Supplementary Results

Neural tracking of hierarchical linguistic structures

To assess neural tracking of hierarchical linguistic structures, we analyzed the ASSR at the sentence rate (0.5 Hz) and word rate (2 Hz). Patients in all three stimulation groups showed clear spectral peaks at the word rate, indicating significant neural tracking of words (spectral peak > noise floor, one-tailed paired t-test, FDR-corrected; Fig.1a-c, left). A subset of patients also showed spectral peaks at the sentence rate and its second harmonic (1 Hz); however, these peaks were not observed reliably across groups or sessions, probably reflecting the fact that the patients had limited consciousness[1]. Overall, we found musical-electric TNS to have no systematic effect on the neural tracking of words or sentences. We observed a reduction in word tracking after beta stimulation ($t_{18} = 2.239$, $p = 0.038$, $d = 0.514$; Fig.1b right); however, this change was not significantly larger than that observed after sham stimulation ($t_{18} = 2.048$, $p = 0.055$, $d = 0.470$; Fig.1d right). Beta stimulation improved sentence tracking (beyond sham stimulation-related changes, $t_{18} = 3.254$, $p = 0.004$, $d = 0.747$; Fig.1d right); however, this change did not render sentence tracking significant in these patients ($t_{18} = 1.523$, $p = 0.145$, $d = 0.349$; Fig.1b). In sum, these supplementary results suggest that the rhythmic musical-electric TNS did not systematically facilitate DOC patients' neural tracking of hierarchical linguistic structures.

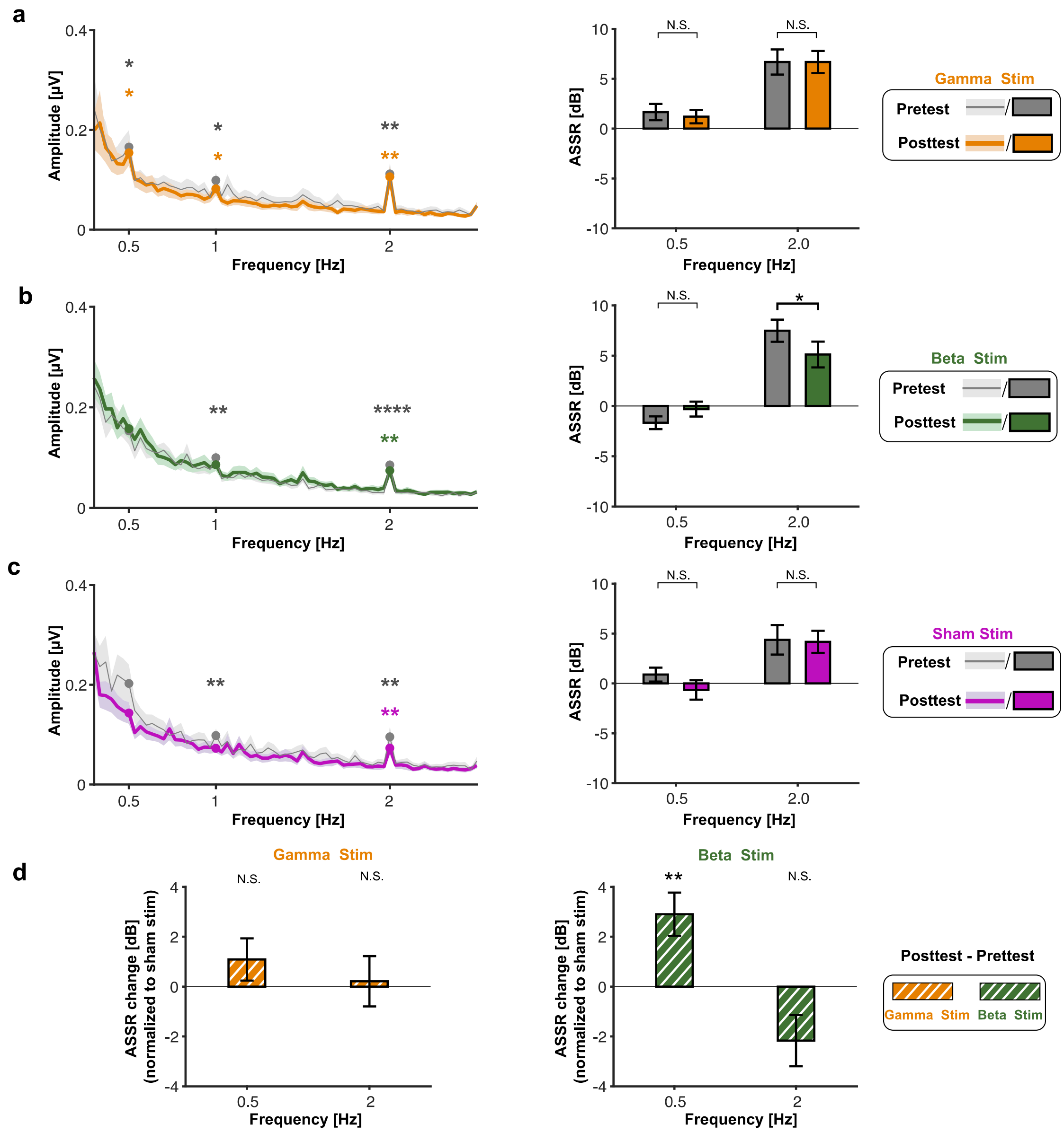

Fig. 1. Neural tracking of hierarchical linguistic structures in DOC patients before and after rhythmic musical-electric TNS or sham stimulation.

(a). Spectral response to hierarchical linguistic structures in pretest (gray) and posttest (orange) for the gamma-stimulation group. The left plot reveals spectral peaks at the word rate (2 Hz) and to a lesser degree at sentence rate (0.5 Hz) and its second harmonic (1 Hz). The bar plot (right) shows the ASSR at word rate and sentence rate in pretest (gray) and posttest (orange).

(b). Same as (a) but for the beta-stimulation group.

(c). Same as (a) but for the sham-stimulation group.

(d). Estimated effect of gamma stimulation (left plot) and beta stimulation (right plot) on ASSR at sentence rate and word rate, after correcting for sham stimulation-related changes (see Methods).

Data are presented as mean ± sem across participants. n.s. non-significant, *$p < 0.05$, **$p < 0.01$, ***$p < 0.001$, ****$p < 0.0001$.

Neural detection of semantic violations

To assess neural detection of semantic violations, we computed ERPs evoked by semantically congruent words vs. semantically incongruent words. This paradigm has been shown to elicit a negative ERP component around 400 ms (relative to the onset of the word) that is commonly thought to encode semantic violations[2,3]. Overall, we did not find this ERP component reliably across patients or sessions, probably due to the fact that patients had limited consciousness (Fig.2a-c, left and center). However, we observed a visibly more negative response to incongruent vs congruent words at around 300-500 ms in the gamma-stimulation group in the posttest (Fig.2a center), suggesting that these patients could detect semantic violations after they underwent gamma stimulation.

To test whether musical-electric TNS improved semantic violation detection we statistically compared the difference waveforms (incongruent minus congruent) in posttest vs pretest. This revealed a significantly enlarged negative difference from 230 to 400 ms after word onset in the gamma stimulation group (Fig.2a, right), supporting our notion above that gamma stimulation improved semantic violation detection. We did not observe such an improvement in the beta or sham stimulation group (Fig.2b-c, right). Analysis of the unbiased neural effect of gamma stimulation (corrected for the observed average sham-stimulation-related change) further corroborated our observation above, revealing a significant increase in semantic violation detection in posttest vs pretest from 220 to 410 ms (Fig.2d, left). No such significant change was detected at any latency in the beta stimulation group (Fig.2d, right). These results indicate that rhythmic musical-electric TNS at gamma, but not beta, frequency may improve neural detection of semantic violations in DOC patients (beyond sham stimulation-related changes).

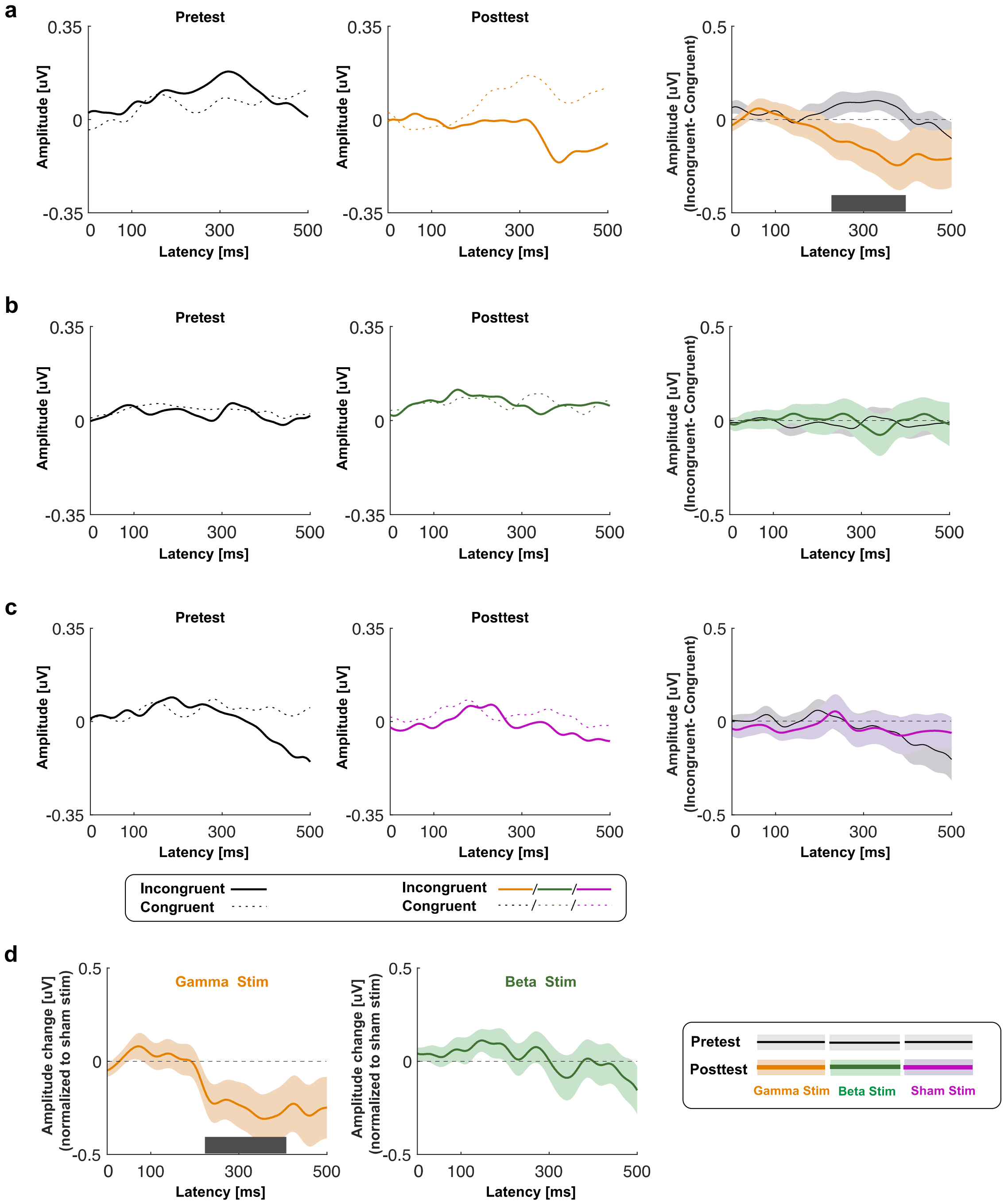

Fig.2. Neural detection of semantic violations in DOC patients before and after rhythmic musical-electric TNS or sham stimulation.

(a). Grand-average ERP waveforms to the same word presented in semantically congruent context (dashed line) or semantically incongruent context (solid line) in pretest (left) and posttest (center) for the gamma stimulation group. Zero latency represents the onset of the word. Semantically incongruent words evoked more negative ERPs at ~300-500 ms than acoustically-matched semantically congruent words in posttest. The right plot shows difference ERP waveforms (incongruent minus congruent) representing the time course of semantic violation detection in pretest (gray) and posttest (orange). Gamma stimulation had a positive aftereffect on putative semantic violation detection throughout a time window between 230-400 ms.

(b). Same as (a) but for the beta-stimulation group.

(c). Same as (a) but for the sham-stimulation group.

(d). Estimated effect of gamma stimulation (left) and beta stimulation (right) on the time course of semantic violation detection, after correcting for sham stimulation-related changes (see Methods). Negative values indicate intervals during which the musical-electric TNS improved semantic violation detection beyond sham stimulation-related changes.

Data are presented as mean ± sem (shaded area in panels a-c, right and panel d) across participants. The black horizontal bars represent clusters of time points showing a statistically significant difference (corrected $p < 0.05$).

References

1. Gui P*, et al.* Assessing the depth of language processing in patients with disorders of consciousness. *Nat Neurosci* **23**, 761-770 (2020).
2. Kutas M, Hillyard SA. Event-related brain potentials to semantically inappropriate and surprisingly large words. *Biol Psychol* **11**, 99-116 (1980).
3. Rohaut B*, et al.* Probing ERP correlates of verbal semantic processing in patients with impaired consciousness. *Neuropsychologia* **66**, 279-292 (2015).