Stuttering: a dynamic motor control disorder

Christy L. Ludlow*, Torrey Loucks

Laryngeal and Speech Section, Clinical Neurosciences Program, National Institute of Neurological Disorders and Stroke, 10 Center Drive MSC 1416, Bldg. 10 Rm. 5D38, Bethesda, MD 20892-1416, USA

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Abstract

The purpose of this review is to determine what neural mechanisms may be dysfunctional in stuttering. Three sources of evidence are reviewed. First, studies of dynamic inter-relationships among brain regions during normal speech and in persons who stutter (PWS) suggest that the timing of neural activity in different regions may be abnormal in PWS. Second, the brain lesions associated with acquired stuttering are reviewed. These indicate that in a high percentage of cases, the primary speech and language regions are not affected but lesions involve other structures, such as the basal ganglia, which may modulate the primary speech and language regions. Third, to characterize the motor control disorder in stuttering, similarities and differences from focal dystonias such as spasmodic dysphonia (SD) and Tourette’s syndrome (TS) are reviewed. This review indicates that the central control abnormalities in stuttering are not due to disturbance in one particular brain region but rather a system dysfunction that interferes with rapid and dynamic speech processing for production.

Educational objectives: The reader will be able to describe: (1) the similarities and differences between stuttering and other speech motor control disorders, (2) which brain lesions are most likely to produce acquired stuttering in adults, and (3) what type of brain abnormality most likely underlies stuttering.

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* Corresponding author. Tel.: +1-301-496-9366; fax: +1-301-480-0803.
E-mail address: Ludlowc@ninds.nih.gov (C.L. Ludlow).
1. Purpose

Our purpose is to identify whether particular neural mechanisms are implicated by the current literature for characterizing stuttering as a neurodevelopmental motor control disorder. Because speech is a dynamic motor function process, it requires a highly synchronized and adaptive network of neural activity in order to function without disruption. We will review the following topics in attempting to fashion an improved understanding of the underlying mechanisms involved in stuttering.

1. Recent evidence on the rapid interplay between multiple systems during speech processing
2. How lesions in many different locations in the brain can disrupt fluency
3. The similarity and differences between stuttering and other speech motor control disorders

2. The rapid interplay between multiple systems required for fluent speech

Speech is a rapid motor control task; movements must occur within a few milliseconds in order for the listener to perceive the correct message. For example, vocal fold opening and closing for voice onset and offset during voiceless and voiced consonant distinctions are less than 20 ms, a time period which is less than a quarter of the time of any other laryngeal movements (Ludlow & Lou, 1996). To produce plosive consonants, the airflow must be sealed long enough for the pressure to build up and then a rapid ballistic opening gesture is needed to provide the necessary burst of air (Borden & Harris, 1984).

To study brain mechanisms involved in the rapid processing of speech, high temporal resolution is needed. Previous studies of brain mechanisms involved in stuttering have used PET scanning which has spatial resolution but poor temporal resolution; brain activity is studied over a minute or more. These studies have shown that many different brain regions are associated with speech production; the left frontal operculum, the right and left sensory and motor regions, the right and left primary and auditory association areas and several subcortical regions including the cerebellum, anterior cingulate, thalamus and the putamen (Braun et al., 1997; Fox et al., 2000). PET scanning, however, cannot provide information concerning the rapid inter-relationships between neural events in different brain regions prior to and during speech gestures or stuttered interruptions. Magnetoencephalography (MEG), on the other hand, has the necessary temporal resolution. This technique can also have some spatial resolution when the recording points are mapped onto brain images obtained using magnetic resonance imaging (MRI). Because of high temporal resolution, within milliseconds, this technique can examine the dynamic relationships between different brain regions during normal speech and language (Helenius, Salmelin, Service, & Connolly, 1998; Levelt,
For example, investigators have examined the dynamic interplay between responses in different brain regions during single word reading (Salmelin, Helenius, & Service, 2000; Salmelin, Schnitzler, Schmitz, & Freund, 2000). When neural events were examined within a 400 ms time period between word presentation and motor execution, predominant processing occurred in the left hemisphere in both persons who stutter (PWS) and controls. However, the sequence of activation differed between groups indicating that the dynamic interplay between brain regions is altered in persons with life-long stuttering. The normal speakers had earlier responses in the left inferior region processing prior to left central motor region activation. The sequence was reversed in the PWS group; these speakers activated the left central MI region for motor execution before the left inferior region for articulation programming.

Reduced activations in auditory association regions in PWS were also found by Fox et al. (2000) and Braun et al. (1997) using PET scanning. This could be interpreted as being an abnormal suppression of auditory feedback while speaking. Using MEG, Numminen et al. were able to examine responses to auditory stimuli during oral reading and found that they were normally suppressed in control subjects by 44–71% in comparison with responses during silent reading (Numminen et al., 1999). A subsequent study by Curio, found that cortical responses to one’s own voice transiently activate the right hemisphere around 100 ms after their utterance by a speaker (Curio, Neuloh, Numminen, Jousmaki, & Hari, 2000). However, on the left side, this was delayed by 11 ms in normal speakers only during speaking and not during listening (Curio et al., 2000). It was suggested that speaking normally both dampens and delays responses in the auditory cortex in the left hemisphere. A similar study was conducted in PWS and controls contrasting auditory responses during silent reading, reading aloud and chorus reading (Salmelin et al., 1998). Responses to auditory stimuli differed during the different conditions in the PWS. The authors suggested that responses to auditory stimuli were most altered during self-paced reading in PWS, when an abnormal pattern of greater auditory suppression occurred on the right and reduced suppression on the left. Surprisingly, the normal pattern of greater auditory suppression on the left and reduced suppression on the right, occurred when the subjects were stuttering. The results implicate different excitatory and inhibitory inter-relationships between brain regions in normal and PWS groups rather than one particular region being dysfunctional.

Subtle fine motor deficits can be found in PWS in other motor systems (Borden, 1983; Forster & Webster, 1991, 2001; Webster, 1990). In addition, sensory function differences have been found in PWS; the effects of sensory deprivation reduces fluency (Hutchinson & Ringel, 1975) while the ability of PWS to use sensory feedback is affected for oral movements but not for hand movements (De Nil & Abbs, 1991; Fucci, Petrosino, Schuster, & Belch, 1991; Petrosino, Fucci, Gorman, & Harris, 1987). Although differences in sensory motor functioning may affect
other motor systems in some PWS, most often the oral-motor system is selectively affected and this is most evident during speech.

Symptom occurrence is intermittent, however — fluent speech occurs the vast majority of the time in PWS, albeit with considerable effort. Stuttering occurs around 10% of the time, although subjects report they consciously monitor their speech to prevent disruptions most of the time. The system seems most easily disrupted when the demands for rapid and dynamic processing increase (Bosshardt, 2002). It may be the functioning of the integrated system that is altered not the individual components per se.

Some have suggested that left hemisphere dominance for the control of speech/language is altered in PWS. Neuroimaging studies demonstrate that both the left and right motor and sensory regions are active in normal speakers during speech production (Braun et al., 1997). However, WADA testing, where a barbiturate is infused into the right or left cerebral arterial system, has demonstrated that the left hemisphere is essential for speech and language expression in most persons who have not sustained a left hemisphere lesion in early childhood (Rasmussen & Milner, 1977). Similarly, the occurrence of aphasia following left hemisphere lesions is much more frequent than following right hemisphere lesions (Mazzocchi & Vignolo, 1979). For speech production, rather than language processing, however, it is unclear to what degree speech production is lateralized (Rasmussen & Milner, 1977). One study used the WADA technique to demonstrate bilateral control of speech in four persons who stuttered following brain injury (Jones, 1966). Another study, however, found that speech was disrupted on the right side only in a patient who had previously had brain injury and aphasia as well as stuttering. The other persons with idiopathic stuttering, only had speech disruption with amytal infusion on the left side, similar to normal (Andrews, Quinn, & Sorby, 1972). Similarly, a study of three PWS without brain injury found all had left hemisphere dominance for speech on WADA testing (Luessenhop, Boggs, LaBorwit, & Walle, 1973). There is no evidence to suggest reversed laterality in PWS, rather the data suggest differences in the functional inter-relationships between brain regions on the right and left sides during speech and language processing in PWS.

Phonemic expression has been suggested to depend upon intact neural mechanisms in the left insula, based on injury data (Dronkers, 1996) and neuroimaging in normal speakers (Wise, Greene, Buchel, & Scott, 1999). That is, left insula functioning is likely involved but must interact with other regions in both the left and right hemispheres occurs during speech. The evidence thus far suggests that speech production may have a different degrees of involvement of right hemisphere mechanisms for speech during stuttering (Braun et al., 1997; Fox et al., 1996, 2000). Wood found inadequate left frontal activation during stuttering using xenon blood flow measures. This normalized after administration of haloperidol to induce fluency (Wood, Stump, McKenhan, Sheldon, & Proctor, 1980). Studies are needed to examine the intricate sequence and timing relationships among these neural mechanisms during ongoing speech both in normally fluent speakers and PWS during both fluent and stuttered utterances. As some of the MEG data
suggest, the ability to effect the dynamic interplay between neural mechanisms may be altered in PWS.

3. Location of brain injury that induces speech dysfluency

A review of the location and types of brain lesions that can induce acquired stuttering can be informative if one hypothesizes that a particular brain region may be essential for fluent speech. To test this hypothesis, the studies reporting on acquired stuttering were reviewed.

Acquired stuttering is qualitatively different from developmental stuttering, possibly because stuttering during development alters emotional and psychological factors associated with speaking. As a result, anxiety, fear and embarrassment may become associated with speech communication in those who have stuttered since childhood. Acquired stuttering is different from uncontrolled rapid festinating syllable repetitions that occur during palilalia (LaPointe & Horner, 1981). Rather, acquired stuttering involves repetitions, vowel prolongations and occasional blocks (Ludlow, Rosenberg, Salazar, Grafman, & Smutok, 1987). The symptoms alone cannot be easily differentiated from developmental stuttering (Van Borsel & Taillieu, 2001). The similarities in the speech symptoms of the developmental and acquired forms, lends credence to the need for analysis of which brain lesions can induce stuttering in adults.

Early studies of acquired stuttering were case reports that lacked imaging data and were unable to determine the location and extent of the brain lesions. More recent reports, however, were able to assess the lesion location (Table 1). These lesion data do not demonstrate that any one brain region is more likely involved in the acquisition of stuttering. Many of the more recent studies, which used neuroimaging, reported involvement of the basal ganglia, with the putamen being listed most often (Abe, Yorifji, 1992; Andy & Bhatnagar, 1991; Carluer et al., 2000; Ciabarra, Elkind, Roberts, & Marshall, 2000; Heuer, Sataloff, Mandel, & Travers, 1996; Kono, Hirano, Ueda, & Nakajima, 1998; Lebrun, Leleux, & Retif, 1987; Leenders et al., 1986; Ludlow et al., 1987; Shibuya, Wakayama, Murahashi, Aoki, & Ozasa, 1998). A few other studies have reported injuries involving the corpus callosum (Hagiwara, Takeda, Saito, Shimizu, & Bando, 2000; Soroker, Bar-Israel, Schechter, & Solzi, 1990; Tsumoto, Nishioka, Nakakita, Hayashi, & Maeshima, 1999). Only a small number of imaging studies suggest that primarily cortical regions are involved (Bijleveld, Lebrun, & van Dongen, 1994; Franco et al., 2000; Grant, Bioussé, Cook, & Newman, 1999; Turgut, Utku, & Balci, 2002) with most of these indicating diffuse cortical injury (Mouradian, Paslawski, & Shuaib, 2000; Rao, 1991). Other older studies do not provide imaging data (Fleet & Heilman, 1985; Helm, Butler, & Benson, 1978; Rosenbek, Messert, Collins, & Wertz, 1978). On the other hand, studies documenting a cessation of stuttering following brain injury involve either diffuse lesions (Miller, 1985) or thalamic injury or stimulation (Andy & Bhatnagar, 1992). One study documented the cessation of stuttering fol-
## Table 1

A review of previously reported cases of acquired stuttering following brain lesions and cases of stuttering cessation following brain lesions

<table>
<thead>
<tr>
<th>Author</th>
<th>Year</th>
<th>Pathology</th>
<th>Imaging</th>
<th>Number</th>
<th>Side</th>
<th>Structures</th>
<th>History of stuttering/LH</th>
</tr>
</thead>
<tbody>
<tr>
<td>Turgut</td>
<td>2002</td>
<td>CVA</td>
<td>CT</td>
<td>1</td>
<td>Left</td>
<td>Parietal</td>
<td>No</td>
</tr>
<tr>
<td>Casado</td>
<td>2000</td>
<td>CVA</td>
<td>MRI</td>
<td>1</td>
<td>Left</td>
<td>Left precentral — left internal carotid occlusion</td>
<td></td>
</tr>
<tr>
<td>Hagiwara</td>
<td>2000</td>
<td>CVA</td>
<td>MRI</td>
<td>1</td>
<td>Right</td>
<td>Right corpus callosum — right anterior artery</td>
<td></td>
</tr>
<tr>
<td>Ciabarra</td>
<td>2000</td>
<td>CVA</td>
<td>MRI</td>
<td>1</td>
<td>Left</td>
<td>Rostromedial infarct</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td>MRI</td>
<td>1</td>
<td>Left</td>
<td>Putamen</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td>MRI</td>
<td>1</td>
<td>Left</td>
<td>Putamen</td>
<td></td>
<td>Left handed</td>
</tr>
<tr>
<td>Mouradian</td>
<td>2000</td>
<td>CVA</td>
<td>MRI</td>
<td>1</td>
<td>Left</td>
<td>Nonspecific white matter changes</td>
<td></td>
</tr>
<tr>
<td>Carluer</td>
<td>2000</td>
<td>CVA</td>
<td>CT</td>
<td>1</td>
<td>Left</td>
<td>Basal ganglia (putamen, caudate and posterior internal capsule)</td>
<td></td>
</tr>
<tr>
<td>Grant</td>
<td>1999</td>
<td>CVA</td>
<td>MRI</td>
<td>1</td>
<td>Left</td>
<td>Middle cerebral artery</td>
<td>Yes</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>1</td>
<td>Left</td>
<td>Temporal lobe</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>1</td>
<td>Right</td>
<td>Parietal</td>
<td>Yes</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>1</td>
<td>Left</td>
<td>Occipital</td>
<td>Left handed</td>
<td></td>
</tr>
<tr>
<td>Tsunoto</td>
<td>1999</td>
<td>CVA</td>
<td>MRI</td>
<td>1</td>
<td>Right</td>
<td>Cerebral artery — involves corpus callosum</td>
<td></td>
</tr>
<tr>
<td>Kono</td>
<td>1998</td>
<td>CVA</td>
<td>CT, MRI</td>
<td>1</td>
<td>Left</td>
<td>Striatocapsular infarct to putamen and caudate</td>
<td></td>
</tr>
<tr>
<td>Shibuya</td>
<td>1998</td>
<td>CVA</td>
<td>MRI</td>
<td>1</td>
<td>Bilateral</td>
<td>Basal ganglia and periventricular white matter</td>
<td></td>
</tr>
<tr>
<td>Heuer</td>
<td>1996</td>
<td>CVA</td>
<td>CT, MRI</td>
<td>1</td>
<td>Right</td>
<td>Periventricular white matter, left thalamus, right caudate</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>Bilateral</td>
<td>Putamen, caudate right cerebral artery</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>1</td>
<td>Left temporal, mesial posterior thalamus</td>
<td>Left handed</td>
</tr>
<tr>
<td>Bijleveld</td>
<td>1994</td>
<td>CVA</td>
<td></td>
<td>1</td>
<td>Left</td>
<td>Frontal and temporal</td>
<td></td>
</tr>
<tr>
<td>Abe</td>
<td>1992</td>
<td>CVA</td>
<td></td>
<td>1</td>
<td>Bilateral</td>
<td>Midbrain and bilateral medial thalamus</td>
<td></td>
</tr>
<tr>
<td>Name</td>
<td>Year</td>
<td>Condition</td>
<td>Procedure</td>
<td>Lesion Description</td>
<td></td>
<td></td>
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<td>-----------------------------------------------------------------------------------</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Andy</td>
<td>1991</td>
<td>Chronic pain</td>
<td>Placement of stimulator</td>
<td>Unclear Mesothalamus</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Rao</td>
<td>1991</td>
<td>Head injury</td>
<td>None</td>
<td>Unclear Closed head injury</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Soroker</td>
<td>1990</td>
<td>CVA</td>
<td>None</td>
<td>Right Callosum</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Ludlow</td>
<td>1987</td>
<td>Missile wounds</td>
<td>CT</td>
<td>5 right, 4 left, 1 bilateral Internal and external capsules, frontal WM, striatum</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Lebrun</td>
<td>1987</td>
<td>CVA</td>
<td>CT, MRI</td>
<td>Right Parietal, subcortical extent</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Leenders</td>
<td>1986</td>
<td>CVA</td>
<td>CT, MRI</td>
<td>Left Brainstem — thalamic. Left striatum</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Fleet</td>
<td>1985</td>
<td>Arteriogram</td>
<td>Right</td>
<td>Internal carotid artery</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Rosenbek</td>
<td>1978</td>
<td>CVA</td>
<td>None</td>
<td>5 left, 1 right, 1 bilateral One had previous stuttering</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Helm</td>
<td>1978</td>
<td>CVA or HI</td>
<td>None</td>
<td>8 bilateral 6 multiple CVAs, 4 head trauma</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Muroi</td>
<td>1999</td>
<td>CVA</td>
<td>MRI</td>
<td>Bilateral Medial thalamus</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Andy</td>
<td>1992</td>
<td>Chronic pain</td>
<td>None — placement of stimulator</td>
<td>Unclear Mesothalamic stimulation</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Miller</td>
<td>1985</td>
<td>Multiple sclerosis</td>
<td>None</td>
<td>Unclear Cerebellar dysfunction</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Jones</td>
<td>1966</td>
<td>Brain tumor</td>
<td>WADA test — bilateral speech</td>
<td>Left Frontal brain tumor since childhood — bilateral speech</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td>Subarachnoid hemorrhage</td>
<td>WADA test — bilateral speech</td>
<td>Right Cerebral artery — bilateral speech</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td>Subarachnoid hemorrhage</td>
<td>WADA test — bilateral speech</td>
<td>Left Anterior communicating artery</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td>Subarachnoid hemorrhage</td>
<td>WADA test — bilateral speech</td>
<td>Left Cerebral artery — bilateral speech</td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

Cessation of stuttering
ollowing unilateral brain injury in four persons who had previously stuttering since childhood and had bilateral speech representation based on the WADA test (Jones, 1966).

The articles listed in Table 1 demonstrated some left hemispheric preference for inducing stuttering: 47% were left sided lesions, 26% were right and 26% were bilateral. Of those with imaging findings reported, 75% involved subcortical regions (basal ganglia, thalamus, internal capsule and corpus callosum). Similar to developmental stuttering, there was a 5:3 male to female ratio when sex was examined across these studies. Further, a normal handedness distribution was found; 80% were right handed and 19% were left handed. Few authors reported whether patients had previously stuttered during childhood; however of 57 cases, 14% reported childhood stuttering. This is a higher frequency than the 1% incidence of stuttering in adults. Apparently, those who recovered from childhood stuttering have a greater vulnerability for acquired stuttering after brain lesions.

The only conclusion that can be made from these studies are that the lesions associated with acquired stuttering rarely involve the primary speech and language regions in the left hemisphere (Broca’s area, the temporal planum, insula or Wernicke’s area). When these regions are involved, patients usually exhibit aphasia, which might mask stuttering symptoms, however, such patients do not exhibit stuttering when they recover (Ludlow et al., 1986). Therefore, the lesions leading to acquired stuttering seem to be those that impinge upon structures that support and modulate rapid communication between brain regions such as the corpus callosum, or areas that exert influence on multiple brain regions such as the basal ganglia and thalamus. The lesions in either the corpus callosum or thalamus could interfere with rapid communication of distributed areas during speech production. On the other hand, they were not disconnection lesions within the speech and language system in the left hemisphere which result in different types of aphasic syndromes (Geschwind, 1965a, 1965b). Rather, these lesions disturb rapid coordinated functioning of the brain networks. Acquired stuttering did not occur when brain regions involved in speech and language functions were irreversibly damaged; rather it occurred when the speech and language areas were not able to inter-relate with other brain regions in a rapid dynamic fashion.

Stuttering may reflect a poorly coordinated speech system possibly because of deficient development of white matter tracts (Sommer, Koch, Paulus, Weiller, & Buchel, 2002) or reduced neural pruning (Foundas, Bollich, Corey, Hurley, & Heilman, 2001). The former was further supported by the recent results of Sommer et al., who found higher thresholds for hand muscle responses to transcranial magnetic stimulation over the motor cortex in stuttering adults (Sommer, Wischer, Tergau, & Paulus, 2003). Stuttering may reflect an instability or loss of control in brain function rather than a loss of function — which makes stuttering similar to some other motor control disorders such as tremor, dystonia or Gilles de la Tourette’s syndrome (TS). To expand this view, a review of the some of the similarities and differences between stuttering and other speech motor control disorders is helpful.
4. The similarity and differences between stuttering and other speech motor control disorders

On first approximation, the phenomenology of stuttering seems commensurate with a neurologically based developmental motor control disorder (Brin, Blitzer, & Stewart, 1998; Kiziltan & Akalin, 1996). If the sensorimotor differences identified in stuttering have more similarities than differences relative to other speech motor control disorders, then this initial approximation is supported.

Speech production takes place during human communication, except in speech science laboratories where subjects are tested while producing meaningless phrases modeled by the tester. Such well controlled speech research tasks rarely elicit stuttering — stuttering is more frequent when subjects are required to formulate meaningful communication (Ratner, Gawronski, & Rice, 1964; Ratner & Sih, 1987). This augmentation of symptoms during communication is more pronounced in stuttering, but is a common feature of most speech and voice motor control disorders (Caligiuri, 1989; Sarno, 1968). In dysarthria and voice disorders, patients are often able to produce the target behavior in the clinical setting when attention is focused on production. After they leave the clinic, however, they tend to revert to impaired performance during conversation with others — a phenomenon referred to as carry-over (Klaff, 1976). In TS, patients can control symptoms for short periods, only to have them emerge in a more frequent pattern when they are no longer monitoring or controlling them.

Stuttering is a task specific disorder — that is, oral-motor dysfunction becomes apparent only during speech and not during humming, singing or chewing. In spasmodic dysphonia (SD), which is a laryngeal dystonia, the voice disruptions are most manifest during speech and much less evident during simple vowel prolongation (Sapienza, Murry, & Brown, 1998) and singing (Bloch, Hirano, & Gould, 1985). In TS, symptoms occur at rest but are increased by 30% during speech (Ludlow, 1993). The separation mentioned earlier, between non-meaningful speech production which is usually symptom free, and linguistic communication with enhanced stuttering (Perkins, Kent, & Curlee, 1991) is also a task dependent attribute. Task related differences also occur in oral-mandibular dystonia where some patients may only have oral-motor muscle abnormalities during speech but not during chewing, while others only have chewing affected with no oral-motor abnormalities during speech (Rosenbaum & Jankovic, 1988).

The difference in the occurrence of symptoms during speech communication and emotional expression is also task related. Laughter and crying are usually normal in both PWS and persons with SD (Bloch et al., 1985). In SD, this difference previously led to the assumption that the disorder was psychogenic. Now this difference is understood as evidence of different vocalization systems being present in human and non-human primates. Singing is thought to involve different brain regions from speech, particularly in the right hemisphere (Riecker, Ackermann, Wildgruber, Dogil, & Grodd, 2000) and simple vocalization and emotional expression may involve the cingulate and periaqueductal grey (Jurgens, 2002). On
the other hand, speech communication involves both cortical and subcortical systems.

Stuttering is more frequent when central processing demands increase with greater speech complexity or dual processing tasks (Bosshardt, 2002; Hall, Yamashita, & Aram, 1993; Starkweather, 2002). Similarly, in SD, motor function and electromyographic abnormalities are more impaired on complex processing tasks (Schaef er et al., 1992).

Both disorders are focal, that is they involve oral-motor or laryngeal musculature but not other motor systems. Reich, for example, conducted similar studies in both disorders, comparing laryngeal and manual reaction times with similar results, the laryngeal or phonatory systems were affected while the manual systems were not (Reich & Till, 1983; Reich, Till, & Goldsmith, 1981).

One difference between these disorders, of course, is the age of onset. Given this difference it is surprising that both groups have similar reactions to their speech disorder. Persons with SD, which onsets in adulthood, develop an adverse reaction to telephone use, become socially isolated and often develop a reactive depression (Cannito, 1991) which resolves with treatment (Murry, Cannito, & Woodson, 1994). Developmental stuttering often involves the development of similar fear and avoidance reactions to the telephone and feelings of social isolation (Miller & Watson, 1992). Persons with either disorders may develop a social anxiety disorder secondary to their voice and speech impairments (Moutier & Stein, 1999).

The task specific attributes of stuttering and SD implicate two possible selective aspects of these disorders. First, they only appear during speech sound production which has more rapid and precise motor control demands on vocal tract motor control (Ludlow & Lou, 1996). Second they implicate that one system is affected, that required for speech production during communication and language, while another is not. The vocal spasms of SD and the repetitions, prolongations and pauses in stuttering point to the intermittent nature of both disorders during speech production. The intermittent nature of these disorders support a serious consideration of whether the central control abnormalities may be similar.

Another disorder with intermittent vocal symptom occurrence is Tourette’s syndrome, a developmental disorder with onset most often between 5 and 12 years of age. This disorder involves multiple and one or more vocal tics occurring either many times a day or intermittently in a year, the tic characteristics can change over time, have onset before 21 years and are idiopathic, that is, not exclusively due to psychoactive substance intoxication or due to known central nervous system disease (Diagnostic and statistical manual of mental disorders, 1987). Speech and vocal tics occur at rest in TS, are exacerbated during speech (Ludlow, 1993; Ludlow, Polinsky, Caine, Bassich, & Ebert, 1982) but occur primarily at the beginning of speech or during speech pauses (Frank, 1978; Martindale, 1976, 1977). No differences in tic production occur with delayed auditory feedback or white noise or reduced speaking rate, which differs from stuttering symptom characteristics (Ludlow, 1993). Different authors have noted, however, that a high proportion of persons affected with TS report stuttered as a child (45%
reported developmental stuttering in one report, Ludlow, 1993), and an association between stuttering and TS in families was reported by one group (Comings & Comings, 1994; Comings, Comings, & Knell, 1989; Comings et al., 1996), although not supported by others (Pauls, Leckman, & Cohen, 1993). Some intriguing similarities, however, are that both disorders are benefited by dopamine receptor blockade (Kossoff & Singer, 2001; Ludlow & Braun, 1993), may be genetically related, wax and wane in severity, start in childhood, and spontaneously remit later in a large proportion of cases. Recent functional neuroimaging has demonstrated that TS involves aberrant activity in the precentral gyrus, insula, anterior cingulate and basal ganglia coupled with hypoactivity in the sensorimotor cortices (Stern et al., 2000). Increased activity in some of the same regions have been associated with the production of stuttering (Braun et al., 1997; Fox et al., 2000). Several TS patients report that tics are preceded by premonitions or urges to tics. Others emphasize that sensations often precede tics and that the tic is a response to a sensory experience. In stuttering, similar premonitions can occur prior to dysfluencies.

TS, however, is not a task specific disorder or focal to the speech musculature as is the case for both SD and stuttering, although vocal and speech tics are a necessary part of the syndrome. Therefore, there are more similarities between stuttering and SD than between stuttering and TS in motor symptoms.

4.1. Sensory deviations

A distinctive attribute of the focal dystonias are sensory anomalies that involve sensory tricks, deviant reflexes, sensory perception differences and abnormal sensory evoked potentials (Hallett, 1995). Sensory tricks are used by individuals with focal dystonias to control symptoms, such as, touching the face in Meige syndrome or chewing tooth-picks in oromandibular dystonia (Rosenbaum & Jankovic, 1988). In SD, a similar reduction in symptoms can occur during fiberoptic nasolaryngoscopy, presumably due to altered sensation during placement of the nasolaryngoscope in the oropharynx. Compensatory speech patterns, such as whispering, that are often observed clinically (Bloch et al., 1985) also alter sensory feedback.

We have studied laryngeal closure reflexes in the thyroarytenoid muscle in response to electrical stimulation of the laryngeal afferents contained in the superior laryngeal nerve in normal speakers and persons with SD. When paired electrical stimuli are presented at less than 1 s intervals for conditioning the late R2 responses (>60 ms latency) are normally suppressed reflecting central inhibitory processes modulating these responses. Conditioning abnormalities of the R2 response of the laryngeal adductor reflex have been found in both the adductor and abductor types of SD suggesting an abnormality in central suppression of muscle responses to sensory feedback (Deleyiannis, Gillespie, Bielamowicz, Yamashita, & Ludlow, 1999; Ludlow, Schulz, Yamashita, & Deleyiannis, 1995). Decreased or altered afferent feedback reduce spasmodic bursts in some of the dystonias (Kaji, Rothwell, et al., 1995; Yoshida et al., 1998).
As mentioned earlier, a number of studies point to corresponding sensory function differences in stuttering. Psychophysical studies indicate PWS have higher perceptual somatosensory thresholds for minimal movements of the jaw, lower lip and tongue and lingual vibrotactile stimuli. Persons who stutter also show deviant kinesthetic perceptions of jaw position on movement accuracy tasks (De Nil & Abbs, 1991). Certain differences relative to SD are noted though. A bilateral blockade of oral sensation was associated with increases in the frequency of stuttering symptoms (Hutchinson & Ringel, 1975), unlike the effects of lidocaine in some of the dystonias (Kaji, Kohara, et al., 1995). Although an influential hypothesis suggested exaggerated reflex gains could lead to stuttering (Zimmermann, Smith, & Hanley, 1981), evidence for marked oral reflex deviations have not been found, although labial reflex gains may be slightly altered in PWS (McClean, 1987).

The observations of so-called secondary or compensatory behaviors in stuttering show a broad similarity to the sensory tricks and compensatory speech adjustments used by persons with focal dystonias (Kiziltan & Akalin, 1996; Mulligan, Anderson, Jones, Williams, & Donaldson, 2001). Reductions in stuttering symptoms are associated with altered speech patterns (whisper, choral speech) and unusual oral gestures or bodily movements. Such movement changes potentially alter auditory and somatosensory inputs in turn helping to avoid or suppress stuttering — and could be interpreted as sensory tricks.

The most profound sensory effects, however, are those of auditory feedback manipulations (delayed auditory feedback, masking, etc.) that significantly suppress stuttering symptoms. The role of auditory feedback has also had a particular role in speech fluency: the paradoxical effects of chorus reading and delayed or altered feedback is pronounced in this disorder (Adams & Ramig, 1980; Stager, Denman, & Ludlow, 1997), although also present in dysarthria in Parkinsonism (Hanson & Metter, 1983). However, extended exposure to altered auditory feedback leads to less dramatic effects (Armson & Stuart, 1998) and it may not be the auditory modality per se but rather any significant change in the speaking context (Kalinowski, Stuart, Rastatter, Snyder, & Dayalu, 2000) that can alter fluency. One small study found no effect of white noise of delayed auditory feedback on symptom occurrence in TS (Ludlow, Nauton, & Bassich, 1984).

Even if sensory abnormalities in either the larynx or orofacial structures are identified in either disorder, the role of sensory abnormalities in these disorders still requires elucidation. It has been long recognized that suppression of sensory information that is possibly redundant or that could interfere with ongoing movement is possibly just as critical for the coordination of movement as the receipt of sensory information. Inappropriate or a lack of inhibition in SD or stuttering could indeed be a central factor in the emergence of vocal spasm or stuttering events, as is suggested for SD by the reduction in R2 conditioning. Studies of abnormal sensory inhibition of brain responses to afferent feedback in stuttering are an avenue that can be addressed with rapid neurophysiological recording using MEG as has been done for auditory feedback (Salmelin, Helenius, et al., 2000; Salmelin, Schnitzler, et al., 2000).
4.2. Muscle interference

Earlier ideas about the physiological basis for dysfluencies in both disorders involved speculation that tonically increased activity in the laryngeal muscles caused speech disruptions in SD and stuttering. In the adductor type of SD, Nash and Ludlow (1996) identified intermittent increases in thyroarytenoid activity during voice breaks, but that the overall level of muscle activity was not abnormal (Van Pelt, Ludlow, & Smith, 1994). Thus, spasmodic bursts in the thyroarytenoid muscles intruded upon otherwise unremarkable muscle recruitment (Nash & Ludlow, 1996). Muscle bursts in the abductor type of SD are more variable across subjects (Cyrus, Bielamowicz, Evans, & Ludlow, 2001), but again tonically elevated muscle tone has not been observed (Van Pelt et al., 1994). The mechanism involved in muscle bursts during voice breaks may arise from deficient suppression of laryngeal sensorimotor reflexes in both SD types. In SD, abnormal central modulation of brain stem mechanisms may result in reduced suppression of laryngeal reflexes in response to the sensory feedback due to speech and voice production, in an otherwise normal neural circuit for phonation.

In stuttering, evidence for elevated tonic activity in the laryngeal or orofacial muscles has not been found during speech disruptions (Smith et al., 1993; Smith, Denny, Shaffer, Kelly, & Hirano, 1996). Tonic co-contraction of the laryngeal muscles during stuttering was first reported by Freeman (Freeman & Ushijima, 1978), but the study was flawed, because of the lack of a control group. Subsequent controlled studies of laryngeal muscle and orofacial muscles have not found tonic over-activity or abnormal co-contraction during fluent speech or dysfluencies in PWS (Smith et al., 1996). Instead, approximately 50% of adults and teens who stutter display high frequency oscillations (6–15 Hz range) in the orofacial and laryngeal muscles during stuttering dysfluencies but not during fluent speech. The oscillations occurred simultaneously in multiple vocal tract muscles and have been likened to tremorogenic activity (Smith et al., 1993). The 50% incidence of the oscillations prevents them from being considered characteristic of stuttering and distances stuttering from SD, which shows a nearly universal incidence for bursting abnormalities in a limited set of muscles during speech breaks. Finer resolution analyses of muscle activity during stuttering may identify other aberrations in muscle activity, but it remains likely that stuttering dysfluencies may involve normal muscle electromyographic amplitudes and spectral characteristics. Although muscle activity during a dysfluency is not characterized by spasms, tremor or excessive co-contraction, questions remain whether the coordination of muscle activation is aberrant or if there is an absence of normal muscle inhibition during stuttering.

Increased cortical excitability in motor regions has been implicated in both SD and stuttering by functional neuroimaging during symptom production (Braun et al., 1997; Fox et al., 1996, 2000; Hirano et al., 2001). Whether cortical excitability is due to decreased cortical inhibition can be examined using transcranial magnetic stimulation using a conditioning paradigm. First, motor thresholds are determined for eliciting a motor evoked potential (MEP) in a hand muscle in
response to cortical stimulation in the primary motor area. Next, cortical inhibition can be assessed using a conditioning paradigm where a sub-threshold conditioning stimulus (at 90% of motor threshold amplitude) precedes a supra-threshold test stimulus at time intervals between 1 and 30 ms. The degree to which the MEP response to the test stimulus is suppressed relative to an MEP to an unconditioned stimulus of the same strength is measured (Kujirai et al., 1993). Increased excitation of hand muscle responses using this paradigm was found in various focal dystonias such as writer cramp and blepharospasm (Sommer, Ruge, et al., 2002).

In a recent study, using the same conditioning paradigm to study hand muscle response inhibition, no abnormalities in inhibition were found in PWS (Sommer et al., 2003). The PWS group, however, had significantly higher motor thresholds for eliciting hand muscle responses than the controls, which was unexpected. These findings may suggest a different pathophysiology in stuttering, that is, a reduced cortico-spinal tract excitability to hand muscles in PWS. Further study is needed to examine whether similar findings occur in SD. Also, conditioning studies of cortical excitability for oral and laryngeal musculature is needed in both SD and TS.

Because stuttering dysfluencies are not specific to a small set of muscles, this may explain why botulinum toxin injections have not and will not likely be appropriate treatment for stuttering (Stager & Ludlow, 1994) even though it is clearly the most effective treatment to date for SD (Truong, Rontal, Rolnick, Aronson, & Mistura, 1991). Botulinum toxin injection, however, suppresses muscle spasms by denervating both the muscle fibers and muscle spindles. Current behavioral treatments for stuttering may also predominantly involve muscle suppression. Treatments that instead target the central mechanisms may be most effective in both disorders, because any abnormal muscle activity in either disorder is secondary to the central pathological mechanisms.

4.3. Central abnormalities

Along with arguments for deviancies in sensori-motor processing and muscle activation in PWS and SD, abnormalities in cortical and/or subcortical processing are thought to be present in both disorders. Only a few studies of brain function have been conducted in either disorder.

A case study of a person with SD using positron emission tomography (H215O PET) indicated reduced regional cerebral blood flow (RCBF) responses in the supplementary motor area (SMA) and increased RCBF in the left superior temporal gyrus during phonation relative to six control subjects (Hirano et al., 2001). Findings for a single subject are difficult to interpret however, due to the high variability of RCBF both between participants and across tasks. Studies in other forms of dystonia have shown deficient central activation in response to sensory feedback (Tempel & Perlmutter, 1990, 1993). Similarly, patterns of hyperactivation and hypoactivation have been found in PWS. Hypoactivation of the left post-central sensory and auditory association regions were found in PWS during dysfluency
evoking tasks by Wu et al. (1995), Fox et al. (1996, 2000), and Braun et al. (1997).
At the same time increased activation in premotor and motor areas have been found in both stuttering and dystonia (Braun et al., 1997; Odergren, Stone-Elander, & Ingvar, 1998). Firm conclusions regarding similar patterns of brain dysfunction in the two disorders cannot be made given the limited data, particularly for SD. However, the corresponding patterns of sensory hypoactivation and frontal motor and premotor hyperactivation make a potential link between the disorders more compelling.

4.4. Basal ganglia abnormalities

Basal ganglia dysfunction has been viewed as the most probable dysfunctional region in primary dystonias, in which the failure of the basal ganglia circuitry to inhibit inappropriate cortical motor control regions may lead to pathological muscle activation and dystonic posturing (Galardi et al., 1996). Given that basal ganglia output modulates cortical motor areas, the logic behind hypotheses of basal ganglia dysfunction in dystonia is attractive. The neuroimaging studies of stuttering also point to atypical basal ganglia activation or abnormal activity in areas receiving basal ganglia output. Wu et al. (1995) reported hypoactivation in the left caudate nucleus during both fluency and dysfluency evoking tasks. In the Braun et al. study (Braun et al., 1997), PWS showed higher activity in the right caudate nucleus and generally lower activation in SMA compared to controls in both the dysfluent and fluent conditions. Consequently, the still limited evidence from neuroimaging indicates atypical activity in the basal ganglia or in areas receiving efferent output from basal ganglia nuclei. The brain lesion data on acquired stuttering reviewed earlier, suggest that basal ganglia dysfunction can induce stuttering in fluent adults.

To date, the focal dystonias have not been found to be responsive to neuropharmacological intervention (Brin et al., 1998) and stuttering is only benefited by dopamine receptor blockade although the side effects usually outweigh the benefits (Ludlow & Braun, 1993). Paroxetine has been reported to have serious side effects (Bloch, Stager, Braun, & Rubinow, 1995) and risperidone has fewer side effects but limited long term benefits (Lee et al., 2001; Maguire et al., 1999; Maguire, Riley, Franklin, & Gottschalk, 2000).

4.5. Vulnerable systems

Stuttering and SD are both idiopathic disorders; that is they are not normally secondary to any known disease or disorder but emerge spontaneously, one during development and the other during adulthood. Both disorders can emerge during stressful events, not because stress is a cause of the disorder but rather because the speech motor system in such persons may be more vulnerable to breakdown when stress is increased. No studies have addressed the rate of co-occurrence of these disorders in families.
Our consideration of the similarities and differences between stuttering and other speech motor control disorders such as SD, is aimed at stimulating new avenues for hypothesis-driven research into the mechanisms of stuttering. Sensory processing irregularities in stuttering that are similar to focal dystonias could be investigated using whole head magnetoencephalography to further assess whether the time courses, amplitudes and source locations of oral somatosensory and/or auditory evoked potentials are deviant in stuttering. Application of functional MRI (fMRI) to neurocognitive and neuromotor processes in stuttering (and SD) have barely been initiated, but the success of fMRI in understanding brain activation for such processes indicates it holds promise for understanding central processes in stuttering. The possibility that cortical pyramidal tract excitation is affected in stuttering (Sommer et al., 2003) needs to be investigated further. Certainly, PET techniques could be used to measure neurotransmitter uptake and to assess basal ganglia function, techniques which have already added improved understanding of the pathogenesis in Parkinson’s disease (Ito et al., 2002). Integrating these research questions with good data on the simultaneous activity in different brain mechanisms should help to parse out the dynamic inter-relationships and how these differ in stuttering both between tasks and from normal.

The major difference between stuttering and focal dystonia is the age of onset. The period of vulnerability for developing stuttering is between 2 years of age and puberty. The neurobiology of development may underlie the bases for the emergence of stuttering in childhood. Developmental neurobiology involves two overall processes, the initial growth stages of cellular proliferation, migration, differentiation and synaptogenesis which occur in the prenatal and early post-natal periods (Purves, 1994) and the later stages of selective refinement. Early childhood, the period of vulnerability for the development of stuttering, may include processes involved in refinement of the neurological system. Reduction and refinement occur through dendritic pruning, programmed cell death and selective enhancement of networks of synaptic connections (Purves, 1994). Reduction and refinement in neural processes may be essential for the development of normal speech motor control based in part, on activity and use. That is, as some synaptic connections are enhanced through use, others are lost through inactivity, shaping the emergence of efficient circuitry for speech function within the central nervous system. Although little information is available on the refinement process within the speech motor control system during childhood, it can be assumed that it follows the same neurodevelopmental processes as the rest of the central nervous system. The recent finding of increased size in the right and left planum temporali in stuttering adults and additional gyri in perisylvian region compared to normal (Foundas et al., 2001) may suggest abnormal pruning. On the other hand, reduced white matter tracts in central areas (Sommer, Koch, et al., 2002) might suggest abnormal growth and refinement processes during development.

In summary, the evidence to date suggests that stuttering is a neurodevelopmental motor control disorder. It has some intriguing similarities to other motor
control disorders, the focal dystonias, in particular. This suggests that conceptual frameworks based on the dynamic interplay between different components of the motor control system and its interface with language processing can be helpful for the study of the pathophysiology of both disorders. Although the etiologies are most likely quite different, the functional abnormalities appear to be related and investigations into the rapid dynamic inhibitory and excitatory processes for speech production may be beneficial to understanding both disorders.

References


CONTINUING EDUCATION

Stuttering: a dynamic motor control disorder

QUESTIONS

1. The brain function abnormalities implicated in stuttering are:
   a. Right language dominance
   b. Left hemisphere injury
   c. Basal ganglia disease
   d. Abnormalities in the function of the neural network for speech

2. Brain injuries which cause stuttering in adults involve:
   a. Lesions only in Broca’s area
   b. Lesions only in Wernicke’s area
   c. Lesions only in the basal ganglia
   d. Lesions outside Broca’s and Wernicke’s area

3. The similarities between stuttering and dystonias are:
   a. Both are task specific and involve emotional expression
   b. Both are task specific, focal and intermittent
   c. Both are affected by auditory feedback
   d. Both affect other disorders besides speech

4. Muscle activity in both stuttering and spasmodic dysphonia:
   a. Is abnormal only intermittently in both disorders
   b. Is constantly too high in spasmodic dysphonia but not in stuttering
   c. Is constantly too high in stuttering but not in spasmodic dysphonia
   d. Is normal all of the time in both disorders

5. Neurophysiological studies of persons who stutter indicates that stuttering involves:
   a. Language abnormalities
   b. Hearing abnormalities
   c. Sensory loss
   d. None of the above