Exploring cross-modal properties of the somatosensory cortex with a novel Paired Associative Stimulation protocol

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Introduction: *In the last years, the evidence that the primary somatosensory cortex (S1) is activated not only during the perception of tactile stimuli but also during their observation, has been widely investigated. A highly influential hypothesis suggests that the cross-modal, mirror-like, activity of S1 may arise from Hebbian associative plasticity: the contingency of seeing a touch and the feeling of a tactile sensation on one's own body may reinforce synapses between visual and somatosensory neurons. However, to date, a causal demonstration is still lacking. To test this hypothesis, we developed a novel cross-modal Paired Associative Stimulation protocol (cm-PAS) where a visual stimulus depicting the palm of a left hand being touched is repeatedly presented (i.e. visual-touch stimulus), time-locked with a Transcranial Magnetic Stimulation (TMS) pulse over right S1.*

Methods: *In 4 within-subjects experiments, we tested temporal (Experiment 1), cortical (Experiment 2) and visual (Experiment 3) specificity of cm-PAS by assessing its effects on tactile acuity. Experiment 3 explored neurophysiological changes in S1 by recording Somatosensory Evoked Potentials (SEPs). The last study (Experiment 4) investigated the role of predictive coding mechanisms through a jittered, unpredictable, cm-PAS version where the frequency between trials was not fixed (at variance with the fixed frequency of 0.1 Hz employed in previous experiments). Temporal constraints were explored by varying the inter-(paired) stimulus interval (ISI), according to different chronometry of S1 activation by touch processing and touch observation (i.e., 20 and 150 ms).*

Results: *Results show that cm-PAS is effective in inducing Hebbian Long-Term Potentiation-like plasticity, increasing tactile acuity at the observer's hand. Importantly, this effect is present only when (a) the ISI between the two stimuli (i.e., the visual-touch stimulus and the TMS pulse) is of 20 ms (Experiment 1), (b) the TMS pulse is delivered over S1 (Experiment 2) and (c) the visual stimulus depicts an hand being touched, not a mere hand action (Experiment 3). The cm-PAS also increases SEPs (i.e., the P40 component peak). Finally, Experiment 4 showed that the unpredictability of temporal occurrence of the paired stimuli changes the temporal window required for integrating the visual-touch stimulus with the cortical activation of S1, now requiring an ISI of 150 ms.*

Discussion:*Our study provides novel insight into the cross-modal, mirroring, activity of S1, and the chance of inducing changes in this area by activating spike-timing-dependent plasticity and, in a broader perspective, Hebbian associative plasticity. Our original protocol, the cm-PAS, effectively modulates S1 functioning, improving tactile acuity and increasing SEPs. Interestingly, the cm-PAS recruits predictive coding mechanisms that act by pre-activating S1, anticipating the upcoming touch. Taken together, our results show how the cm-PAS can be a very useful non-invasive stimulation protocol to cross-modally induce neuroplasticity in the human brain, as well as uncovering the underpinning of mirroring mechanisms and the shaping role of predictive coding.*

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