

Figure S1. Cerebral blood flow (CBF) measured by ASL-fMRI.

- **A)** Comparison between placebo and ibuprofen recipients using a summary measure of brain regions associated with pain (the NeuroSynth pain map). In the placebo group, note the apparent placebo effect between 0 and 15 minutes followed by a uniform increase in CBF between 15 and 30 minutes.
- **B)** To avoid confounding by the placebo effect, the slope of CBF change between 15 and 30 minutes was used to compare the two groups. (* p<0.05, Wilcoxon test).
- **C)** Whole-brain topologic inference on the slope between 15 and 30 minutes highlighting areas that survive an uncorrected p<0.05. Nothing survived false discovery rate estimation due to the low number of analyzable images in the placebo group. Slopes were not evaluable in 5 out of 10 subjects in the placebo group and 8 out of 19 subjects in the ibuprofen group primarily due to motion artifacts. Despite this limitation the image illustrates the brain areas with the most pronounced numeric changes: insula, anterior cingulate cortex and secondary somatosensory cortex.