing Research, 23*, 122-136.

Zimmermann, G., & Knott, J. R. (1973). CNVs related to spoken words in stutterers and nonstutterers. *Electroencephalography and Clinical Neurophysiology, 36*, 216.

Zimmermann, G., & Knott, J. R. (1974). Slow potentials of the brain related to speech processing in normal speakers and stutterers. *Electroencephalography and Clinical Neurophysiology, 37,* 599-607.

APPENDIX

Stimulus words:

Battlefield	Blackberry	Passenger	Pinball machine
Balancing	Blackmailing	Parallel	Plantation
Baltimore	Boycotting	Pacific	Platinum
Bargaining	Bodybuilder	Patrolman	Plexiglas
Barbecue	Bodily	Pakistan	Popular
Bacteria	Bookkeeping	Parliament	Politics
Battery	Borrowing	Particle	Politician
Baptism	Botany	Paradise	Potato
Basketball	Bottleneck	Paperweight	Policeman
Bankruptcy	Boulevard	Paprika	Poetry
Balcony	Bootlegging	Paragraph	Poverty
Ballplayer	Brutality	Patio	Pollution
Barbarian	Broadcaster	Patriot	Poisonous
Bachelor	Broadcaster	Parasite	Portugal
Bachelorette	Brotherhood	Panama	Pottery
Barricade	Brazilian	Parenthood	Polyester
Believing	Brevity	Pennsylvania	Porcelain
Belonging	Bricklayer	Permanent	Porcupine
Beautiful	Bricklaying	Perfection	President
Beethoven	Brotherly	Peculiar	Property
Behavior	Breathtaking	Peanut butter	Probation
Benjamin	Businesses	Pedestal	Promises
Biblical	Bulletin	Peppery	Professor
Bitterness	Buffalo	Performer	Presentation
Biography	Budapest	Pedestrian	Prisoner
Birmingham	Buddhism	Pessimist	Publicity
Biology	Businessmen	Piano	Punishment
Bicycle	Burglary	Pittsburg	Publisher
Biologist	Buttering	Picasso	Puritans
Birthday party	Bystander	Pineapple	Punctuation