Spasmodic Dysphonia: An Evidence-Based Clinical Update

Balaji Rangarathnam, PhD, CCC-SLP, and Gary H. McCullough, PhD

ABSTRACT
• Objective: To provide an evidence-based clinical update on the pathophysiology, assessment, and treatment of spasmodic dysphonia (SD).
• Methods: We reviewed the extant literature on SD spanning predominantly the past 2 decades. References were extracted from Medline and PubMed using search terms of spasmodic dysphonia, pathophysiology, assessment, and treatment since 1990.
• Results: Whereas technological advances have clearly defined SD as a neurologically based disorder with possible genetic and environmental links, specific neurologic underpinnings remain elusive. Best practice continues to be treatment via botulinum toxin injection, though results are significantly better for adductor than abductor type SD. Surgical interventions are being reported with increasing success.
• Conclusions: Research should examine long-term outcomes in botulinum toxin versus surgical intervention and continue to define the neurologic substrates of SD.

Spasmodic dysphonia (SD) is a type of focal dystonia that is specific to the control of laryngeal muscles [1] affecting voluntary speech production, while involuntary acts such as laughter and cry are largely preserved [2]. Two types of spasmodic dysphonia have been widely reported: adductor type (ADSD), involving spasms of the thyroarytenoid and lateral cricoarytenoid muscles during adduction of vocal folds for voice production during vocalic sounds, and an abductor type (ABSD), affecting the posterior cricoarytenoid muscle and presenting itself as spasms during abduction of vocal folds typically heard in voiceless consonants. Mixed spasmodic dysphonia, characterized by both abductor and adductor spasms, occurs in about 2% of all reported cases [3]. About a third of all patients also have action-induced vocal fold tremor. SD has strong epidemiological data with usual onset around middle age [1] and a high preponderance in females [4]. Symptoms typically begin gradually, though a recent report suggests almost a quarter of patients experience a more sudden onset. For most, symptoms worsen over time until they plateau. This plateau may happen in the first year or 2, but in about a third of all patients that plateau is not reached until 10 or more years [3]. Patients who suffer SD report feeling a lack of control over the disorder and experience significant emotional impact [5].

The pathophysiology and differential diagnosis of spasmodic dysphonia from other vocal disorders and abnormalities in speech motor control have received significant research interest. With the advent of advanced neuroimaging methods and voice assessment procedures, our understanding of the disorder as a whole has improved significantly, though not completely; questions remain regarding the differential diagnosis of the disorder as well as the most effective treatment for reducing symptoms and improving quality of life.

PATHOPHYSIOLOGY OF SD
Neurological Underpinnings

Once believed to be purely psychogenic, primarily because of the task specificity of the symptoms, research over the past couple of decades has established strong neural underpinnings of the disorder. Earlier work with EMG [6] and muscle histology [7] hinted at this, showing changes in muscle activity with SD and in the number of type II fibers present in affected thyroarytenoid and lateral cricoarytenoid musculature that suggested CNS involvement—possibly CNS interneurons affecting changes in motor neurons which could, in turn, alter muscle. More recently, with rapid improvements in brain imaging and advanced neuroimaging techniques, the role of the nervous system in the development and perpetuation of the disorder has become clearer. Functional magnetic resonance imaging (fMRI) has been used to study the activity of different regions of the brain during speech production in patients with SD, and the results have been consistent with the hypothesis that the disorder involves a disruption of the corticobulbar tracts, which are responsible for motor control of the larynx.

From the Department of Communication Sciences and Disorders, East Carolina University, Greenville, NC (Dr. Rangarathnam) and the Department of Communication Sciences and Disorders, University of Central Arkansas, Conway, AR.
imaging, studies [8] have demonstrated widespread cortical and subcortical abnormalities [9–11]. Dystonias are usually associated with significantly reduced inhibitory basal ganglia output, poor cortical inhibition, abnormal sensorimotor integration, and maladaptive plasticity [12].

Still, no definitive correlation exists between clinical abnormalities and a specific region of the brain for SD. Since SD is observed only in volitional speech tasks, it is not unreasonable to suspect impairment in neural circuits related to speech production, while those involved in emotional sound production such as laughter or cry remain intact [1]. Haslinger and colleagues [9] conducted functional magnetic resonance imaging (fMRI) scans on 12 subjects with laryngeal dystonia and reported reduced activation in primary sensorimotor, premotor and sensory association cortices during vocalization. Simonyan and colleagues [10] used diffusion tensor imaging (DTI) to investigate white matter changes in individuals with SD. They reported right-sided decrease of fractional anisotropy in the genu of the internal capsule and bilateral increase of overall water diffusivity in the white matter along the corticobulbar/corticospinal tract. Water diffusivity was also reported to be bilaterally increased in the lentiform nucleus, ventral thalamus and cerebellar white and grey matter in the patients. Simonyan and colleagues [11] used diffusion tensor imaging (DTI) to investigate white matter changes in individuals with SD. They reported right-sided decrease of fractional anisotropy in the genu of the internal capsule and bilateral increase of overall water diffusivity in the white matter along the corticobulbar/corticospinal tract. Water diffusivity was also reported to be bilaterally increased in the lentiform nucleus, ventral thalamus and cerebellar white and grey matter in the patients. Simonyan and colleagues [11] studied neural activations in patients with SD on symptomatic (vocal) production and asymptomatic tasks (whimpering) using fMRI. They reported increased activation in the primary sensorimotor cortex, insula, and superior temporal gyrus for both the tasks and decreased activation in the basal ganglia, thalamus, and cerebellum during asymptomatic tasks.

The brainstem is believed to host the central pattern generators for voluntary speech production and emotional vocal production [13]. Pathophysiology of SD, therefore, cannot be entirely attributed to the brainstem. An isolated disturbance in voice production related to volitional speech alone would not make sense. But the brainstem does appear to be involved. Post-mortem brainstem tissues in 2 patients with focal laryngeal dystonia were noted to have small clusters of inflammation in the reticular formation surrounding the solitary tract, spinal trigeminal and ambiguus nuclei, inferior olive and the pyramids [11]. In addition, the authors reported degeneration in the substantia niagra and locus coeruleus.

**Genetic Influence**

Recent reports have pointed to a genetic basis of the disorder. At least 17 different types of gene mutations have been studied in generalized dystonia numbered as DYT1-DYT17 [14]. Specifically, DYT6 has been strongly associated with laryngeal focal dystonia [14,15]. Studies have reported mutations in thanatos-associated protein (THAP), within DYT6, in individuals with general dystonia [16]. Djamarti and colleagues [17] studied THAP related mutations in spasmodic dysphonia and reported that mutations in THAP1 (thanatos-associated protein 1) can be associated with early onset focal laryngeal dystonia, although the role of the mutation can be a minor one, given the fact only 1% of the subjects screened among a group of patients with general dystonia showed abnormalities in THAP1 mutations. The physiological changes caused due to these mutations are unclear.

In summary, the pathophysiology of the disorder remains unclear (Table 1); however, technological advances suggest a strong association of impairments in the somato-sensory areas and the perisylvian regions involved in voluntary speech production and the sub-cortical structures of basal ganglia and thalamus. Motor inhibition is likely affected due to these impairments which have been well documented. It is unclear if connectivity impairment exists due to diaschisis of one structure affecting the function of another or if there is a combinatorial effect of more structures. The brainstem plays a potential role, as well, though this aspect of the puzzle is even less clearly understood. Genetics play a role, but further research investigating patients of different onset and progression patterns and different ethnicities needs to be conducted. It is very possible that a combination of genetic factors and environmental influences may facilitate the development of the disorder.

**VOCAL ASSESSMENT IN SD**

**Acoustics and Perception**

Extensive research has been carried out in the direction of identifying auditory-perceptual, acoustic, laryngeo-

<table>
<thead>
<tr>
<th>Knowledge</th>
<th>Needs</th>
</tr>
</thead>
<tbody>
<tr>
<td>Cortical involvement: somatosensory and perisylvian</td>
<td>Better understanding of specific pathways</td>
</tr>
<tr>
<td>Subcortical involvement: basal ganglia and thalamus</td>
<td>Better localization, especially within possible brainstem areas</td>
</tr>
<tr>
<td>Genetic influence</td>
<td>Possible DYT6/THAP1</td>
</tr>
</tbody>
</table>
scopic and aerodynamic markers in the diagnosis of SD. Of recent interest, Cannito et al [18] studied perceptual features in patients with ADSD before and after treatment with botulinum toxin. This research defined hyperadduction and hypoadduction underlying the primary perceptual variables. Overall voice quality, roughness, and brokenness—representing hyperadduction—formed a coherent set distinct from breathiness—representing the hypoadduction component. Pre-treatment, ADSD voices appeared heavily loaded with the first set of variables (poor quality, roughness, brokenness). Post–botulinum toxin injection changes indicated distinct improvement in brokenness but minimal change in breathiness, indicating a stronger hypoadduction factor in ADSD than previously considered—one that is more prominent post-treatment. This breathiness factor continues to impact voice quality. Acoustic measures of phonation breaks, aperiodic segments, frequency shifts and cepstral peak prominences correlated well with these findings.

Ludlow and colleagues [19] emphasized perceptual (patient and clinician) measures in suggesting research priorities for SD. They reported several key perceptual features. For ADSD, breaks on vowels and 1 or more breaks per 3 sentences in repeated adductor sentences (glottal stops and vowels). For ABSD, prolonged voiceless consonants and 1 or more breaks per 3 sentences while repeating abductor sentences (/p/, /t/, /k/, /s/, /h/, /f/). In both types of SD, they reported less strain perceived in higher pitches and breaks on vowels or prolonged voiceless consonants during counting tasks. It is also a common for symptoms to be exacerbated in voiced consonants [20]. In differentiating SD from muscle tension dysphonia and tremor, the relative ease of shouting and whispering compared to normal speech and the presence of sustained irregular laryngeal posturing were most salient.

Whereas their pilot data differentiating SD from MTD were promising, prior research suggests the task of differential diagnosis will not come easily. Overlapping perceptual features often lead to wrong diagnosis and, in turn, inappropriate care. Prior investigations have been conducted examining differences between the 2 disorders visually, acoustically, and perceptually [20–22]. Leonard & Kendall [23] attempted a phonoscopic evaluation of ADSD and MTD. Six laryngeal behaviors were studied and none accurately differentiated the disorders. The most useful behaviors were tremor and paradoxical movements of the true and false vocal folds that were absent in MTD but were present in at least a few of the subjects with ADSD. Higgins, Chait, and Schulte [21] compared subjects with MTD and SD on mean airflow rate and found no significant differences between the groups and large inter-subject variability in phonatory airflow. Houtz and colleagues [24] attempted to differentiate the disorders by analyzing the long term average acoustic spectrum of subjects with ADSD and MTD. Only Moment 2 in the spectral analyses appeared to differentiate the disorders with any reliability—and this only in women. Another study [25] used spectrographic analyses in differentiation of the disorders and reported reliable differential diagnosis with the technique.

A couple of newer diagnostic tools have been proposed with some promise for diagnosing SD. Whereas the multidimensional voice profile (MDVP) is only useful for evaluation sustained phonation and only on voices with reasonably preserved periodicity, the auditory model-based pitch extraction (AMPEX) produces a 27 dimensional feature vector every 10 seconds with 23 spectral parameters [26]. It can be used with sustained phonation or running speech. Significant correlations were observed with perceptual evaluation. Of particular note is “average voicing evidence,” which indicates problems with voiced–voiceless contrasts and was clearly distinct between SD and normal voicing. Perceptual measures were drawn from the IIINFVo scale (overall impression, impression of intelligibility, noise, fluency, and voicing).

**Voice Handicap/Quality of Life**

Some research [27] suggests measures of voice handicap and quality of life, such as the VHI, VHI-10, and V-RQOL, correlate well with SD symptoms and severity and improve with treatment (botulinum toxin). Other studies have called into serious question the relationship between improvement in clinician-based perceptual measures (ie, CAPE-V) and patient-perspective measures (ie, V-RQOL). In a patient-centered health care model, the V-RQOL would arguably carry more weight than a clinician-based rating system. V-RQOL ratings have been reported to improve over time despite a lack of improvement in condition, indicating patients with SD may learn to cope with the disorder better over time.

Summarizing vocal assessment of SD, spasms in the vocal folds during speech production that are absent during emotional sound production is a hallmark feature of SD (Table 2). This feature is seen on voiced consonants...

---

**Table 2**

<table>
<thead>
<tr>
<th>Condition</th>
<th>Visible Features</th>
</tr>
</thead>
<tbody>
<tr>
<td>ADSD</td>
<td>Tremor, paradoxical movements</td>
</tr>
<tr>
<td>MTD</td>
<td>Absent in MTD but present in at least a few of the subjects with ADSD</td>
</tr>
</tbody>
</table>

---

**Notes:**

2. Ludlow and colleagues [19] emphasized perceptual measures in suggesting research priorities for SD.
3. Leonard & Kendall [23] attempted a phonoscopic evaluation of ADSD and MTD.
5. Houtz and colleagues [24] attempted to differentiate the disorders by analyzing the long term average acoustic spectrum.
6. AMPEX produces a 27 dimensional feature vector every 10 seconds with 23 spectral parameters.
7. IIINFVo scale is used for perceptual measures.
8. VHI, VHI-10, and V-RQOL are measures of voice handicap and quality of life.
9. V-RQOL ratings improve with treatment and carry more weight than clinician-based measures.
Spasmodic Dysphonia in ADSD and on voiceless consonants in ABSD [19]. Perceptually, ADSD voice is strained and strangled with intermittent phonatory breaks predominantly perceived on voiced sounds. ABSD voice is less rough with greater breathiness. Acoustic and aerodynamic data have not provided concrete diagnostic markers yet. It is also important to note that ADSD mimics the features of MTD and markers of differential diagnosis with reports of sensitivity, specificity and likelihood rations are warranted.

**TREATMENT OF SD**

**Botulinum Toxin**

Owing to the poorly understood pathophysiology of the disorder, it is no wonder that the best method of treatment remains a matter of debate (Table 3). The most common and widely accepted and clinically proven line of care is injection of botulinum toxin into the vocal folds [28,29], though changes post-botulinum toxin are far from uniform and results reported in studies may be affected by the type of assessment (ie, clinician vs. patient perception) and even gender of the patient [30]. Caution should, therefore, be exercised when drawing overall conclusions about the effects of botulinum toxin on SD. Botulinum toxin injections are believed to induce inhibitory responses that control the spasms. The use of botulinum toxin has been clinically proven and improvements in various outcome measures have been proposed. Improvements in perceptual vocal quality, voice acoustics, voice related quality of life have been widely reported, though results are temporary and only address symptoms of the disorder [31,32]. More than a decade ago it was clear that laryngeal muscle bursts, reported with electromyography, decreased after botulinum toxin injections [6], and that symptoms were alleviated per clinician report. Whereas CAPE-V ratings suggest significant benefit from the injections, V-RQOL ratings only weakly support this method of treatment [32]. Results are highly dependent upon SD type as well, with the abductor type appearing to have much less benefit [33]. Injection of botulinum toxin into the PCA may suppress abductor spasm, but inadequate glottal closure remains a problem due to vocal fold weakness. The result is continued breathiness. Moreover, only 1 PCA can be injected at a time in order to preserve respiration, limiting the impact of the treatment. Improved results for abductor SD has been reported with increased doses (10–25 units) to the dominant side affected [33].

The best method and dosing for injection, even for adductor SD, remains in question. Fulmer, Merati, and Blumin [34] reported no difference between EMG-guided and non-EMG guided injection in a cohort of 64 patients. A “point-touch” technique, relying on anatomical structures rather than EMG, has also been reported with some success [35]. And though larger unilateral doses of botulinum toxin have been reported to be successful for abductor SD, a more minimalist approach, 1.25 units compared with even 2.5 units, has been advocated for adductor SD, increasing as necessary to achieve maximal benefit. As long term effects of botulinum toxin injections have not been clearly defined, the minimalist approach may have merit [36]. It is generally believed that botulinum toxin injections must be tailored to the individual, considering their occupation, symptoms, and side effects [37,38]. When tremor is observed in conjunction with SD, injection of the interarytenoid muscle, in addition to the thyroarytenoid muscle, has been reported to improve most measures of acoustic and perceptual function; 67% of subjects opted to continue both injections [39]. Results, however, are even more inconsistent when tremor and SD coexist than with SD alone, and benefits reported overall are markedly reduced [40].

Support for botulinum toxin is scant in research correlations with brain activation patterns [9]. Earlier work

### Table 2. Assessment of Spasmodic Dysphonia

<table>
<thead>
<tr>
<th>Knowledge</th>
<th>Needs</th>
</tr>
</thead>
<tbody>
<tr>
<td>Perceptual strain (adductor) or breathiness (abductor)</td>
<td>Improve ability to obtain acoustic data on aperiodic voicing and running speech</td>
</tr>
<tr>
<td></td>
<td>Clarify impact of spasms on acoustic and airflow measures as well as voice handicap</td>
</tr>
</tbody>
</table>

### Table 3. Treatment of Spasmodic Dysphonia

<table>
<thead>
<tr>
<th>Knowledge</th>
<th>Needs</th>
</tr>
</thead>
<tbody>
<tr>
<td>Botulinum toxin</td>
<td>Decreases laryngeal muscle bursts</td>
</tr>
<tr>
<td></td>
<td>Acoustic/perceptual improvement</td>
</tr>
<tr>
<td>Surgery--reinnervate RLN with ansa-cervicalis with better QOL/patient perception</td>
<td>Why low impact on QOL/patient perception?</td>
</tr>
<tr>
<td></td>
<td>Best method of injection</td>
</tr>
<tr>
<td></td>
<td>More long-term data</td>
</tr>
</tbody>
</table>
utilizing electromyography demonstrated decreases in laryngeal muscle bursts post botulinum toxin injection in both injected (TA-thyroarytenoid) and non-injected (LCA-lateral cricoarytenoid) muscles. Decreases correlated with decreased speech symptoms but were not related to normalized levels of muscle activity within muscle pre- or post-treatment, indicating changes in central pathophysiology must have occurred [6]. Histological study suggests changes in injected (TA) and non-injected (LCA) musculature—predominantly by increase in type II fibers. It has been suggested that laryngeal motor neurons may change from tonic to phasic, thereby influencing the changes in muscle fiber type.

Surgical Intervention

Surgical treatment options have also been reported by various authors. The most widely known method is the resection of a part of the recurrent laryngeal nerve (RLN). The symptoms have completely resolved after the surgery but reinnervation of the thyroarytenoid muscle, and sometimes the impact of nearby nerves, causes relapse [41]. Since then, the more common procedure has been to reinnervate the distal RLN with the ansa cervicalis. Case studies [42] and small group cohorts [43] have been reported with good results. When comparing surgery to botulinum toxin, VHI-10 scores were actually better in the surgical group, though no controls for severity were employed. Caution may be necessary with surgical approaches at this time due to the lack of long-term outcome data [36].

Type II thyroplasty (lateralization of vocal folds/laryngeal framework surgery) has also been successfully used to reduce the symptoms [44] and improve acoustic and aerodynamic measures. This procedure, employed rarely and on few subjects, serves to limit the tightness of the closure by incising the thyroid cartilage at midline and pulling the edges of the cartilage apart from 2 to 5 mm until optimal voicing is achieved.

Another procedure which remains highly experimental at this time is lateral laser thyroarytenoid myotomy [45]. In this procedure, transverse cuts are made in the thyroarytenoid muscle for a segmental myotomy. Four patients achieved positive results and maintained those results at 2.5 years without additional botulinum toxin [45].

Behavioral voice therapy on its own is generally not well regarded as an option [46]. The addition of voice therapy to botulinum toxin has been reported with mixed results [47,48]. Increasing pitch and adjusting consonant and vowel production (depending on SD type) may provide some benefit but with little evidence for benefit in quality of life.

Finally, deep brain stimulation is a relatively new method that has received attention. Deep brain stimulation of the basal ganglia has provided favorable results in general dystonia [49,50]. It remains to be seen how well spasmodic dysphonia responds to this method. Targeting the brain directly means that the core of the disorder is targeted rather than the symptoms alone. However, since the actual pathophysiology itself remains somewhat unclear, specific structures of target for stimulation need to be further explored.

SUMMARY

Whereas advances in technology have improved our understanding of SD, specific pathophysiology, best diagnostic markers, and treatments producing the most beneficial and lasting effects have not been established. Diagnosis is best accomplished by a team of voice professionals with experience evaluating and treating SD, tremor, and MTD. Though the primary treatment for SD remains botulinum toxin injection, advances in surgical techniques are increasingly reported. Long term effects, outcomes, and side effects must be carefully studied and defined before newer treatments become standard clinical options.

Corresponding author: Gary H. McCullough, PhD, University of Central Arkansas, 328 Torreyson West, 201 Donaghey Ave., Conway, AR 72035, gmccullough@uca.edu.

Financial disclosures: None.

Author contributions: conception and design, BR, GHM; drafting of article, BR, GHM.

REFERENCES


