

Left posterior inferior parietal cortex causally supports the retrieval of action knowledge

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ABSTRACT

Conceptual knowledge is central to human cognition. The left posterior inferior parietal lobe (pIPL) is implicated by neuroimaging studies as a multimodal hub representing conceptual knowledge related to various perceptual–motor modalities. However, the causal role of left pIPL in conceptual processing remains unclear. Here, we transiently disrupted left pIPL function with transcranial magnetic stimulation (TMS) to probe its causal relevance for the retrieval of action and sound knowledge. We compared effective TMS over left pIPL with sham TMS, while healthy participants performed three different tasks—lexical decision, action judgment, and sound judgment—on words with a high or low association to actions and sounds. We found that pIPL-TMS selectively impaired action judgments on low sound–low action words. For the first time, we directly related computational simulations of the TMS-induced electrical field to behavioral performance, which revealed that stronger stimulation of left pIPL is associated with worse performance for action but not sound judgments. These results indicate that left pIPL causally supports conceptual processing when action knowledge is task-relevant and cannot be compensated by sound knowledge. Our findings suggest that left pIPL is specialized for the retrieval of action knowledge, challenging the view of left pIPL as a multimodal conceptual hub.

1. Introduction

Conceptual knowledge is central to numerous cognitive abilities, including object use and word comprehension (Kiefer and Pulvermüller, 2012; Lambon Ralph, 2014; van Elk et al., 2014). The left posterior inferior parietal lobe (pIPL) is the most consistently activated region in functional neuroimaging studies on conceptual processing (Binder et al., 2009). Together with the fact that it is located between and connected with many modality-specific cortices (Margulies et al., 2016; Seghier, 2013), this suggests that left pIPL constitutes a “convergence zone” for conceptual knowledge which integrates information from multiple perceptual-motor modalities (Binder and Desai, 2011; Damasio, 1989; Mesulam, 1998; Price et al., 2015). Importantly, recent neuroimaging evidence suggests that left pIPL is not amodal but multimodal, that is, it remains sensitive to the individual modalities (Fernandino et al., 2016; Kuhnke et al., 2020). For instance, in a recent fMRI study (Kuhnke et al., 2020), we found that left pIPL (particularly areas PFm/PGA) responds to

both action and sound features of word meaning. Notably, pIPL activation strongly depended on the task: Left pIPL selectively responded to action features (high vs. low action words) during action judgments, and to sound features (high vs. low sound words) during sound judgments.

However, as neuroimaging is correlational, it remains unknown whether left pIPL plays a *causal* role as a multimodal conceptual region, or instead shows activation that is incidental to behavioral performance (Price and Friston, 2002). While some studies have provided evidence that left pIPL is functionally relevant for conceptual processing in general (Hartwigsen et al., 2016; Sliwinska et al., 2015; Stoeckel et al., 2009), no study has tested the functional relevance of left pIPL for processing multiple different conceptual features. Crucially, the neuroimaging literature seems to conflict with patient studies which predominantly associate left IPL lesions with deficits in object-directed motor actions (Buxbaum et al., 2005a, 2005b; Culham and Valyear, 2006), suggesting a potential specialization for action knowledge.

The causal relevance of a brain region for a cognitive function can be

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determined in healthy human subjects using repetitive transcranial magnetic stimulation (rTMS) applied during the task-of-interest (“online”) (Pascual-Leone et al., 2000; Walsh and Cowey, 2000). Compared to structural brain lesions and rTMS protocols applied before the task (“offline”), online rTMS has the advantage that its effects are transient and thus unconfounded by reorganization processes (Devlin and Watkins, 2008; Hartwigsen et al., 2015).

Here, we used online rTMS to investigate whether left pIPL is functionally relevant for the processing of sound and action features of concepts, and to what extent its involvement depends on the task. We compared effective rTMS over the left pIPL with (ineffective) sham rTMS over the vertex, while healthy participants performed three tasks—lexical decision, sound judgment, and action judgment—on words with a high or low association to sounds and actions (e.g. ‘telephone’ is a high sound–high action word).

Based on our fMRI results (Kuhnke et al., 2020), we hypothesized that left pIPL is multimodal and causally relevant for the processing of both sound and action features of concepts, where its contribution depends on the relevance of a conceptual feature for the concept and the task. Compared to sham stimulation, rTMS over left pIPL should impair behavioral performance (accuracy and/or response times) on both sound judgments and action judgments (which require sound and action features respectively) but not lexical decisions (which do not require access to conceptual knowledge). Action judgments should be modulated differentially for high vs. low action words, and sound judgments should be modulated differentially for high vs. low sound words.

2. Materials and methods

2.1. Participants

Data from 26 native German speakers (14 female; mean age: 27.7 years, SD: 4.0, range: 20–35) entered the final analysis. 29 participants

were initially recruited, but 3 were excluded due to technical failure during the experiment. The sample size was determined based on comparable previous TMS studies (e.g. Klaus and Hartwigsen, 2019; Kuhnke et al., 2017; Vukovic et al., 2017) and counterbalancing requirements (see subsections 2.2 and 2.3). All participants were right-handed (mean laterality quotient: 86.8, SD: 9.99; according to Oldfield, 1971) and had no history of psychiatric, neurological, or hearing disorders. They were recruited via the subject database of the Max Planck Institute for Human Cognitive and Brain Sciences, Leipzig, Germany. Written informed consent was obtained from each subject prior to the experiment. The study was performed according to the guidelines of the Declaration of Helsinki and approved by the local ethics committee of the University of Leipzig.

2.2. Experimental procedures

Fig. 1 depicts the experimental procedure. The study employed a 2 x 3 x 2 x 2 within-subject design with the factors TMS (left pIPL, sham), TASK (lexical decision, sound judgment, action judgment), SOUND (high, low association), and ACTION (high, low association). The experiment consisted of two sessions (one for each TMS condition) separated by at least 7 days (mean inter-session interval: 7.38 days, SD: 1.08) to prevent carry-over effects of TMS. Session order was counterbalanced across participants.

In each session, participants performed three tasks on 104 words denoting concrete objects with a low or high association to sounds and (human) actions. In the lexical decision task, participants decided whether the presented stimulus was a real word or pseudoword. In the sound judgment task, participants judged whether the object denoted by the word was strongly associated with sounds. Finally, in the action judgment task, participants judged whether the object was strongly associated with actions. The lexical decision task acted as a control task which did not require sound or action features of word meaning, and was always performed first so that the participants’ attention was not

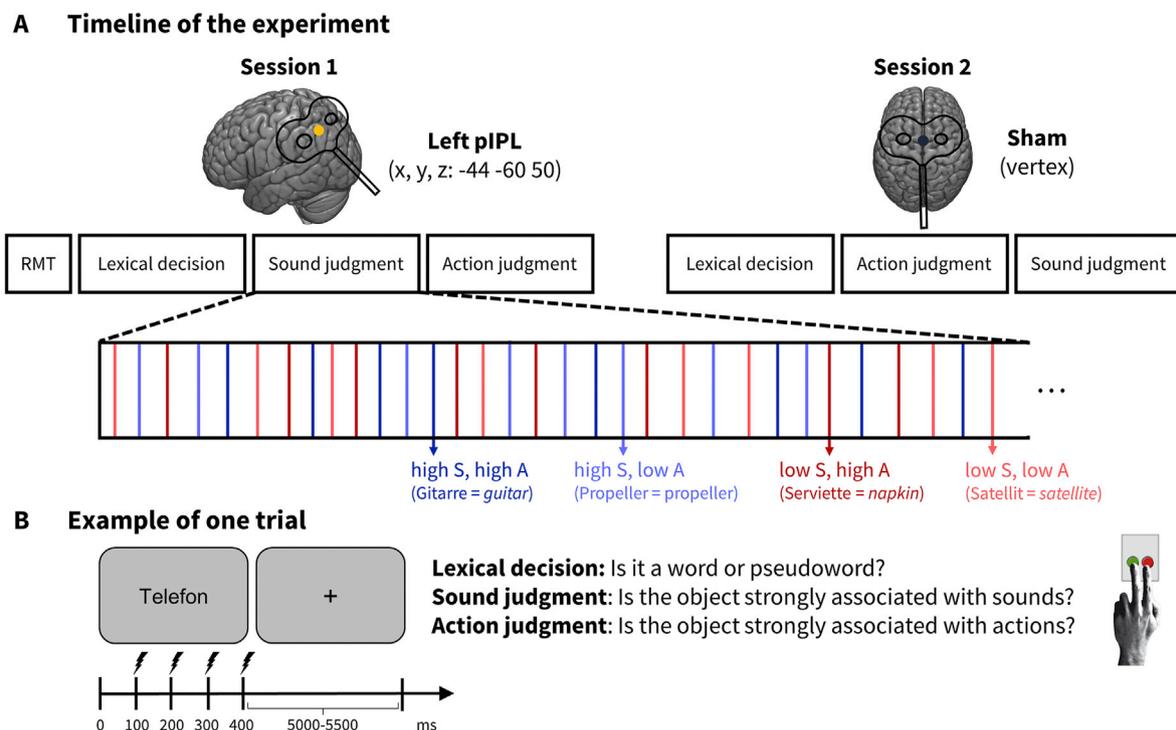


Fig. 1. Experimental procedure. (A) Each subject participated in two TMS sessions. In one session, they received effective rTMS over left pIPL, and in the other session, sham rTMS over the vertex (order counterbalanced across subjects). At the beginning of session 1, the individual resting motor threshold (RMT) was determined. Participants performed three different tasks—lexical decision, sound judgment, and action judgment—on words from the categories 1) high sound–high action (dark blue), 2) high sound–low action (light blue), 3) low sound–high action (dark red), and 4) low sound–low action (light red). (B) During each trial, a word was presented for 400 ms and 4 pulses of 10 Hz rTMS were applied at 100% RMT. Participants responded via button press.

explicitly directed towards sound or action features (cf. Kuhnke et al., 2020). The sound and action judgment tasks explicitly required retrieval of sound or action features, respectively; their order was counterbalanced within and across subjects. Within each task, trials for the four word types were pseudo-randomized (maximally 3 successive trials of a type).

The trial structure was identical in all tasks. A word was shown for 400 ms, followed by an inter-trial interval (fixation cross) of 5–5.5 s (to avoid inter-trial interference by TMS; Kiers et al., 1993). 4 pulses of 10 Hz rTMS were applied starting 100 ms after word onset to interfere with the earliest (~150 ms; Hauk and Tschentscher, 2013; Kiefer and Pulvermüller, 2012) until latest (~400 ms; Lau et al., 2008) conceptual processing stages, while sparing stimulus encoding and response execution processes (cf. Devlin et al., 2003; Hartwigsen et al., 2016). Participants responded via button press using the index and middle fingers of their left hand. They were instructed to respond as fast and as accurately as possible. Before each task, participants practiced with 8 trials (4 without and 4 with TMS) excluded from the actual experiment. Stimuli were presented using the *Presentation* software (Neurobehavioral Systems, Inc., Berkeley, CA, www.neurobs.com) on an EIZO 19" LCD monitor positioned ~1–1.5 m in front of the participant.

2.3. Stimuli

We used an extended stimulus set of our previous fMRI study (Kuhnke et al., 2020). 208 written German nouns denoting concrete objects, which exhibited a high or low association with sounds and actions, yielded four categories of 52 words each: 1) high sound–high action, 2) high sound–low action, 3) low sound–high action, and 4) low sound–low action (see Fig. 1 for examples). To prevent learning effects, different words were used in the two TMS sessions. Thus, the stimulus set was split into two lists of 104 words; list-to-session assignment was counter-balanced across subjects.

163 volunteers who did not participate in the TMS study rated an initial set of 891 words for their association with sounds, actions, and visual features, as well as their familiarity on a 1-to-6 scale (for a similar procedure, see Fernandino et al., 2016a; Kiefer et al., 2008). We selected 52 words for each category such that within and across lists, high and low sound words differed selectively in their sound ratings ($p < 0.001$), whereas high and low action words differed only in their action ratings ($p < 0.001$). Categories were matched on all other rating criteria, as well as on number of letters and syllables, word frequency, bi- and trigram frequencies, and number of orthographic neighbors (see Tables S3–S6). Stimuli for all word categories were selected from the same superordinate categories of animals, inanimate natural entities, and man-made objects (Goldberg et al., 2006; Kiefer et al., 2008). For the lexical decision task, a pseudoword was generated for each word matched in length, syllable structure, and transition frequencies between subsyllabic elements using the *Wuggy* software (<http://crr.ugent.be/Wuggy>; Keuleers and Brysbaert, 2010).

2.4. Transcranial magnetic stimulation

To investigate the causal role of left pIPL in conceptual processing, we applied short trains of 10 Hz rTMS *during* different tasks (“online”). The main advantage of online rTMS over the application before a task (“offline”) is the more precise timing of the interference that allows for measuring its acute and transient consequences (Siebner et al., 2009). Whereas common offline rTMS protocols can induce adaptive changes in brain activity and connectivity that may outlast the stimulation period for up to 30–50 min depending on the particular protocol (Siebner and Rothwell, 2003; Wischniewski and Schutter, 2015), the effects of brief online rTMS bursts are too short-lasting to elicit adaptive reorganization (Bergmann et al., 2016; Hartwigsen et al., 2015; Rotenberg et al., 2014). Therefore, we are confident that online rTMS allows us to assess the functional relevance of left pIPL in conceptual tasks, unconfounded by reorganization processes.

We used stereotactic neuronavigation (TMS Navigator, Localite GmbH, Sankt Augustin, Germany) to precisely navigate the coil over the target area and maintain its location and orientation throughout the experiment. To this end, the participant’s head was co-registered onto their T1-weighted MR image at the beginning of each session. T1 scans were obtained beforehand with a 3T MRI scanner (Siemens, Erlangen, Germany) using an MPRAGE sequence (176 slices in sagittal orientation; repetition time: 2.3 s; echo time: 2.98 ms; field of view: 256 mm; voxel size: 1 x 1 x 1 mm; no slice gap; flip angle: 9°; phase encoding direction: A/P).

MNI coordinates for the left pIPL target (44–60 50 mm) corresponded to the group activation peak for both action and sound feature retrieval (conjunction of [action judgment: high > low action words] ∩ [sound judgment: high > low sound words]) in our previous fMRI study which employed the same paradigm (Kuhnke et al., 2020). To precisely target these coordinates in each individual participant, they were transformed from MNI to subject space using the *SPM12* software (Wellcome Trust Center for Neuroimaging, University College London, UK) (cf. Hartwigsen et al., 2016; Kuhnke et al., 2017). The vertex was determined manually as the midpoint between the lines connecting nasion toinion and the tragi of left to right ear (Klaus and Hartwigsen, 2019). Vertex was used for sham stimulation to increase participant blinding, that is, participants were told that any differences in sensations between TMS sessions were due to a different location of the TMS coil on the head.

Biphasic rTMS bursts were applied via a MagPro X100 stimulator (MagVenture, Farum, Denmark) equipped with a passively cooled MCF-B65 figure-of-eight coil. For sham stimulation, we employed the corresponding placebo coil (MCF-P-B65), which features the same mechanical outline and acoustic noise as the effective coil, but reduces the magnetic field strength by ~80%.

For effective rTMS over left pIPL, the coil was oriented perpendicular to the target gyrus (using the brain segmentation and rendering tools of the neuronavigation software) to maximize the strength of the induced electrical field (Opitz et al., 2011; Thielscher et al., 2011). Stimulation intensity was set to 100% of individual resting motor threshold (RMT), which corresponded to $49.5 \pm 9.3\%$ (mean \pm SD) of maximum stimulator output (where 100% = 144 A/ μ s). RMT was determined before the first experimental session as the lowest stimulation intensity producing at least 5 motor evoked potentials of ≥ 50 μ V in the relaxed first dorsal interosseus muscle of the right hand when single-pulse TMS was applied over the hand region of left primary motor cortex 10 times.

2.5. Analysis

Response times (RTs) for correct trials and response accuracies (% correct responses) were analyzed. To factor out any differences between conditions unrelated to effective rTMS, the data for pIPL-rTMS were normalized to sham stimulation. That is, differences in response accuracy or RT were calculated between each condition under pIPL-rTMS and their sham equivalents (cf. Devlin et al., 2003; Kuhnke et al., 2017; Vukovic et al., 2017).

Statistical inference was then performed using 3-way repeated-measures ANOVAs on sham-normalized accuracies and RTs with the factors TASK (lexical decision, sound judgment, action judgment), SOUND (high, low association), and ACTION (high, low association). We report p-values corrected for non-sphericity using the Huynh-Feldt method. Significant interactions were resolved using step-down analyses and Bonferroni-Holm corrected post-hoc comparisons on estimated marginal means.

We ran several control analyses to ensure that our results were not confounded by TMS-unrelated variables. To test for potential session order effects, we performed a mixed ANOVA (Huynh-Feldt corrected) with the same within-subject factors and an additional between-subject factor ORDER (sham first, pIPL-rTMS first). Moreover, Shapiro-Wilk tests indicated for some conditions that sham-normalized accuracies were not normally distributed ($p < 0.05$). Importantly, however,

repeated-measures ANOVAs are known to be robust against violations of the normality assumption (Blanca et al., 2017; Salkind, 2010; Schmider et al., 2010). Nevertheless, to ensure that our results were not driven by violations of distributional assumptions, we also conducted non-parametric Wilcoxon signed rank tests.

Since null hypothesis significance testing cannot provide evidence for null effects, we performed a complementary Bayesian analysis using the JASP program (<https://jasp-stats.org/>; Wagenmakers et al., 2018). For each experimental condition, Bayesian comparisons tested whether the data were better predicted by the null hypothesis (i.e. performance does not differ between pIPL-rTMS and sham stimulation) or alternative hypothesis (i.e. performance differs between pIPL-rTMS and sham). We used the default prior distribution in JASP, a two-sided Cauchy($0, \frac{1}{2}\sqrt{2}$) distribution. BF_{10} denotes the Bayes Factor in favor of the alternative hypothesis, whereas BF_{01} refers to the Bayes Factor in favor of the null hypothesis ($BF_{01} = 1/BF_{10}$). For example, $BF_{10} = 3$ means that the data were 3 times more likely under the alternative hypothesis than under the null hypothesis (Lakens et al., 2020).

2.6. Electrical field simulations

To characterize the location, extent and strength of the electrical field induced by rTMS over left pIPL in each individual subject, we performed electrical field simulations using SimNIBS v3.1 with high-resolution isotropic finite element models (FEMs; Saturnino et al., 2019; Thielscher et al., 2015). Individual head models were generated from T1-weighted MR images using the mri2mesh pipeline described in Nielsen et al. (2018), employing FreeSurfer (<http://surfer.nmr.mgh.harvard.edu/>; Dale et al., 1999; Fischl et al., 1999) and FSL (<https://fsl.fmrib.ox.ac.uk/fsl/fslwiki/FSL>; Jenkinson et al., 2012; Smith et al., 2004). The head models were composed of $\sim 2.3 \times 10^6$ nodes and $\sim 13 \times 10^6$ tetrahedra. T1 images were used for segmenting the main tissues of the head: scalp, skull, grey matter (GM), white matter (WM), and cerebrospinal fluid (CSF). Instrument markers recorded by the neuro-navigation software during the experiment were used to define the individual position and orientation of the coil (Weise et al., 2020). The electrical field was calculated for 1 A/ μ s and scaled with the respective stimulator intensity. We used the following isotropic conductivity values: $\sigma_{Scalp} = 0.465$ S/m, $\sigma_{Skull} = 0.01$ S/m, $\sigma_{GM} = 0.275$ S/m, $\sigma_{WM} = 0.126$ S/m, $\sigma_{CSF} = 1.654$ S/m (Thielscher et al., 2011; Wagner et al., 2004). The quality of the head reconstructions and electrical field simulations was checked visually (see Figures S3 and S4). Each subject's electrical field was mapped to the fsaverage and MNI spaces for group analyses.

We extracted the average electrical field strengths from maximum probability maps of anatomical regions-of-interest in the SPM Anatomy toolbox version 2.2c (Eickhoff et al., 2005, 2006) to provide descriptive statistics of the electrical field distribution (Table 2). For visualization on the group-average electrical field image, these regions were transformed from MNI to fsaverage space (Wu et al., 2018).

To test for a potential relationship between behavioral impairments and stimulation intensity in left pIPL, we correlated the individual behavioral effect of pIPL-rTMS (accuracy change for action judgments on low sound–low action words; see Results section) with the individual mean electrical field strength in the left pIPL region engaged for action feature retrieval (Action judgment: high > low action words) in our previous fMRI study (Kuhnke et al., 2020). To determine whether this relationship was specific to action knowledge retrieval, we also correlated the electrical field strength in the same region with the accuracy change for sound judgments on the same words. Finally, to test whether the relationship between electrical field strength and action judgment performance was anatomically specific to left pIPL, we performed the same correlation in left SPL 7PC—the region outside left pIPL that received the strongest stimulation (see Table 2). Bayesian statistics again tested for evidence in favor of the null or alternative hypothesis. We used a completely uninformed prior distribution.

3. Results

3.1. rTMS over left pIPL selectively increased errors on action judgments

A repeated-measures ANOVA on sham-normalized response accuracies revealed a significant TASK x SOUND x ACTION interaction ($F_{2,50} = 3.877$, $p = 0.038$, $\text{partial-}\eta^2 = 0.134$). Step-down analyses by TASK revealed that this effect was driven by a SOUND x ACTION interaction in the action judgment task ($F_{1,25} = 5.768$, $p = 0.024$, $\text{partial-}\eta^2 = 0.187$), whereas no significant effects were present in the lexical decision task (SOUND: $F_{1,25} = 1.435$, $p = 0.24$; ACTION: $F_{1,25} < 0.01$, $p = 1$; SOUND x ACTION: $F_{1,25} = 0.103$, $p = 0.75$), or in the sound judgment task (SOUND: $F_{1,25} = 0.358$, $p = 0.56$; ACTION: $F_{1,25} = 0.624$, $p = 0.44$; SOUND x ACTION: $F_{1,25} = 1.5$, $p = 0.23$).

Post-hoc comparisons showed that rTMS over left pIPL selectively impaired response accuracies for action judgments on low sound–low action words, as compared to sham stimulation (Fig. 2; $t_{287} = -3.582$, $p = 0.002$, Cohen's- $d = 0.625$). pIPL-rTMS did not significantly affect action judgments on the other word types (high sound–high action: $t_{287} = -0.39$, $p = 0.7$; high sound–low action: $t_{287} = -0.231$, $p = 0.82$), albeit low sound–high action words showed a trend towards facilitation ($t_{287} = 1.862$, $p = 0.064$, Cohen's- $d = 0.366$). The impairment of low sound–low action words was greater than that of low sound–high action words ($t_{141} = -3.582$, $p < 0.001$, Cohen's- $d = 0.991$) and high sound–low action words ($t_{140} = -2.242$, $p = 0.027$, Cohen's- $d = 0.579$, does not survive correction). Crucially, low sound–low action words were selectively disrupted during action judgments: pIPL-rTMS did not significantly alter lexical decisions ($t_{287} = 0.155$, $p = 0.88$) or sound judgments ($t_{287} = 0.621$, $p = 0.54$) on the same words, and the performance decline (pIPL vs. sham) was significantly greater during action judgments than during lexical decisions ($t_{196} = 2.366$, $p = 0.019$, Cohen's- $d = 0.656$) and sound judgments ($t_{196} = 2.697$, $p = 0.008$, Cohen's- $d = 0.747$).

A control analysis showed that our results were not confounded by session order effects (Table S1). Importantly, this analysis corroborated our previous results: The TASK x SOUND x ACTION interaction remained significant ($F_{2,48} = 3.811$, $p = 0.04$, $\text{partial-}\eta^2 = 0.137$) with no other significant effects. Furthermore, to exclude that our results were driven by violations of distributional assumptions (e.g. normality), we conducted non-parametric Wilcoxon signed rank tests. These tests confirmed that pIPL-rTMS significantly disrupted action judgments on low sound–low action words ($p = 0.018$) and no other conditions ($p > 0.2$).

As null hypothesis significance testing cannot provide evidence for the absence of an effect, we performed a complementary Bayesian analysis. This analysis confirmed that pIPL-rTMS impaired action judgments on low sound–low action words, and crucially provided evidence for a null effect of pIPL-rTMS on all other conditions. For action judgments on low sound–low action words, the data were ~ 3 times more likely under the alternative hypothesis that pIPL-rTMS affected performance than under the null hypothesis of no TMS effect ($BF_{10} = 3.054$). In contrast, for all other conditions, the data were ~ 3 –4 times more likely under the null hypothesis (Table 1).

3.2. pIPL-rTMS did not alter response times (RTs)

A repeated-measures ANOVA on sham-normalized RTs revealed no significant effects (Figure S2; TASK: $F_{2,50} = 0.98$, $p = 0.37$; SOUND: $F_{1,25} = 1.66$, $p = 0.21$; ACTION: $F_{1,25} = 3.312$, $p = 0.08$; TASK x SOUND: $F_{2,50} = 2.355$, $p = 0.12$; TASK x ACTION: $F_{2,50} = 0.284$, $p = 0.68$; SOUND x ACTION: $F_{1,25} = 0.408$, $p = 0.53$; TASK x SOUND x ACTION: $F_{2,50} = 1.882$, $p = 0.17$). Corroborating this result, Bayesian statistics provided evidence in favor of a null effect of pIPL-rTMS for all experimental conditions (Table S2).

3.3. Localizing the TMS effect using electrical field simulations

To better characterize the relationship between the behavioral effects

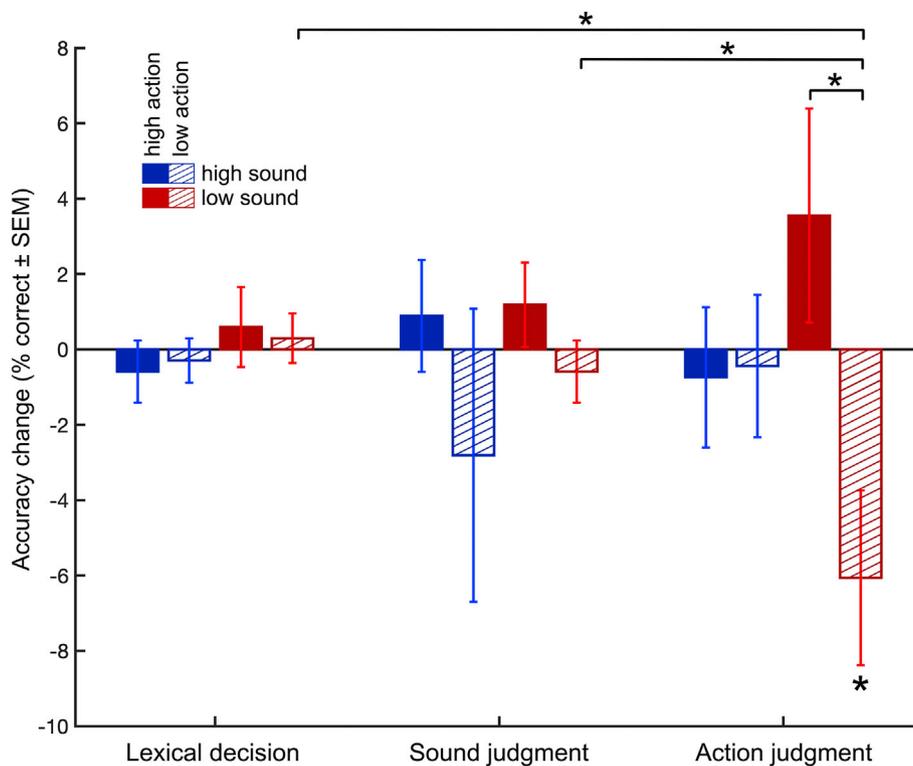


Fig. 2. rTMS over left pIPL selectively impaired response accuracy for action judgments on low sound–low action words. Change in response accuracy for pIPL-rTMS vs. sham stimulation. Error bars represent standard error of the mean (SEM). *: $p < 0.05$ (Bonferroni-Holm corrected).

Table 1
Results of the Bayesian analysis on sham-normalized accuracies.

	Mean	95% credible interval	BF ₁₀	BF ₀₁
L: high SF, high AF	-0.592	[-2.332, 1.149]	0.259	3.859
L: high SF, low AF	-0.296	[-1.533, 0.941]	0.232	4.318
L: low SF, high AF	0.592	[-1.635, 2.819]	0.238	4.208
L: low SF, low AF	0.296	[-1.088, 1.680]	0.226	4.416
S: high SF, high AF	0.888	[-2.229, 4.004]	0.243	4.123
S: high SF, low AF	-2.811	[-10.979, 5.357]	0.261	3.838
S: low SF, high AF	0.148	[-0.971, 1.267]	0.214	4.664
S: low SF, low AF	1.183	[-1.173, 3.540]	0.336	2.979
A: high SF, high AF	-0.740	[-4.646, 3.166]	0.222	4.501
A: high SF, low AF	-0.444	[-4.406, 3.519]	0.212	4.709
A: low SF, high AF	3.550	[-2.425, 9.525]	0.405	2.470
A: low SF, low AF	-6.065	[-10.942, -1.189]	3.054	0.327

L: lexical decision; S: sound judgment; A: action judgment; SF: sound feature; AF: action feature; BF₁₀: Bayes Factor for the alternative hypothesis; BF₀₁: Bayes Factor for the null hypothesis (where BF₀₁ = 1/BF₁₀). Bold font highlights evidence in favor of one hypothesis over the other.

and the effectively stimulated region in left pIPL, we performed computational simulations of the electrical field induced by pIPL-rTMS in each individual subject. Importantly, we used the actual position and orientation of the coil recorded during the experiment for these simulations to maintain individual specificity.

Fig. 3 shows the average (A) and standard deviation (B) of the electrical field magnitude across subjects, and Table 2 lists the average electrical field strengths in anatomical regions-of-interest. As expected, the left posterior IPL (anatomical regions PFm and PGa) was stimulated with the highest intensity (~50 V/m at peak). However, surrounding areas were also stimulated with relatively high intensities (20–40 V/m). These regions included parts of left anterior IPL (e.g. region PFt) and intraparietal sulcus (IPS; areas hIP1-3), somatosensory cortex (especially area 1), and the superior parietal lobe (SPL; particularly areas 7PC, 7A).

3.4. Stronger stimulation of left pIPL specifically predicted worse action judgment performance

We reasoned that if left pIPL is indeed causally relevant for action knowledge retrieval, subjects whose action-related pIPL region was stimulated more strongly should show worse performance on action judgments. To test this, we correlated the individual behavioral effect of pIPL-rTMS (i.e. the accuracy change for action judgments on low sound–low action words, as compared to sham stimulation) with the electrical field strength in the left pIPL region that was activated for action knowledge retrieval in our previous fMRI study (Fig. 3C). Indeed, the electrical field strength in the action-related pIPL area was negatively correlated with the individual accuracy change (Fig. 3D; $r = -0.46$, $p = 0.018$, BF₁₀ = 3.461), supporting the hypothesized association between higher electrical field strengths and larger individual impairments of action judgments. In contrast, the electrical field strength was not associated with behavioral performance for sound judgments on the same words (Figure S5; $r = 0.08$, $p = 0.71$, BF₁₀ = 0.260), indicating that left pIPL is specialized for action knowledge retrieval. Moreover, left SPL 7PC—the region outside left pIPL that received the strongest stimulation—did not show a significant relationship between electrical field strength and action judgment performance (Figure S6; $r = -0.15$, $p = 0.46$, BF₁₀ = 0.344). This suggests that the behavior–electrical field relationship was anatomically specific to left pIPL. Note that the region-of-interest in left pIPL was selected based on the results of our fMRI study with a completely different group of subjects, and was thus unbiased with respect to the current data.

3.5. Errors caused by pIPL-rTMS were associated with a typical RT

To further elucidate the nature of the behavioral impairment caused by rTMS over left pIPL, we analyzed the response times (RTs) for errors during action judgments on low sound–low action words. As compared to sham stimulation, pIPL-rTMS predominantly increased errors with a “typical” RT, close to the individual mean ($t_{25} = 2.628$, $p = 0.01$,

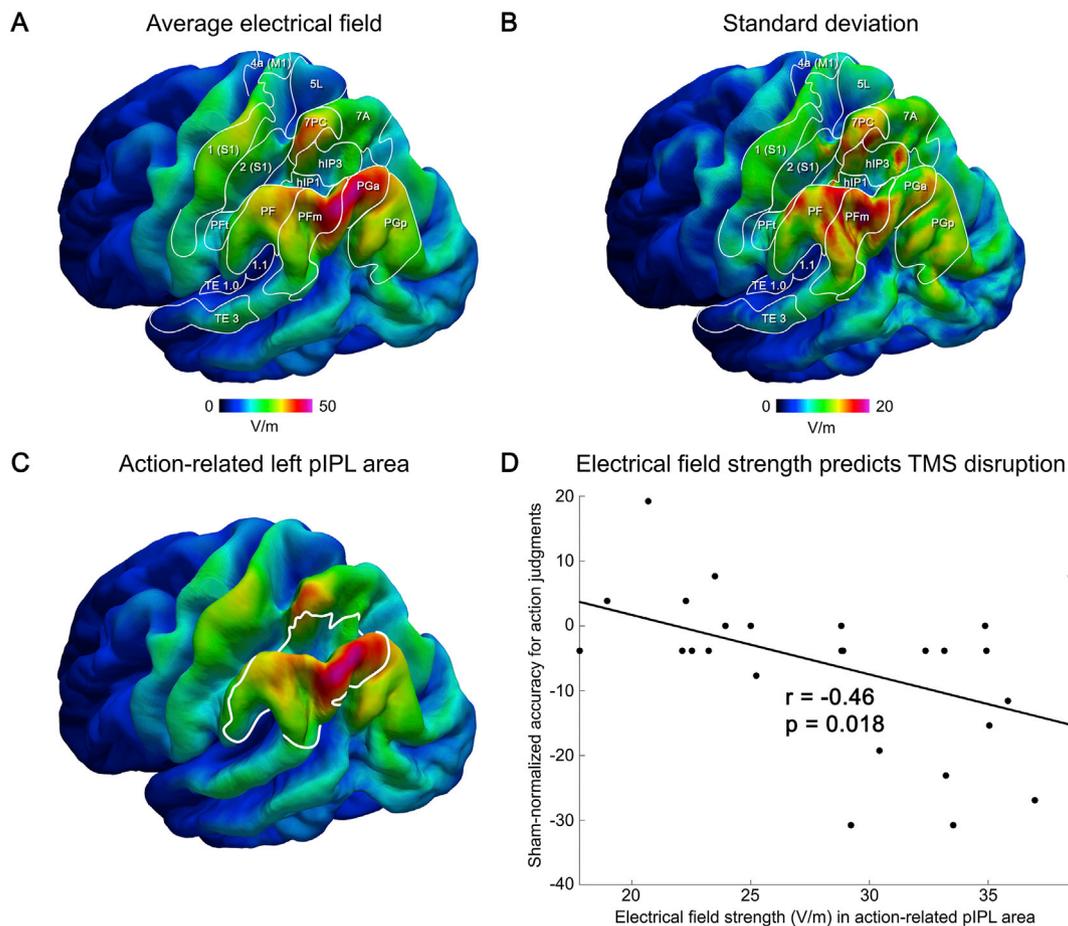


Fig. 3. Results of electrical field simulations. (A) The average strength of the induced electrical field across subjects is displayed on the normalized cortical surface (fsaverage). Anatomical regions from the SPM Anatomy toolbox (Eickhoff et al., 2005, 2006) are outlined in white. (B) The standard deviation of the electrical field strength across subjects. (C) The action-related region-of-interest in left pIPL is outlined on the average electrical field image. (D) Correlation between the electrical field strength in action-related left pIPL and individual behavioral impairment of action judgments for low sound-low action words (i.e. accuracy change in % for pIPL-rTMS vs. sham stimulation).

Cohen's $d = 0.515$; Fig. 4; Table 3). This indicates that subjects erroneously decided that a low sound-low action word was action-related in a normal period of time, and renders it highly unlikely that the TMS effect reflects a speed-accuracy tradeoff.

4. Discussion

This study tested the causal role of left pIPL as a multimodal convergence zone in conceptual processing. Specifically, we investigated the functional relevance of left pIPL for processing action and sound features of concepts. We found that rTMS over the left pIPL selectively increased errors for action judgments on low sound-low action words, as compared to sham stimulation. Electrical field simulations provided the first evidence that stronger stimulation of left pIPL is associated with worse performance on action but not sound judgments. These findings strongly suggest that left pIPL is causally relevant for processing action but not sound knowledge. Therefore, our results question the view that left pIPL acts as a multimodal conceptual hub.

Our data indicate that the causal involvement of left pIPL in conceptual processing strongly depends on the task. Low sound-low action words were selectively disrupted during action judgments, whereas the same words were not affected during lexical decisions or sound judgments. This suggests that left pIPL selectively supports conceptual processing when action knowledge is task-relevant. This result supports theories that assume conceptual processing to rely on a flexible, task-dependent architecture (Binder and Desai, 2011; Hoenig et al., 2008;

Kemmerer, 2015; Popp et al., 2019). The neural representation of a concept is not a static, task-independent entity, but it is flexibly shaped to the requirements of the current context (Lebois et al., 2015; Yee and Thompson-Schill, 2016).

In addition to the task, the critical involvement of left pIPL also depends on the relevance of action and sound knowledge for word meaning. Considering action feature relevance, pIPL-TMS impaired low sound-low action words, but tended to facilitate the corresponding high action words. As a potential mechanism for these effects, we propose that rTMS increased action-related activity in left pIPL (Miniussi et al., 2013). In case of both word types, rTMS increased the likelihood to judge an object as action-related. In addition, errors caused by pIPL-rTMS were associated with a “typical” response time close to the individual mean. This indicates that participants made the intentional decision that a low-action word was action-related. These facts suggest that rTMS increased action-related activity in left pIPL, leading to a higher likelihood to judge an object as action-related, even if it was not.

Regarding sound feature relevance, pIPL-rTMS selectively affected low-sound, but not high-sound words, during action judgments. This finding might be explained via “action-sound coupling” mechanisms (Lemaitre et al., 2018). Actions often elicit typical sounds (e.g. hammering, guitar playing). Thus, in the case of high-sound words, participants might leverage the sound feature to support action judgments. Such action-sound coupling could provide some functional “degeneracy” (Price and Friston, 2002) to the neural representations of sound and action features, and robustness against disruption (e.g. by TMS

Table 2
Average electrical field strength (in V/m) in anatomical regions-of-interest.

Region	Mean e-field (SD)	Region	Mean e-field (SD)	Region	Mean e-field (SD)
Left IPL		Left SPL		Left motor	
PFt	21.73 (6.69)	7A	23.12 (7.37)	4a	11.79 (3.47)
PF	27.88 (8.16)	7PC	30.82 (8.34)	4p	13.17 (3.24)
PFm	31.84 (7.77)	7P	13.97 (4.50)	Left auditory	
PGa	31.52 (6.64)	7M	6.76 (2.74)	TE 1.0	7.08 (2.56)
PGp	29.38 (7.20)	5L	15.92 (6.69)	TE 1.1	4.87 (2.17)
PFop	18.18 (5.42)	5M	6.47 (2.52)	TE 1.2	8.07 (2.09)
PFcm	11.52 (4.41)	5Ci	7.39 (1.37)	TE 3	14.47 (3.76)
Left IPS		Left somatosensory			
hIP1	21.80 (5.30)	1	26.31 (5.75)		
hIP2	27.56 (7.10)	2	20.30 (4.80)		
hIP3	24.14 (5.31)	3a	12.82 (2.69)		
		3b	20.66 (4.79)		

To facilitate readability, the table is colored according to average field strength: <15 (dark blue), 15-20 (light blue), 20-25 (green), 25-30 (orange), >30 V/m (red). IPL = inferior parietal lobe; IPS = intraparietal sulcus; SPL = superior parietal lobe. Anatomical regions were derived from the SPM Anatomy toolbox v2.2c (Eickhoff et al., 2005, 2006).

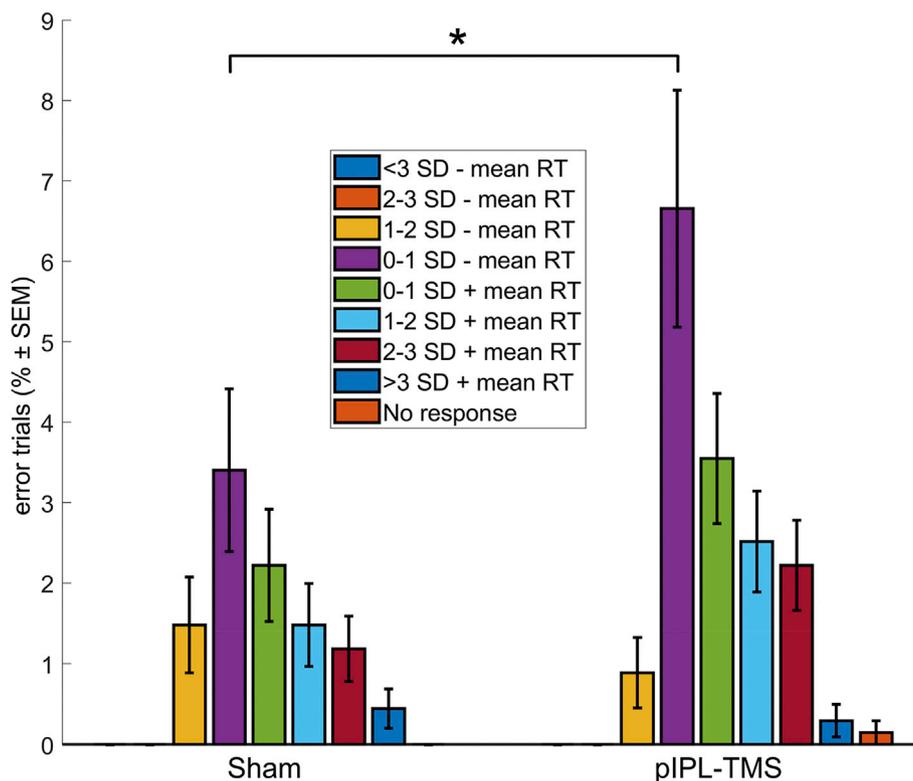


Fig. 4. Response times (RT) for errors during action judgments on low sound–low action words. Errors caused by pIPL-rTMS had a “typical” RT close to the individual mean (mean RT – 0–1 SD). Bars display mean percentage of trials with an error in a given RT bin. Error bars represent standard error of the mean (SEM). *: $p < 0.05$.

Table 3
Response times (RTs) for errors during action judgments on low sound–low action words.

RT bin	Sham (SEM)	pIPL-rTMS (SEM)	Difference (SEM)	t	p
Typical RT					
mean RT – 0–1	3.40	6.66 (1.47)	3.26 (1.21)	2.628	0.01
SD	(1.01)				
mean RT + 0–1	2.22	3.55 (0.81)	1.33 (0.69)	1.887	0.07
SD	(0.70)				
Fast RT					
< mean RT – 3	0 (0)	0 (0)	0 (0)	0	1
SD					
mean RT – 2–3	0 (0)	0 (0)	0 (0)	0	1
SD					
mean RT – 1–2	1.48	0.89 (0.43)	–0.59 (0.54)	–1.072	0.29
SD	(0.59)				
Slow RT					
mean RT + 1–2	1.48	2.51 (0.63)	1.03 (0.68)	1.494	0.15
SD	(0.52)				
mean RT + 2–3	1.18	2.22 (0.56)	1.04 (0.71)	1.428	0.17
SD	(0.41)				
> mean RT + 3	0.44	0.30 (0.20)	–0.14 (0.25)	–0.570	0.57
SD	(0.24)				
No response	0 (0)	0.15 (0.15)	0.15 (0.15)	1.0	0.33

or brain lesions). In contrast, low-sound words cannot employ action–sound coupling and are therefore vulnerable to disruptions of action feature representations.

In contrast to our hypotheses, pIPL-rTMS did not affect sound judgments. Note that this inference is based not merely on a non-significant result, but Bayesian statistics provided evidence for a null effect of pIPL-rTMS. This finding conflicts with our previous fMRI study that found task-dependent activation of left pIPL for both action and sound knowledge (Kuhnke et al., 2020). It also challenges the view that left pIPL represents a multimodal conceptual region (Binder and Desai, 2011; Fernandino et al., 2016). Indeed, one possible reason for the lacking disruption of sound judgments is that left pIPL is not causally relevant for processing sound knowledge. Sound-related activation in fMRI might be incidental to behavioral performance (Price and Friston, 2002). Alternatively, it is possible that left pIPL is functionally relevant for sound feature retrieval, but rTMS did not disrupt sound feature processing strongly enough to cause an observable behavioral impairment as it was stabilized by other sound-related regions. In line with this view, electrical field simulations indicated that pIPL-rTMS did not strongly affect other sound-related regions: Auditory areas (TE 1.0, 1.1, 1.2, 3), as well as prefrontal areas associated with sound-related conceptual processing (Fernandino et al., 2016; Kuhnke et al., 2020) were all stimulated at relatively low intensities (see Fig. 3; Table 2). Intact functioning of these regions may have compensated for the disruption of a single critical node. Such compensatory mechanisms could be further investigated in future studies employing combined TMS-fMRI (Hartwigsen, 2018).

In contrast, pIPL-rTMS might have affected nearby action-related regions, leading to a strong disruption of the action network as a whole. Electrical field simulations showed that pIPL-rTMS induced relatively high stimulation intensities not only in left pIPL itself, but also in surrounding areas such as left aIPL/IPS, SPL, and somatosensory cortex. All of these regions have previously been associated with action-related conceptual processing (Fernandino et al., 2016; Kuhnke et al., 2020). Thus, stimulation of surrounding action-related areas may have contributed to the observed behavioral impairment of action judgments. However, the electrical field strength within left pIPL (Fig. 3D), but not left SPL (Figure S6), correlated with the individual behavioral impairment on action judgments. This strongly suggests that left pIPL itself is crucial for action knowledge retrieval, and not only surrounding areas.

Note that we used a state-of-the-art computational pipeline for head reconstruction (Nielsen et al., 2018) and electrical field modeling (Saturnino et al., 2019; Thielscher et al., 2015). While electrical field modeling may include inaccuracies, it seems highly unlikely that they drove the correlation between electrical field strength and behavioral performance. Modeling errors are random and not systematically related to behavior. Moreover, the correlation was both task-specific to action (but not sound) judgments, and anatomically specific to left pIPL (and not SPL). Finally, we averaged electrical field strength over a large cortical area, which greatly reduces the influence of small errors. Therefore, we are confident that our results indicate that stronger stimulation of left pIPL is associated with worse performance for action knowledge.

Left IPL has previously been implicated in action knowledge retrieval. Meta-analyses of functional neuroimaging studies show consistent engagement of left IPL during action-related conceptual processing on words or pictures (Binder et al., 2009; Watson et al., 2013). However, as neuroimaging is correlational, these studies do not provide evidence for a behavioral relevance of left IPL for processing action knowledge. Two previous TMS studies provided evidence for a causal role of left IPL in action knowledge retrieval (Ishibashi et al., 2011; Pobric et al., 2010). In these studies, offline rTMS over left IPL impaired picture naming of manipulable but not non-manipulable objects (Pobric et al., 2010), and slowed matching of tool names by manipulation but not by function (Ishibashi et al., 2011). However, Pobric et al. exclusively varied the relevance of action knowledge for the concept, but not for the task, and vice versa in the study by Ishibashi et al. Therefore, neither study could assess potential interactions between task and feature relevance. Moreover, both studies only manipulated the relevance of action knowledge and no other modalities (e.g. sound). Thus, it remained unclear whether left IPL was indeed action-specific, or rather multimodal (i.e. sensitive to the relevance of multiple different conceptual features). Finally, in contrast to online rTMS, offline rTMS can lead to large-scale functional reorganization (Hartwigsen, 2018; Hartwigsen et al., 2017; Jung and Lambon Ralph, 2016). This renders it ambiguous whether the behavioral effects were indeed related to the stimulated area or other, distant nodes. To avoid these limitations, we applied online rTMS over left pIPL, while participants performed three different tasks on words that systematically varied in their association with both actions and sounds. We substantially extend the previous findings by showing that pIPL-rTMS interacts with task, action and sound knowledge: Left pIPL is necessary for conceptual processing selectively when action knowledge is task-relevant and cannot be compensated by sound knowledge via action–sound coupling.

Left IPL is not only implicated in action knowledge retrieval, but also in real motor action. Neuroimaging studies consistently find left IPL activation during action execution, imitation, observation, and imagery (Hardwick et al., 2018; Papitto et al., 2019). Neurons in the homologue region of the macaque monkey (area PF/PFG) code the behavioral intention of an action. For instance, Fogassi et al. (2005) found monkey IPL neurons to respond specifically when the monkey grasps a piece of food to eat it, but not to place it somewhere else, or vice versa. Ideomotor apraxia, a deficit in producing skilled object-directed movements (Culham and Valyear, 2006), is specifically associated with damage in and near left IPL (Buxbaum et al., 2005a, 2005b; Haaland et al., 2000). Ideomotor apraxics are impaired at performing and pantomiming the appropriate movements for object use, while retaining the ability to grasp objects based on their physical properties (Buxbaum et al., 2003). These facts suggest that left IPL represents the motor skills for object-directed actions (Culham and Valyear, 2006; Johnson-Frey, 2004; van Elk et al., 2014).

The common role of left IPL in both real motor action and action-related conceptual processing supports grounded theories of cognition, and conflicts with amodal theories. Amodal theories posit that concepts consist of abstract symbols represented outside perceptual-motor systems (Fodor, 1975; Pylyshyn, 1984). In contrast, grounded theories propose concept retrieval to involve a “simulation”—a partial reinstatement of activity in perceptual-motor brain areas during actual experience

(Barsalou, 2008; Kiefer and Pulvermüller, 2012; Pulvermüller, 1999). For instance, to retrieve action knowledge about guitars, neural activity in motor-related regions during guitar playing is partially reinstated (Sim et al., 2015). Together with previous evidence, our findings suggest that action knowledge retrieval involves a simulation of object-use motor skills in left IPL.

It is important to consider whether the behavioral effects of piPL-rTMS were confounded by stimulation-unrelated factors. Unlike sham stimulation, effective TMS produces a somatosensory stimulus on the scalp that can be unpleasant, and the level of discomfort correlates with behavioral impairments (Holmes and Meteyard, 2018). This raises the concern that any effects of effective TMS could be related to unpleasantness and/or task difficulty. However, this is highly unlikely in the present study. Firstly, rTMS over left piPL produces little to no discomfort (Meteyard and Holmes, 2018). Secondly, piPL-rTMS was highly condition-specific and selectively disrupted action judgments on low sound–low action words. Crucially, this condition was not the most difficult (see Figures S1 and S2). In contrast, the most difficult condition (sound judgments on high sound–low action words) was not affected by piPL-rTMS. Finally, piPL-rTMS even tended to improve performance for action judgments on low sound–high action words. These facts render it highly unlikely that the behavioral effects of piPL-rTMS were related to unpleasantness or task difficulty. Moreover, control analyses showed that our results were not confounded by session order effects or violations of distributional assumptions. Therefore, we are confident that the impairment of action judgments on low sound–low action words was caused by left piPL stimulation, indicating a causal role of left piPL in action knowledge retrieval.

As our study exclusively compared effective rTMS over left piPL with ineffective sham stimulation, it remains unclear whether stimulation of other brain regions leads to similar, different, or no effects. In particular, future TMS studies should target potential sound-specific areas such as left posterior superior/middle temporal gyrus (Kiefer et al., 2008; Trumpp et al., 2013), and other potential multimodal convergence zones like medial prefrontal cortex (Binder, 2016; Fernandino et al., 2016; Kuhnke et al., 2020) to test for selective effects on sound knowledge retrieval or both sound and action knowledge retrieval, respectively. Moreover, “chronometric” TMS studies could systematically manipulate the stimulation timing to determine the precise timepoint(s) when a certain region causally contributes to conceptual tasks (Schuhmann et al., 2012; Stoeckel et al., 2009). For example, a recent chronometric TMS study showed that primary motor cortex is crucially involved in processing literal and metaphoric action sentences after 300 ms (Reilly et al., 2019).

5. Conclusions

In conclusion, our data strongly support a selective causal role of left piPL in the processing of action knowledge. rTMS over left piPL interfered with conceptual processing specifically when action knowledge was task-relevant and could not be compensated by sound knowledge. Electrical field simulations revealed that stronger stimulation of left piPL led to worse performance on action judgments. To our knowledge, this study is the first that directly relates the electrical field induced by TMS to behavior in a cognitive task. We believe our novel approach could benefit future TMS studies of cognition since it provides much stronger evidence for a behavioral relevance of the stimulated cortical area than the classical testing for a group effect of TMS alone.

Declaration of competing interest

The authors declare no competing interests.

CRedit authorship contribution statement

Philipp Kuhnke: Conceptualization, Data curation, Formal analysis,

Investigation, Methodology, Writing - original draft, Writing - review & editing. **Marie C. Beaupain:** Data curation, Investigation. **Vincent K.M. Cheung:** Data curation, Investigation, Formal analysis, Methodology, Writing - review & editing. **Konstantin Weise:** Formal analysis, Methodology, Writing - review & editing. **Markus Kiefer:** Conceptualization, Writing - review & editing. **Gesa Hartwigsen:** Conceptualization, Funding acquisition, Supervision, Project administration, Writing - review & editing.

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Appendix A. Supplementary data

Supplementary data to this article can be found online at <https://doi.org/10.1016/j.neuroimage.2020.117041>.

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Data and code availability

Analysis code, raw and derived data are available via the Open Access Framework: https://osf.io/63vbr/?view_only=778ed65cdd4040f7a15bfb9829bd5517.

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