Pain-related gamma-band oscillations in the human insula
How does pain emerge from the brain?

Bingel & Tracey (Physiol 2008)
1. Connections with the spinothalamic tract
2. Lesions of the insula and pain perception
3. Focal insular epilepsy and direct stimulation of the human insula
4. Brain activity related to sustained nociceptive input
5. Local field potentials (LFPs) recorded from the human insula
Insula and pain

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Local field potentials (LFPs) in the human insula

Direct intracerebral recordings have shown that nociceptive stimuli elicit robust LFPs in the human operculo-insular cortex.

Frot & Mauguière (Brain 2003)
Does the insula exhibit pain-specific responses?

- Depending on the **exclusivity** of the relationship between these responses and the experience of pain:
  - Stimuli perceived as painful elicit responses in the insula (**sufficiency**) ✓
  - These responses are elicited *if and only if* the stimulus is painful (**necessity**) ?
Intracerebral EEG

Aim: determine whether or not the insula exhibits **nociceptive-specific** responses

- 8 patients (19-43 years)
- 9 insulae
  - 7 left
  - 2 right
- 53 insular contacts
  - 25 posterior
  - 28 anterior
Sensory stimulation

- 4 modalities
  1) Nociceptive (CO₂ laser)
  2) Tactile (mechanical vibration)
  3) Auditory (tones)
  4) Visual (LED)

- Blocked design
- Ipsilateral and contralateral
- 40 stimuli per block
- Stimulus duration: 50 ms
- ISI: self-paced by experimenter

Intensity ratings
- After each stimulus
- NRS: 0-10

Liberati et al. (PLoS Biol 2016)
LFP waveforms

Liberati et al. (PLoS Biol 2016)
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Non phase-locked gamma-band oscillations (GBOs)

Transient nociceptive stimuli elicit an early-latency increase of the magnitude of gamma-band power with a spatial distribution compatible with activity originating from S1.

Gross et al. (PLOS Biol, 2007)

Hu et al. (NIMG, 2013)

Zhang et al. (J Neurosci, 2013)
GBOs: insular responses specific to pain?

Liberati et al. (under review)

GBO power magnitude normalized across subjects
- Perception has been proposed to emerge from the temporal binding or synchronization of stimulus-evoked neural activities through GBOs (Engel et al., 2001; Fries et al. 2009)

- GBOs generated in the insula could reflect cortical activity through which the perception of pain arises from nociceptive input

*Liberati et al. (under review)*
Conclusions

• Nociceptive low-frequency LFPs elicited in the insula are not specific for nociception, but rather reflect multimodal activity
  – Could represent mechanisms of arousal and/or attentional re-orientation towards salient stimuli

• The enhancement of stimulus-evoked GBOs recorded from the human insula could possibly reflect nociceptive-specific stages of cortical processing