Critically Appraised Topic

Title: Repetitive Transcranial Magnetic Stimulation (rTMS) for Adults with Hemiparesis following a Stroke

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CLINICAL SCENARIO

Condition/Problem

A cerebrovascular accident (CVA), more commonly known as a stroke, occurs when blood flow to the brain is obstructed, which results in decreased blood flow and tissue death. The two main types of strokes are ischemia and hemorrhage. An ischemic stroke occurs when there is insufficient blood flow to the brain due to an embolism. A hemorrhagic stroke occurs when there is bleeding in the subarachnoid space and oxygenated blood is not able to get to other parts of the brain. The effects of a stroke depend on the artery that was involved and thus the area of the brain that was damaged. Possible impairments include hemiplegia, left unilateral body and visual neglect, hemianopia, decreased sensation, motor apraxia, abnormal behaviors, gaze preference, expressive aphasia, and receptive aphasia. Many individuals make gains in these areas, but full gains may not be made in every aspect of recovery. In addition to the symptoms listed above, other residual problems may include depression, psychosocial adjustment, and cognitive impairments ("Stroke", 2017, August 15).

Incidence/Prevalence

Every year, more than 795,000 Americans have a stroke and approximately 610,000 of these are first-time strokes. About 140,000 Americans die every year due to strokes ("Stroke", 2017, September 6). About 40% of stroke survivors have severe impaired function in the affected arm, 40% have mild to moderate impairments, and 20% have normal arm function three months’ post-stroke (Schub & RainesGass, 2017).

Impact of the Problem on Occupational Performance

Many areas of occupational performance in ADL’s and IADL’s are affected after experiencing a stroke, but every individual is different with the severity of the impairment. When an individual has a stroke, they experience weakness or total loss of motor function and sensory impairments in their extremities. With that being said, individuals may have difficulty performing upper extremity (UE) and lower extremity (LE) dressing due to the requirement of bilateral use of the extremities. Dressing requires joint and soft-tissue integrity, voluntary movement and function of the UE, postural adaptations, visual-perceptual skills, cognitive skills and emotional reactions (sequencing, etc.) (Radomski & Trombly, 2014).

There have been many studies showing that bathing and climbing stairs are tasks that need the most assistance after a stroke (Radomski & Trombly, 2014). Bathing can be difficult because it also requires bilateral use of the extremities when washing areas of the body as well as, cognitive and perceptual skills. For example, sequencing, attention span, motivation, and frustration tolerance may be involved for this specific ADL. Other areas of ADL’s that might be difficult for stroke patients include: eating, toileting, personal hygiene, and grooming (Daily Living, n.d.). Patients often neglect the affected extremity and have trouble doing tasks without the use of their unaffected side. This is encouraged, when possible, to promote relearning of bilateral use of their UE’s. These ADL’s require
sequencing steps, motor planning, strength in bilateral UE's, and visual-perceptual skills (Radomski & Trombly, 2014).

Some IADL's that are affected by the stroke include homemaking, home management, and community mobility, which require higher level cognitive function, problem-solving, social skills, and interaction with the social and physical environment (Radomski & Trombly, 2014). When experiencing difficulties with ADL's and IADL's, individuals become frustrated and lose motivation when improvements are not achieved. It can be particularly frustrating when individuals cannot express their thoughts or communicate due to aphasia. Depression and/or anxiety often occur in about 2/3 of patients after having a stroke which will affect the memory, cognition, and motivation aspect of completing ADL's and IADL's. When patients lose motivation, it interferes with the leisure, work, and all areas of their life, depending on the severity of their depression or anxiety (Emotional and Personality Changes after Stroke Fact Sheet, n.d.)

Intervention (Description and Detailed Protocol)

High frequency (> 1 Hz) rTMS was used with a train of 20 pulses at 10 Hz and 80% resting motor threshold (RMT) for a total of 2 seconds over the target motor cortex area (figure of eight coil) corresponding with the paretic hand (Kim, You, Ko, Park, Lee, Jang, Yoo, & Hallett, 2006). The session lasted 8 minutes where the train was repeated 8 times with a total of 160 pulses delivered with a 58 second intertrain interval (Kim, et al., 2006). During the intertrain intervals, the participants were required to practice a block of sequential finger motor tasks for 40 seconds (Kim, et al., 2006). The last 28 seconds were a rest period. After the rest period, the participants completed a repetitive push button task using 7 digits displayed on a computer screen (Kim, et al., 2006). The digits comprised a 1, 2, 3, or 4 with each digit corresponding with a finger (index=1, middle=2, ring=3, little finger=4). When the number was displayed on the screen, the participant would push the corresponding finger button (Kim, et al., 2006). Motor evoked potentials (MEP) were also recorded with 10 sweeps during each intertrain interval (Kim, et al., 2006).

Low frequency (≤ 1 Hz) was used in the part of the contralateral hemisphere motor cortex where TMS evoked the largest MEP in the first dorsal interosseous muscle (Kakuda, Abo, Kaito, Ishikawa, Taguchi, & Yokoi, 2010). 1 Hz TMS was administered using a figure eight coil for 90% resting motor threshold for 20 minutes, totaling 1,200 pulses (Kakuda, et al., 2010). Intensive OT using both 1 on 1 training and 1-hour self-training then followed. The treatment was over 6 consecutive days in the hospital, with ten treatments total (Kakuda, et al., 2010).}

Comparison of low frequency and high frequency rTMS included a 70-mm figure eight coil and Magstim Rapid Stimulator (Sasaki, Mizutani, Kakuda, & Abo, 2013). For the high frequency group, 10 Hz rTMS was given in the lesional hemisphere in 10 second trains with 50 seconds between intervals for 10 minutes, a total of 1,000 pulses (Sasaki, Mizutani, Kakuda, & Abo, 2013). For the low frequency group, 1 Hz rTMS in the nonlesional hemisphere was given for 30 minutes for a total of 1,800 pulses (Sasaki, Mizutani, Kakuda, & Abo, 2013). Both were given at 90% RMT (Sasaki, Mizutani, Kakuda, & Abo, 2013).

Intervention schedule

High frequency rTMS occurred twice within a one week interval (Kim, et. al., 2006). Low frequency rTMS occurred 6 consecutive days in the hospital with 10 sessions including low frequency rTMS and intensive OT, each for 1 hour (Kakuda, et al., 2010). Patients received sessions for 5 consecutive days for the high frequency vs. low frequency rTMS (Sasaki, Mizutani, Kakuda, & Abo, 2013).
OT Theoretical Basis

rTMS falls under the motor learning and control frame of reference which examines increasing movement with intensive practice. Interventions include specific ways of organizing and breaking up practice. Some examples may be working on task specific practice and whole vs. part practice. Many repetitions and practice sessions are needed to create new neural pathways in the brain. Clients learn or relearn motor skills using activity (Ciuffrida, 2003). In addition to a patient receiving the rTMS, they also will be performing a functional task, range of motion training, exercise, gait training, or ADL. The rTMS is hypothesized to help reorganize neuronal connections to facilitate motor learning (Gross, 2008).

Science Behind the Intervention

rTMS relies on the laws of electromagnetic induction to stimulate the brain. More specifically, a coil is placed over the primary motor cortex resulting in “a current passing through a coil of wire which generates a magnetic field perpendicular to the current direction in the coil” (Gross, 2008). When there is a rapid change of this magnetic field, it produces a transient electric field which influences the membrane potential of the surrounding neurons. The change in membrane potential may lead to depolarization and neuron discharging (Gross, 2008). This stimulates the damaged neurons and promotes recovery.

While receiving rTMS, the patients also received conventional rehabilitation which included range of motion training, exercises, gait training, ADL training, etc. Including these rehabilitation activities into the patient’s schedule is important based on the theory of motor learning and control. For a patient to relearn a motor skill, it requires more than just receiving neuron stimulation via rTMS, but rather practice through therapeutic and functional activities. This will help to ensure that the patient has truly learned the motor skill and that they will be able to transfer and generalize those skills (Jarus, 1994).

Intervention Related to OT

rTMS can be identified as a preparatory method that focuses on motor control learning under the OT framework. This is because it is a device that prepares the client to perform a functional task for their occupational performance. The client does not actively participate, but rather relaxes as rTMS is stimulating the brain and neurons to create new connections. This helps prepare their brain and promotes the restoration of a client’s movement in their UE to enhance occupational performance. After receiving rTMS, the client completes repetitive task practice when their neurons have been stimulated by rTMS and are ready to fire to activate motor neurons. This is appropriate for many reasons and can address the deficits that a client may face with ADL and IADL tasks and limit the amount of disuse after stroke (Gross, 2008).

rTMS also addresses client factors in both the processing and motor categories including higher level functioning, mental functions of seeking complex movement, neuromuscular and movement-related functions, muscle functions, and movement functions which are components of the OT framework. This treatment is appropriate for OTs if they have the skill and training or assistance from another professional to operate the rTMS device.

FOCUSED CLINICAL QUESTION:

In adults with stroke, is rTMS combined with conventional occupational therapy more effective than sham treatment with conventional occupational therapy for improving upper extremity function and performance skills?
A literature review was conducted through six different databases that investigated transcranial magnetic stimulation and its effects on upper extremity hemiparesis and movement in individuals following a stroke. Five studies were located that included relevant information related to the focused clinical question, and three studies were selected and critiqued. Two of the studies are randomized control trials and one study is a case control study. Selection of the articles was based on specific inclusion/exclusion criteria such as outcome measures, population, intervention, and the comparison intervention. Two of the selected studies were 1b (moderate) level of evidence and one study was 4 (weak) level of evidence.

CLINICAL BOTTOM LINE:
Based on these three articles, there is not strong supporting evidence for rTMS and occupational therapy being an effective intervention for upper extremity movement and performance skills for adults following a stroke. It shows statistical significance, but larger studies are need to be conducted to determine if rTMS has clinical significance using functional outcome measures.

Limitation of this CAT: This critically appraised paper (or topic) has been reviewed by occupational therapy graduate students and the course instructor.

TABLE 1: SEARCH STRATEGY

<table>
<thead>
<tr>
<th>Search Terms</th>
<th>Inclusion and Exclusion Criteria</th>
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<tbody>
<tr>
<td>Stroke+Transcranial Magnetic Stimulation</td>
<td>Inclusion: Published in 2006 or after, acute or chronic stroke, peer reviewed, and full text available</td>
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<tr>
<td>Stroke+rTMS+Occupational Therapy</td>
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<tr>
<td>Stroke+rTMS</td>
<td>Exclusion: Published prior to 2006 or lower extremity</td>
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<tr>
<td>Stroke+Hemiplegia</td>
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<tr>
<td>Stroke+Upper Extremity</td>
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<tr>
<td>CVA+rTMS</td>
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<td>CVA+rTMS</td>
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<tr>
<td>CVA+Occupational Therapy</td>
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</tbody>
</table>

TABLE 2: SUMMARY OF STUDY DESIGNS OF ARTICLES RETRIEVED
<table>
<thead>
<tr>
<th>Level</th>
<th>Study Design/ Methodology of Articles Retrieved</th>
<th>Total Number Located</th>
<th>Citation (Name, Year)</th>
</tr>
</thead>
<tbody>
<tr>
<td>1a</td>
<td>Systematic Reviews or Metanalysis of Randomized Control Trials</td>
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<tr>
<td>2a</td>
<td>Systematic reviews of cohort studies</td>
<td></td>
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<tr>
<td>2b</td>
<td>Individualized cohort studies and low quality RCT’s (PEDro ≤4)</td>
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<tr>
<td>3a</td>
<td>Systematic review of case-control studies</td>
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<tr>
<td>3b</td>
<td>Case-control studies and non-randomized controlled trials (quasi experimental or clinical trials)</td>
<td>1</td>
<td></td>
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<tr>
<td>4</td>
<td>Case-series and poor quality cohort and case-control studies</td>
<td>1</td>
<td>Kakuda, et al., 2010</td>
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<tr>
<td>5</td>
<td>Expert Opinion</td>
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STUDIES INCLUDED

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<thead>
<tr>
<th></th>
<th>Study 1</th>
<th>Study 2</th>
<th>Study 3</th>
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<tbody>
<tr>
<td><strong>Design</strong></td>
<td>RCT</td>
<td>Single blind RCT</td>
<td>Case Series</td>
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<tr>
<td><strong>Level of Evidence</strong></td>
<td>1b (Moderate)</td>
<td>1b (Moderate)</td>
<td>4 (Weak)</td>
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<tr>
<td><strong>Rigor Score</strong></td>
<td>7/11</td>
<td>8/11</td>
<td>8/9</td>
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<tr>
<td><strong>Population</strong></td>
<td>N: 29&lt;br&gt;Age: 45 - 80 years old&lt;br&gt;Post-Stroke: 6 – 29 days; No disturbance of consciousness; No apparent cognitive deficits demonstrated by their ability to follow verbal commands; Able to begin rTMS within 30 days of admission.</td>
<td>N: 15 (13 male, 2 female)&lt;br&gt;Age: 43-65 years old&lt;br&gt;Post Stroke: 3 months after onset of first ever stroke; Motor deficits of unilateral upper limb that had improved to the extent of being able to move fingers individually.</td>
<td>N: 5&lt;br&gt;Age: 58-72 years old&lt;br&gt;Post-Stroke: ≥12 months; History of single stroke only; No excessive spasticity ≥3 on the Modified Ashworth Scale (MAS); Brunnstrom stage 4 or 5 for both UE and hand-finger; MCP and IP joints of all fingers extend at least 10°; Mini-mental state exam score ≥26; No history of neurolytic nerve block to affected limb; No increase in Fugl-Meyer Assessment found in monthly evaluation for latest 3 months; No active physical or mental illness requiring medical management.</td>
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<tr>
<td><strong>Intervention Investigated</strong></td>
<td>Low frequency and high frequency rTMS (LF-rTMS and HF-rTMS) for 30 minutes and 10 minutes respectively, for 5 consecutive days. Participants received 40 - 80 minutes of conventional occupational therapy for 3 days on average after onset.</td>
<td>High frequency rTMS (HF-rTMS) induced cortical excitability and the associated motor skill acquisition in chronic stroke patients. Participants received 8-minutes of HF-rTMS, 2 times for 1-week. Patients immediately practiced a 40 second motor practice task block 8 times after receiving HF-rTMS.</td>
<td>Low frequency rTMS (LF-rTMS) for 20 minutes immediately followed by 1 hour of one-on-one training and self-training with occupational therapy to complete repetitive task practice with affected UE; 2 times per day for 6 days. The same evaluation was performed 4 weeks after completion of 6-day protocol at clinic.</td>
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<td><strong>Comparison Intervention</strong></td>
<td>Sham rTMS for 10 minutes for 5 consecutive days. Participants received 30 – 80 minutes of conventional occupational therapy for 3 days on average after onset.</td>
<td>Participants received 8-minutes of sham rTMS, 2 times a week for 1 week. Patients immediately practiced a 40 second motor practice task block 8 times after sham rTMS.</td>
<td>20 minutes of LF-rTMS followed by 1 hour of one-on-one treatment and 1 hour of self-training twice daily for 6 days.</td>
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<td><strong>Dependent Variables</strong></td>
<td>1) UE strength 2) Skilled movement and movement speed through tapping frequency</td>
<td>1) UE coordination 2) UE movement through movement accuracy (MA) and movement time (MT) of individual fingers</td>
<td>1) UE strength 2) UE coordination 3) Dexterity</td>
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<tr>
<td><strong>Outcome Measures</strong></td>
<td>1) Grip strength using a handheld Jamar dynamometer 2) Tapping frequency over 30 seconds</td>
<td>1) Movement accuracy determined through SuperLab 2.0 software and represents the total number of correct button presses of the maximal potential score 2) Movement time determined through SuperLab 2.0 software representing the time required to complete the motor task</td>
<td>1) Fugl-Meyer Assessment (FMA) 2) Wolf Motor Function Test (WMFT) 3) Ten-second tests: finger individual movement test, hand pronation and supination test, finger tapping test 4) Grip strength using a Jamar dynamometer 5) Pinch force using a pinch gauge</td>
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</table>
| **Results**                | P < .05. There was a statistically significant difference between grip strength and tapping frequency at baseline and post treatment for the Hf-rTMS and LF-rTMS groups however, no significant increase for the sham rTMS. | There were no significant group X time factor interaction effects for both MA (p<0.01) and MT (p<0.01). There was a significantly larger increase in both MA and MT scores for Hf-rTMS plus motor practice compared to sham rTMS plus motor practice (p<0.05). There was no significant carryover effect between the first and second session crossover design block (p=0.17). There was no carryover effect between the first and second session crossover design block (p=0.17). | Statistics were not provided. The FMA scores increased in all participants and did not decrease at 4 weeks (with an exception of 1 participant). Time to complete the 15 WMFT tasks decreased. Ten-second test scores after treatment increased in all three categories. Grip and pinch strength also increased compared to before treatment. The MCID was 5.25 for the Fugl-Meyer. Participants all showed change greater than 5.2, which was...
**SYNTHESIS SECTION:**

**PICOT Question:**
In adult patients with stroke, how does repetitive Transcranial Magnetic Stimulation (rTMS) compared to the control group affect hemiparesis after 3 weeks of treatment?

**Overall Conclusions:**

**Outcome Measures Variables**

**Performance Skill Variables**
- Performance skill variables that were measured including movement accuracy and time with tapping, tapping frequency, finger individual movement, forearm pronation and supination.

**Upper Extremity Movement Variables**
- UE client factor variables that were measured included grip strength, pinch strength, motor function, and UE dexterity.

**Results:**

**Performance Skills**
Participants that received rTMS in addition to conventional occupational therapy achieved statistically significant improvement in performance skills including movement accuracy and time, tapping frequency, finger individual movement, and forearm and hand pronation and supination.

- Treatment Dosage

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<th>Effect Size</th>
<th>Unknown</th>
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<tr>
<td>Conclusion</td>
<td>Statistically significant improvements are achievable for grip strength and tapping frequency through both LF-rTMS and HF-rTMS when combined with conventional OT. However, this isn't indicative of clinical change.</td>
<td>There was a statistically significant increase in motor performance however, this is not indicative of clinical change. Having a crossover design did not have any implications in the results.</td>
<td>Improvements are achievable for UE strength, coordination, and dexterity through LF-rTMS plus intensive occupational therapy.</td>
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*Clinically significant. The MCID was 5kg for the Jamar hand dynamometer. 1 participant showed a change greater than 5kg for the grip strength.*

Minimum treatment included 1 Hz of LF-rTMS in the contralateral hemisphere for 20 minutes and 1,200 pulses or 1 Hz for 30 minutes and 1,800 pulses. HF-rTMS included 10 Hz for 8 minutes for 160 pulses with a 58 second intertrain interval or 10 Hz in the lesional hemisphere in 10 second trains with 50 seconds between intervals for 10 minutes, for a total of 1,000 pulses. HF-rTMS was given for two sessions in one week, or in the comparative study, 5 consecutive days. LF-rTMS was given for 6 consecutive days for 10 sessions, each one hour, or for the comparative study, 5 consecutive days.

- **Tapping Frequency**
  - Increased significantly in both high and low frequency groups (p<.05), the exact p-value was not given. The sham group did not show significant increase in tapping (p=.23).
  - No significant difference between the high frequency and low frequency rTMS group (p=.81). The high-frequency group has statistically significant increase in tapping frequency than that in the sham group (p<.05). There were no statistically significant differences between low-frequency rTMS and the sham group (p=.11).

**UE Movement**
Participants that received rTMS, both high frequency and low frequency, had significant increases in grip strength and tapping frequency. A more significant increase in grip strength and tapping frequency in the HF-rTMS group compared to the sham.

- **Treatment Dosage**
  - The minimum treatment included 1 Hz of LF-rTMS for 20 minutes for 6 days for a total of 1200 pulses. The maximum treatment included 10 Hz of HF-rTMS for 10 minutes for a total of 1000 pulses.

- **Fugl-Meyer Assessment**
  - Scores increased from 1-9 points and did not decrease 4 weeks post treatment.

- **Dexterity, Grip, and Pinch Strength**
  - Improvement of dexterity, grip, and pinch strength in affected limb.
  - Grip strength increased significantly in both high and low frequency groups (p<.05), the exact p-value was not given. The sham group did not show significant increase in grip strength (p=.10).
  - No significant difference between the high frequency and low frequency rTMS group (p=.28). When compared to the sham stimulation group for grip strength, the HF-rTMS showed significant differences (p < .05), where the LF-rTMS group did not (p=15).

- **Movement Accuracy and Time**
  - Significant difference in group by time factor interaction effects for both MA and MT (p<0.01 for both).
  - No significant carryover effect between the first and second session crossover design block (p=0.17).
  - Significant difference between the real rTMS plus motor practice in both MA and MT scores than sham rTMS (p<0.05).
No significant difference between the block 1 MA and MT of the first session in the sham-first group and those of the second session in the real-first group (p=0.15 for MA and p=0.33 for MT, respectively).

Results: Similarities
All studies had the experimental group use rTMS combined with traditional therapy and a common diagnosis, with no adverse sides effects noted. In the randomized control trial studies, participants that received HF-rTMS showed statistically significant improvements in UE movement and performance skill variables.

- Coil Placement
  - LF-rTMS, the contralateral brain hemisphere was used for application of the coils.
  - HF-rTMS, the ipsilateral hemisphere was used for application of the coils. In all the studies, there were no adverse side effects noted by any of the participants.

Results: Differences
All three studies differed in the frequency, dosage of rTMS, occupational therapy rehabilitation, hemisphere of the brain the rTMS was applied to, MEP muscles used, and the time between onset of stroke to implementation of rTMS.

- Dosage and frequency of rTMS
  - For the experimental groups, the studies varied in the usage of frequency from low-frequency (1 Hz) to high-frequency (10 Hz).
  - In the LF-rTMS, the treatment time varied from 20 minutes for 1,200 pulses to maximum of 30 minutes for 1,800 pulses.
  - The HF-rTMS also had varied treatment time, ranging from 8 minutes with a train repeated 8 times with a total of 160 pulses and a 58 second intertrain interval to a 10 second train with 50 seconds between intervals for 10 minutes, totaling 1,000 pulses.

- Hemisphere rTMS was applied to
  - LF-rTMS was applied to the contralateral hemisphere.
  - HF-rTMS was applied to the ipsilateral hemisphere.

Boundaries:
There was a total of 49 participants, 36 males and 13 females, ages 18 to 80 years old. All participants had experienced at least one stroke affecting their UE function with time since stroke ranging from 30 days to ≥ 12 months. Participants varied in active finger movement from individual finger movement to at least 10 degrees of active MCP and IP joints in all fingers. Participants received at least a 5 on verbal response and 4 on eye opening for the Glasgow Coma Scale as well as, no pathologic conditions that interfere with rTMS. Participants had no cognitive deficits so they could follow verbal directions.

Implications for Practice:
- All three studies showed statistical significant improvements in UE movement and performance skills however, larger studies need to be conducted to determine if rTMS has clinical significance using functional outcome measures.
The outcome measures chosen were not able to effectively measure function.

These studies demonstrated that rTMS combined with conventional occupational therapy results in statistically significant improvement in performance skills for movement accuracy and speed with 16 minutes of total treatment time of rTMS.

These studies demonstrated rTMS combined with conventional occupational therapy results in improvement in UE movement for grip strength, pinch strength, and dexterity with 120 total treatment minutes of rTMS.

These studies demonstrated grip strength and tapping frequency had more significant improvements with high frequency rTMS when compared to low frequency rTMS with 500 minutes or total treatment time.

Effect size could not be calculated for any of the studies due to insufficient data.

In all the studies, there was no adverse side effects resulting from the treatment of rTMS.

rTMS is considered an experimental treatment and should not be used in practice currently.

REFERENCES

Critiqued Articles


Related Articles (Not Individually Appraised)


**Other Related Information**


