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Supplemental Information

Phase-Locked Stimulation during Cortical Beta Oscillations Produces Bidirectional Synaptic Plasticity in Awake Monkeys

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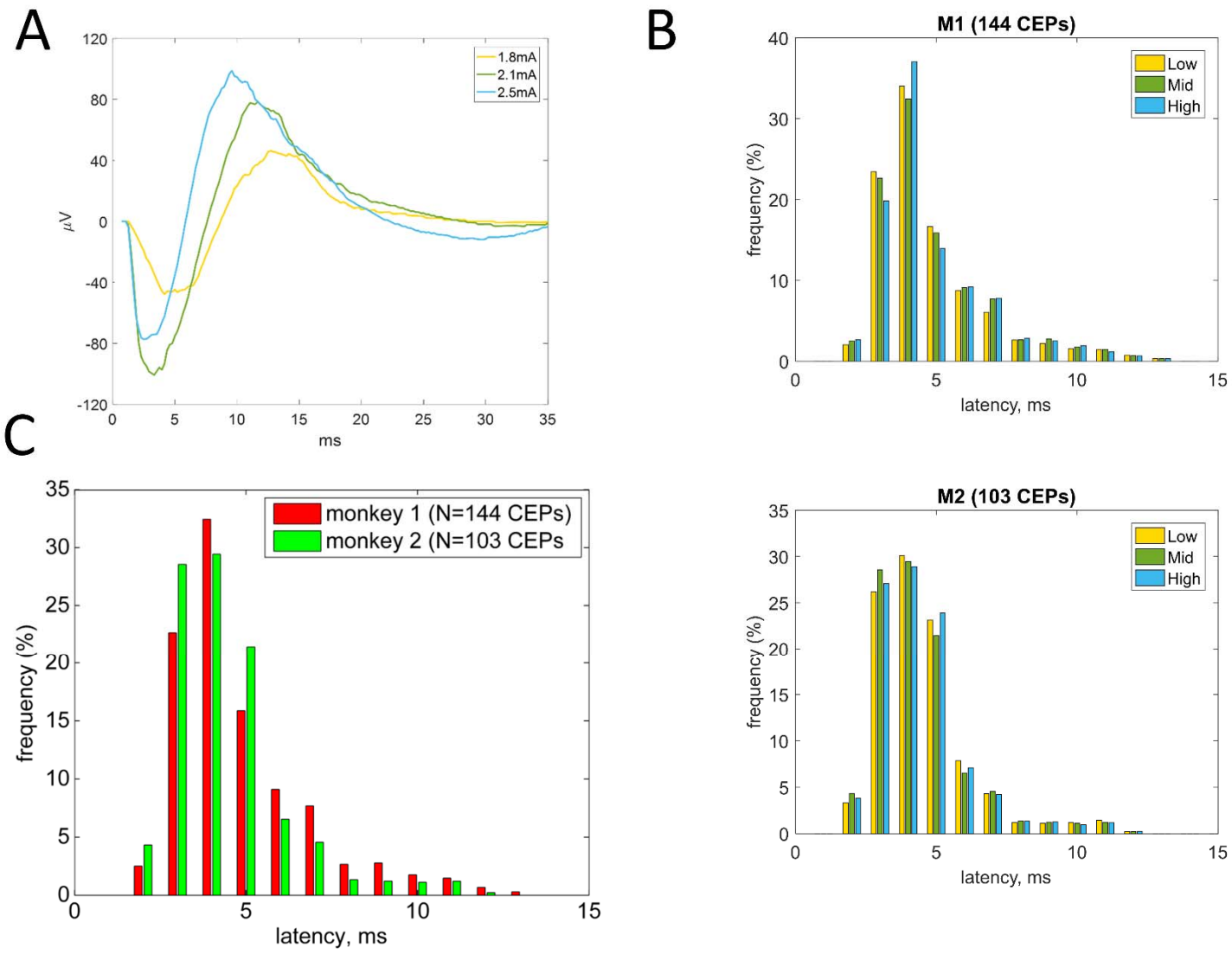

Figure S1. Cortically-evoked potentials (CEPs), CEP latency and effect of stimulation intensity, Related to Figure 2.

(A): Stimulation intensity at a given site was set to approximately 110% of the current that elicited clear CEPs. In this example clear CEPs were elicited at 1.8mA and larger CEPs were elicited at progressively larger intensities. Conditioning was performed using current intensity of 2.1mA.

(B): Distributions of latencies of the first CEP component for different current intensities: low (threshold for eliciting a clear CEP), mid (110% of threshold), high (typically 120-150% of threshold). Left panel: monkey 1, right panel: monkey 2. For each monkey, the distributions were not significantly different in pair-wise comparisons.

(C): Histogram of latencies of the peak of the first, typically surface-negative, component of cortically-evoked potentials in the 2 monkeys.

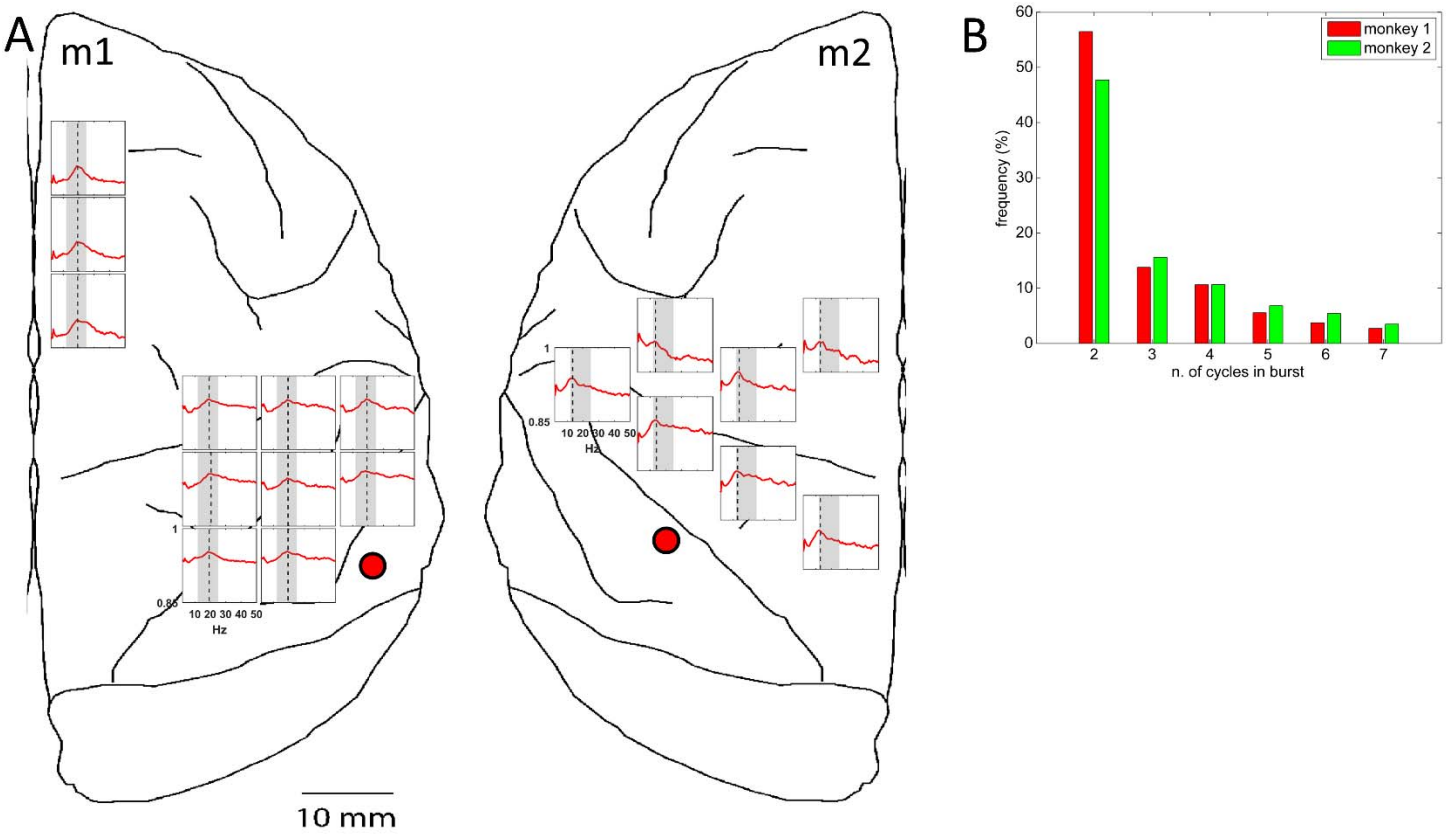

Figure S2. Synchrony of spontaneous beta oscillations in sensorimotor cortex, Related to Figure 2.

(A): Coherence spectra between a trigger site (red dot) and other cortical sites. Vertical grey ribbon denotes the beta band as was defined in our study (12-25 Hz); the dotted line denotes the frequency associated with the peak of the coherence spectrum. The positions of the panels on the brain map approximate the locations of the cortical electrodes; the distances between them are not representative of the actual distances between the electrodes. (B): Histogram of number of cycles occurring within oscillatory bursts, in each of the 2 animals.

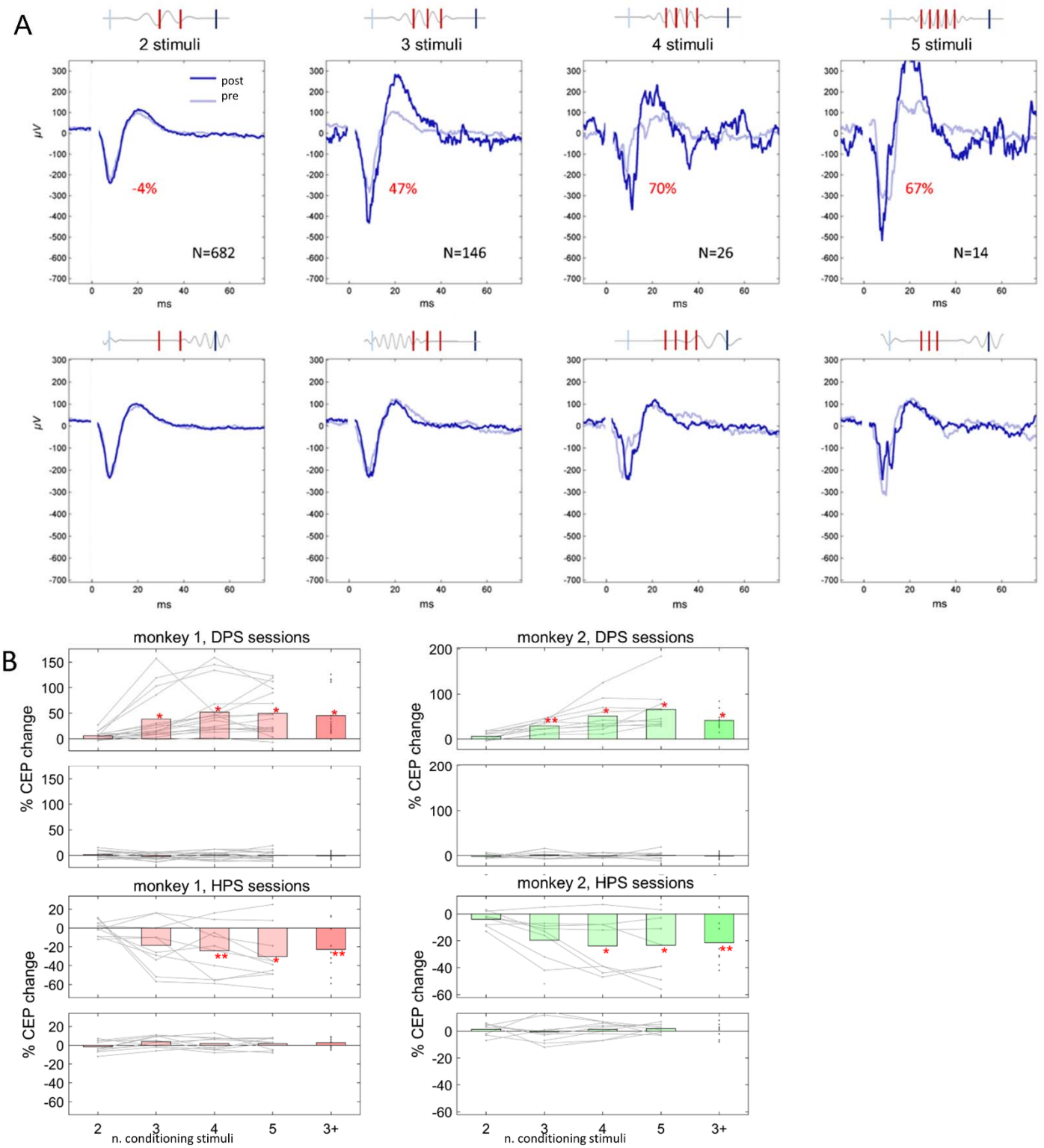

Figure S3. Magnitude of conditioning effect increases with number of cycle-triggered stimuli, Related to Figure 3.

(A) (Top row): Conditioning episodes from same session separated by number of cycle-triggered, conditioning stimuli. Percent values indicate change in post- vs pre-episode test CEPs. N is number of available episodes. (Bottom row): Corresponding control session with the same sequence of stimuli produced no effect.

(B): Average magnitude of the conditioning effect as a function of the number of conditioning stimuli. Each panel shows change in CEP amplitude after stimulation bursts, relative to pre-burst CEP amplitude, as a function of the number of conditioning stimuli. Left and right: animal 1 and 2; top and bottom: depolarizing and hyperpolarizing phase sessions. Dots connected by grey lines represent measurements in individual sessions. Colored bars indicate the average CEP change for that number of conditioning stimuli across

all sessions included in that panel. Panels show closed-loop conditioning experiments (upper) and corresponding control (lower). Single asterisk denotes significant difference in CEP change relative to CEP change seen in bursts with 2 stimuli in the same experiment ($p<0.05$, one-way ANOVA, with number of conditioning stimuli as group variable); in each case, CEP change was also significantly different than 0 (0 = no change from pre-burst CEP amplitude) ($p<0.05$, one-way ANOVA). Two asterisks denote significant difference of CEP change relative to 0, but not from the CEP change seen in bursts with 2 cycles.

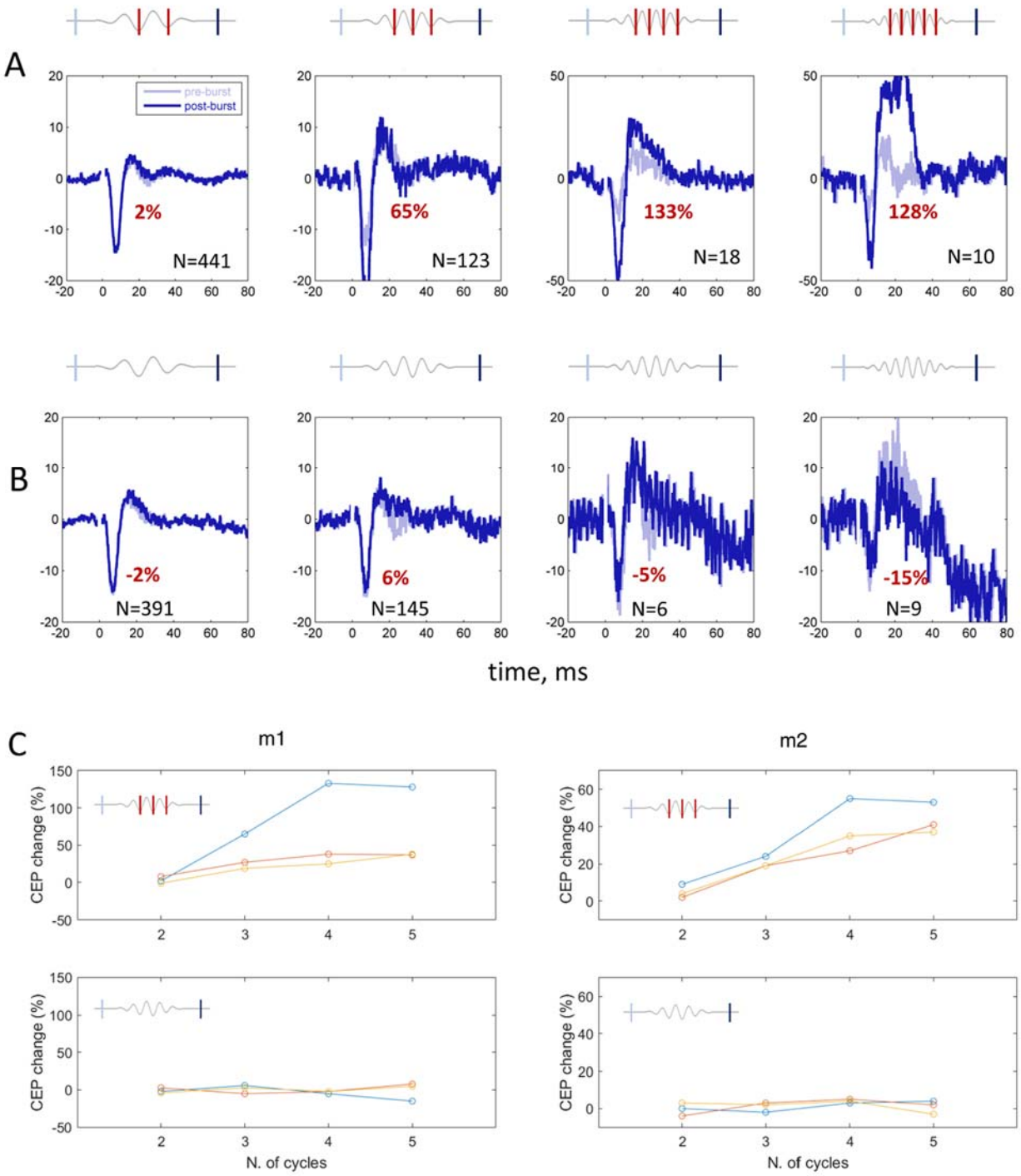

Figure S4. Occurrence of oscillatory episodes, without cycle-triggered stimulation, is not associated with changes in CEP amplitude, Related to Figure 3.

(A): Potentiation of CEP amplitude after depolarizing phase stimulation. Potentiation is significant in conditioning episodes of 3 or more cycles.

(B): In a subsequent experiment in the same animal, test stimuli were delivered and CEPs were registered at the same sites as in (A), before and after oscillatory episodes, in the same way as before; however, no conditioning stimuli were delivered during those episodes. No changes in the CEP amplitude were seen.

(C): CEP changes associated with depolarizing phase stimulation (top panel) and, in the same site, associated with oscillatory episodes without stimulation (bottom panel), as a function of the number of oscillatory cycles per episode; each colored curve corresponds to a different experiment and site. Three experiments are shown for animal 1 (m1) and 3 for animal 2 (m2).

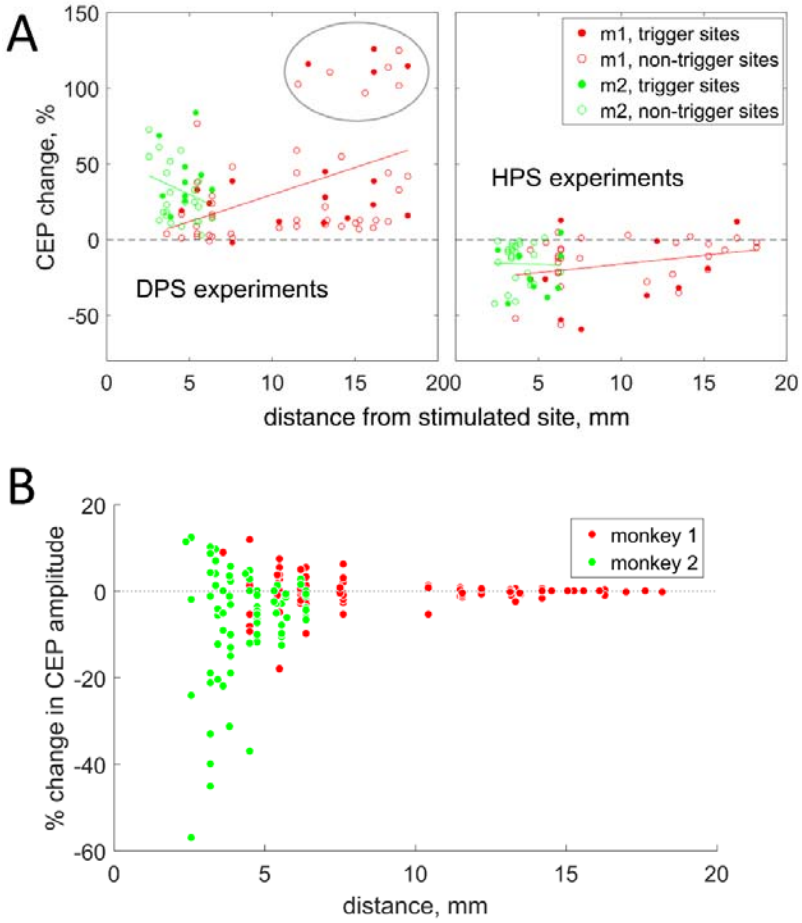

Figure S5. Short-term and long-term changes in CEP amplitude with conditioning in triggering and non-triggering sites, as a function of their distance from the stimulated site, Related to Figure 5.

(A): Short-term changes in CEP amplitude, between pre- and post-episode test pulses, in episodes of 3 or more cycles. The conditioning effect is shown separately for DPS and HPS experiments (left and right panels). Filled circles represent triggering sites, open circles represent non-triggering sites at which CEPs were registered. Lines represent least square linear fits. Red circles and lines correspond to data from animal 1, green from animal 2. Correlation coefficients between % CEP change and distance from the stimulated site were for DPS experiments, 0.44 and -0.26 for animal 1 and animal 2, respectively ($p<0.01$ and p NS, respectively), and for HPS experiments 0.28 and -0.02 (p NS for both). The grey circle in the left panel denotes strong conditioning effects from DPS experiments in animal 1. All of these measurements were between M1 and SMA sites.

(B): Long-term changes in CEP amplitude with conditioning between the beginning and end of stimulation sessions. These changes were inversely related to the distance from the stimulated site. Virtually no changes in monkey 1, the animal with more widespread electrode coverage, were seen at distances over 10 mm.

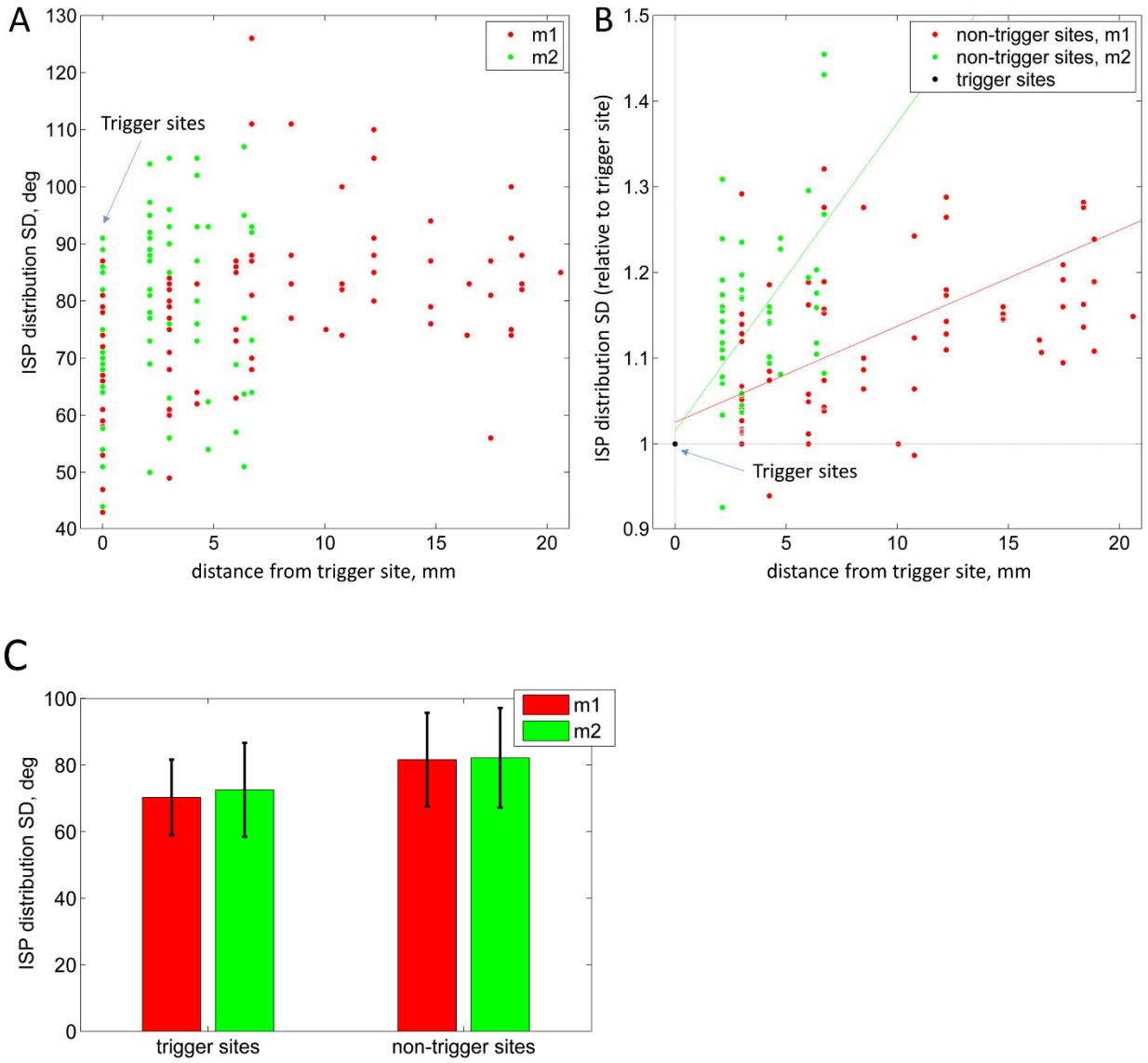

Figure S6. Consistency of instantaneous stimulation phase in triggering and non-triggering sites, Related to Figure 5.

(A): Standard deviation (SD) values of the instantaneous stimulation phase (ISP) distributions at all triggering and non-triggering sites with CEPs, from all experimental sessions in both animals, as a function of distance from the corresponding triggering site. The data points at distance=0 represent the triggering sites.

(B): The same data, normalized by the SD at C_{TRIG} for that experimental session. The 2 colored dashed lines represent the least-squares regression lines, one for each animal.

(C): Summary of SD values of the ISP distribution in triggering sites (left) and in non-triggering sites (right), for the 2 animals. Bars represent means, error bars represent +/-SD from means.