Primary Progressive Apraxia of Speech: A Distinct Neurodegenerative Syndrome

Apraxia of speech (AOS) is a disorder of speech motor planning or programming that affects the sequencing of sounds in syllables and words. It often results from left-hemisphere stroke where it rarely progresses and may even improve over time. But AOS can also occur in neurodegenerative diseases — commonly in conjunction with aphasia. Then it is associated with slow onset and progressive loss of speech production, with some patients eventually becoming mute.

AOS can be difficult to distinguish from aphasia — a syndrome characterized by a problem with the use of words rather than their formation — and is often overlooked or ignored in patients who receive an aphasia diagnosis. AOS can also be confused with dysarthria, which arises from a disruption of the neuromuscular control of speech rather than the inability to generate motor programs for speech movement.

Despite similarities among the various disorders, Mayo Clinic researchers have shown that AOS is a distinct syndrome — called primary progressive apraxia of speech (PPAOS). It differs from primary progressive aphasia and can be the sole presenting sign of neurodegenerative disease. Their findings appeared in the May 2012 issue of Brain.

For the study, investigators recruited 37 patients presenting with a neurodegenerative speech and language disorder between 2010 and 2011. All underwent speech and language, neurological, and neuropsychological evaluations as well as neuroimaging analysis, including head magnetic resonance imaging and fluorodeoxyglucose positron emission tomography scanning.

Based solely on speech and language tests, 12 patients were found to have AOS without aphasia — the main criterion for PPAOS. The consensus diagnosis

Figure. Three-dimensional surface renderings showing regions of gray matter volume loss (A, red), white matter volume loss (B, green) and fluorodeoxyglucose-PET hypometabolism (C, blue) in patients with PPAOS compared with controls. Results are shown uncorrected for multiple comparisons, p < 0.001.LA.
CONNECT Trial Tests Effectiveness, Feasibility of Remote TBI Care

Between 2001 and 2010, traumatic brain injury (TBI)-related emergency department visits rose 70 percent, with the greatest increase occurring among young children and adults older than 65. Many of these vulnerable patients lack access to specialized post-acute care, especially in rural areas.

Mayo Clinic’s specialty brain rehabilitation practice has provided services to patients around the region, often in remote communities, with positive results. Now, Mayo’s TBI Model System Center is undertaking a first-of-its-kind study funded by the National Institute on Disability and Rehabilitation Research. Called the CONNECT Trial, it will determine whether partnering remotely with local providers for TBI-related treatment is feasible and effective. “The CONNECT Trial is totally aligned with our mission of reaching out to regional health systems and other providers around the country that may not have the specialty care that Mayo has,” explains Thomas Bergquist, Ph.D., L.P., a clinical neuropsychologist and specialist in brain rehabilitation at Mayo Clinic in Minnesota.

Features of apraxia of speech*

1. Slow overall speech rate†
2. Lengthened intersegment durations between sounds, syllables, words or phrases; possibly filled, including intrusive schwa†
3. Increased sound distortions or distorted sound substitutions with increased utterance length or increased syllable and word articulatory complexity
4. Syllable segmentation within words greater than one syllable†
5. Sound distortions†
6. Syllable segmentation across words in phrases and sentences†
7. Audible or visible articulatory groping, speech initiation difficulty, false starts and restarts‡
8. Lengthened vowel or consonant segments or both†
9. Distorted sound substitutions
10. Deliberate, slowly sequenced, segmented or distorted (including distorted substitutions) speech sequential motion rates in comparison with speech alternating motion rates‡
11. Increased sound distortions or distorted sound substitutions with increased speech rate
12. Distorted sound additions (not including intrusive schwa)
13. Sound or syllable repetitions
14. Sound prolongations beyond lengthened segments‡
15. Inaccurate (off-target in place or manner) speech alternating motion rates, as in rapid repetition of puh puh puh‡
16. Reduced words per speech breath group relative to maximum vowel duration

*Features are ordered from most to least prevalent among the participants in this study. Features one through five were present in all 12 participants. All features were present in at least one participant. Note that both prosodic and articulatory abnormalities were captured in several of the listed features.
†Can also be present in spastic dysarthria (only two subjects had unequivocal spastic dysarthria).
‡Can also be present in aphasia, but none of the 12 subjects were otherwise aphasic.

Mary M. Machulda, Ph.D., L.P.

For more information
Dr. Bergquist says local providers have expressed great interest in getting real-time advice from Mayo specialists through traditional means, such as phone calls, as well as through Web-based and social media platforms. “Patients may not get exactly the same treatment they would at Mayo, but through these connections, they get something very close to it in their own communities,” he says. This model of care has not been directly tested, however, and no published data indicate whether it provides any advantage over treatment as usual. The CONNECT Trial aims to fill that gap.

Patient recruitment and care
Working with partners in Minnesota, Iowa, and North and South Dakota, CONNECT will recruit 500 patients recently discharged from the hospital with a diagnosis of TBI. Half will receive the usual care available in their community. The rest will be treated by local providers receiving TBI-specific education and consultative support from resources at Mayo’s Brain Rehabilitation Center.

Patients in the intervention group will receive a comprehensive evaluation and needs assessment from the clinical team before being connected to local physicians, therapists and community agencies.

In addition to partnering with providers, the Mayo team will connect with patients and families. “The family is extremely important in any patient’s recovery, and we will provide families with support and education,” Dr. Bergquist explains. “If family members are disengaged, with no defined roles or relationships, they can really struggle. And patients are less likely to have a positive outcome for reasons unrelated to their medical condition. As a brain injury rehabilitation provider, I see this every day.”

The CONNECT Trial will also connect patients and families with each other for peer support and the opportunity to discuss common experiences and problems. Patients in both groups will be followed for up to 18 months and will be assessed on a variety of measures based on the International Classification of Functioning, Disability and Health, which captures how people function in daily life rather than focusing on the presence or absence of disease.

Primary outcome measures for patients will include impairment, activity limitations and participation (independent living, employment and quality of life) as well as satisfaction with the services provided. Families also will be asked about their satisfaction with services along with any changes in their coping and caregiver burden. And providers will report whether the provided services have improved their confidence and competence in working with brain-injured patients. The combined responses will help determine whether outcomes among remote care patients are superior to those in the treatment-as-usual group.

“If the data support this model of care, our hope is that it will become the standard of care for what we do every day,” Dr. Bergquist says. “We will have a hub-based system of remotely coordinated brain rehabilitation services with different providers that will provide the same model of care that patients receive here.”

For more information

New Trial Evaluates rTMS for Adolescent Depression

The need for new therapies for adolescent depression is critical. As many as 40 percent of young people with major depressive disorder fail to respond to pharmacotherapy and psychotherapy, leading to an increased risk of psychiatric hospitalization, poor psychosocial development, and attempted or completed suicide. For these patients, repetitive transcranial magnetic stimulation (rTMS) may be a safe, well-tolerated and effective therapeutic option.

A noninvasive modality, rTMS uses brief magnetic pulses to depolarize neurons in the brain. The magnetic field penetrates the skull, producing electrical currents in cortical tissue. Most studies have used high-frequency rTMS to enhance excitability in the left dorsolateral prefrontal cortex (DLPFC), although some research has focused on the use of low-frequency stimulation to normalize overactivity in the right DLPFC.

Treatment is usually administered five times a week for a total of 30 sessions (3,000 pulses per session at 120 percent motor threshold) over a four- to six-week period. The procedure
is approved for use in adults with major depressive disorder, and evidence supports its safety and efficacy in this population. But little is known about rTMS in children.

According to psychiatrist Paul E. Croarkin, D.O., of Mayo Clinic in Minnesota, “A number of studies have shown that rTMS is not associated with adverse neuropsychological events in adults, and some studies have indicated time-limited improvements in attention, memory and learning after treatment. But we are not sure whether this is true for young patients.” So Dr. Croarkin and colleagues conducted two prospective, open pilot trials of active rTMS using treatment sites and dosing parameters based on guidelines established in adult studies. The results appeared in the December 2013 issue of *Frontiers in Psychiatry*.

“Most of the 14 children who completed the trials had some benefit for their depression, which is encouraging,” Dr. Croarkin says. “It’s also reassuring to note that none of the patients or family members reported any changes in memory, cognitive function or attention. In fact, there was a modest improvement in these areas. These findings reflect what we have seen in clinical practice. Still, you must be careful and skeptical with an open-label trial. It may be there are benefits to just having kids coming in every day for four to six weeks.”

The next step is a large, randomized, double-blind, sham-controlled study, currently recruiting patients at Mayo Clinic. “This approach will allow us to validate rTMS treatment outcomes in a scientifically rigorous manner using all the protocols and parameters developed in definitive adult studies,” Dr. Croarkin explains, adding, “Many of the patients enrolled in our trials have not done well on multiple medications. If we see positive results in this trial, we may be able to offer rTMS to depressed patients who don’t want to take medicine or don’t respond to it. We’re also hoping we can expand the use of neurostimulation to other disorders, including bipolar disorder and autism.”

In addition to evaluating the antidepressant effects of rTMS, the sham-controlled study will use proton magnetic resonance spectroscopy to map the distribution of brain metabolites and determine whether certain neurochemical resonances are associated with remission or improvement of clinical depressive symptoms after rTMS therapy. “We’re trying to understand not only if this works, but the mechanisms as well. For child psychiatry to evolve, we need to understand what happens in brains that are stressed by depression and how they respond to various treatments,” Dr. Croarkin says.

**For more information**