Semantic priming in the motor cortex; evidence from combined rTMS and ERPs

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Abstract

Reading action verbs is associated with activity in the motor cortices involved in performing the corresponding actions. Here, we present new evidence that the motor cortex is involved in semantic processing of bodily action verbs. In contrast to previous studies, we used a direct, non-behavioural index of semantic processing after repetitive transcranial magnetic stimulation (rTMS). Participants saw pairs of hand-related (e.g., to grab – to point) or mouth-related (e.g., to speak – to sing) verbs while semantic priming was assessed using event-related potentials (ERPs). Presentation of the first verb coincided with rTMS over the participant's cortical-left hand area and event-related brain potentials were analysed time-locked to the presentation onset of the second verb. Semantic integration –indexed by the N400 brain potential– was impaired for hand-related but not for mouth-related verb pairs after rTMS. This finding provides strong evidence that the motor cortex is involved in semantic encoding of action verbs, and supports the "embodied semantics" hypothesis.

Keywords: Semantic embodiment; Transcranial magnetic stimulation; Event-related potentials; N400

Introduction

The existence of a “seat” of meaning in the human brain has been a topic of debate for centuries. A recent view put forward by Pulvermuller and colleagues entails that meaning is distributed over interactive neuronal assemblies, each coding a specific aspect of conceptual representations [1,2]. This view has received support from studies showing that reading verbs related to particular bodily actions is associated with activation in areas of the motor cortex underpinning these actions [3,4].

However, there are two concerns regarding the evidence for, but also against [5], the semantic embodiment hypothesis. Firstly, most of the evidence available to date is based on manual reaction times (RTs) after application of TMS to a given cortical area (e.g., the hand motor cortex) that has also been found activated by relevant verbs [6]. However, TMS can increase excitability of the stimulated neural tissue [7,8]. Hence, stimulation of the hand motor cortex, for instance, possibly makes this area more sensitive to hand-related words irrespective of their meaning.

Secondly, much of the current evidence is based on lexical decision tasks in the absence of control over or manipulation of semantic relatedness between stimuli. Thus, RTs in such tasks do not necessarily reflect semantic processing of the stimulus, because, even though target word meaning is likely activated, lexical decision does not hinge upon/require semantic access. For instance, baboons can successfully perform this task, suggesting that lexical decision can be achieved based on the statistical regularity of letter arrangements [9]. In sum, RTs in lexical decision tasks may not accurately reflect semantic processing of target words because a) semantic priming was not controlled and b) the task can be performed via a non-semantic route.

The evidence we present here does not rely on motor responses on the part of the participant and can only be explained by semantic encoding of bodily action verbs.

We applied sham or rTMS to the cortical-left hand motor cortex while participants passively viewed hand- or mouth-related prime-target verb pairs. Importantly, we applied rTMS during presentation of the prime stimulus only, and measured the event-related potential (ERP) amplitude elicited by the subsequently presented target verb. The extent to which prime and target stimuli are semantically related was indexed by N400 amplitude, which has proved a reliable index of semantic priming [10,11]. The more a stimulus is semantically unrelated to its context, the more negative the amplitude of the N400 (e.g., [10]). If the hand motor cortex is important for understanding hand-related verbs, rTMS or sham stimulation applied to this area would differentially affect the N400 amplitude for these verbs. By contrast, assuming that the hand area does not code meaning of mouth verbs, stimulation of the hand area should not differentially affect the N400 or mouth and hand verbs.

Materials and Methods

Participants

12 participants (all right-handed, 4 female, mean age 22.8 years) were recruited from Bangor University's participant panel. Written informed consent was obtained from all participants. In addition, participants completed a safety screening questionnaire for TMS [12]. Handedness was assessed with the Edinburgh Handedness Inventory [13]. Three participants were excluded from the analyses due to technical problems or too few artefact-free trials per condition (< 20). The experiment was designed according to ethical standards of the Declaration of Helsinki and approved by Bangor University's ethics committee.

Materials

Stimulus pairs were created with 40 hand-related verbs (e.g., to write) and 40 mouth-related verbs (e.g., to speak), which were paired with one word of each category preventing phonological overlap within pairs. The sets of hand and mouth verbs were matched (all paired t-tests p >.3) for frequency (hand: 20 ± 9.9, mouth: 43 ± 33), familiarity (hand: 542 ± 10, mouth: 537 ± 19), concreteness (hand: 451 ± 33, mouth: 449 ± 23), and word length (hand: 4.5 ± 0.3, mouth 4.7 ± 0.3; MRC Psycholinguistic Database, [14]. Relatedness of the verb pairs was assessed by ratings from a separate group of 10 university students on a scale from 0 to 5 (standard error): hand–hand pairs (e.g., to clap - to type) 1.5 (0.1); mouth–mouth pairs (e.g., to grin–to talk) 1.9 (0.1); mixed pairs (e.g., to giggle–to squeeze) 0.7 (0.1). The critical conditions in this experiment were hand- or mouth-related verb pairs while cross-category pairs were used as fillers to prevent predictability of the second stimulus and to keep the participant engaged in the experiment. Filler items were excluded from the analysis because the relatedness scores indicated rather low relatedness for some within-category and cross-category pairs overall, while some cross-category pairs (e.g., to wave–to smile, average rating 3.8) had a higher relatedness rating than within-category pairs (to scratch–to press, average rating 0.8). These factors make it difficult to predict and interpret the relative N400 amplitudes between within- and cross-category conditions. Moreover, we could not make any predictions with regard to the direction of the N400 modulation for sham vs. stimulation in the case of cross-category pairs because both include hand verbs in stimulated or target position and stimulation could also have affected processing of the target stimulus. Stimuli were presented in their infinitive form (e.g., “to clap”) to ensure their interpretation as verbs rather than nouns.

Procedure

All participants underwent a structural MRI scan in separate session prior to the experiment. The T1-weighted anatomical scans were acquired using a 3T Philips MRI scanner with a SENSE phased-array head coil (175 sagitally-oriented slices; 1 mm isotropic voxels; TR=8.4 ms, TE= 3.8 ms; flip angle = 8°). The hand area of the left motor cortex was identified in each subject based on anatomical landmarks [15]. Brainsight neuronavigation software (Rogue Research, Montreal, Canada) was used to determine the optimal TMS coil position, and this position was marked on the electrode cap. Before the experiment, the resting motor threshold (rMT) of the right hand was determined for each participant by finding the minimum amount of stimulation that was required to elicit a clearly visible hand twitch. Next, we reduced the stimulation to 90% of rMT, and confirmed that this intensity neither elicited a visible hand twitch, nor resulted in any reported sensations in the subject's hand during the experiment. This intensity (90% rMT) was used for the experiment. Sham stimulation was applied with the TMS coil resting on its side at the marked spot on the EEG cap. Participants wore earplugs to attenuate the noise of the coil discharge and were seated in a comfortable chair approximately one meter away from a computer monitor with a refresh rate of 100 Hz. Stimulus presentation was controlled by E-prime [16] and stimuli were presented in a random order, printed in grey (18pt; visual angle approx. 3^{o}) on a black background. Each trial started with the presentation of a fixation cross (700 ms duration) followed by the first verb (450 ms duration), a blank inter-stimulus interval (black screen; duration 450 ms), presentation of the second verb (duration 1000 ms), and ended with a inter trial interval (ITI) of 4300 ms (Fig. 1). To ensure that participants attended to the stimuli and semantically processed them, they received a comprehension question on 30 % of the trials during the ITI. Questions were randomly drawn from a set of 12 about whether one uses their hands, mouth, feet, or eyes for the first, second, or both verbs (e.g., Do you use you hands for the first action?). Subjects responded by pressing a YES or NO key on a response box with the non-dominant (left) hand. Hence, on any given trial, participants neither knew whether they would receive a question about the stimuli nor what question it would be. Even when a response was required, response selection was made well after the relevant ERP was recorded. Answers to the intermittent questions were 92.8% correct on average, confirming semantic processing of the verb pairs. Participants were instructed to keep their right hand relaxed on the armrest of the chair and to keep their left hand also relaxed, but close to the response box in case a question appeared on the screen. It was pointed out to the participant that responses should be accurate, not fast. Five TMS pulses were administered at a rate of 10 Hz: at 100 ms, 200, 300, 400, and 500 ms relative to the onset of the prime stimulus, i.e., the first TMS pulse was delivered 100 ms after prime onset and the last TMS pulse was given 50 ms after prime offset which was 400 ms before the onset of the second/target verb. After each block of 32 trials, participants received a short break during which the TMS coil was replaced to prevent overheating. Stimulation type (sham or real stimulation) was alternated between blocks, with the order counterbalanced across participants.

Data acquisition

Electrophysiological data were recorded in reference to Cz at a rate of 1 kHz from 64 Ag/AgCl electrodes placed according to the extended 10-20 convention. At each TMS pulse, the EEG amplifier was blocked for 50 ms. Impedances were kept below 5 kΩ. On-line EEG activity was band-pass filtered between 0.1 and 200 Hz and off-line filtered with a 30 Hz low pass zero-phase shift digital filter (slope 48 db/Oct).

Eye-blinks were mathematically corrected using Scan 4.4 (Compumedics, USA) and epochs exceeding ±75 µV activity at any electrode site were discarded. Epochs ranged from -100 to 900 ms relative to the onset of the second verb, and were baseline corrected in reference to the 100 ms pre-stimulus activity. Individual averages were digitally re-referenced to the global average reference. The minimal number of artefact free trials per condition was 22 and the average was: stimulated hand-hand 32, mouth-mouth 35, sham stimulated hand-hand 35, mouth-mouth 36. An ANOVA on the individual number of sweeps revealed a significant effect of stimulation ($F_{1,8} = 5.4$, $p < .05$, $\eta 2p = .4$) showing that real stimulation lead to a greater loss of trials due to artefacts than sham stimulation.

Statistical analysis

We calculated individual mean ERP amplitude over the time window (300-500 ms relative to the onset of the second verb) and the electrodes traditionally associated with the N400 (Cz, C2, CPz, CP2; [10], albeit omitting 2 left electrodes sites too close to the area of stimulation (C1 and CP1). A repeated measures ANOVA with electrode (Cz,C2,CPz,CP2), stimulation (sham vs. real stimulation), and verb type (hand vs. mouth related verb pairs) as within participants factors was performed on individual mean N400 amplitude and latency. An additional ANOVA was performed on global field power (GFP; [17] to test whether the effect of stimulation did not globally affect repeated hand and mouth verb pairs differently. If this were the case then any different modulation of hand and mouth verbs could be due to other than semantic integration processes.

Results

To test whether the hand motor cortex is involved in semantic encoding of hand-related verbs, we analysed mean N400 amplitude elicited by the second verb in a pair of hand- or mouth-related verbs after sham or rTMS applied over the right-hand motor cortex (Fig 2). Inspection of the grand average GFP amplitude revealed that even though the last TMS pulse was delivered 700 ms before onset of the target verb, GFP amplitude was increased after TMS compared to sham stimulation (Fig. 3). This global increase due to stimulation was nearly significant at the electrode sites (Cz, C2, CPz, CP2) and time window (300-500 ms) associated with the N400 [10]; $F_{1,8} = 4.7$, $p = .06$, $\eta^2_p = .37$). Importantly however, there was no interaction between verb type (hand- vs. mouth-related pairs) and stimulation (rTMS vs. sham) ($p >.1$) allowing further analysis of N400 amplitude at the typical sites of maximal amplitude modulation by semantic priming.

An ANOVA with electrode (Cz, C2, CPz, CP2), stimulation (sham vs. real), and verb type (hand- vs. mouth-related) as within-participant factors was conducted on individual mean N400 amplitude. There was a main effect of electrode ($F_{3,24} = 15.1$, $p < .001$, $\eta^2_p = .65$) and an interaction between stimulation and verb type ($F_{1,8} = 13.9$, $p < .01$, $\eta^2_p = .63$, Fig. 4). Subsequent ANOVAs for hand and mouth verbs separately, revealed that for the hand verbs, there was a significant effect of electrode ($F_{3,24} = 11.2$, $p < .01$, $\eta^2_p = .58$) and a significant effect of stimulation ($F_{1,8} = 6.0$, $p < .05$, $\eta^2_p = .41$), but no significant interaction between electrode and stimulation. For mouth-related verbs, there was a significant effect of electrode ($F_{3,24} = 12.4$, $p < .01$, $\eta^2_p = .60$) , but no effect of stimulation ($p > .3$). Hence, rTMS of the hand motor cortex significantly increased N400 amplitude for hand-related verbs but it had no effect on the N400 of mouth-related verbs. The ANOVA on N400 latency did not reveal any significant effects (all $p > .3$).

Discussion

We investigated whether neural activity of the hand motor area when reading hand-related verbs is required for processing the meaning of these verbs. Contrary to previous studies, our results do neither rely on behavioural measures that could be affected by TMS, nor did we measure behaviour which could have been influenced by other than semantic factors (e.g., changes in neural excitability), and crucially, our measure was purely a semantic one.

As mentioned in the introduction, previous research already suggests motor cortex involvement in action verb processing. However, none of these studies has provided solid evidence that neural activity at the motor cortex elicited by bodily action verbs reflects semantic encoding of these verbs. For example, [18] used Theta burst stimulation (TBS) over the left or right motor cortex as participants made lexical decisions (using a manual response) on manual action verbs. They found *quicker* responses after TBS over the cortical-left than right hand motor cortex to manual action verbs only. In this case, the same neural tissue is stimulated, activated by the critical verbs, and required for the response. Response time modulations may therefore have been caused by a complex interaction of factors unrelated to the semantic encoding of manual action verbs. Indeed, one would expect slower responses when TBS supposedly interferes with semantic encoding. In addition, semantic priming between trials or prime stimuli in the lexical decision task was not experimentally manipulated, therefore, RTs in this task did not necessarily reflect semantic processing.

The advantages of our design are that a) the participant was only involved in stimulus semantic processing without a requirement for response preparation, and b) given the semantic priming paradigm, the N400 ERP measure is purely an index of semantic processing. Focal attention to printed words leads to semantic processing of these words, which, in turn, leads to priming of semantically related words [19]. The N400 is a sensitive and reliable measure of such semantic priming [10,11] and the extent to which prime and target stimuli are semantically related is reflected in N400 amplitude elicited by the target stimulus. The hand motor cortex is thus important for understanding hand-related verbs, because when neural computation is disrupted in this region, semantic priming is reduced between hand-related verbs. By contrast, semantic priming between mouth-related verbs was unaffected by disruption of hand motor cortex function.

Such category selective disruption of semantic processing contrasts with the general semantic processing impairment observed after application of TMS to Wernicke's area [20,21], the left inferior frontal gyrus, or posterior middle temporal cortex [22]. Taken together our findings, the observations of general impairments in semantic processing, the finding of taxonomic category specific semantic processing [23], and lexical class-specific semantic processing [24] fit well with the idea that lexical-semantic knowledge is distributed in the brain [1]. Stimulation of, or a lesion in one of these regions may therefore influence comprehension of a stimulus, but stimulus processing in un-stimulated / intact brain regions will not be affected. As a consequence, conceptual knowledge may be protected from complete loss when one component of the network is damaged, which also explains patterns of e.g., category-specific semantic loss in stroke patients [25].

We note, however, that in the current study we only tested hand verb representation in left M1. Hence it is not known whether stimulation of different cortical sites would disrupt semantic processing of (hand) verbs. In addition to using different stimulation sites, further studies may shed light on the extent of embodiment of abstract verbs or nouns.

To conclude, our finding of a hand-verb selective N400 increase after TMS at the hand motor cortex provides compelling evidence in support of the “embodied semantics” hypothesis in that semantic encoding of manual action-verbs, but not e.g., mouth action-verbs, involves the hand motor cortex.

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Legends

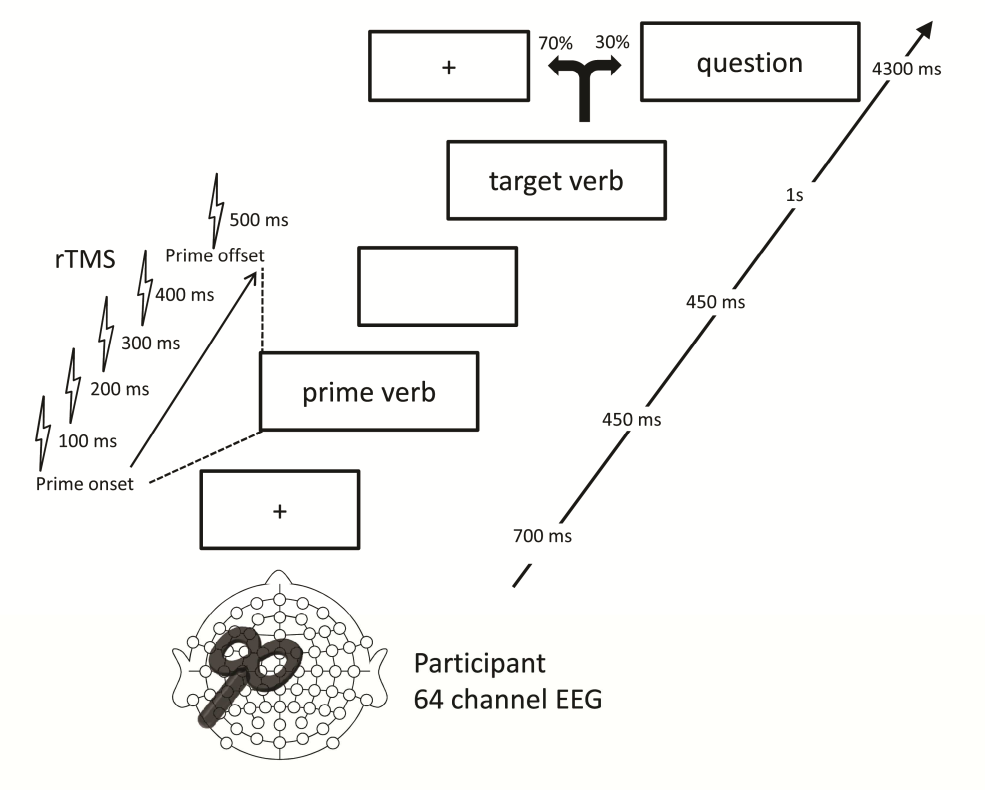
Figure 1. Trial procedure. Note that vertical and horizontal ocular electrodes are not represented.

Figure 2. Grand average ERP waveforms of four electrodes typically associated with the N400 (Cz, C2, CPZ, CP2) excluding those close to the stimulation site (C1, CP1).

Figure 3. Grand average ERP waveforms of Global Field Power for hand and mouth verb pairs.

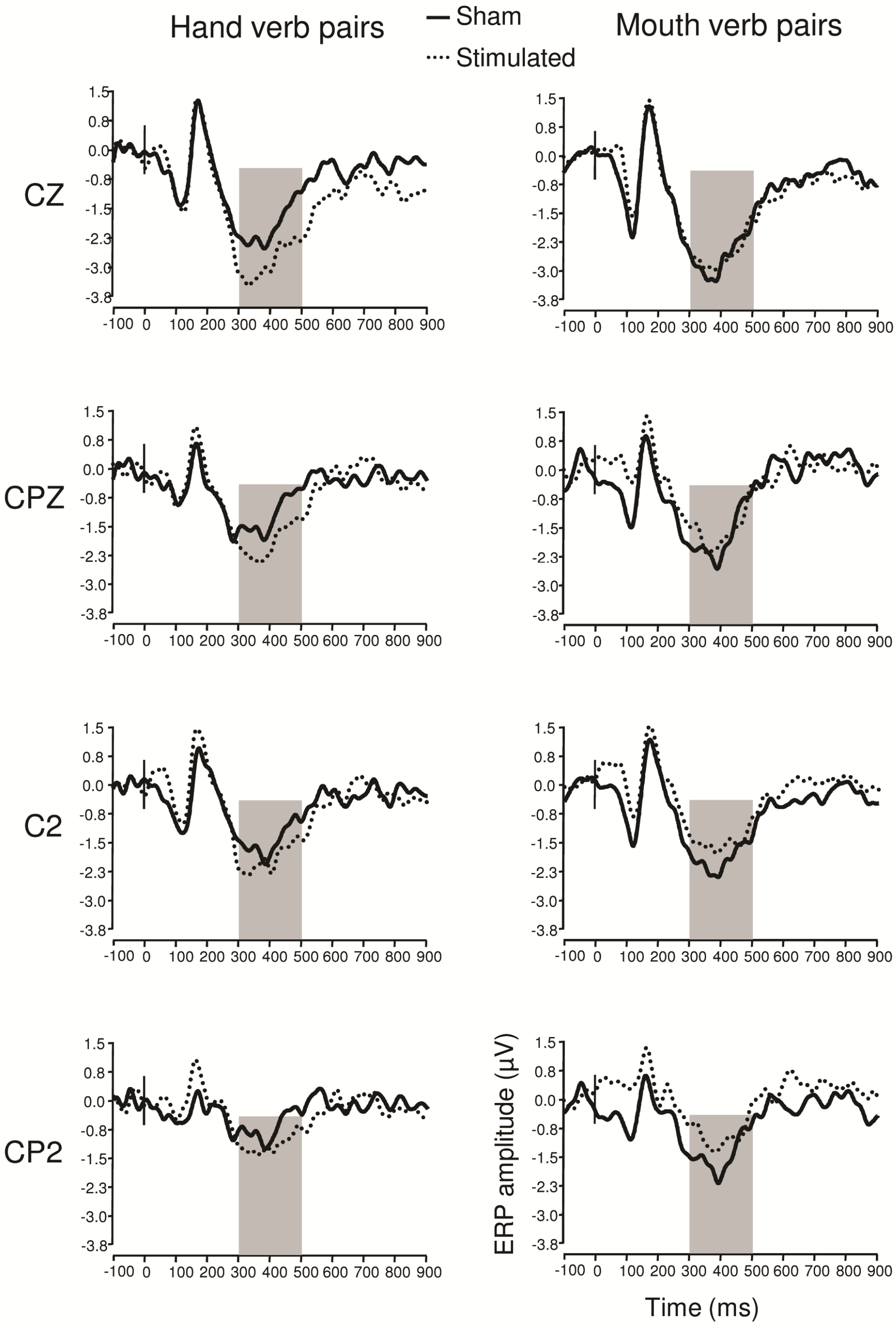
Figure 3. N400 amplitude modulations. Mean N400 amplitude (300-500ms) of 4 centro-parietal electrodes (C2, Cz, CP2, CPZ). Error bars depict the standard error of the means.

Figure 1.



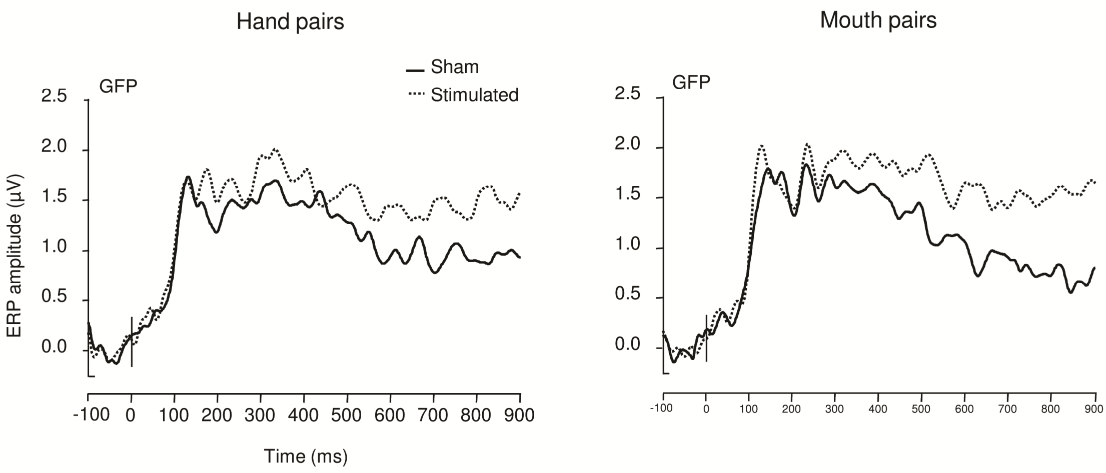
+
70%
30%
question
4300 ms
target verb
1s
500 ms
rTMS
Prime offset
400 ms
300 ms
450 ms
200 ms
prime verb
450 ms
100 ms
Prime onset
+
700 ms
Participant
64 channel EEG

Figure 2.



Hand verb pairs
Sham
Stimulated
Mouth verb pairs
CZ
CPZ
C2
CP2
1.5
0.8
0.0
-0.8
-1.5
-2.3
-3.0
-3.8
-100 0 100 200 300 400 500 600 700 800 900
ERP amplitude (µV)
Time (ms)

Figure 3.



Hand pairs
Mouth pairs
Sham
Stimulated
GFP
ERP amplitude (µV)
2.5
2.0
1.5
1.0
0.5
0.0
-100 0 100 200 300 400 500 600 700 800 900
Time (ms)

Figure 4.