Rapid electrophysiological activations within anterior insula anticipate spontaneous pupil dilation

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Introduction

- Spontaneous activations within neuronal populations can emerge similarly to the "task-evoked" activations commonly elicited during cognitive performance or sensory stimulation.
- We hypothesized that spontaneous activations within a brain region implicated in higher-order cognitive functions– the dorsal anterior insular cortex (daIC)– have comparable functional and physiological significance to task-evoked activations.
- We combined human intracranial electroencephalography (iEEG) with pupillometry to investigate the relationship between daIC activations (task-evoked and spontaneous) and pupil dilation, a sensitive marker of ongoing fluctuations in arousal and cognition.[1]
- We recently developed an iEEG paradigm that allows reliable functional localization of task-evoked activations within the salience network, including the insula.[2]
- Here we report novel and independent analyses within a subset of the subjects from our past work who had extensive electrode coverage within the insula and who underwent pupillometry during iEEG recordings.

Methods

Participants

- Three subjects (S1, S2, S3) with intractable epilepsy had depth electrodes (stereo-EEG) implanted for clinical purposes

Intracranial EEG and Pupillometry Acquisition

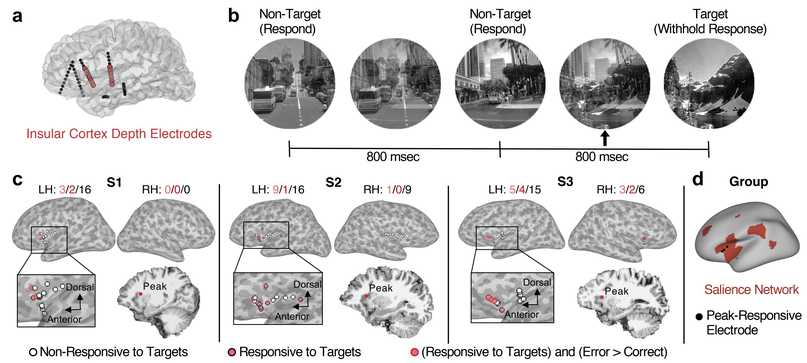
- All subjects had electrode coverage within the insular cortex
- Pupil diameter was recorded with a SensoMotoric Instruments (Teltow, Germany) Remote Eye Tracking Device (250 Hz sampling rate)
- Subjects participated in two task conditions, each in 6 minute runs (3-8 runs per condition):
  - **1)** The gradual onset continuous performance task (GradCPT)[3]
  - **2)** "Resting state" visual fixation

Data Preprocessing and Analysis

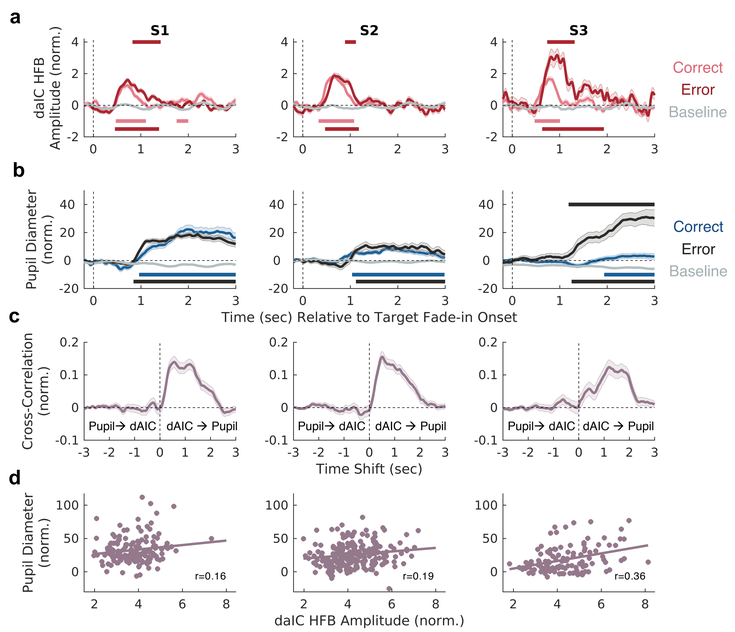
- Preprocessing: Line noise filtered out, common average re-referencing (without spikey/pathological channels), time-frequency decomposition (Morlet wavelet transform), log-normalization of time series
- Frequency band averaging: *δ* (1-3 Hz), *θ* (4-7 Hz), *α* (8-12 Hz), *β1* (13-29 Hz), *β2* (30-39 Hz), *γ* (40-70 Hz) HFB (70-170 Hz).
- Cluster-based permutation tests to identify significant iEEG-HFB responses and pupil responses to targets (mountains)
- ROC curves used to identify optimal HFB amplitude and duration parameters associated with task evoked responses[4]
  - True responses defined as activations on mountain (target) trials, false responses defined as activations on city (non-target) trials.
- Frequency of HFB activations during task versus rest compared with Wilcoxon rank sum test
- Pupillary time courses aligned to real and null (10,000 permutations) HFB activation peaks from responsive daIC electrodes in task and rest data
  - Area under curve computed for 2-sec window following HFB peak for real vs. null pupil responses

Results

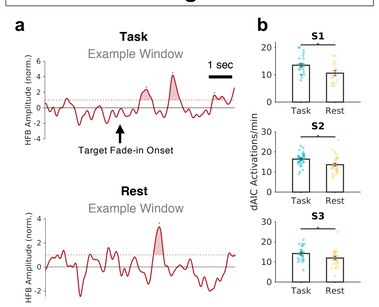
Functional localization of dorsal anterior insular cortex sites



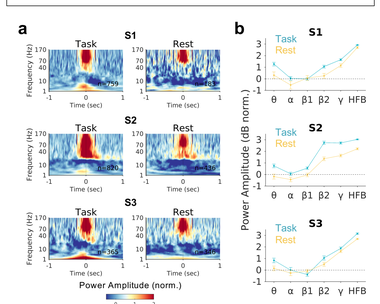
Task-evoked daIC activation precedes pupil dilation



daIC activations detected during resting state

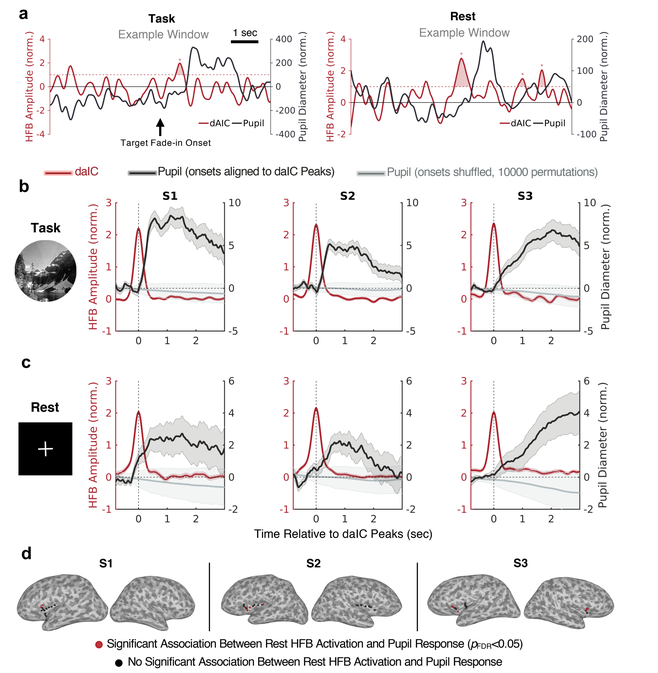


Spectral properties of task-evoked vs. rest activations



Results

Spontaneous daIC activation at "rest" precedes pupil dilation



daIC
Pupil (onsets aligned to daIC Peaks)
Pupil (onsets shuffled, 10000 permutations)

Discussion

In summary, we report several novel findings:

- 1) Spontaneous activations occur within the same neuronal populations and with the same spectro-temporal profiles as task-evoked activations;
- 2) Spontaneous activations are time locked to pupillary responses in a manner similar to task-evoked brain and pupillary responses;
- 3) Task-evoked responses directly recorded from human daIC, sensitive to behavioral errors, precede and correlate with the magnitude of evoked pupil dilations.
- We suggest that spontaneous temporal coupling between the daIC and pupil dilation could signify the emergence of self-generated cognitive processes with shared attributes to explicitly evoked cognition.

References

[1]Joshi et al., *Neuron* (2016); [2]Kucyi et al., *Nat Commun* (2020); [3]Esterman et al., *Cereb Cortex* (2013); [4]Dastjerdi et al. *Nat Commun* (2013)

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