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Broca's Area: Long-term Treatment for Non-fluent Aphasia with Repetitive Transcranial Magnetic Stimulation

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Abstract

Long-term treatment to Broca's area for language recovery is a topic of deep interest in the neuroscience community. Many questions regarding treatment methods remain unanswered in the journey towards diagnosis for non-fluent aphasia patients with damage to the dominant left hemisphere of Broca's area. Studies have noted functional imaging studies on aphasia patients with damage on the left hemisphere of Broca's area to have over activation in their right language hemisphere. Application of repetitive transcranial magnetic stimulation (rTMS) to the right region of Broca's area may result in long-term language improvements. This experiment will take place on patients with non-fluent aphasia who are 3-10 years post stroke. In efforts to enhance the results of a short term trial, this study proposes that a long-term trial of rTMS treatment is a reasonable approach towards language improvement in non-fluent aphasia patients.

Background and significance:

Since 1861 the neuroscience community has accepted Broca's area as the language power system of the brain [4]. Evidently, functional and anatomical re-defining of Broca's area has been a pressing issue as the search for treatment of damaged Broca's area rapidly increases (4). Broca's aphasia is the most common non-fluent aphasia [5]. The site of damage after a stroke generally occurs on the left frontal lobe, in most cases leaving the right region free from damage (2). Finger, Buckner, and Buckingham proclaimed that Broca was amongst one of the first scientist that hypothesized that the right hemisphere may become dominant in the case that the dominant language region of the left hemisphere experienced damage (2). Today, researchers have observed the significance of the right hemisphere of Broca's area as essential in the pursuit of language recovery in aphasia patients (7).

Scientists know the left region of Broca's area is dominant and plays a key role in most language functions generally including: reading, writing, speech production, and comprehension (2). Recently, functional imaging studies have shown high activation levels, during language task, on the right hemisphere of Broca's region in

patients with non-fluent aphasia due to damage on the left hemisphere (3,7). The theory that the right hemisphere can take on language responsibilities in the event of damage to the left hemisphere of Broca's area has been considered since Broca's era (2). This observation has sparked the exploration of re-organizing the right hemisphere to be the dominant sphere for language abilities (7). Researchers have turned to rTMS as method for altering the right hemisphere of Broca's area in purse to language improvement (7).

Open trials testing the effect of rTMS on the right hemisphere of Broca's area suggest rTMS as a feasible novel treatment for aphasia patients (1,7). Multiple studies have shown patient's language abilities over the course of treatment improve based on the given assessment language tests (1,7). Many studies have supported past studies and observed progression in speech production, auditory comprehension, and picture naming (1). Other reports have shown that damage to the right hemisphere of Broca's area in patients that partly recover from trauma to the left hemisphere also experience a decrease in language abilities (2). The digression of language abilities in patients that encounter right hemispheric damage after recovering from the effects of a left hemispheric lesion suggests more influence than documented of the right hemisphere (1).

Brain recovery for language after damage to the left hemisphere of Broca's Area after stroke for patients with aphasia remains unknown (7). Though there have been experiments that conclude with language improvements after rTMS treatment the mechanisms of the treatment are still unclear (1,7). Improvements in aphasia patients 5-10 plus years post-stroke is remarkable yet, there is no concrete knowledge as to why rTMS worked for the patients (7). The largest obstacle with this treatment is understanding how rTMS and the right hemisphere work together at improving language abilities (7). The possibility of rTMS as future treatment lies on researchers ability to document changes in activation and take into account any signs of brain re-organization (2).

This experiment is significant for a multitude of reasons. If funded, this will be one of the longest documented trials of actual and sham rTMS (7). Scientists will be able to observe any long-term changes in patients

language abilities by standard test methods and functional imaging (3). As the patients experience changes in their language abilities scientists will be able to observe activation patterns in the brain and identify how rTMS stimulates the language capacities of the right hemisphere (2). As the field moves towards rTMS as a method of treatment for non-fluent aphasia the closer neuroscientists move toward clarity on brain re-organization and the distribution of responsibilities in the brain, specifically Broca's area (2,7).

Method:

Repetitive transcranial magnetic stimulation to the right region of Broca's area in patients with damage to the left region of Broca's area will show improvement in language abilities. However, scientists must have access to laboratory space and proper equipment to conduct this study. This experiment will take place in a state of the art laboratory assembled with a functional magnetic resonance imaging machine. A minimum of ten post-stroke patients with non-fluent aphasia ranging from moderate to severe and patients who recovered from Broca's aphasia will be needed. Equipment necessary for this experiment includes fMRI and rTMS. Questionnaires needed are the Boston Naming Test (BNT) and parts of the Boston Diagnostic Aphasia Exam (BDAE). These exams were chosen based on efforts to support claims of past studies and to be an accurate comparison source for future studies (4). In addition, BNT and BDAE test are commonly used in the neuro-science community (7).

This study will be carried out over the span of two years. Prior to the initial treatment, patients will be tested for their baseline abilities. Five patients chosen randomly will take place in sham rTMS and the other five will participate in actual rTMS. The first year will consist of rTMS treatment for 25 minutes a day 3 times a week with continuous language assessment tests. The second year will be strictly for follow up language assessment tests to observe the long-term effects of rTMS on language abilities. There will be bimonthly fMRI scans to account for any changes in anatomical activation patterns throughout both years. The total activities involve one baseline language test, weekly assessment language tests, bimonthly fMRI scans, actual rTMS , and sham rTMS.

All experiments require patient's consent. Each patient will also be informed of the methods excluding the difference between sham rTMS and actual rTMS. Patients will not be fully informed on how the language test scores will combine with the rTMS treatments. Up to date, there have been no harmful side effects reported from rTMS treatment and all patients will be participating voluntarily.

Rationale:

The experiment addresses improving language for non-fluent aphasia patients with damage to Broca's area in measurable respects. Scientists will be able to record language improvements with the BNT and BDAE test after rTMS treatments. There will also be fMRI scans to complement the changes in patient's individual language abilities. The fMRI data will be important for observing any activation changes that may occur during the course of treatment. Baseline testing will be significant in recording changes in language abilities from one week pre-rTMS to one year post-rTMS. All elements in the experiment work towards addressing the hypothesis and beyond. The results of fMRI throughout this experiment will also aide in understanding the mechanisms of rTMS. The long-term trial may help scientists identify how rTMS alters the brain to increase language abilities. Continuous language tests and fMRI scans one year post- rTMS treatments will aid in measuring the effectiveness of the treatment and the probability of rTMS becoming a novel treatment for those with aphasia due to damage of the left hemisphere of Broca's area.

This study explores the possibility of new treatment for restoring speaking abilities in patients who experience aphasia due to damage to Broca's area. In addition, exploring long-term treatment of rTMS provides the neuroscience community the opportunity to discover if rTMS assists with re-organization of the brain or modifies pathways necessary for speech production (4). There have been studies with similar theories that administer rTMS treatments and observe the results of this treatment with BNT and BDAE tests but do not follow up with functional imaging (7). This experiment serves to analyze rTMS as treatment for non-fluent aphasia patients and assist scientists with discovering the action mechanisms of rTMS.

Exploration of rTMS treatment for aphasia patients will first and foremost positively impact post-stroke patients past the spontaneous recovery phase. Beyond the field of neuroscience, the community will have access to information regarding brain re-organization and behavioral changes that occur via rTMS. Once the mechanisms of rTMS are fully defined, scientists may adapt their use of rTMS on other areas of the brain for treatment of other forms of brain damage. The general public will benefit from this experiment measurably in the long run. Methods of treatment for neurologically impaired individuals will change remarkably.

Budget

Below is an estimated budget to conduct a long-term rTMS trial study. Prices are subject to change as more resources become available.

Need	Cost (USD)
Portable lab including fMRI	$186,000.00
Neuroscientist/ Researcher:	$56,540-$106,410
Repetitive Transcranial Magnetic Stimulation Equipment:	$25,000
Patients:	Voluntary
Estimated Total:	$ 311,000

Data Management Statement:

Researchers will be required to manually and digitally record language test results after each sham and actual rTMS treatment. There will be a database for images collected during fMRI. Images will be labeled with the date image collection occurs and patient information.

Lay Proposal:

Communicating questions, concerns, and opinions are abilities that many individuals take for granted each day. My granny is unable to communicate the way she did prior to her stroke. Granny's stroke damaged the part of her brain responsible for language. "But...yea...bye" are some of the only words Granny is able to say. Granny's stroke damaged a location on the left side of her brain responsible for language.The part of Granny's brain that is damaged is called Broca's area. In many cases, damage to Broca's area on the left hemisphere results in non-fluent aphasia. An aphasia is a language deficit and non-fluent aphasia is the inability to speak smoothly. Granny is a prime example of a non-fluent aphasia patient. Similar to Granny, other non-fluent aphasia patient's vocabulary will typically consist of short words such as: yes, no, but, okay and bye. Today, researchers are working towards a treatment that will help patients who cannot speak due to damage on the left hemisphere of Broca's area.

Broca's area has regions on the left and right hemisphere of the brain that are responsible for language abilities. After a stroke brain cells experience extreme injury or cell death leaving the damaged area of the brain unable to participate in maintaining vital functions. Stroke patients, like Granny, commonly experience cell damage to the left region of Broca's area, leaving the right region undamaged. Scientists today are devoted to restore language by stimulating the undamaged right hemisphere of Broca's area. The current method under investigation to restore language capabilities for non-fluent aphasia patients with damage to the left side of Broca's area is repetitive transcranial magnetic stimulation (rTMS). Repetitive transcranial magnetic stimulation is an external method that causes activation or deactivation of brain cells. Other studies have shown significant improvement in patient's language abilities by applying rTMS to the undamaged right hemisphere Broca's area.

Repetitive transcranial magnetic stimulation targets the undamaged right side of Broca's area in efforts to take on the responsibilities that the damaged left side cannot. Treatment aims to improve language capabilities for non-fluent aphasia patients. However, in order to continue studies toward discovering long-term treatment for those with damage to the left hemisphere of Broca's area financial assistance is required. Contributions from the community will fuel efforts toward establishing long-term treatment for those who suffer from non-fluent aphasia due to injury to Broca's Area. Financially supporting this experiment will positively impact the scientific community and general public. In addition, if results support rTMS as a successful treatment method this study may pave the way for many more treatments for patients with damage to other regions of the brain. Supporting this experiment gives Granny and so many others hope for regaining the ability to communicate with their loved ones again.

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