

The Functional Role of Response Suppression during an Urge to Relieve Pain

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Abstract

■ Being in the state of having both a strong impulse to act and a simultaneous need to withhold is commonly described as an “urge.” Although urges are part of everyday life and also important to several clinical disorders, the components of urge are poorly understood. It has been conjectured that withholding an action during urge involves active response suppression. We tested that idea by designing an urge paradigm that required participants to resist an impulse to press a button and gain relief from heat (one hand was poised to press while the other arm had heat stimulation). We first used paired-pulse TMS over motor cortex (M1) to measure corticospinal excitability of the hand that could press for relief, while participants withheld movement. We observed increased short-interval intracortical inhibition, an index of M1

GABAergic interneuron activity that was maintained across seconds and specific to the task-relevant finger. A second experiment replicated this. We next used EEG to better “image” putative cortical signatures of motor suppression and pain. We found increased sensorimotor beta contralateral to the task-relevant hand while participants withheld the movement during heat. We interpret this as further evidence of a motor suppressive process. Additionally, there was beta desynchronization contralateral to the arm with heat, which could reflect a pain signature. Strikingly, participants who “suppressed” more exhibited less of a putative “pain” response. We speculate that, during urge, a suppressive state may have functional relevance for both resisting a prohibited action and for mitigating discomfort. ■

INTRODUCTION

The concept of “urge” is often used in movement disorders such as Tourette’s syndrome (Leckman, Walker, & Cohen, 1993) and psychiatric disorders such as obsessive compulsive disorder (da Silva Prado et al., 2008), and some have argued that craving is a kind of urge, in the context of substance use disorders (Berke, 2003). Urge is also an interesting state in everyday cognitive control, having connotations of drive, conflict, control, and effort and their interrelation. Yet the components of urge are poorly understood. A target article about urge by Jackson, Parkinson, Kim, Schüermann, and Eickhoff (2011), which was published along with a dozen commentaries, proposed the idea that the urge state can be defined as the experience of two conflicting demands: an impulse to act and a need to refrain from acting. Notable in the commentary was the idea that action-withholding, sometimes at least, involves an active process of response suppression. Support for this comes from fMRI studies in which brain regions implicated in motor stopping and motor control, such as the right inferior frontal gyrus (rIFG) and the pre-SMA, are activated in urge scenarios. For example, Berman, Horovitz, Morel, and Hallett (2012) reported activation of the rIFG during the urge to blink, and Mazzone, Cole, Ando, Egan, and Farrell (2011) found that greater activation of the pre-SMA and rIFG corresponded to a heightened urge to cough and

also see (Lynn, Demanet, Krebs, Van Dessel, & Brass, 2016; He et al., 2014; Lerner et al., 2008; Mazzone, McLennan, McGovern, Egan, & Farrell, 2007; Kuhtz-Buschbeck et al., 2005; Banzett et al., 2000; Hsieh et al., 1994). However, these same brain areas are activated by many diverse task demands and are thus not selective to response suppression. It is therefore difficult to know if increased activation of these areas during the withholding of blinking, for example, reflects a top-down suppression of blinking muscles or instead increased effort, arousal, difficulty, discomfort, or something else. We reasoned that a strong test of a response suppression process during urge requires more specific measurements with appropriate control conditions.

Here, we designed a new task (a heat pain paradigm) to generate an urge. In the Heat condition, each trial began with a quick ramping of temperature via a thermode on the left arm, whereas the right index finger was positioned near a button. The participant had to wait a variable number of seconds before the word “Press” was presented on a screen; then, they could press to get quick relief (the thermode temperature plummeted). The participant understood that pressing early would incur a large financial penalty.

In Experiments 1 and 2, we used paired-pulse TMS to measure short-interval intracortical inhibition (SICI) of M1 contralateral to the finger that was “waiting” to press. SICI is thought to reflect the activity of GABA-A-mediated inhibitory interneurons in M1 (Rothwell, Day, Thompson,

& Kujirai, 2009; Di Lazzaro et al., 1998, 2000, 2005; Chen, 2004; Kujirai et al., 1993). Although SICI is often used to capture phasic changes in GABAergic inhibition (e.g., during preparation for a movement), it appears that it can also measure more tonic effects (discussed in more detail below; Albers, Walton, Gamble, McNeill, & Hummer, 2017; Beck et al., 2008; Ortu, Deriu, Suppa, Tolu, & Rothwell, 2008; Di Lazzaro et al., 2002; Ziemann, Lönnecker, & Paulus, 1995). We predicted that SICI would be increased for the task-relevant finger, but not a task-irrelevant finger, and that this increased SICI state would be maintained for several seconds.

In Experiment 3, we used scalp EEG to measure the power of beta oscillations in sensorimotor cortex. An influential hypothesis is that above-baseline increases in beta power oscillations reflect an akinetic or suppressed state, reviewed by Kilavik, Zaepffel, Brovelli, MacKay, and Riehle (2013) and Engel and Fries (2010). Accordingly, we predicted an increase in sensorimotor beta contralateral to the hand that could press for relief (i.e., the right hand). We were also interested in a putative signature of heat pain—a below-baseline reduction in beta power from the arm contralateral to the heat thermode (i.e., the left arm; Misra, Ofori, Chung, & Coombes, 2016; Misra, Wang, Archer, Roy, & Coombes, 2016). If we detected both of these effects, we were interested in testing how they might be related—could more motor suppression correspond to less “heat pain?”

Alternative outcomes to these studies were that we would not detect increases in SICI nor increases in sensorimotor beta power contralateral to the hand that could press. Such results would suggest that, in this paradigm, there is no active process of response suppression, and instead, people simply postpone action using a strategy such as mental distraction.

EXPERIMENT 1

We used paired-pulse TMS over primary motor cortex (M1) during the heat paradigm. The TMS coil was placed over the left M1 corresponding to a spot that could measure corticospinal excitability of both index and pinky fingers of the right hand (the right index finger was poised to press, the pinky served as a control). We delivered single and paired pulses in an alternating fashion. The paired-pulse technique was used to calculate SICI in both the task-relevant index finger and the pinky control finger. As mentioned above, SICI provides an index of GABA-A inhibitory interneuron activation in M1 at the time of stimulation. Although many researchers use SICI to capture phasic changes in GABAergic inhibition (e.g., during preparation for a movement), there are several demonstrations that SICI can be modulated for an extended period of time and that it may even relate to tonic GABA-A receptors. For example, studies of tonic muscle contraction have shown reduced SICI across several seconds of contraction (Beck et al., 2008; Ortu et al.,

2008); other studies have shown that tonic GABA-A receptors are sensitive to ethanol (Albers et al., 2017); yet others have shown that SICI is affected by ethanol (Ziemann et al., 1995)—providing pharmacological evidence that SICI can also relate to tonic GABA-A receptors. Finally, a repetitive TMS study over M1 reported modulation of SICI lasting 1–10 min poststimulation (Di Lazzaro et al., 2002). Thus, because SICI can be modulated across several seconds, we anticipated it would be a good probe for our hypothesis. Furthermore, because several studies have specifically reported increases in SICI in relation to stopping an action (Coxon, Stinear, & Byblow, 2006; Sohn, Wiltz, & Hallett, 2002), we reasoned that if a motor suppressive mechanism is engaged as participants resist the impulse to press, SICI would increase in the task-relevant index finger. We also aimed to examine the “drive” to perform the action. Previous work in motor control suggests that corticospinal excitability (“drive”) and GABAergic inhibitory mechanisms (“control”) may represent two distinct processes that can be measured independently with single-pulse and paired-pulse TMS, respectively (Floeter & Rothwell, 1999). Consequently, in addition to assessing changes in SICI, we aimed to use single-pulse TMS data to independently measure the “drive” to press.

Before data collection, we outlined the methods and study plan described below in a preregistered report (uploaded March 11, 2017).¹

Method

Participants

Twenty-five participants were recruited. Two were excluded due to an operating error with the heat machine, five were excluded due to an insufficient number of motor evoked potentials (MEPs; i.e., <10 MEPs per condition), and one participant withdrew. The remaining 17 participants (11 women, right-handed, mean age = 20 years, *SD* = 2.32 years) were included in the analysis. Each participant provided written informed consent (UCSD IRB 071912) and completed a TMS safety questionnaire (Rossi, Hallett, Rossini, & Pascual-Leone, 2009). Participants were compensated \$15/hr with an opportunity to earn an additional \$15 according to task performance.

Apparatus

We applied heat to the participant’s left arm using a thermode attached to the TSA-II Medoc system (TSA II Medoc). We set the temperature of the thermode according to each participant’s reported heat threshold; a temperature rated as highly uncomfortable yet not intolerable. This was based on the “method of limits” that is common in pain research (Lerman et al., 2016; Yarnitsky & Sprecher, 1994). First, we conducted three trials in which the temperature of the thermode continuously increased until the participant pressed a button to

indicate that they could no longer tolerate the temperature. Participants experienced the average temperature (calculated from those three trials) for 10 sec. They then rated the severity on a scale from 1 to 5 (1 = *not painful at all* and 5 = *absolutely unbearable*). We adjusted the temperature until the participant rated the severity as a 4.

The study was conducted using an Apple Computer iMac with a 21.5-in. monitor and a standard small keypad. We presented task stimuli using custom MATLAB code (The MathWorks) and Psychtoolbox Version 3 (Brainard, 1997).

We performed paired-pulse TMS using two MagStim 200² units connected with a Bistim module (Magstim) and a figure-of-eight coil (70-mm diameter). The bistim configuration allowed us to perform paired-pulse TMS by using one unit to deliver the initial pulse and the second unit to deliver a subsequent pulse only 2 msec later (see TMS Methodology section below for more detail).

Task Design

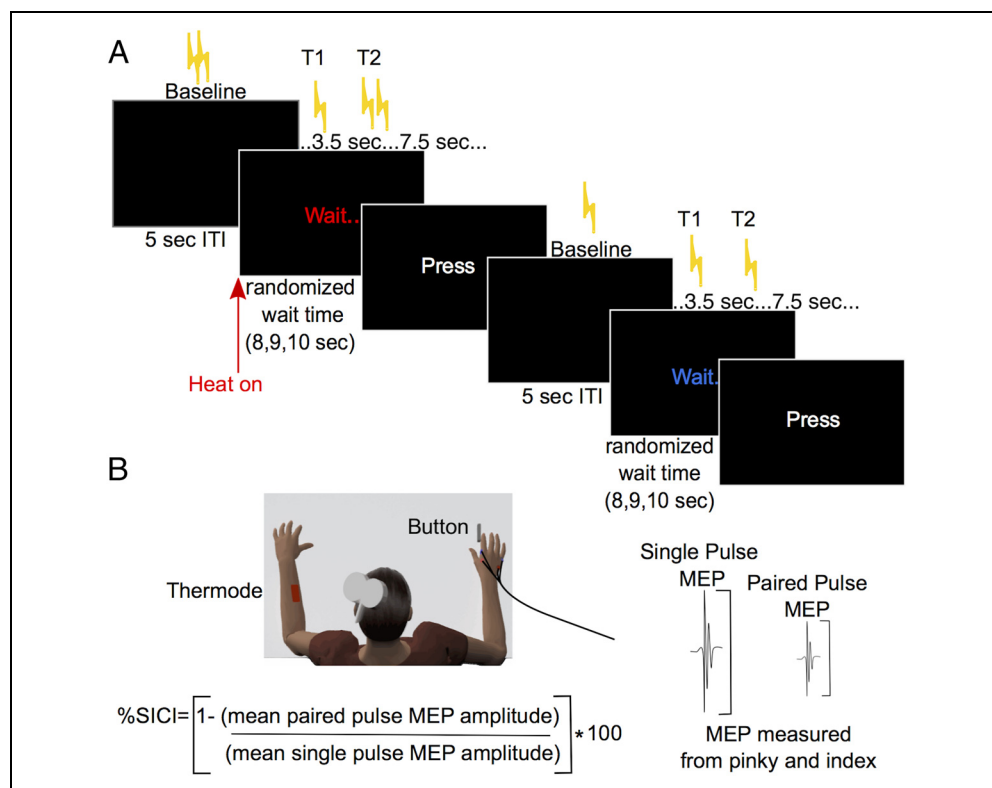
The task included both Heat and No Heat trials presented in alternating order (Figure 1A). On Heat trials, the word “Wait” appeared on the screen, and the

temperature of the thermode immediately increased to the participant’s predetermined heat threshold. “Wait” remained on the screen for 8, 9, or 10 sec. This randomization was meant to obviate the fact that motor suppression can also occur during preparation for a movement when the timing is predictable (Bestmann & Duque, 2016). For each trial, after the wait time elapsed, the word “Press” was displayed, indicating that the participant could press the button to turn off the heat. After each heat stimulus, participants were probed with one of two questions, either (1) how strongly they had wanted to press the button or (2) the severity of their recent discomfort. This rating scale was presented as a line with “Weak” on the left side and “Strong” on the right. Participants verbally reported where their response fell on the line. Both rating questions were presented in a pseudorandomized order. No Heat trials had the same design, except that during the Wait period there was no application of heat and there was no subsequent rating question. “Wait” was written in red for Heat trials and in blue for No Heat trials. All trials were followed by a 5-sec intertrial interval during which the participants were reminded to relax their hand.

To induce an urge state with both a drive to act (i.e., to relieve heat) and an incentive to withhold, participants were informed that pressing early would result in a \$15

Figure 1. Task design

Experiment 1. (A) Each trial began with a brief baseline period. On Heat trials, the word “Wait” appeared, and the temperature of the thermode increased to the participant’s pain threshold. The participant had to wait a number of seconds (8, 9, or 10) until they saw “Press,” meaning they could safely press the button to turn off the heat. There was a severe penalty (lose \$15 and start over) for pressing early. The No Heat trials had the same design, but there was no heat during the wait period. The task alternated between Heat and No Heat trials. Paired- and single-pulse data were collected at three times during Heat trials (baseline: before heat; T1: 3.5 sec into Wait; T2: 7.5 sec into Wait) to calculate changes in SICI across the time of urge. Only single-pulse data were collected from the three times in No Heat trials. (B) MEPs were collected from the task-relevant index finger that could press for relief and the pinky, serving as a control. We used a formula to calculate SICI, our index of motor suppression. SICI reflects the level of activation of GABAergic interneurons in M1 at the time of stimulation, and a greater percentage of SICI indicates higher inhibition.



penalty and restarting the entire task. The full task included three blocks with 36 trials per block, resulting in a total of 108 trials (54 Heat and 54 No Heat).

TMS Pulse Times

TMS pulses were delivered at three time points during each trial: baseline (before the “Wait” stimulus), T1 (3.5 sec into the wait period), and T2 (7.5 sec into the wait period). The single- and paired-pulse arrangement is described below. Additionally, for No Heat trials, the third pulse “toggled” between the original T2 time (7.5 sec into the wait period) and 200 msec after the “Press” stimulus appeared on the screen (T2Late). T2Late was included as an internal validation of our TMS procedures. Specifically, because response time to press was expected to be approximately 400–500 msec, the behavioral response should be preceded by a ramping of corticospinal excitability in the 200 msec before response (post “Press” instruction; e.g., Jahfari, Stinear, Claffey, Verbruggen, & Aron, 2010). T2Late was designed to capture this pre-movement ramping and to serve as validation of the TMS methods.

Measuring SICI

Calculating SICI for Heat trials required MEP data from both paired- and single-pulse TMS. Paired-pulse trials involved an initial subthreshold pulse that was delivered at an intensity too weak to produce an observable MEP itself but instead designed to target lower threshold GABAergic inhibitory interneurons. We delivered a second suprathreshold pulse (the conditioned pulse or “C” pulse) 2 msec later at an intensity that would produce an MEP. The amplitude of the MEP from the second pulse is expected to be affected by the initial subthreshold pulse and to vary according to the inhibitory state of M1. For instance, a smaller amplitude would reflect a higher level of inhibition (Rothwell et al., 2009). Single-pulse trials only included a single suprathreshold TMS pulse (the nonconditioned or “NC” pulse) that would produce an MEP and provide a measure of net corticospinal activity. We calculated SICI as a percentage with data from both single- and paired-pulse trials: $SICI (\%) = [1 - C / NC] \times 100$, where C is the conditioned pulse or the mean MEP amplitude elicited from paired-pulse trials and NC is the nonconditioned pulse or the mean MEP amplitude produced by single-pulse trials (Coxon et al., 2006; see Figure 1B). A larger percentage of SICI indicates a higher level of inhibition. To acquire paired- and single-pulse data for each of the three time points during Heat trials, the pulse type was alternated, such that single- and paired-pulse TMS was delivered an equal number of times for baseline, T1, and T2. Note that SICI was only measured on Heat trials. No Heat trials only included single-pulse TMS. MEP data were collected for 27 single pulses and 27 paired pulses at each of the three

pulse times (baseline, T1, and T2) in Heat trials. For No Heat trials, MEP data were collected for 54 single pulses for baseline and T1, 27 single pulses for T2, and 27 single pulses for T2Late.

TMS Methodology

EMG recording. We recorded EMG for two fingers of the same hand: the first dorsal interosseous (FDI) of the right index finger (the task-relevant finger) and the abductor digiti minimi (ADM) of the right pinky finger (the control finger). We also recorded the root mean square (RMS) of the EMG trace 200 msec before each pulse time (baseline, T1, T2, and T2Late) to check that the muscle was appropriately at rest preceding each pulse.

Determining the locus of stimulation. We conducted a hotspotting procedure to determine the locus for stimulation, that is, the part of M1 that evokes MEPs corresponding to the right index and pinky fingers. We placed the coil 5 cm lateral and 2 cm anterior to the vertex and adjusted the position to identify the optimal location that produced the largest and most consistent MEPs.

Single-pulse TMS (NC). We determined the participant’s resting motor threshold defined as the minimum intensity required to evoke MEPs with amplitudes approximately 0.05 mV peak-to-peak in 5 of 10 consecutive pulses (Rossini et al., 1994). We then increased the stimulator intensity until approximately 5 of 10 consecutive pulses produced an MEP of 1 mV amplitude (peak to peak). The first Magstim unit was set to this intensity and was used to deliver single pulses (NC) in addition to the second pulse on all paired-pulse trials.

Paired-pulse TMS (C). Participants tensed their right FDI muscle by pinching together their right pinky and thumb. We then gradually decreased the pulse intensity (from resting motor threshold) to determine the participant’s active motor threshold (AMT). AMT was defined as the minimum intensity required to elicit barely discernable MEPs against the background EMG in 5 of 10 consecutive pulses. We set the intensity of the conditioning pulse to 80% of the participant’s AMT on the second Magstim unit. We used a 2-msec ISI between pulses for paired-pulse trials.

Data Processing

We used in-house MATLAB software to identify MEPs and exclude trials if the RMS of the EMG trace (200 msec before the pulse) exceeded 0.01 mV (i.e., the hand was not entirely at rest before the pulse). Additionally, we excluded MEP amplitudes below 0.05 mV on single-pulse

trials. The 0.05-mV exclusion criterion was not applied to paired-pulse trials as there could be 100% or close to 100% motor suppression on these trials. MEP amplitudes 2 mV or larger (outside amplifier resolution) were also excluded for all trials except for No Heat trials when the pulse was delivered at T2Late. Because T2Late was designed to capture the ramping of MEP amplitude before a button press, MEPs reaching the ceiling measure (2 mV) still served as a valid indication of ramping. We manually reviewed each 2 mV trial included in the analysis to ensure that the MEPs being measured occurred before the EMG burst for the movement itself.

The remaining MEPs (after the above exclusions) were winsorized for each condition separately (i.e., T1 single-pulse heat condition, T1 paired-pulse Heat condition, T2 single-pulse Heat condition, etc.). This was done for individual participants before calculating any group means. To winsorize, the top 10% of data points were replaced with the maximum value before the 90% cutoff, and the bottom 10% of data points were replaced with the minimum value prior to the bottom 10% cutoff. We then calculated the mean single-pulse MEP amplitude for each time point in the No Heat condition. We also calculated the mean MEP amplitude for each time point according to pulse type (single or paired) for the Heat condition. SICI was then computed for each muscle (FDI, ADM) at all three times (baseline, T1, and T2) in the Heat condition.

Preregistered Hypotheses

- Participants will actively suppress the right index finger while trying to withhold the pressing response during heat. Specifically, we expected increased SICI at T1 and T2 compared with baseline. Second, we predicted that SICI would increase across time (i.e., $T2 > T1$) as the urge to press grew.
- In the context of urge, we aimed to test whether single- and paired-pulse MEPs represent two distinct processes, corticospinal excitability (“drive”) and intrinsic-to-M1-GABAergic “control,” respectively (Floeter & Rothwell, 1999). We predicted larger single-pulse MEPs at T2 versus T1 reflecting a growing drive to press as the time of withholding persisted. We warranted, however, that single-pulse MEP is often used as a net measurement and could reflect a compound of increasing corticospinal excitability plus increasing GABAergic control during urge, in which case there might be no detectable change.
- The expected increases in both SICI (our measure of motor suppression) and single-pulse MEP amplitude (our measure of drive) will be specific to the finger relevant to the alleviating action, the right index finger: that is, there will be a difference compared with the pinky.
- On No Heat trials, there will be no drive or impulse to press and thus no change in single-pulse MEP amplitudes across the Wait period.
- As validation of our TMS measurement fidelity, we expected a strong increase in single-pulse MEP amplitude at T2Late (immediately before pressing) in the No Heat condition.
- The level of SICI late during the withholding period of urge (T2) will be positively correlated with the rating of desire to press or the severity of discomfort.

Results

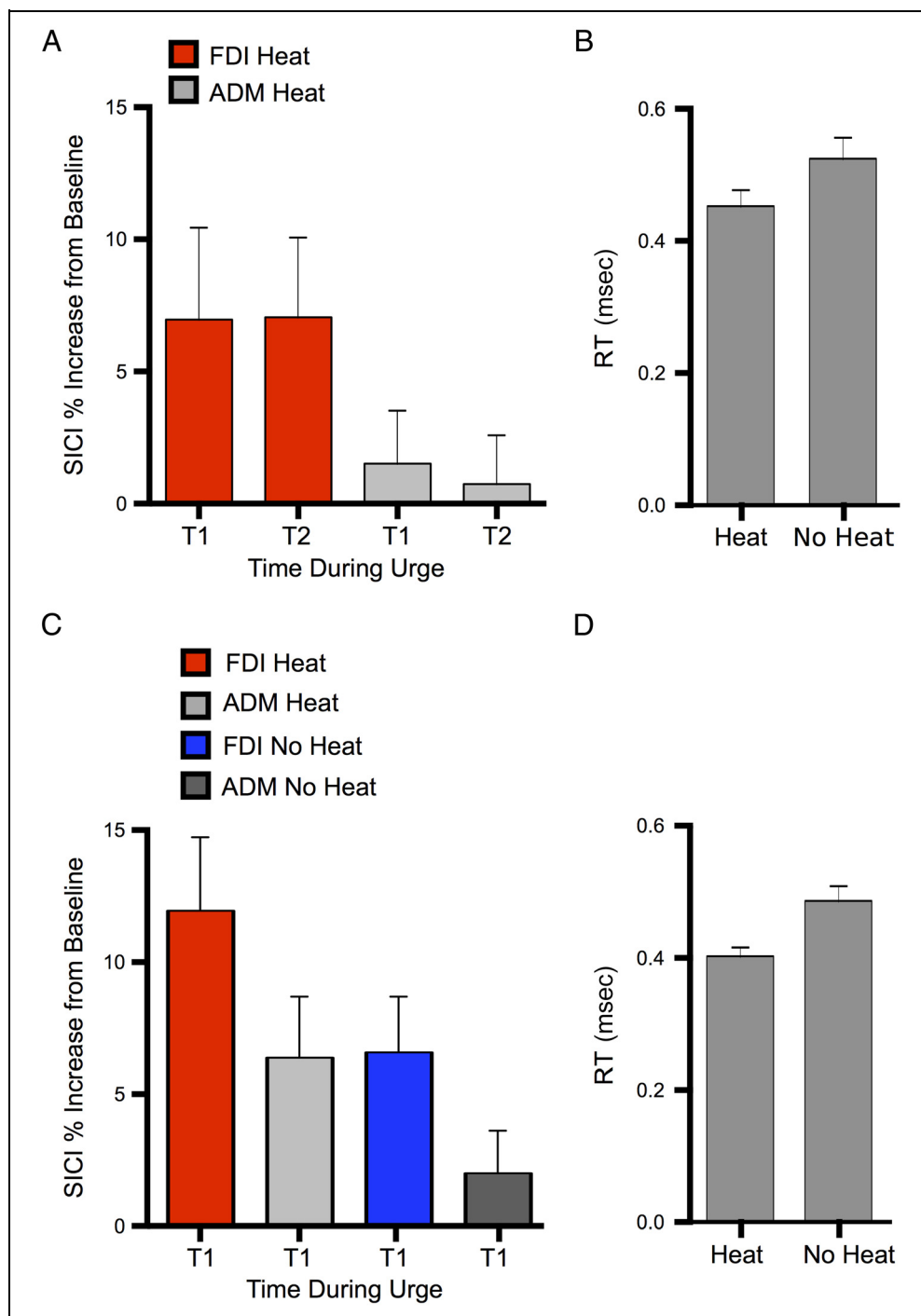
Motor Suppression

To test for motor suppression specific to the task-relevant finger during urge, percent SICI was analyzed using a 2×3 repeated-measures ANOVA with Finger (FDI, ADM) and Time (baseline, T1, and T2) as the factors. There was a significant interaction between Finger and Time, $F(2, 32) = 3.39$, $p = .046$. Subsequent tests were done to examine the change in SICI in FDI across the time of urge, with a Bonferroni-adjusted alpha level of .017 (.05/3). Because our preregistered document specifically predicted increased SICI during the withholding period of urge, these tests were conducted as one-tailed t tests. There was an increase in SICI at T1 compared with baseline, not significant with correction, $t(16) = 2.02$, $p = .030$, and significantly greater SICI at T2 compared with baseline, $t(16) = 2.35$, $p = .016$, $d = .570$. There was no significant difference between T1 and T2, $t(16) < 1$. As indicated by the interaction, these effects were specific to FDI (Figure 2A). This shows that there was an increase in motor suppression that was sustained across multiple seconds of urge and was specific to FDI, the task-relevant muscle. Note that raw MEPs for all conditions are shown in Supplementary Figure 1.²

Drive to Relieve the Heat Pain

To examine changes in the drive to act during urge, we used a repeated-measures ANOVA with Finger (FDI, ADM) and Time (baseline, T1, and T2) as factors and single-pulse MEP amplitude in the Heat condition as the dependent measure. There was an interaction between Time and Finger, $F(2, 32) = 3.36$, $p = .047$, and a main effect of Finger, $F(1, 16) = 5.07$, $p = .039$. To test whether single-pulse MEP amplitude in FDI increased across time of urge, further tests were conducted (Bonferroni-adjusted alpha of .017 per test [.05/3]). There was no difference between single-pulse MEP amplitude in FDI at T1 versus baseline, $t(16) = 0.64$, $p = .267$. Similarly, there was no difference between T2 and baseline, $t(16) = 0.83$, $p = .209$, or T1 and T2, $t(16) = 1.41$, $p = .089$. To summarize, the main effect indicates that there was a heightened MEP amplitude in FDI compared with ADM during the urge to press. However,

Figure 2. Results from TMS Experiments 1 and 2. (A) In Experiment 1, there was an increase in SICI at T1 (3.5 sec into the wait period) compared with baseline and at T2 (7.5 sec into the wait period) compared with baseline. This increase in suppression during the withholding period of urge was specific to the task-relevant index finger. (B) Experiment 1 showed quicker response times for Heat compared with No Heat trials. (C) Experiment 2 replicated the core finding from Experiment 1 showing an increase in SICI at T1 compared with baseline. This again was specific to the task-relevant index finger in Heat. Suppression at T1 was also observed in the No Heat condition. (D) Experiment 2 also showed quicker response times for Heat compared with No Heat trials.



there was no indication that the amplitude in FDI was significantly greater during the withholding period of urge compared with baseline.

RMS and Validation of TMS Procedures

Analysis of the RMS EMG for 200 msec before each TMS pulse revealed no main effects or interactions of Time and Finger, indicating that the results reported above were not confounded by differences in the pre-TMS period (all $ps > .439$).

To further validate our TMS procedure, the No Heat condition included T2Late, when the pulse was delivered 200 msec after the Press stimulus and immediately before the button press movement. A repeated-measures ANOVA with Finger (FDI, ADM) and Time (baseline, T1, T2, and T2Late) as the factors was used to compare mean MEP amplitudes of single-pulse TMS at each time point in the No Heat condition. The results indicated a main effect of Finger, $F(1, 16) = 8.96, p = .009$, and a main effect of Time, $F(3, 48) = 15.78, p < .001$. Additionally, there

was a Time \times Finger interaction, $F(3, 48) = 38.83$, $p < .001$. Specifically, there was a robust increase in MEP amplitude at T2Late compared with T2, $t(16) = 5.60$, $p < .001$, and this was specific to FDI with no difference between T2Late and T2 in ADM, $t(16) = 0.86$, $p = .405$. This ramping of MEP amplitude before the button press at T2Late validates our TMS methodology.

Correlations

There was no correlation between reported level of discomfort and SICI in FDI at T2, $p = .506$, nor for reported level of desire to press, $p = .447$. To probe the validity of the self-report rating, we also tested the relationship between response time in Heat, an objective proxy for desire to press, and the reported desire to press. There was no significant relationship, $p = .155$.

Response Time

A paired-samples t test demonstrated significantly quicker response times in the Heat compared with No Heat condition, $t(16) = -4.10$, $p < .001$ (Figure 2B).

Discussion

We used paired-pulse TMS to measure changes in intracortical inhibition as participants tried to withhold an impulse to act and gain relief from intense heat. By directly probing the state of M1 during an urge to act, we demonstrated increased SICI, which we interpret as increased cortical motor suppression. This suppression was maintained across multiple seconds of urge and was specific to FDI, the muscle relevant for gaining relief. The specificity to the finger that could press is important, because it rules out the possibility that increases in SICI merely reflect processes such as arousal, catecholamine release, or pain state.

To examine potential changes in the drive to press, we also looked at single-pulse MEPs during heat. Although single-pulse MEP amplitudes were greater in the task-relevant index finger compared with the pinky control, there was no change from baseline and thus no evidence of an increase in amplitude during the urge to press. This finding of no change compared with baseline could be explained on the view that single-pulse MEPs reflect a net measurement of corticospinal excitability (i.e., the combination of drive and control during urge results in no discernable amplitude change). Thus, although the SICI measurement captured suppression as predicted, the single-pulse MEP is more ambiguous.

We did not detect a relationship between reports of discomfort and SICI at T2 nor reports of desire to press (also see Brown et al., 2017). Possibly our method of garnering subjective reports was ineffective. Indeed, reported desire to press did not even relate to response speed. Thus, other kinds of rating scales may be

necessary to capture these relationships. An alternative explanation is that reports of urge may in fact not be linked to the degree to which an individual suppresses. Instead, they may be more closely tied to other components not measured well here (e.g., how strongly one feels compelled to act, fatigue, or how long an individual has endured).

Notwithstanding, the main finding of this study was that, in the Heat condition, SICI was increased above baseline for multiple seconds, and this was specific to the finger that was relevant for pressing for relief. Although the literature on “urge” often assumes an inhibitory process, few have demonstrated it as we do here.

EXPERIMENT 2

We now aimed to replicate and refine the core finding from Experiment 1. Accordingly, we tested a larger sample and slightly modified the study procedures to improve the design and better capture the suppressive process under study.

Method

Participants

Twenty-five new participants were recruited. We removed extreme outliers ($>3 \times$ interquartile range) identified in any of the SICI conditions (i.e., SICI in index at T1, SICI in pinky at T1, etc.) leaving a total of 21 participants for analysis (12 women, right-handed, mean age = 23 years, $SD = 6.42$ years; this same data check was done in Experiment 1, but no participants were identified as extreme outliers). Informed consent and compensation were the same as for Experiment 1.

Procedure Modifications

The procedure was identical to Experiment 1 but for a few minor modifications. First, though Experiment 1 did show a SICI increase from baseline in the Heat condition, we wondered whether participants could have proactively begun to suppress during baseline in anticipation of a Heat trial. In Experiment 2, we thus randomized the presentation of Heat and No Heat trials to remove any expectation of condition type—our thinking was that this might increase the relative difference of SICI between Heat and baseline. Second, because the ratings in Experiment 1 proved ineffective, we removed them. Third, for more thorough comparisons between conditions, SICI was now measured for both Heat and No Heat trials. Fourth, wait times were extended to 9, 10 or 11 sec to better ensure the TMS machines had sufficient time to recharge between pulses (we lost some MEP measurements in Experiment 1 due to insufficient recharge time). Lastly, we included the UPPS Impulsive Behavior Scale as a measure of impulsivity (Whiteside & Lynam, 2001). We planned to examine scores

on the negative urgency subscale, a measure of the propensity to act impulsively when experiencing distress.

Preregistered Hypotheses

1. Based on the core finding from Experiment 1, we predicted that in the Heat urge condition, SICI would be increased at T1 and T2 compared with baseline. Again, we expected the effect to be specific to the task-relevant right index finger.
2. Because the No Heat condition was not expected to produce an urge, we predicted no change in SICI across the time points in No Heat.
3. We supposed that poor inhibitory control and impulsivity may relate to difficulties in withholding during urge. Thus, we expected higher negative urgency scores on the UPPS to relate to lower SICI (less motor suppression).

Results

Motor Suppression

Comparing SICI across conditions requires that RMS EMG is roughly equivalent between conditions. As we show below, this was not the case for T2. Thus, we proceed here by only analyzing the data in baseline and T1 for this experiment. First, to specifically test whether we could replicate the original result from Experiment 1, we did a repeated-measures ANOVA on the Heat condition alone with Finger (FDI, ADM) and Time (baseline, T1) as factors. Again, we found a Finger \times Time interaction, $F(1, 20) = 5.13, p = .035$, and a main effect of Time, $F(1, 20) = 17.01, p < .01$. The interaction replicates the core finding from Experiment 1 and demonstrates that participants were suppressing the task-relevant finger during the urge to act.

Here, we now also compare Heat and No Heat conditions in a $2 \times 2 \times 2$ repeated-measures ANOVA with Finger (FDI, ADM), Time (baseline, T1), and Condition (Heat, No Heat) as factors. There was a main effect of Time, $F(1, 20) = 22.87, p = .000$, and Condition, $F(1, 20) = 6.87, p = .016$, as well as an interaction between Finger and Time, $F(1, 20) = 7.05, p = .015$, and also an interaction between Condition and Time, $F(1, 20) = 4.43, p = .048$, but not a reliable three-way interaction between Finger, Time, and Condition (Figure 2C). Thus, as predicted, SICI was greater in Heat versus No Heat, although this was not specifically the case for the task-relevant finger. Note that raw MEPs for all conditions are shown in Supplementary Figure 1.

Root Mean Square

Analysis of the RMS EMG for 200 msec before each pulse revealed a main effect of Time, $F(2, 40) = 12.16, p = .001$,

a main effect of Condition, $F(1, 20) = 8.61, p = .008$, and a Time \times Condition interaction, $F(2, 40) = 7.86, p = .001$. Follow-up paired-samples t tests showed that, in both FDI and ADM, mean RMS at T2 was greater for Heat compared No Heat: $t(20) = 3.80, p = .001$ and $t(20) = 3.85, p = .001$, respectively. As described above, because this between-condition difference in RMS at T2 could confound the SICI results, we excluded T2 from the analyses.

Impulsivity Scale

One correlation was conducted to examine the relationship between SICI at T1 and negative urgency scores on the UPPS. There was no relationship, $p = .386$.

Response Time

Consistent with Experiment 1, participants had quicker response times in the Heat versus No Heat trials, $t(20) = -5.70, p < .001$ (Figure 2D).

Discussion

We successfully replicated the primary finding from Experiment 1 that, in the Heat condition, there was increased SICI during the wait period versus baseline, more so for index than pinky. We interpret this, again, as evidence of an effector-specific suppressive mechanism engaged during the urge to act. Additionally, consistent with our hypothesis of a Heat versus No Heat difference, there was a greater SICI increase for the Heat condition. However, this was not specific to the task-relevant finger. Our explanation of this is that there might have been some degree of response suppression in the No Heat condition itself (although not as much as in the Heat condition). This may have occurred because the word “Wait” in the No Heat condition may have inherited the withholding requirement via a conditioning process (Verbruggen & Logan, 2009). More specifically, it has been shown that stress impairs the ability to learn to perform an action—presumably via a Pavlovian link between inaction and aversive states (de Berker et al., 2016). In the current task, this Pavlovian effect could have generalized to the No Heat condition. Yet another possibility is that participants actively suppressed to avoid penalty even in No Heat.

Finally, in contrast to our hypothesis, the results did not reveal any relationship between negative urgency, an impulsivity trait measure, and SICI measurements. This suggests that the degree to which a motor suppressive process is engaged during urge may be independent of trait impulsivity. Again, impulsivity may be more closely associated with other aspects of urge and self-control such as how vulnerable individuals are to the occurrence of urges (i.e., some may be more easily triggered or tempted to act than others) or the strength of the impulse to act.

EXPERIMENT 3

We now used scalp EEG to test whether a motor suppressive process is engaged during urge. We aimed to analyze EEG signals contralateral to the hand that could press for relief, and we predicted an increase in beta band power (~ 13 – 30 Hz). This is based on a large literature showing that increases in beta power oscillations reflect an akinetic or suppressed state (reviewed by Kilavik et al., 2013; Engel & Fries, 2010).

The use of EEG also permitted the investigation of an additional element: the neural response to heat pain and how this might relate to motor suppression during urge. As the thermode was over the left arm, we planned to test for a separable “pain” response in right sensorimotor cortex. Based on studies of heat pain with EEG (Misra, Ofori, et al., 2016; Misra, Wang, et al., 2016; Ploner, Gross, Timmermann, Pollok, & Schnitzler, 2005), we expected that heat pain, or at least the sensory processing of heat, would produce a below-baseline reduction in right sensorimotor beta. If we did identify this signature, we planned to test how it related, within participants, to the putative motor suppressive process in the opposite hemisphere.

Method

Participants

Thirty-two participants were recruited. We had to exclude eight participants (leaving 26 for analysis) because heat pain led to substantially increased artifacts in the EEG data compared with a typical study. The excluded participants had lost more than 25% of the task events due to muscle artifact contamination. All participants were right-handed and recruited from the University of California, San Diego (mean age = 19 years, $SD = 1.3$ years, 18 women). Informed consent and compensation were the same as the above experiments.

Urge Task Modifications

We made minor modifications to the task of Experiments 1 and 2 (Figure 3 task design). First, to eliminate any potential behavioral effects caused by the visual instruction “Wait,” the initiation of each wait period was instead indicated by a cue shape (see below) that appeared in the center of the screen. Second, there were now three task conditions: Heat (as before), No Heat Risk (where pressing early would also deliver a \$15 penalty), and Safe (pressing early had no penalty). Lastly, the required wait times were reduced to 3, 4, or 5 sec (mainly to save time in the overall experiment). In more detail: On Heat trials, a red square appeared on the screen and the temperature of the thermode immediately increased to the participant’s predetermined heat threshold. The red square cue remained on the screen for the randomized wait period (3, 4, or 5 sec), after which the screen displayed “Press,” indicating that the participant could then safely press the button to turn off the heat. Consistent with the previous exper-

iments, participants were informed that pressing too early would result in a \$15 penalty and restarting the entire task. On No Heat Risk trials, an orange triangle appeared on the screen and remained on the screen for the randomized wait period. The participant then saw the word “Press,” indicating it was permissible to press and advance to the next trial. The No Heat Risk condition had the same penalty for pressing too early (lose \$15 and start entirely over), but there was no heat applied to the participant’s arm during the required wait period. On Safe trials, a green circle was displayed on the screen. After the randomized wait period, participants saw the word “Press” and were able to press to advance to the next trial. The Safe condition did not include any heat during the wait period, and there was no penalty for pressing too early. There was also, however, no advantage to pressing early (i.e., pressing early did not advance the task to the next trial any quicker than it would if the participant waited the appropriate time to press). The two control conditions, No Heat Risk and Safe, were included to try to more explicitly test whether a risk of penalty alone was sufficient to invoke a suppressive process. The urge task now consisted of three blocks with a total of 54 trials per condition (Heat, No Heat Risk, and Safe).

EEG Recording

EEG data were recorded with a 64-electrode actiCAP electrode system (Brain Products Co. Ltd.), with electrode placement in the 5% International 10/20 System. The ground was placed at electrode location Fpz. The data were recorded reference free. EEG electrodes were placed bilaterally over mastoids for later use of offline re-referencing. All electrode impedances were reduced to < 10 k Ω before the recording.

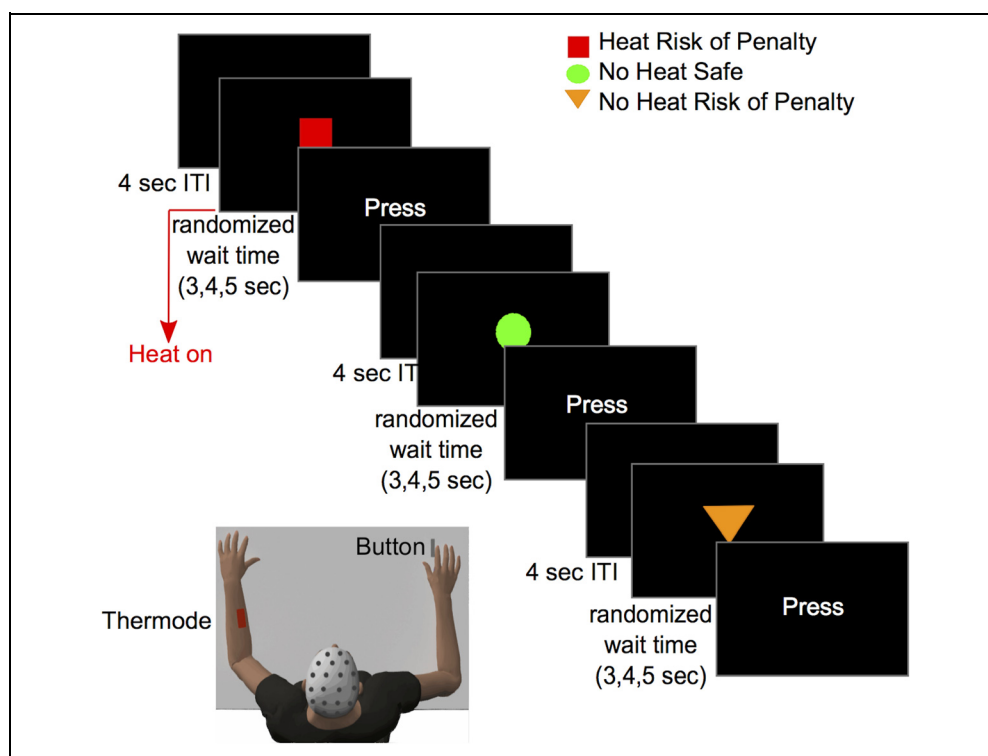
Additional electrodes were placed at each canthus, and one electrode was placed below the right eye to monitor for eye movements and blinking. The EEG and EOG data were sampled at 1000 Hz and recorded using PyCorder (Brain Products).

EEG Preprocessing

EEG analysis was done in EEGLAB 14.1.1b (Delorme & Makeig, 2004) in MATLAB2015b (The MathWorks). The data were low-pass filtered using a MATLAB built-in polyphaser anti-aliasing filter and down-sampled to 500 Hz. The data were then offline re-referenced to an average of the two mastoid electrodes. The data were then high-pass filtered at 2 Hz (FIR order 3300). Additionally, a notch filter at 60 and 180 Hz (FIR order 846) was used to reduce electrical noise caused by the TSA-II Medoc system used for the heat stimulus. EEG channels with substantial artifacts were identified by visual inspection and removed. Next, the data were re-referenced to a common average. Visual inspection was used to manually reject stretches in the continuous data that were contaminated

Figure 3. Task design

Experiment 3 scalp EEG. The task was modified to have three conditions: Heat, No Heat Risk, and Safe. Each trial began with a brief baseline period. Next, on Heat trials, a red square appeared on the screen and the temperature of the thermode was increased to the participant's predetermined heat pain threshold. The participant had to wait a randomized number of seconds (3, 4, or 5) until "Press" appeared and they could safely press the button to turn off the heat. Pressing too early again resulted in a \$15 penalty and restarting the entire task. On No Heat Risk trials, an orange triangle appeared on the screen. After the randomized wait period, the word "Press" appeared indicating it was permissible to press and advance to the next trial. The No Heat Risk condition had the same penalty for pressing early, but there was no heat during the wait period. On Safe trials, a green circle was displayed on the screen. After the randomized wait period, the word "Press" appeared, and the participant could press to advance to the next trial. The Safe condition did not include any heat during the wait period, and there was no penalty for pressing too early. 64-channel scalp EEG was recorded during the task.



by substantial artifact. Participants with fewer than 75% of the study events after visual inspection were excluded from analysis. After preprocessing, we applied independent component analysis (ICA) decomposition to the data (Makeig, Bell, Jung, & Sejnowski, 1996). ICA was used to remove artifact components (e.g., blinks, muscle tension) and to select components relevant to the research questions of interest (see below).

Independent Component Analysis

We used ICA and a clustering algorithm to select the clusters of interest: a left sensorimotor cluster (to test for motor suppression of right hand) and before a right sensorimotor cluster (to test for a pain signature contralateral to the heat on the left arm). We now explain the ICA analysis steps.

Running ICA. Continuous EEG data (with all three conditions: Heat, No Heat Risk, and Safe trials) were submitted to extended Infomax ICA for each participant, providing the same number of independent components (ICs) as channels (Makeig et al., 1996; Bell & Sejnowski, 1995).

Artifact rejection. Non-brain components were rejected according to visual inspection of scalp maps, power spectra, and IC time courses. We also computed

a best fitting single ECD matched to the scalp projection of each IC source (Delorme, Palmer, Onton, Oostenveld, & Makeig, 2012; Oostenveld & Oostendorp, 2002), using a standardized three-shell boundary element head model implemented in the DIPFIT toolbox in EEGLAB. We removed ICs whose equivalent dipole model explained less than 85% of variance of the IC scalp map.

Clustering. The above steps result in a variable number of ICs per participant. The challenge is then to group common ICs across participants, specifically a left sensorimotor cluster for the right hand and a right sensorimotor cluster for the left arm. Although this clustering can be done by eye, a more objective method is to use an algorithm. Our clustering method was based on the assumption that the same left sensorimotor cluster related to the execution of the button press would also relate to the withholding of the button press. We focused on Safe trials only, time-locked to the button press for which there would be an event-related desynchronization (Miller et al., 2007; Pfurtscheller & Lopes Da Silva, 1999; Crone et al., 1998; Pfurtscheller & Aranibar, 1977; Pfurtscheller, Neuper, Andrew, & Edlinger, 1997; Jasper & Penfield, 1949).

a. Creating feature vectors. Having extracted the event-related desynchronization time-locked to the button press on Safe trials, we then used that information from each IC to derive feature vectors: (a) IC dipole location,

- (b) scalp projection, (c) power spectra in the range of 3–200 Hz, (d) event-related spectral perturbations (ERSPs; 3–20 Hz, 0–1000 msec; Makeig et al., 2002).
- b. Preclustering dimensionality reduction. Before clustering, we reduced the dimensionality of the features as follows. First, we selected the relevant parts of each feature. For example, for the power spectra, we selected the average spectra over trials in the range of 3–200 Hz, which resulted in approximately 197 data points (given one bin at each frequency). We then reduced these 197 points to 10 dimensions using PCA. PCA finds orthogonal subspaces that explain maximal variance of the data, with the first principal component explaining the largest part of the variance of the data. We applied the same procedure to the ERSP and scalp maps. Dipoles inherently have only three dimensions (the Tailarach coordinates x, y, z). We thus ended up with four feature vectors, three each with 10 dimensions and one with three dimensions (related to dipoles) for each IC.
 - c. Weighting of feature vectors. The dimensionally reduced feature vectors were then weighted for subsequent clustering (dipole locations: weight 12; scalp projection: weight 4; power spectra: weight 3; ERSs: weight 5). These weights were chosen based on our decision to cluster according to movement execution on Safe trials: We expected an event-related mu and beta decrease and subsequent increase (8–30 Hz) relative to the button press, with a scalp distribution over the left motor cortex (hand area)—contralateral to the hand that was pressing and a timing from 0 to 1000 msec after the button press.
 - d. Concatenation and clustering. The four feature vectors were then concatenated for each IC and further reduced to 10 principal components using PCA. We then ran k -means clustering ($k = 16$).
 - e. Outlier cluster. ICs were identified as outliers if their locations in the clustering vector space were 4 SD s from the cluster centers. Clusters were then screened for remaining artifact ICs by visually inspecting single IC spectra and ERSP images for broadband activity from 20 to 100 Hz. It is possible that some ICs contain cortical activity mixed with EMG or that the clustering algorithm did not correctly assign all ICs containing muscle activity to a separate cluster. Those ICs were moved to the outlier cluster.
 - f. Group-level cluster selection. We inspected clusters for typical characteristics of motor activity (1) spatial topography and dipole location over/in motor cortical hand area, (2) event-related spectral power changes showing event-related desynchronization in mu and beta bands before and during movement and event-related synchronization after movement offset. We identified two clusters related to motor activity: a right and a left sensorimotor cluster. Both clusters included ICs from 19 participants. If a cluster contained two or more

components from a single participant, we selected the IC that was closest to the cluster centroid dipole and removed the other additional ICs.

Approach to EEG Hypothesis Testing

Having identified 19 participants with ICs in a left sensorimotor cluster, we next tested our hypothesis about response suppression during Heat. Based on many studies showing that sensorimotor beta increases occur in participant-specific frequency bands, we first had to estimate the appropriate frequency for each participant. We focused on the “postmovement beta rebound” on Safe trials. In so doing, we made the assumption that the beta-rebound reflects an inhibition process in common with that recruited during the withholding period of urge. There is a precedent for this idea, especially the finding that the same frequency band that increased during postmovement beta rebound was also increased during the withholding of foot movements (Solis-Escalante, Müller-Putz, Pfurtscheller, & Neuper, 2012; also see Alegre, Alvarez-Gerriko, Valencia, Iriarte, & Artieda, 2008; Cassim et al., 2001).

We likewise faced the challenge of identifying a right sensorimotor “pain signature” in each participant. Because beta band is also implicated in pain processing (Misra, Ofori, et al., 2016; Misra, Wang, et al., 2016; Ploner et al., 2005; Raij, Forss, Stancák, & Hari, 2004), our approach was to remain consistent and examine the above same participant-specific beta band for the right sensorimotor cluster. We predicted that motor suppression of the right hand would lead to an *increase* in beta band power in left sensorimotor cortex, and we predicted that a pain response over the left arm would lead to a *decrease* in this beta band power over the right sensorimotor cortex. The detailed procedure was as follows:

Determining participant-specific beta frequency. Within each participant’s left sensorimotor component, the data were segmented into epochs [0 3 sec] time locked to the button press on Safe trials. We chose this time window since postmovement beta rebound starts around 0.5 sec—lasting up to 3 sec after movement offset (Neuper & Pfurtscheller, 2001). We then computed power spectral density with Welch’s method (Welch, 1967) in the window [0 3 sec]. Power spectral density was computed by dividing the 3-sec time window into 1-sec segments with 3/4 overlap, 200 points zero-padding and multiplied with a Hamming window, resulting in a frequency resolution of 0.08. The spectrum was then log-transformed. To determine the participant’s peak frequency, we detected the highest local maximum in the 13–30 Hz band. To do this, we first removed the $1/f$ component of the spectrum, as this obscures the peaks in the beta range (13–30 Hz) by strongly biasing lower frequencies. To compensate for the $1/f$ effect, linear regression (least-squares fit) was used

to fit a linear model to the log-transformed spectrum from 3 to 40 Hz excluding mu and beta ranges 7–25 Hz (since high alpha and beta peaks would distort the linear trend). The fitted linear trend was then subtracted from the spectrum, allowing for a more reliable beta peak frequency estimate (cf. Haegens, Cousijn, Wallis, Harrison, & Nobre, 2014; Nikulin & Brismar, 2006). We then selected the local maximum in the 13–30 Hz band. We chose the participant specific band by selecting a band around the identified beta peak frequency (i.e., individual beta frequency peak ± 1.3 Hz; Figure 4A).

Motor suppression (left sensorimotor cortex). In the left sensorimotor cluster, we tested how the above selected beta band changed during the first 3 sec of withholding for each condition. Specifically, data were segmented for the first 3 sec of the wait period with each epoch time-locked to the wait cue in each condition: green circle for Safe, orange triangle for No Heat Risk, and red square for Heat. Relative changes in power were computed using a sliding window approach and wavelets (parameters for wavelets: three cycles at lowest frequency with a linear increase in cycles, with factor 0.5). The values were converted to log power, and a baseline (the average log individual beta band power in the pre-cue period [–1 0 sec]) was subtracted, to obtain event-related power changes. We used a common baseline for all conditions.

Pain signature (right sensorimotor cortex). For consistency and to later compare beta power between the clusters, the same participant-specific band was examined for the right sensorimotor cluster. Again, data were segmented for the first 3 sec, time-locked to the wait cue in each condition. Relative changes in right sensorimotor beta were computed as described above.

Results

Left Sensorimotor Cluster (Motor Suppression)

Figure 4B shows the average event-related beta power in a left sensorimotor cluster over 19 participants (using participant-specific beta). There was an initial beneath-baseline decrease in beta power that we speculate is related to the initial preparation for an impending movement at the start of each trial. It is curious that there would be such preparation, but perhaps it relates to the fact that there was ~4 sec of time between trials, jittered, so the occurrence of the wait cue for each trial was unpredictable. As soon as the wait cue occurred, participants knew that a response was now relevant. After the initial decrease, there was an increase in beta power, evidently greater in the Heat condition. To test this statistically, for each condition and each participant, we calculated the average of late beta power over the time window 1000–2500 msec post shape cue, minus the

average of early beta power (the average over the period with the initial decrease, 0–1000 msec post shape cue). We used a repeated-measures ANOVA to determine whether this change in beta varied between conditions (Heat, No Heat Risk, and Safe). There was a main effect of Condition, $F(2, 36) = 7.38, p = .005$. Subsequent tests were done to examine how the conditions differed, using a Bonferroni-adjusted alpha of .025 (.05/2). Paired t tests revealed a greater increase in beta for Heat compared with No Heat Risk, $t(18) = 2.83, p = .011$, and for Heat compared with Safe, $t(18) = 3.25, p = .004$. To test whether beta power remained consistently higher throughout the late period (1000–2500), a 3×3 ANOVA was run with three conditions (Heat, No Heat Risk, and Safe) and three time periods (1000–1500 msec, 1500–2000 msec, 2000–2500 msec post shape cue). There was a significant main effect of Condition, $F(2, 36) = 5.66, p = .007$. We interpret these results as further evidence that participants are suppressing the task-relevant hand while trying to resist the impulse to press during heat.

Right Sensorimotor Cluster (Pain Response)

Figure 4B shows the average event-related beta power in the right sensorimotor cluster over 19 participants (using participant-specific beta). There was a decrease in beta power across the time that participants had to endure the heat and suppress the impulse to act. Specifically, we compared the average relative beta in the same above “late” time window (i.e., when left beta shows a sustained increase; 1000–2500 msec post shape cue), across conditions. We conducted a one-way repeated-measures ANOVA with Condition as the factor (Heat, No Heat Risk, and Safe) and right sensorimotor beta power as the dependent measure. There was a main effect of Condition, $F(2, 36) = 13.56, p < .001$. Post hoc tests showed reduced beta during Heat compared with No Heat, $t(18) = -4.10, p = .001$, and Heat compared with Safe, $t(18) = -4.42, p < .001$ (Bonferroni-adjusted alpha levels of .025 [.05/2]). Thus, there was a stronger beta desynchronization in the Heat condition during the wait period compared with other conditions—we interpret this as a brain signature of the pain response.

Relationship between Right and Left Sensorimotor Beta

Between-participant robust regression. We now tested for a relationship between the level of motor suppression exerted by a participant and the magnitude of the putative pain response. Our specific index of motor suppression was the average beta power in the left sensorimotor cluster during the late period of withholding (1000–2500 msec postcue). We assumed a greater level of left beta signified more motor suppression. Our specific index of the pain response was the average beta power in the right sensorimotor cluster during the same late window. We assumed that a greater decrease in right

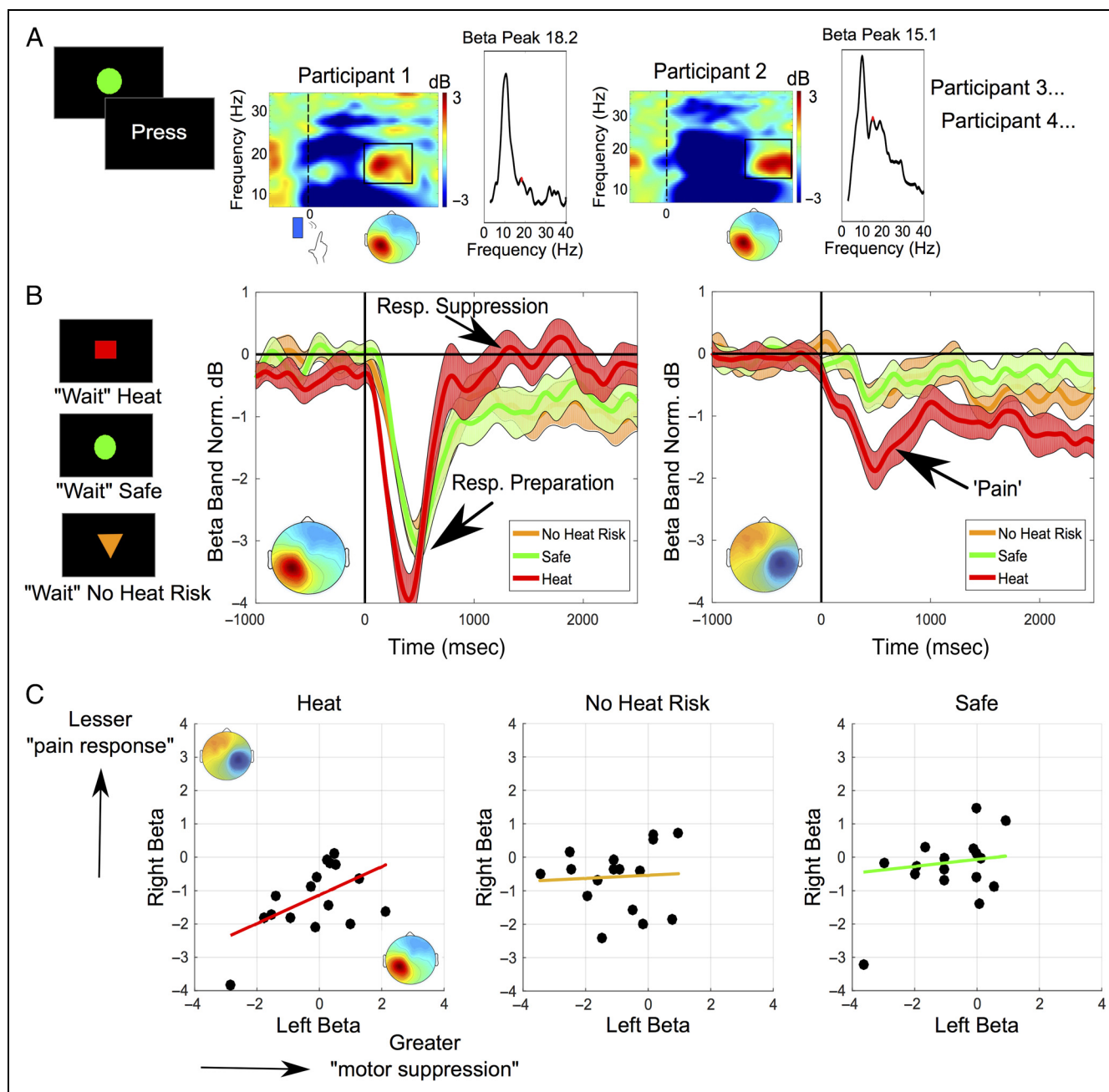


Figure 4. EEG results from Experiment 3. (A) To select a participant-specific beta band, we identified the peak beta band in the postmovement beta rebound (PMBR) of the Safe trials. Here, two participants are illustrated. In each case a left sensorimotor component is found corresponding to the right (task-relevant) hand. The ERS is time-locked to the response on Safe trials and shows typical beneath-baseline reductions followed by PMBR (the power increase in the box). Peak frequency is extracted from this PMBR period for each subject. (B) "Response suppression" and "Pain" correspond to left and right hemispheres, respectively. We time-locked the data to the start of each trial (when the cue shape appeared) for both the left sensorimotor component (task-relevant hand) and the right sensorimotor component (corresponding to the thermode). For the left sensorimotor component, we split the timing into an early phase (0–1000 msec, putatively corresponding to response preparation) and a later phase (1000–2500 msec, putatively corresponding to response suppression). The increase of "response suppression" was greater for Heat compared with the two control conditions. For the right sensorimotor component, there was a larger decrease in beta power for Heat compared with the others—presumably reflecting a "pain" or sensory response to heat. (C) Participants who "suppressed" more demonstrated a lesser "pain" response. A robust regression shows that increases in left sensorimotor beta corresponded to higher right sensorimotor beta (or less of the putative pain response) in the Heat condition only.

beta signified a stronger pain response. We performed robust fit regressions for all three conditions: Heat, No Heat Risk, and Safe. In particular, we wanted to know whether participants who on average suppressed more also

exhibited more or less of a pain response to heat. We found a marginally significant regression for the Heat condition, $F(1, 14) = 4.6$, $p = .050$, with an R^2 of .247 and a β coefficient of .426. Thus, participants who motor

suppressed more in the Heat condition (i.e., greater increase in left beta) had a mitigated reduction in right sensorimotor beta (Figure 4C). The same regression was not significant for No Heat Risk, $R^2 = .004$, $p = .818$, nor Safe conditions, $R^2 = .065$, $p = .343$.

Between-participant (single trial) robust regression. For each participant, we now log-transformed the beta power values for each single trial and subtracted the average log beta power computed over the single trial baseline period. We next calculated robust regressions to test whether single trial measures of left sensorimotor beta during the late time window were predictive of single trial measures of right sensorimotor beta in the same time window. This analysis provided a β coefficient for each subject in each condition. We then used paired-samples t tests to determine whether these β coefficients were significantly different across participants. All three conditions had β coefficients that significantly differed from 0 (all $ps < .001$). Thus, unlike the between participant analysis above, the within trial relationship between putative motor suppression and pain was not selective to the Heat condition.

Relationship between Right Sensorimotor Beta and Thermoder Temperature

Because some prior work suggests that beta decreases may reflect stimulation intensity rather than pain (for a review, see Archibald, Warner, Ortiz, Todd, & Jutzeler, 2018), we tested for a correlation between right sensorimotor beta, using the same above late time window, and temperature of the thermoder. There was no relationship ($R = -.037$, $p = .896$). This suggests that the decrease in right sensorimotor beta was not simply an indication of stimulus intensity.

Discussion

We made minor adaptations to the heat paradigm and recorded 64-channel EEG. We ran ICA on each participant's EEG data to generate components. We automatically clustered these across participants to derive left and right sensorimotor clusters. We then identified a participant-specific beta band based on the postmovement beta rebound after the response on Safe trials. Using a participant-specific band, we tested the differences between Heat, No Heat Risk, and Safe conditions for left and right sensorimotor areas during the withholding period.

We found a significant increase in left sensorimotor beta for Heat versus No Heat Risk and for Heat versus Safe, and this was sustained across multiple seconds of urge. Furthermore, we found a decrease in right sensorimotor beta, contralateral to heat stimulation, that we suggest may reflect a pain response or the sensory processing of heat. This decrease was significantly stronger

for the Heat versus No Heat Risk and for Heat versus Safe. Interestingly, there was a positive relationship between right and left sensorimotor beta such that participants who suppressed more exhibited a mitigated pain response. This relationship was not evident for No Heat and Safe conditions, although the strength of the relationship in Heat was only marginally significant. The relevance of these results is discussed below in the wider context of Experiments 1 and 2.

GENERAL DISCUSSION

We designed a new task to create an urge state in which people wanted to perform an action at the same time as they needed to withhold it. Experiment 1 used TMS over primary motor cortex in the left hemisphere, which was contralateral to the hand that could press to get relief. We found increased SICI for the wait period on Heat trials compared with baseline, and this was specific for a task-relevant finger. Experiment 2 replicated this result. There was, however, increased SICI for the task-relevant finger even in the No Heat condition. This result was a puzzle but could reflect that even in the No Heat condition the participant had to wait to press under fear of penalty or that there was some conditioning so that the Wait cue instantiated an inhibitory state even in the No Heat case. Experiment 3 used scalp EEG and ICA to derive putative motor suppression and heat pain components. For the left sensorimotor component, for all conditions, Heat, No Heat Risk, and Safe, there was a rapid event-related desynchronization in the beta band, followed by an increase that was greatest in the Heat condition. We interpret this increase in the Heat condition as the EEG corollary of the SICI results—that is, a motor suppressive state during urge. For the right sensorimotor component, there was an event-related desynchronization for the Heat condition versus the others; this is a putative signature of heat pain or the sensory aspects of the stimulation. Strikingly, across participants, a robust regression showed that increases in left sensorimotor beta (more putative motor suppression) corresponded to less beta desynchronization in the right sensorimotor component (less putative heat pain signature)—raising the prospect that these are related (we discuss this further below).

Convergent Evidence for Motor Suppression in Urge

The consistency between the EEG result (relatively increased beta band power for the left sensorimotor component for Heat versus the other conditions) and the TMS findings (increased SICI in the Heat condition during the urge period relative to baseline in two studies and specific to the task-relevant finger) strongly suggests that a motor suppressive process is at work in this urge state.

Although it has often been conjectured that an urge state involves inhibitory control (Berman et al., 2012; Filevich & Haggard, 2012; Jackson et al., 2011; Mazzone et al., 2007, 2011; Nachev, 2011; Lerner et al., 2008; Athwal et al., 2001), this is perhaps the clearest demonstration, using two kinds of evidence. For example, fMRI studies on both blink and cough suppression have reported activation of a cortical node such as rIFG that in other work is critical for top-down inhibitory control, but the activations in these particular studies could reflect any of impulse, discomfort, arousal, or control. By contrast, we specifically point to increased SICI and increased beta band power, both of which are linked to increased GABAergic levels in M1 (Kilavik et al., 2013; Muthukumaraswamy et al., 2013; Gaetz, Edgar, Wang, & Roberts, 2011; Hall, Barnes, Furlong, Seri, & Hillebrand, 2010; Rothwell et al., 2009; Di Lazzaro et al., 2000, 2005; Jensen et al., 2005; Chen, 2004; Baker & Baker, 2003). Our study, however, is focused on the sensorimotor system and leaves open the question of which prefrontal/executive systems instantiate a motor suppressive state during urge. Based on a broader literature on response suppression, one might anticipate that prefrontal areas such as the rIFG (Aron, Robbins, & Poldrack, 2014) and the dorsal frontomedian cortex (Kühn, Haggard, & Brass, 2009; Brass & Haggard, 2007) are involved in top-down control over urges.

Alternative Accounts

It could be argued that the increased SICI in the Heat condition in Experiments 1 and 2 reflects a process other than motor suppression. Indeed, changes in corticospinal excitability could occur for a number of reasons, including increased arousal or stress (Coelho, Lipp, Marinovic, Wallis, & Riek, 2010; Milani et al., 2010), catecholamine release (Ziemann, Tergau, Bruns, Baudewig, & Paulus, 1997), and sensory processing (Valeriani et al., 1999, 2001; Tokimura et al., 2000). However, what speaks against an arousal/stress account is that, in both experiments, the SICI increase was specific to the finger that could press (the right index) and not the right pinkie. An alternative view is that increased SICI in the index finger reflects a (inhibitory) process related to movement preparation rather than a top-down suppression of the movement. Indeed a large body of work has used TMS to demonstrate inhibitory processes in movement preparation (for reviews, see Duque, Greenhouse, Labruna, & Ivry, 2017; Bestmann & Duque, 2016). However, several considerations speak against this account. First, in both Experiments 1 and 2, we observed increased SICI at Time Point 1, only ~3 sec into a wait period that participants knew lasted at least 8 sec long. This is not compatible with inhibitory mechanisms in movement preparation, which are usually seen only several hundred milliseconds before an anticipated movement (Lebon et al., 2015; Duque, Lew, Mazzocchio, Olivier, & Ivry, 2010) and not several seconds before. Second, in Experiment 3, the left sensori-

motor beta increase was greater in the Heat versus No Heat Risk and Safe conditions, even though movement preparation occurred in all cases.

Regarding our heat pain signature in Experiment 3, the right sensorimotor cortex contralateral to the arm with the heat showed a beta desynchronization. This is consistent with prior studies (Misra, Ofori, et al., 2016; Misra, Wang, et al., 2016), and we interpret it as a pain response. However, an alternative view is that this reflects a movement tendency—to move the arm with the thermode to “get away” from the pain. Although this would be ineffective in this situation (as the thermode was attached to the arm), such a response may be built in. Indeed, studies have shown that heat pain readies the motor cortex for movement and speeds movement (Misra, Ofori, et al., 2016). Although we cannot fully refute this “movement account,” it is not so easy to reconcile with our finding that, in the Heat condition, across participants, a greater left sensorimotor beta increase corresponded to less right sensorimotor reductions, that is, if right sensorimotor beta reductions reflect readiness to move the arm (to get away from heat), it is unclear why this effect is weaker in those who show more putative suppression of the other hand (especially since suppression was finger specific in Experiments 1 and 2).

How Valid Is Our Heat Pain Model for Urge?

The question arises whether heat pain is a good model of an urge state. Everyday urges involve such things as preventing oneself from coughing, scratching, or even indulging in sweets. Clinically, urges are epitomized by Tourette’s syndrome where a patient has a tendency to perform a movement that is, for example, socially inappropriate. We suppose that our heat pain paradigm is a fair model of some of these scenarios at least; perhaps particularly those where there is a specific action that the individual wants to perform but must withhold.

A related question is why is there a motor suppressive process at all? It stretches credulity that in our paradigm the participant needs to literally suppress the finger in the Heat case so that it does not “jump away” and press the button prematurely. We speculate that the participant engages the sensorimotor suppressive state not only for motor control but because the suppressive state may somehow help to reduce the discomfort. Indeed, we observed across participants that increased left sensorimotor beta power (more motor suppression) was predictive of relatively less beta desynchronization over the right sensorimotor component (lesser heat pain signature). Although we cannot of course infer from this relationship that suppressing causally affects pain, other studies do support a functional link between the motor system and pain processing. For instance, Misra, Ofori, et al. (2016) show that a greater pain-related beta response (i.e., greater reduction in beta)

corresponds to motor facilitation and quicker responding (this is complementary to our finding that relatively less beta reduction relates to more motor suppression). Another study shows that preparing to make a movement, often associated with inhibitory mechanisms (Bestmann & Duque, 2016), leads to reduced subjective pain ratings and pain-related evoked potentials (Le Pera et al., 2007). Overall, stronger conclusions about whether and how suppressing a motor response during urge affects one's subjective experience is a ripe topic for further investigations with causal methods.

Limitations

First, although Experiments 1 and 2 were preregistered with a clear analytic procedure, Experiment 3 was much more exploratory. The particular mode of analysis relies on several somewhat arbitrary assumptions. For example, we selected time windows for the late versus early comparison in the withholding period based on the pattern of the overall data themselves and then tested between-condition differences. Clearly, more study—and replication—using the EEG method is warranted. Second, as discussed above, we cannot definitively conclude that the beta desynchronization in the arm contralateral to the thermode reflects a pain response rather than a preparatory response to move (albeit moving the arm with the thermode attached would not help). A future study could include a condition where heat pain is applied without any possibility of movement. Third, we did not manipulate the level of heat or ask for subjective reports of pain. This is pertinent to the intriguing result that motor suppression related to the heat pain signature. It is not clear presently if it really relates to the actual felt pain or merely to an EEG signature correlated with heat pain. Future studies could parametrically vary the heat pain and test if the beta desynchronization scales accordingly and test whether the motor suppressive state relates to subjective changes in heat pain. Such studies could also test whether the putative motor suppressive state is causal to changes in heat pain.

Conclusion

Using both paired-pulse TMS (SICI) and scalp EEG, we provide converging evidence that a motor suppressive process is voluntarily recruited as participants try to suppress an impulse to act during urge. Specifically, we found both an increase in SICI and an increase in left sensorimotor beta during the urge to press. Additionally, with whole brain data from EEG, we discovered distinct changes in left (increase) and right (decrease) sensorimotor beta, which we infer to reflect motor suppression and a putative pain response, respectively. Furthermore, those participants who exerted more putative motor suppression during the urge task also exhibited a reduction in our putative pain signature. These results provide novel

information about the functional role of motor suppression in urge.

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Notes

1. Preregistered study plan at: <https://osf.io/kysu8>.
2. Supplemental material can be retrieved from <https://osf.io/kysu8>.

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