Control over brain activation and pain learned by using real-time functional MRI

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techniques: real-time fMRI to reduce pain perception; GLM
**Introduction**

**real-time fMRI** - subjects given online feedback about their brain activity and attempt to control it.

**questions in the study:**
Can subjects learn to control a pain-associated brain area (rACC) with rtfMRI?

If so, will this affect pain perception in healthy subjects and patients with chronic pain?
**Background**

**Rostral Anterior Cingulate Cortex (rACC)**

- **amygdala** (fearful emotions)
- **frontal cortex** (decision making, expectations, evaluation)

- rACC activated by feeling and observing pain (empathy)
- Pain perception modified by psychological factors, and rACC maybe important (expectation, placebo, attention)

- rACC has spindle cells found only in humans, higher apes, elephants, whales and dolphins (all have large, social brains)
Methods

**pain stimulus:** 30s heat plate applied to left palm, 46.8-48.6 deg C; pre-tested to be maximally painful stimulus subject could tolerate without moving.

**instructions for healthy subjects:**
“learn to control activation of a localized brain region associated with pain” attempt to increase and decrease and give real-time feedback using any of these strategies:

1. **Attention.** Attend toward the painful stimulus vs. away from it (to the other side of the body).
2. **Stimulus quality.** Attempt to perceive the stimulus as a neutral sensory experience vs. a tissue-damaging, frightening, or overwhelming experience.
3. **Stimulus severity.** Attempt to perceive the stimulus as either low or high intensity.
4. **Control.** Attempt to control the painful experience, or allow the stimulus to control the percept.

**instructions for pain subjects:**
the same but no external pain stimulus applied
Methods

**Figure 1**

- **experiment:**
  - 1 localizer scan,
  - three training runs (13 min) - one post-test run (rate each stimulus)

- **subjects:**
  - 8 healthy controls
  - 8 chronic pain patients

- **feedback:**
  - 2 visual displays of rACC activity level (relative to that of a larger background region)

- **control group 1 (n=8)** same instructions, no rtfMRI feedback
- **control group 2 (n=8)** same instructions, no rtfMRI feedback, but even more training time
- **control group 3 (n=8)** same instructions, but rtfMRI from another unrelated brain area
- **control group 4 (n=4)** same instructions, but rtfMRI feedback of a group 1 subject’s rACC (i.e. identical visual stimulation as a group 1)
Results

Figure 2

GLM contrast:

\[ \left( \text{fMRI}_{\text{inc}} \text{ vs. } \text{fMRI}_{\text{dec}} \right)_{\text{final}} - \left( \text{fMRI}_{\text{inc}} \text{ vs. } \text{fMRI}_{\text{dec}} \right)_{\text{initial}} \]

additional brain areas showing this pattern: supplementary motor cortex, insula superior cerebellum.
Results

Figure 3

evidence of learning: difference in activity between “increase” and “decrease” blocks grow over training runs.

pain perception: difference in pain rating between “increase” and “decrease” blocks also grow over training runs.

correlation between learning and change of pain perception
Results

Figure 4 - control groups

no improvement in the pain ratings

Figure 5 - patient groups

improvement in the pain ratings and they correlate with changes in rACC activity
Conclusions

Normal subjects and pain patients learned to control rACC activity with rtfMRI training.

Reduced fACC activity with associated with reduced pain perception (~30% change in pain rating).

Across subjects, strength of rACC control correlated with strength of pain relief.
Discussion

Why did this work?

Did subjects consciously learn to control their own “placebo” effect?

Can this be a useful strategy for management of chronic pain?

Once trained, can subjects apply strategy to reduce pain outside of the MRI scanner?

Mix of strategies, is there a best strategy?