Spasmodic Dysphonia
An Abnormality in Laryngeal Sensori-motor control

Pathogenesis =
- Genetic predisposition
- Abnormality in Neural Function
- Environmental trigger

Pathophysiology =
- Abnormal modulation of Synaptic excitability
- Laryngeal Manipulation
  - Transient changes
  - 2-5 years maximum
- Voice Symptoms

Purpose of Functional and Structural Neuroimaging
Underlying neurological abnormality
Must be independent of symptoms
Can be modified short term by neurophysiological manipulation by Botox, Nerve Section, or therapy
Ali et. al., 2006 using PET showed brain function altered after Botox
Haslinger et al., 2005 using fMRI showed brain function altered by Botox
Brain Physiology is plastic and can be manipulated

Neural Central Control Systems Involved in Human Voice
- Animal vocalization system for emotional expression, laughter, cry, shout, pain
  - Involves the Cingulate Cortex, PAG and brain stem
  - Unaffected in spasmodic dysphonia
- Learned Voice Control involves cortical control of voice for speech,
  - Involves Cortex, corticobulbar pathway & brain stem
  - Affected in spasmodic dysphonia
Central Nervous System- The Motor Pathway

**The Cortico-Bulbar System rapidly conducts to the Laryngeal Muscles in ~12 ms**

- **Motor Cortex**
- **Corticobulbar pathway**
- **Brain stem**
- **Laryngeal Muscle**

**Stimulate at cortex**

Response

200 µV

10 ms

15 ms

50

**Structural Studies of the Brain**

- **Diffusion tensor Imaging (DTI)**—arrangement of water molecules in the brain

  - Diffusivity
  - Anisotropy

- **Alignment of water molecules shows the degree of integrity of the white matter tracts**
- **Less alignment, greater diffusivity in reduced white matter tracts**

**Slice through the Brain with Neuroimaging MRI**

- **Cortical control of the Laryngeal muscles**
- **Internal capsule**
Simonyan et al. 2008, *Brain*
DTI Study showing white matter abnormalities in SD
14 ADSD, 6 ABSD

Head and neck region in the genu of the right internal capsule

Similar Findings of White Matter abnormalities in other dystonias
- Carbon et al., 2004 in persons carrying the DYT1 mutation

Simonyan et al., *Brain* 2008 also found Structural Differences in the Thalamus and Cerebellum in Spasmodic Dysphonia

Axonal Thinning in the Genu of the Internal Capsule

Increased Mean Diffusivity in Thalamus and cerebellum
Relationship of severity of SD and Increased Diffusivity in the Thalamus

Increased breaks in patients with increased diffusivity in thalamus

Studies of a post Mortem Brain of a Patient with AD Spasmodic Dysphonia

Axonal Thinning in the Internal Capsule

Region in internal capsule control Patient with SD

Post Mortem Abnormalities in SD

Deposits in Brain Tissue of SD patient

Some accumulation of mineral deposits in the brain of a SD patient in Regions showing increased mineral accumulations of calcium, iron, phosphorous
Using 7Tesla MRI to Identify a Biomarker

- To determine if we can identify these abnormalities in white matter and basal ganglia in individuals for diagnosis of SD on the basis of brain structure
- High resolution MRI 7Tesla

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Transient changes
2-5 years maximum

Voice Symptoms

NIH Workshop resulted in a Consensus
White paper

Research priorities in spasmodic dysphonia


Highest priority is a valid diagnostic tool for identifying SD for research
Diagnostic Criteria for Spasmodic Dysphonia

- 3 stage process, possible, probably and confirmed
- Items
  - 2 patient questions,
  - breaks in sentences and voice quality ratings and
  - nasoendoscopy findings
- Pilot study at NIH comparing with team diagnosis in 30 patients
- 4 groups
  - ADSD
  - ABSD
  - Vocal tremor
  - Muscular tension dysphonia

Pilot Study results 97% accuracy conducted 2007
No difference between ADSD and ABSD if count the number of breaks