Optimal timing of pulse onset for language mapping with navigated repetitive transcranial magnetic stimulation.

Within the primary motor cortex, navigated transcranial magnetic stimulation (nTMS) has been shown to yield maps strongly correlated with those generated by direct cortical stimulation (DCS). However, the stimulation parameters for repetitive nTMS (rTMS)-based language mapping are still being refined. For this purpose, the present study compares two rTMS protocols, which differ in the timing of pulse train onset relative to picture presentation onset during object naming. Results were correlated with DCS language mapping during awake surgery. Thirty-two patients with left-sided perisylvian tumors were examined by rTMS prior to awake surgery. Twenty patients underwent rTMS pulse trains starting at 300 ms after picture presentation onset (delayed TMS), whereas another 12 patients received rTMS pulse trains starting at the picture presentation onset (ONSET TMS). These rTMS results were then evaluated for correlation with intraoperative DCS results as gold standard in terms of differential consistencies in receiver operating characteristics (ROC) statistics. Logistic regression analysis by protocols and brain regions were conducted. Within and around Broca's area, there was no difference in sensitivity (onset TMS: 100%, delayed
TMS: 100%), negative predictive value (NPV) (onset TMS: 100%, delayed TMS: 100%), and positive predictive value (PPV) (onset TMS: 55%, delayed TMS: 54%) between the two protocols compared to DCS. However, specificity differed significantly (onset TMS: 67%, delayed TMS: 28%). In contrast, for posterior language regions, such as supramarginal gyrus, angular gyrus, and posterior superior temporal gyrus, early pulse train onset stimulation showed greater specificity (onset TMS: 92%, delayed TMS: 20%), NPV (onset TMS: 92%, delayed TMS: 57%) and PPV (onset TMS: 75%, delayed TMS: 30%) with comparable sensitivity (onset TMS: 75%, delayed TMS: 70%). Logistic regression analysis also confirmed the greater fit of the predictions by rTMS that had the pulse train onset coincident with the picture presentation onset when compared to the delayed stimulation. Analyses of differential disruption patterns of mapped cortical regions were further able to distinguish clusters of cortical regions standardly associated with semantic and pre-vocalization phonological networks proposed in various models of word production. Repetitive nTMS predictions by both protocols correlate well with DCS outcomes especially in Broca's region, particularly with regard to TMS negative predictions. With this study, we have demonstrated that rTMS stimulation onset coincident with picture presentation onset improves the accuracy of preoperative language maps, particularly within posterior language areas. Moreover, immediate and delayed pulse train onsets may have complementary disruption patterns that could differentially capture cortical regions causally necessary for semantic and pre-vocalization phonological networks.