Video Article

Combining Transcranial Magnetic Stimulation and fMRI to Examine the Default Mode Network

Mark A. Halko, Mark C. Eldaief, Jared C. Horvath, Alvaro Pascual-Leone
Berenson-Allen Center for Noninvasive Brain Stimulation, Beth Israel Deaconess Medical Center

Correspondence to: Jared C. Horvath at Jhorvat2@bidmc.harvard.edu

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Abstract

The default mode network is a group of brain regions that are active when an individual is not focused on the outside world and the brain is at "wakeful rest."[1,2,3] It is thought the default mode network corresponds to self-referential or "internal mentation".[2,3]

It has been hypothesized that, in humans, activity within the default mode network is correlated with certain pathologies (for instance, hyper-activation has been linked to schizophrenia [4,5,6] and autism spectrum disorders [7] whilst hypo-activation of the network has been linked to Alzheimer's and other neurodegenerative diseases [8]). As such, noninvasive modulation of this network may represent a potential therapeutic intervention for a number of neurological and psychiatric pathologies linked to abnormal network activation. One possible tool to effect this modulation is Transcranial Magnetic Stimulation: a non-invasive neurostimulatory and neuromodulatory technique that can transiently or lastingly modulate cortical excitability (either increasing or decreasing it) via the application of localized magnetic field pulses.[9]

In order to explore the default mode network's propensity towards and tolerance of modulation, we will be combining TMS (to the left inferior parietal lobe) with functional magnetic resonance imaging (fMRI). Through this article, we will examine the protocol and considerations necessary to successfully combine these two neuroscientific tools.

Protocol

1. Preparation

a. To begin, obtain a baseline anatomical scan of your subject. This should be done several days before the actual experiment.
b. Next, load the scan into your frameless stereotactic software package.
c. Finally, locate and target your stimulation coordinates. In this case, we will be targeting the left inferior parietal lobule.

2. The Initial Scan

a. On the day of the experiment, your subject will, once again, start in the MRI machine.
b. Begin with an anatomical scan.
c. Next, conduct three functional experimentation runs. For this experiment, the task is quite simple: A fixation point is presented in the subject's central field of vision, and he/she is to simply stare at it passively.

3. TMS Preparation

a. Because the effects of rTMS are transitory, time is of the essence when combining TMS and fMRI. It is imperative you get the subject back into the scanner as soon as possible after stimulation cessation. Because of this, you'll want to use a portable TMS device stationed in a room adjacent to or as close as possible to the scanning-bay as possible. In this case, we're using a portable set-up in an observation suite next door to the scanner.
b. Load your subject's pre-targeted baseline MRI into the stereotactic software package.
c. Finally, link and calibrate your stimulating coil with the stereotaxy equipment - in this case, we'll align a set of infrared sensors to register coil centrality.

4. Determining TMS Parameters

a. When the subject arrives, sit him/her comfortably in a chair.
b. Next, calibrate your subject's head with the sterotaxy equipment. In this case, we'll use infrared sensors to register several positioning anchors: both ears, the nose, and the nasion.
c. Determine your subject's resting motor threshold.
d. If we want to excite the subject's cortex, we will set the TMS machine to 20 Hz with a stimulation power of 110% motor threshold. If we want to inhibit the subject's cortex, we will set the TMS machine to 1 Hz at 110% motor threshold. Although you'll want to explore both parameters throughout the course of a full study, we will only look at a 20 Hz excitatory rTMS chain in this article.
e. Finally, set up a stimulation pattern of 2 second trains with 28 second rest periods.

5. TMS Stimulation

a. Prior to stimulation, prepare the subject to go directly in the scanner following TMS. This includes removal of metal and ensuring the subject has used the restroom.
b. Holding the coil tangential to the scalp, use your stereotaxy equipment to locate and target the subject's stimulation site.
c. Turn on the machine's coil cooling system.
d. Begin stimulation! For this protocol, we will conduct 45 total stimulation trains. At 2 seconds a train with 28 second breaks, we will have a total stim time of 23 minutes.

6. Back to the Scanner

a. Once stimulation is complete, it is important to get the subject back into the scanner as soon as possible. To make this transition as seamless as possible, ensure your scanner is prepared and ready to go. Our advice is to raise the body platform, and reduce the number and duration of localizer scans to a bare minimum.

7. Final Scan

a. Because the effects of rTMS are transitory, the final scanning session should begin with the functional runs. Again, we'll conduct three, 6-minute runs of passive fixation.
b. After the experimental runs are complete, finish with an anatomical scan.

8. Representative Results

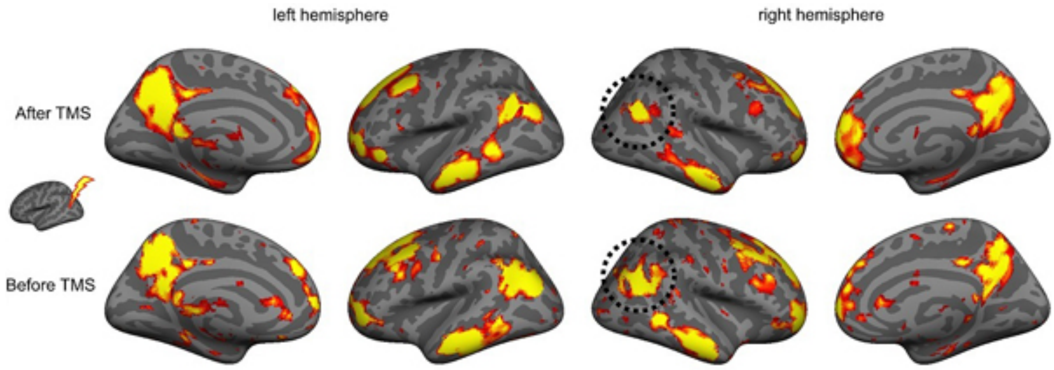

Figure 1. The data suggests that 20 Hz rTMS stimulation to the left inferior parietal lobule, although facilitating local excitability, acts to decrease functional connectivity within the default network.

Discussion

When conducting an offline TMS/MRI experiment, arguably the most important consideration involves the swift and effortless transition from the site of stimulation to the MRI bay. As such, it would be worth revisiting several of the aforementioned ideas suggested to aid in this transition. First: use a portable TMS machine set up in a location as close to the MRI bay as possible. Two: circumvent any automatic stand-by or equivalent mechanism programmed into the MRI equipment. Three: ensure the platform is raised and the stimuli are loaded before the subject completes TMS. And, finally, four: don't attempt to do all this alone. Always have a minimum of two active researchers available and involved with each experimental session - one in charge of the TMS portion, the other in charge of the MRI portion.

Disclosures

No conflicts of interest declared.

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