Supporting Information

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SI Methods

Functional MRI Acquisition Parameters. MRI data were acquired using a 3.0-T whole-body scanner (Phillips, Achieva), equipped for echo planar imaging with a 12 channel head coil. Head movements were restricted using foam cushions. Structural images were acquired via a high resolution, T1-weighted 3D MPRAGE sequence (TR = 6.787 ms, TE = 3.13 ms, flip angle = 8°, voxel size = $1.0 \times 1.0 \times 1.2$ mm), which was collected for the positioning of subsequent scans. Functional images (i.e., blood oxygenation level dependent signal or BOLD) were acquired using T2*-weighted sequences (TR = 2,500 ms, TE = 28 ms, flip angle = 90°, voxel size = $3 \times 3 \times 3$ mm, slice thickness = 3.0 mm, number of slices = 40). Functional data were collected by using an asymmetric spin-echo, echo-planar sequence sensitive to BOLD contrast during three 6-min functional runs. A fixation dot (a white dot placed in the center of a black background) was displayed to subjects via a rear projection system. During all functional MR runs participants were instructed to keep their eyes open, stare at the fixation dot, and "think about whatever they want."

Repetitive Transcranial Magnetic Stimulation Procedures. First, each subject's resting motor threshold was determined by placing the transcranial magnetic stimulation (TMS) coil over primary motor cortex. The motor threshold was defined by the minimum single-pulse intensity required to produce a visible twitch on more than 5 of 10 consecutive trials in the hand contralateral to the site of stimulation. Repetitive TMS (rTMS) was administered with a Magstim Rapid System (Magstim), using a 70-mm figure-of-eight air-cooled coil. For the 1-Hz sessions, stimulation was delivered at 110% of the participant's resting motor threshold at 1 Hz continuously over 30 min for a total of 1,800 pulses. The 20-Hz stimulation was delivered at 110% of the participant's resting motor threshold via 45 trains of 2-s 20-Hz rTMS (i.e., 40 pulses per train), each of which was followed by intertrain pauses of 28 s, for 22.5 min and a total of 1,800 pulses (the same number of total pulses delivered during 1-Hz stimulation). Both 1-Hz and 20-Hz stimulation parameters used are within recommended safety limits for rTMS (1).

During rTMS, targeting of left posterior inferior parietal lobule (lpIPL) was achieved by loading a participant's baseline functional connectivity data into a frameless stereotactic optical tracking neuronavigation system (Brainsight, Magstim, Rogue Research). This system permitted lpIPL to be reliably stimulated within each session, across sessions, and across participants. Specifically, the system allowed for monitoring of the TMS coil position relative to the individual participant's head and brain in real-time, thus allowing for coil placement to be constantly monitored throughout stimulation to achieve maximal targeting accuracy. Notably, such targeting using neuronavigation guided by individualized functional imaging data represents the most accurate method of localizing a cortical target for TMS (2).

Functional Connectivity MRI Data Analysis. Functional MRI data were analyzed using a combination of freely-available software packages [e.g., Functional Magnetic Resonance Imaging of the Brain (FMRIB) Software Library (FSL) (http://www.fmrib.ox.ac.uk/fsl/index.html); Freesurfer (http://surfer.nmr.mgh.harvard.edu/); Statistical Parametric Mapping (SPM) (http://www.fil.ion.ucl.ac.uk/spm/)] and custom, in-house software. We first applied a stringent in house data quality control program to each dataset, described in Yeo et al. (3). If any single run of fMRI data (any one of the three pre-TMS or any one of the three post-TMS runs for 1-Hz or 20-Hz stimulation) exhibited low signal-to-noise or excessive head movement, that subject's dataset was excluded from additional analysis. Eight subjects were removed, resulting in a total of 17 subjects for analysis.

The first stage of preprocessing consisted of spatial normalization to a standard Montreal Neurological Institute (MNI) 152 template brain, slice-timing correction, and motion correction. A second preprocessing stage removed nuisance variables (global mean, motion, white matter, and cerebrospinal fluid), temporally band-passed the data for signals >0.08 Hz, and smoothed the data spatio-temporally (7 mm FWHM Gaussian blur). After preprocessing, region-to-region correlation strengths, the main outcome measure of interest, were calculated with volumetric seed-based functional connectivity analyses: correlation maps were produced by extracting the BOLD time course from a "seed" region in the brain, and then computing the correlation coefficient between that time course and the time course from all other brain voxels. This method has been described in several other paradigms (4–7). To assess the impact of rTMS upon functional connectivity in the default network, we performed the same seed-based functional connectivity MRI (fcMRI) analysis of functional MRI data acquired before and after rTMS stimulation in each participant. The following six default network seeds were used for the analysis: right (r) and left (l) pIPL, posterior cingulate cortex/ventral precuneus (pCC), medial prefrontal cortex (mPFC), and right and left hippocampal formation (HF). The regions of interest (ROI) used to assess changes in functional connectivity as a result of rTMS were defined a priori on the basis of each subject's individualized baseline fMRI resting-state data. Default network seeds were spherical in shape and 8 mm in diameter. The mean MNI coordinates of these six seeds across all participants are displayed in Table S1. Functional connectivity between two given network ROIs was measured by the Pearson's correlation coefficient (r). There was no numerical cutoff for r values, so that all r values were included in the analysis. We used a Fisher's r-to-z conversion which transformed r values to corresponding values within the z distribution for all subsequent statistical analyses. To measure the region-to-region correlation changes as a result of rTMS (i.e., the difference between post-rTMS and pre-rTMS z values), a paired t test was performed to compare changes in z scores before and after stimulation.

Localization of Control Seeds. Additional control seed regions were placed in primary auditory cortex (A1), primary visual cortex (V1), and primary motor cortex (SM1). These regions were defined by their anatomical structure: the A1 seed was placed within the transverse temporal gyrus; the V1 seed was placed within the posterior calcarine sulcus; and the SM1 seed was placed in the hand area on the knob of the precentral gyrus (8).

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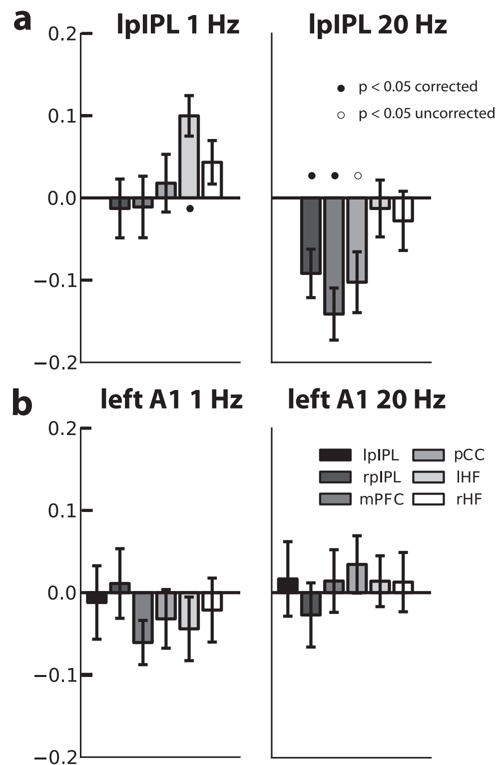

Fig. S1. Comparison of rTMS induced changes in functional connectivity between lpIPL and the default network and between left A1 and the default network. The *y* axes represent changes in *z*-transformed region-to-region correlation strength as a result of rTMS from either a lpIPL seed (*A*) or a left primary auditory cortex (A1) seed (*B*). The ROIs used for the functional connectivity analysis with either lpIPL or left A1 are shown in the legend in *B*. Error bars represent one SEM. One-hertz rTMS significantly increased functional connectivity between lpIPL-lHF (*A*, *Left*), and 20 Hz rTMS significantly decreased functional connectivity between lpIPL-rpIPL and lpIPL-mPFC (corrected) and between lpIPL and pCC (uncorrected) (*A*, *Right*). No significant changes in region-to-region correlations were appreciated between left A1 and any default network ROI following either stimulation frequency (*B*).

Table S1. Mean coordinates for the six default network ROIs across participants

Default network seed	Average MNI coordinates	Broadmann area
lpIPL (stimulation site)	−46 −70 31	39
rpIPL	50 −65 29	39
mPFC	1 53 −3	10
pCC	−1 −56 26	31
lHF	−25 −19 −24	35
rHF	27 −21 −21	35