Stimulating The Facial Nerve To Treat Ischemic Stroke: A Review

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Disclosure

The authors report no relevant disclosures.
Introduction

❖ Stroke is the fifth leading cause of death in the United States, with approximately 795,000 people experiencing a new or recurrent stroke each year.

❖ The goal of modern stroke treatment facilities is to rapidly reperfuse the ischemic area, predominantly via endovascular thrombectomy or tissue plasminogen activator (tPA).

❖ Both treatments have a very short window of time for effective treatment, indicating the need for further innovation.

❖ Ganglion stimulation to induce vasodilation serves as a good potential treatment to extend potential treatment times of thrombectomy or tPA. In this review we discuss current innovative strategies and assess the causes of their current limited success.
Methods

A review was conducted through three electronic databases:

- **Study:**
  - Randomized-controlled trials, open label safety trials, and animal models
- **Population:**
  - Patients with ischemic stroke
  - Animals with induced stroke
  - Healthy humans and animals
- **Intervention:**
  - Facial nerve neuromodulation
  - Ganglion stimulation
- **Comparison:**
  - Control - Sham stimulation (when applicable)
- **Outcome:**
  - Safety and tolerability of intervention(s)
  - Increased cerebral and collateral blood flow
  - mRS score at 90 days
  - Brain infarct volume and growth
  - Neuronal survival
  - Improved neurological outcome

Exclusion Criteria

- Reviews, observational studies, meta-analyses, and commentaries
- Hemorrhagic stroke
- Ganglia stimulation for other indications (e.g., chronic headache, rhinitis) or stroke rehabilitation
## Key Results

### Table 2: Trial Endpoints within Invasive Ganglion Stimulation to Treat Ischemic Stroke

<table>
<thead>
<tr>
<th>Trial</th>
<th>Primary Endpoint</th>
<th>Secondary Endpoint(s)</th>
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<tbody>
<tr>
<td><strong>ImpACT-1</strong></td>
<td>Mortality</td>
<td>mRS</td>
</tr>
<tr>
<td>(67)</td>
<td>Serious adverse events</td>
<td>Dichotomized mRS‡</td>
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<tr>
<td></td>
<td>Procedural complications</td>
<td>Binary NIHSS§</td>
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<td></td>
<td>Device-related adverse events</td>
<td>Independence^</td>
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<td></td>
<td>Early treatment terminations</td>
<td></td>
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<tr>
<td></td>
<td><strong>ImpACT-24A</strong></td>
<td>Improvement beyond expectation specifically among patients</td>
</tr>
<tr>
<td>(54)</td>
<td>Improved mRS score at 3 months beyond expectation</td>
<td>with aphasia at entry*</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Neurological recovery at 3 months**</td>
</tr>
<tr>
<td></td>
<td><strong>ImpACT-24B</strong></td>
<td>Functional independence (mRS 0-2)</td>
</tr>
<tr>
<td>(56)</td>
<td>Improved mRS score at 3 months beyond expectation</td>
<td>Bodily self-care (mRS 0-3)</td>
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<tr>
<td></td>
<td></td>
<td>Stroke-Related Quality of life (SIS-16)</td>
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<tr>
<td></td>
<td></td>
<td>Disability-Related Quality of life (UW-mRS)</td>
</tr>
<tr>
<td>NCT04014621</td>
<td>Core expansion volume</td>
<td>Infarct volume (follow-up) between baseline CTP core volume and follow up NCCT infarct volume</td>
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<tr>
<td>(clinicaltrials.gov)</td>
<td></td>
<td>Infarct volume (day 5)</td>
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<tr>
<td></td>
<td></td>
<td>mRS (90 days)</td>
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<tr>
<td></td>
<td></td>
<td>Blood flow***</td>
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<tr>
<td></td>
<td></td>
<td>Hand motor performance****</td>
</tr>
</tbody>
</table>

mRS = modified Rankin Scale  
SIS-16 = Stroke Impact Scale 16  
UW-mRS = Utility-Weighted Modified Rankin Scale  
‡Proportion of positive outcomes, where a positive outcome was an mRS score between 0 and 2  
§ Proportion of positive outcomes, where a positive outcome was a complete recovery (NIHSS 0 or 1) or an improvement by 9 or more points when comparing day 90 to baseline  
^Barthel index  
*mRS score one or more points lower than expected based on a prognostic model incorporating baseline NIHSS score, age, and stroke side  
**NIHSS score ≤1 or improved by ≥9 from baseline  
***Common Carotid Doppler  
****Hand dynamometer
Discussion & Summary Points

❖ Augmentation of collateral blood flow by stimulation of the sphenopalatine ganglion or geniculate ganglion is clearly achievable in clinical settings.

❖ SPG stimulation remains a promising treatment option to improve clinical outcomes for ischemic stroke patients.

❖ Further innovation is required to find a workable integration of ganglion stimulation into current operating procedures.

❖ The inherent focus needs to focus on freezing the ischemic core to allow for more time until mechanical thrombectomy or tPA.

❖ Solutions should look to benefit these current treatment options instead of supplanting them, and finding a way to be used by first responders and non-stroke centers. Planned future trials indicate that this shift is already occurring within key research groups.