On the functional anatomy of the urge-for-action: an fMRI and low-intensity focused ultrasound study

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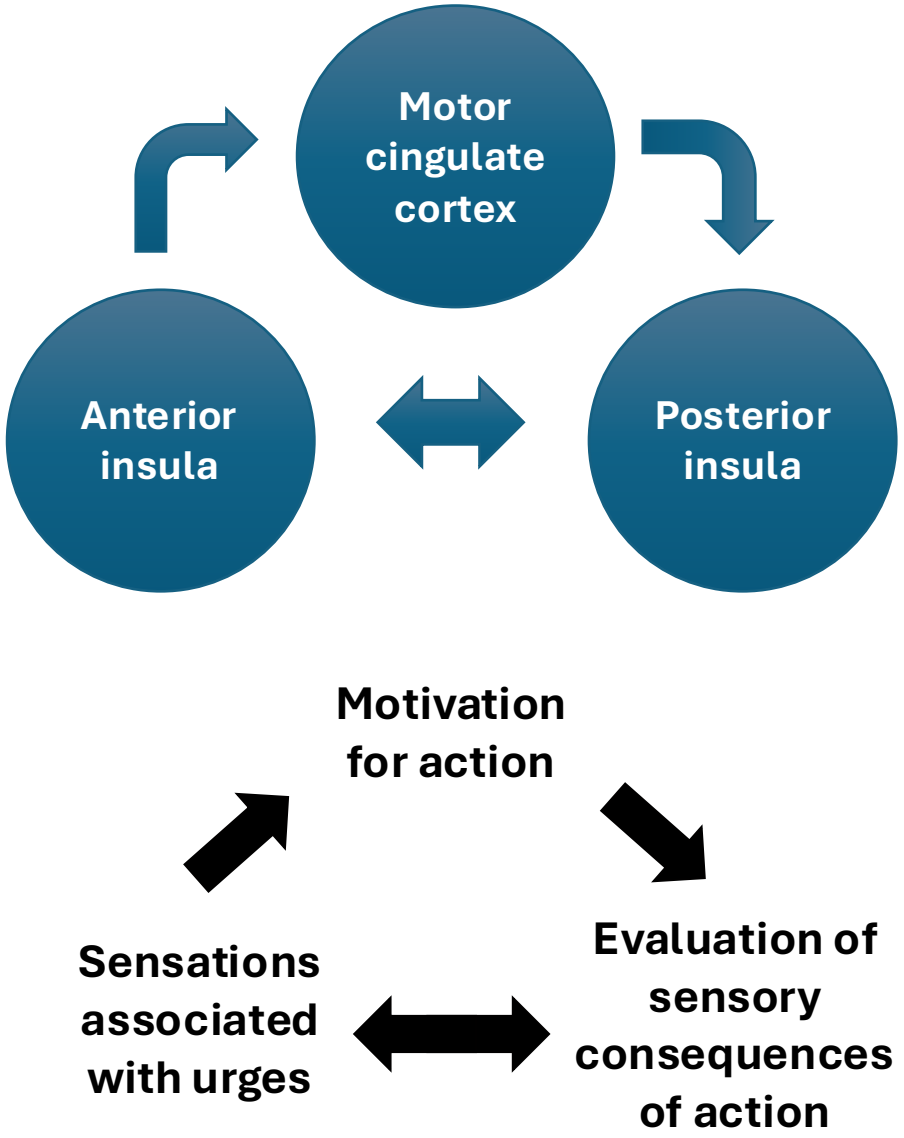
Urge-action-evaluation circuit



We identified the **insula** and **motor cingulate** cortex as key nodes in an urge-action-evaluation circuit.

Anterior insula – processes sensations associated with the urge-for-action, encodes unpleasantness

- **I have an itch**

Motor cingulate area – provides motivational drive to act and links urge → motor plan

- **I need to scratch the area that itches**

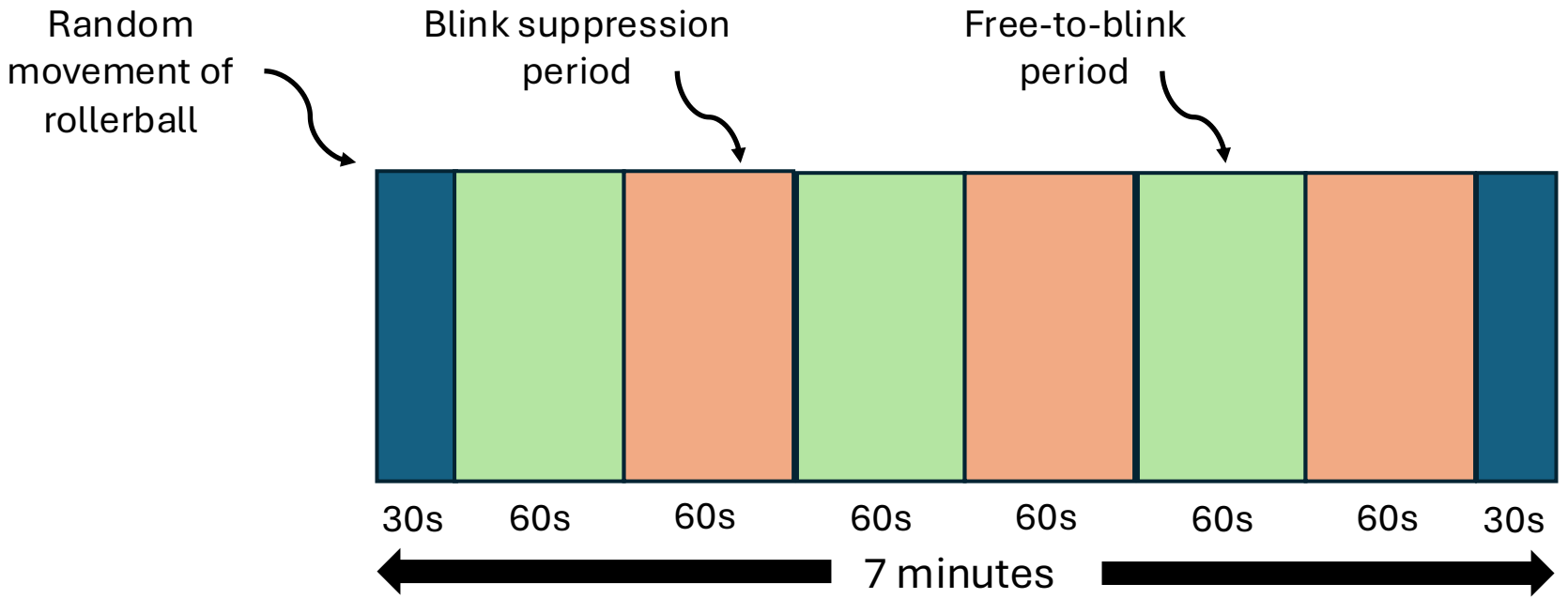
Posterior insula – evaluates the sensory consequences of the action,

- **Do I still have an itch?**

Jackson et al., *Cognitive Neuroscience*, 2011

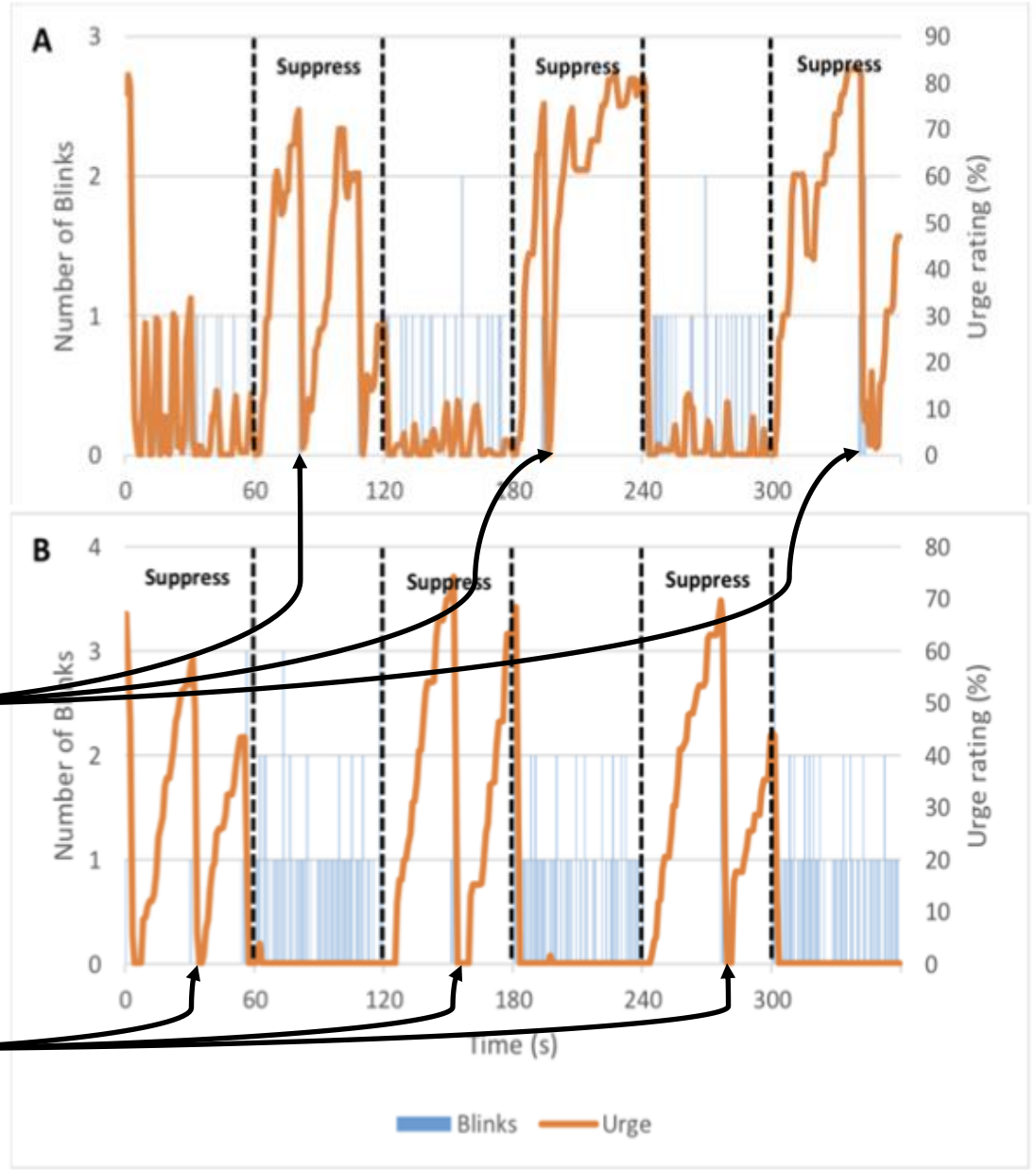
Study 1: 3T fMRI investigation of blink suppression

- **Sample** 20 healthy young adults (mean age 28 ± 5.2 years)
- **Design**
  - 7-minute fMRI session
  - Initial and final 30s = random movement of rollerball
  - Alternating 60s 'blink suppression' periods and 'free-to-blink periods
  - Order counterbalanced across participants
- **Contrasts used in analysis**
  - **Suppress:** blink suppression > free-to-blink periods
  - **Urge:** urge estimate **rollerball movements** > random rollerball movements



Urge-to-blink as a proxy for the urge-to-tic in TS

- Blinks are substantially reduced during periods of blink suppression.
- Urges increase during blink suppression
- Suppression isn't always completely effective and 'escape blinks' can occur during blink suppression periods
- Urges decrease when blinks are executed and likely arise due to the act of suppression



Escape blinks

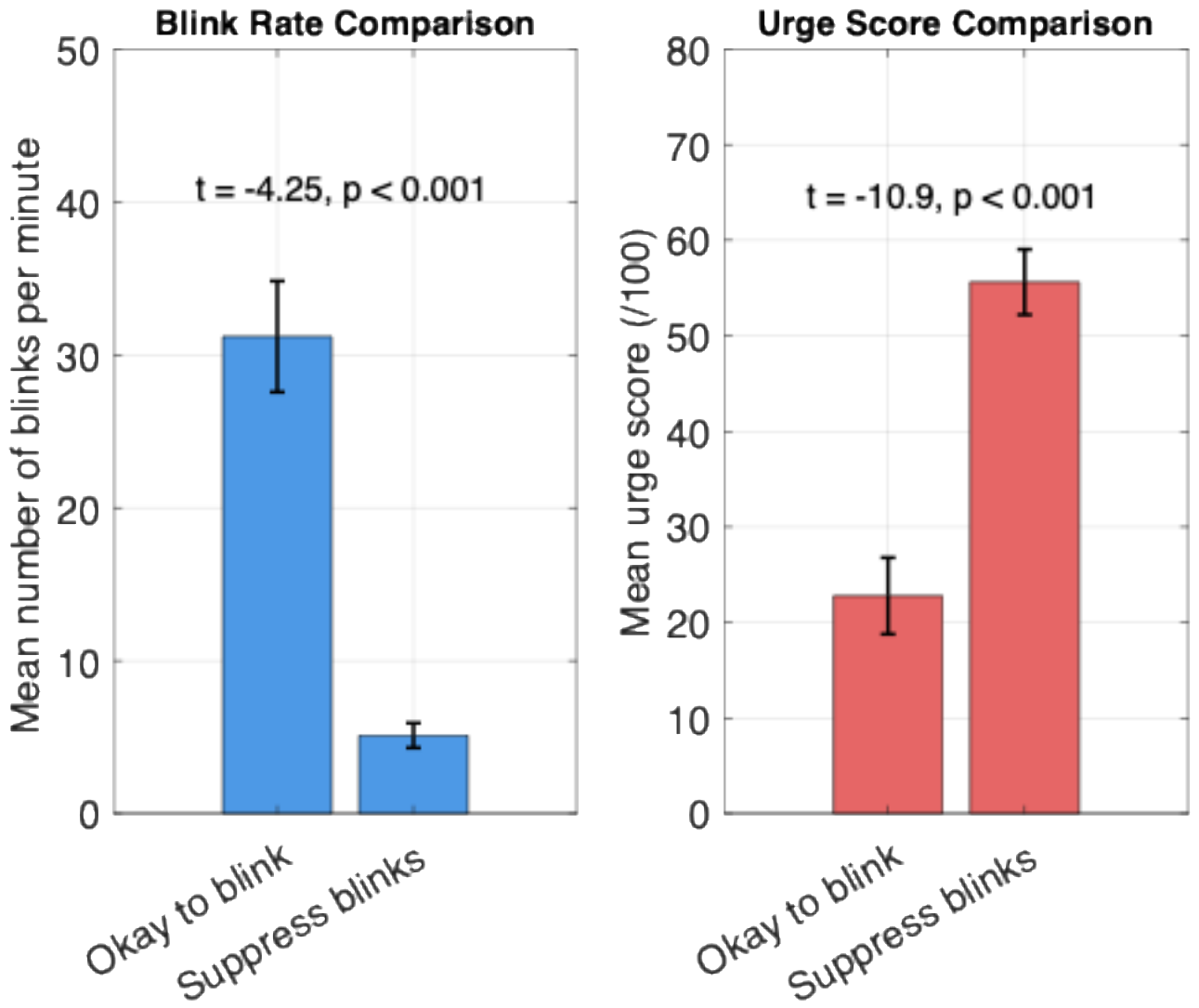
Escape blinks

Houlgreave et al. *Imaging Neuroscience*, 2025

Behavioural results

Key results

- Blink rate decreases during blink suppression
- Urge-to-blink increases during blink suppression



Houlgreave et al. *Imaging Neuroscience*, 2025

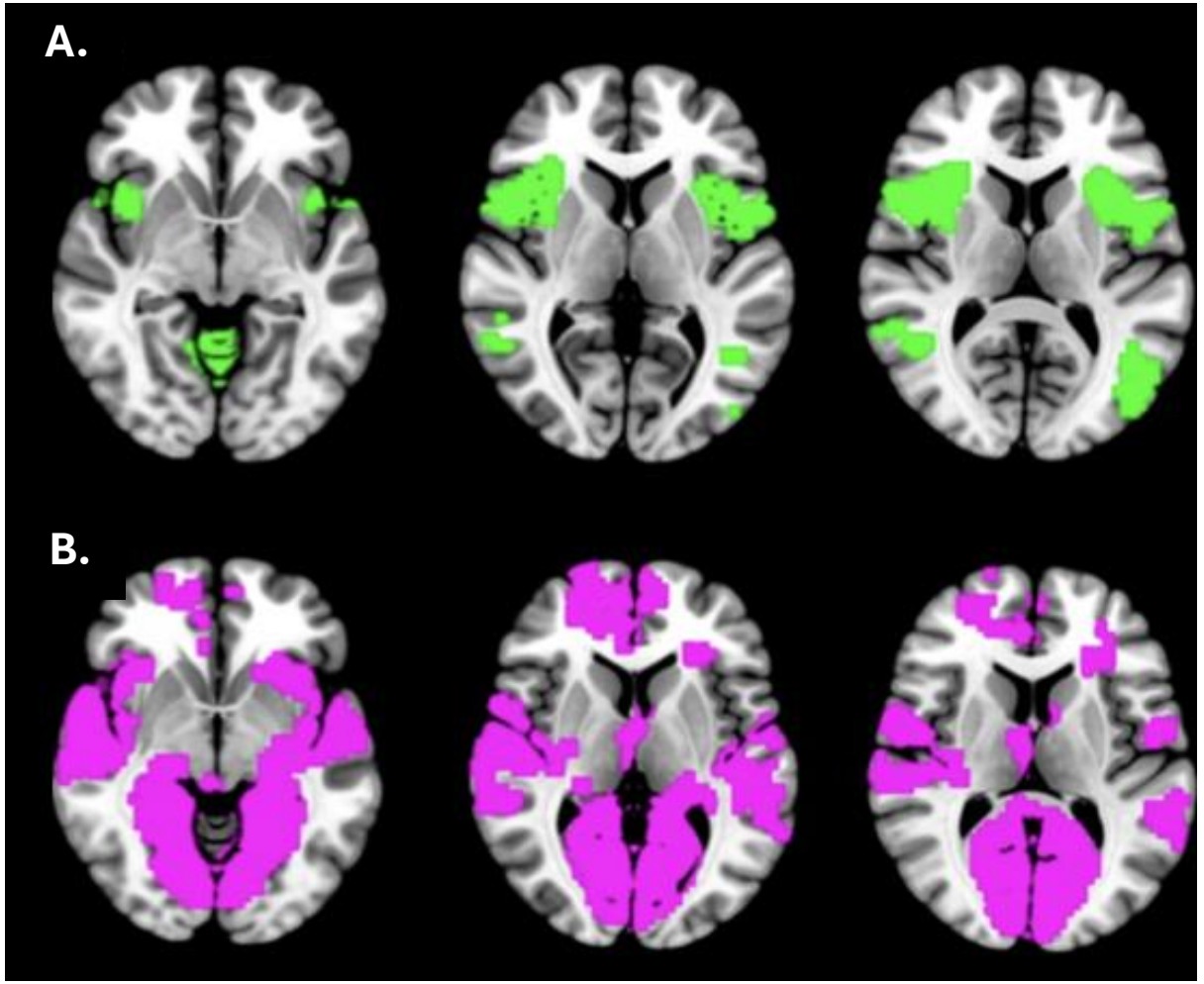
Results of fMRI study of urge-to-blink

A. Blink suppression (contrast: Suppress > Free-to-blink)

   Associated with **bilateral increases** in activity in the **dorsal anterior insula**, the **mid-cingulate cortex**, and **supplementary motor area**

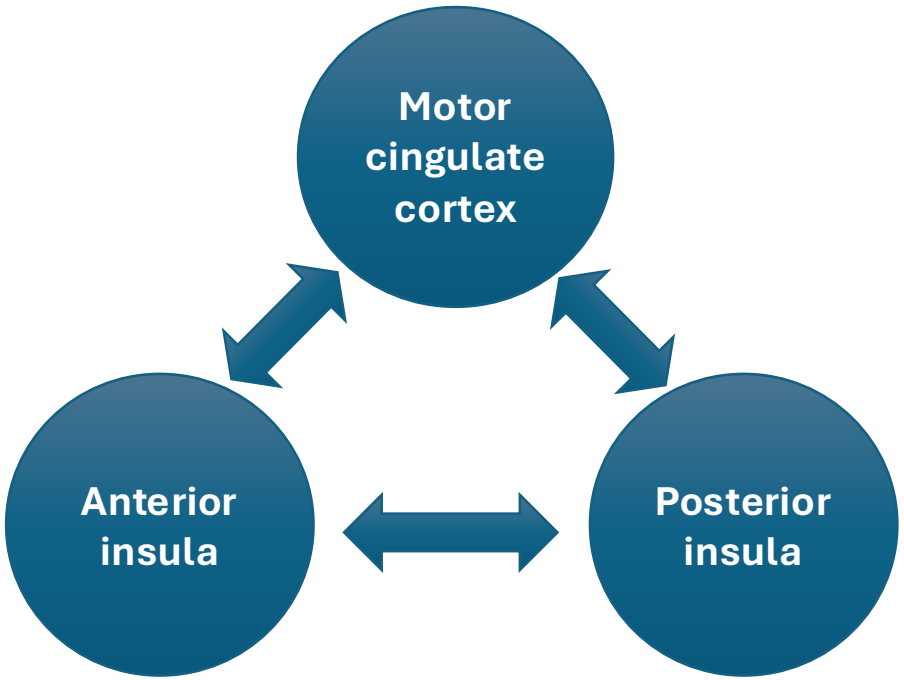
B. Urge-to-blink (Contrast: urge movements > random movements)

   Positively associated with **bilateral increases** of activity in areas that include the **ventral anterior insula** and **posterior insula**



Houlgreave et al. *Imaging Neuroscience*, 2025

Interim conclusions



<u>Conclusions from Study 1</u>

Neural correlates of the urge-to-blink

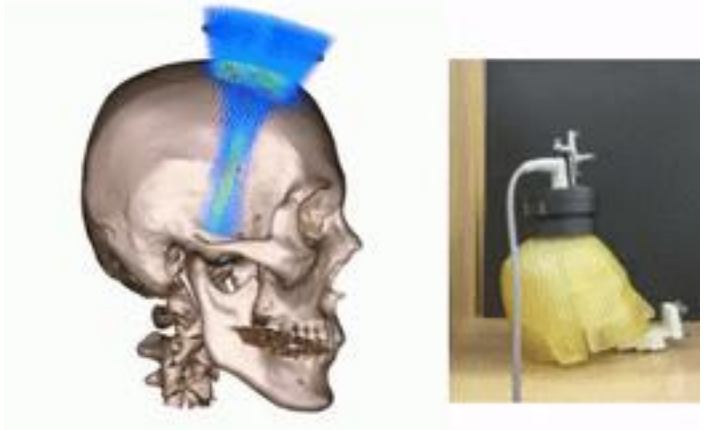
- Sensations may be processed by the **posterior insula** and, through integration of information in the **ventral-anterior insula**, become emotionally salient.
- Connections between the posterior insula and motor cingulate/SMA, may contribute to the release of a blink in response to the urge or to continuation of blink suppression.

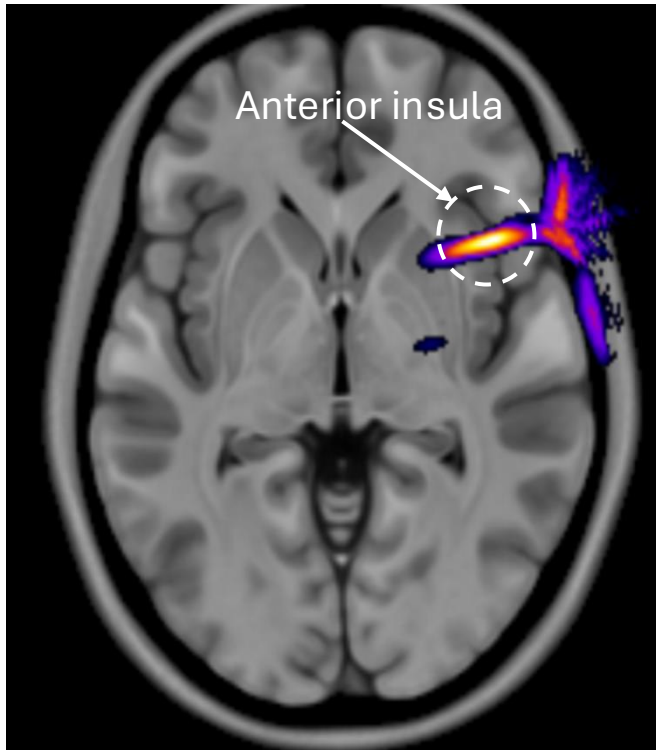
Neural correlates of action suppression

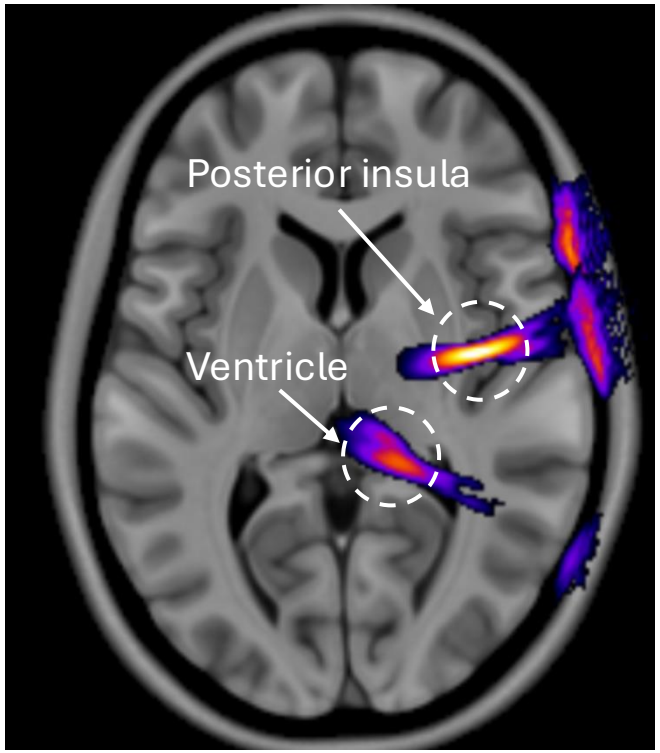
- **Dorsal-anterior insula**, along with inferior frontal cortex, motor cingulate and SMA may contribute to action suppression.

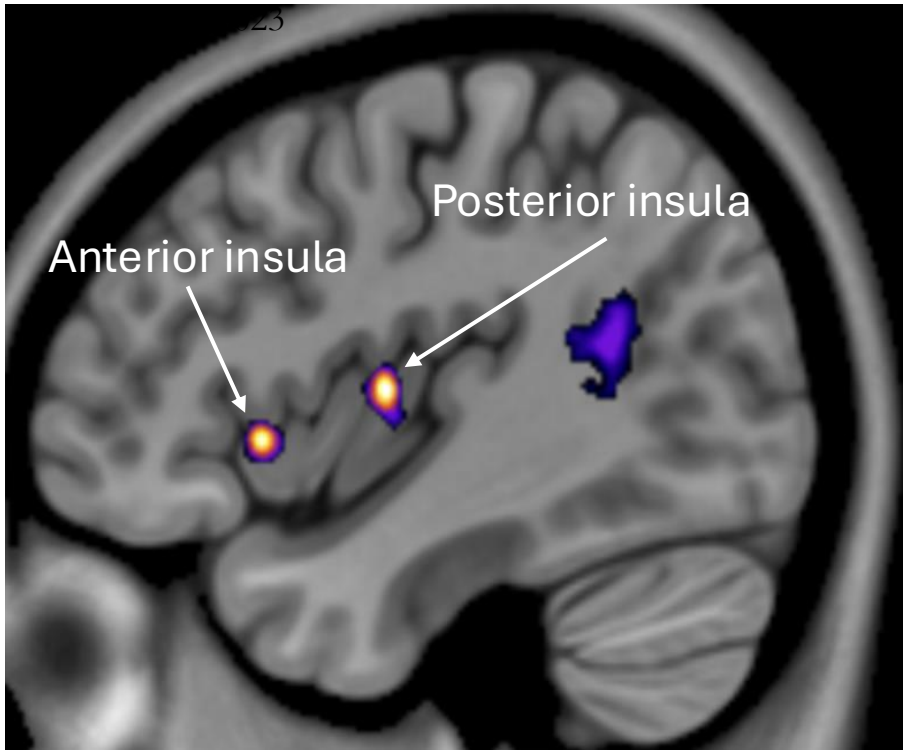
Study 2: Low intensity fUS investigation of blink suppression

- 20 adults underwent 3 fUS sessions targeting:
  - Right anterior insula
  - Right posterior insula
  - Right posterior ventricle (control site)
- Within-subject, crossover design.

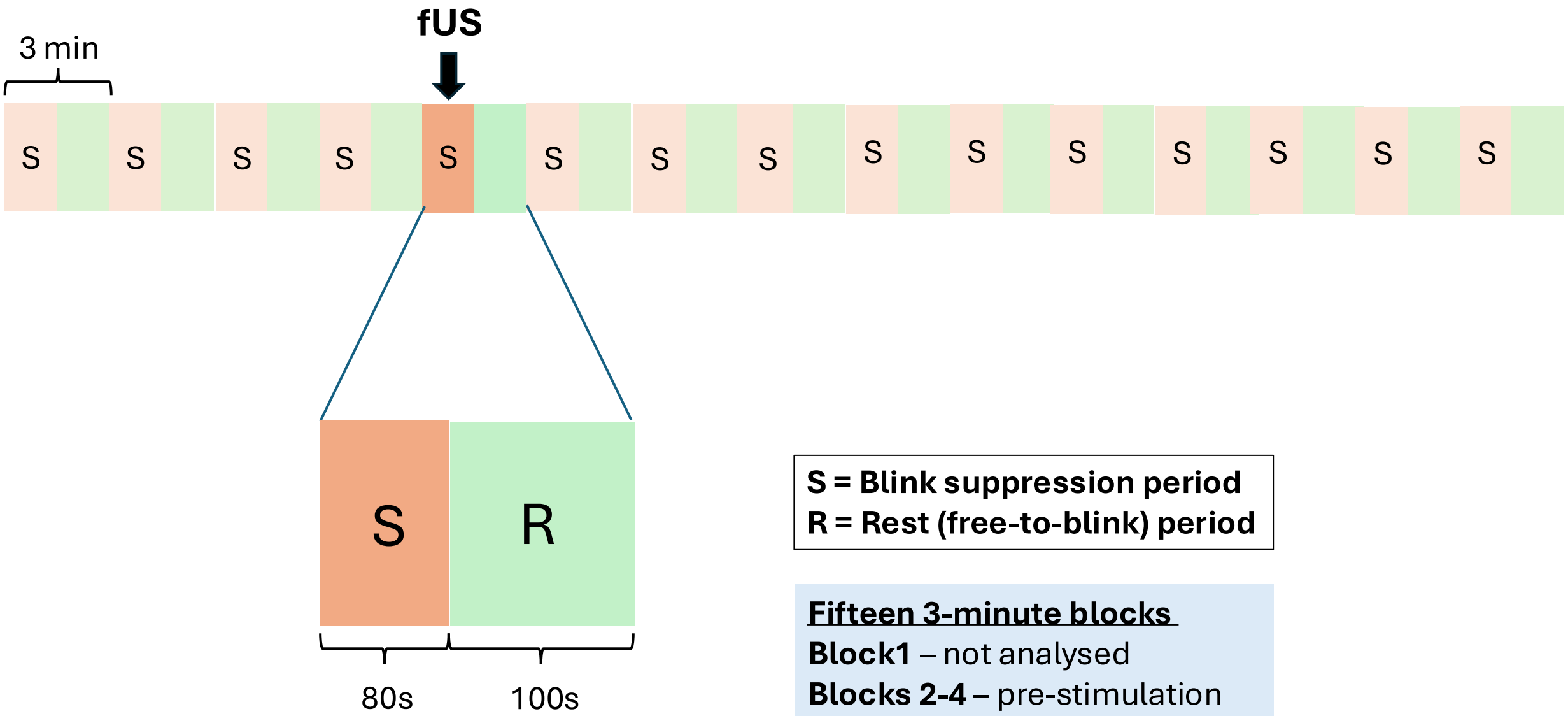








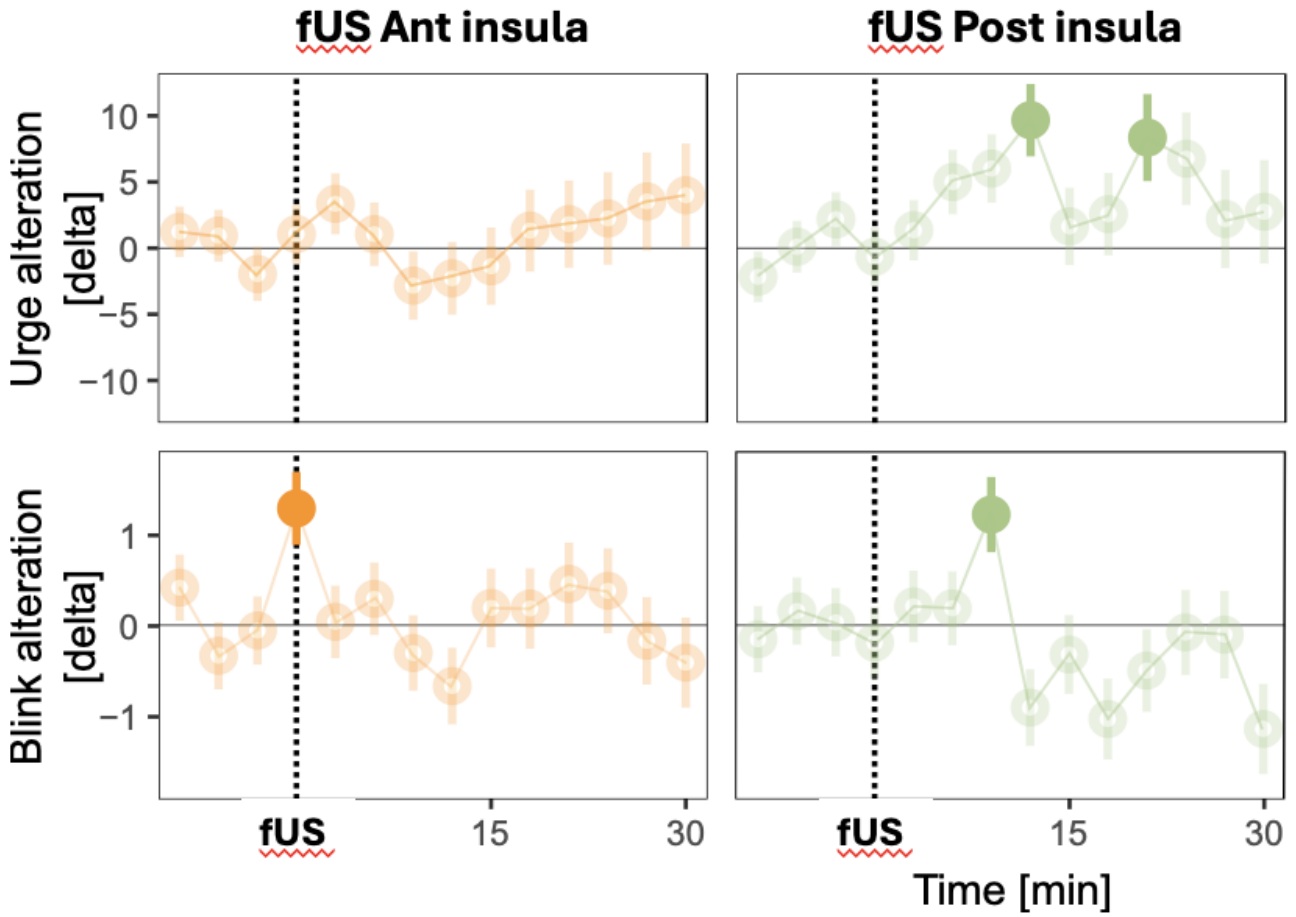
Design for fUS study of blink suppression



S = Blink suppression period
R = Rest (free-to-blink) period

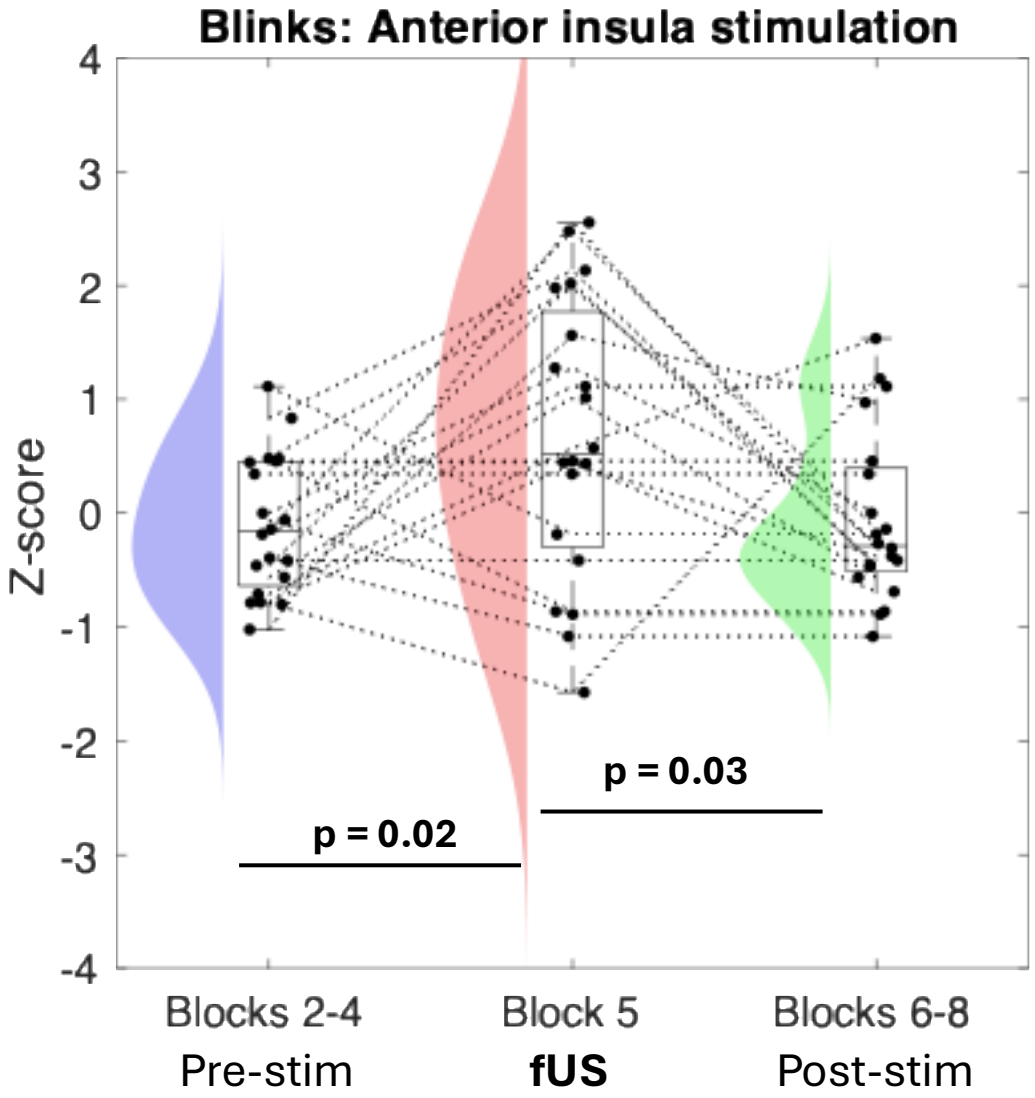
Fifteen 3-minute blocks
Block1 – not analysed
Blocks 2-4 – pre-stimulation
Block 5 – stimulation
Blocks 6-15 – post stimulation

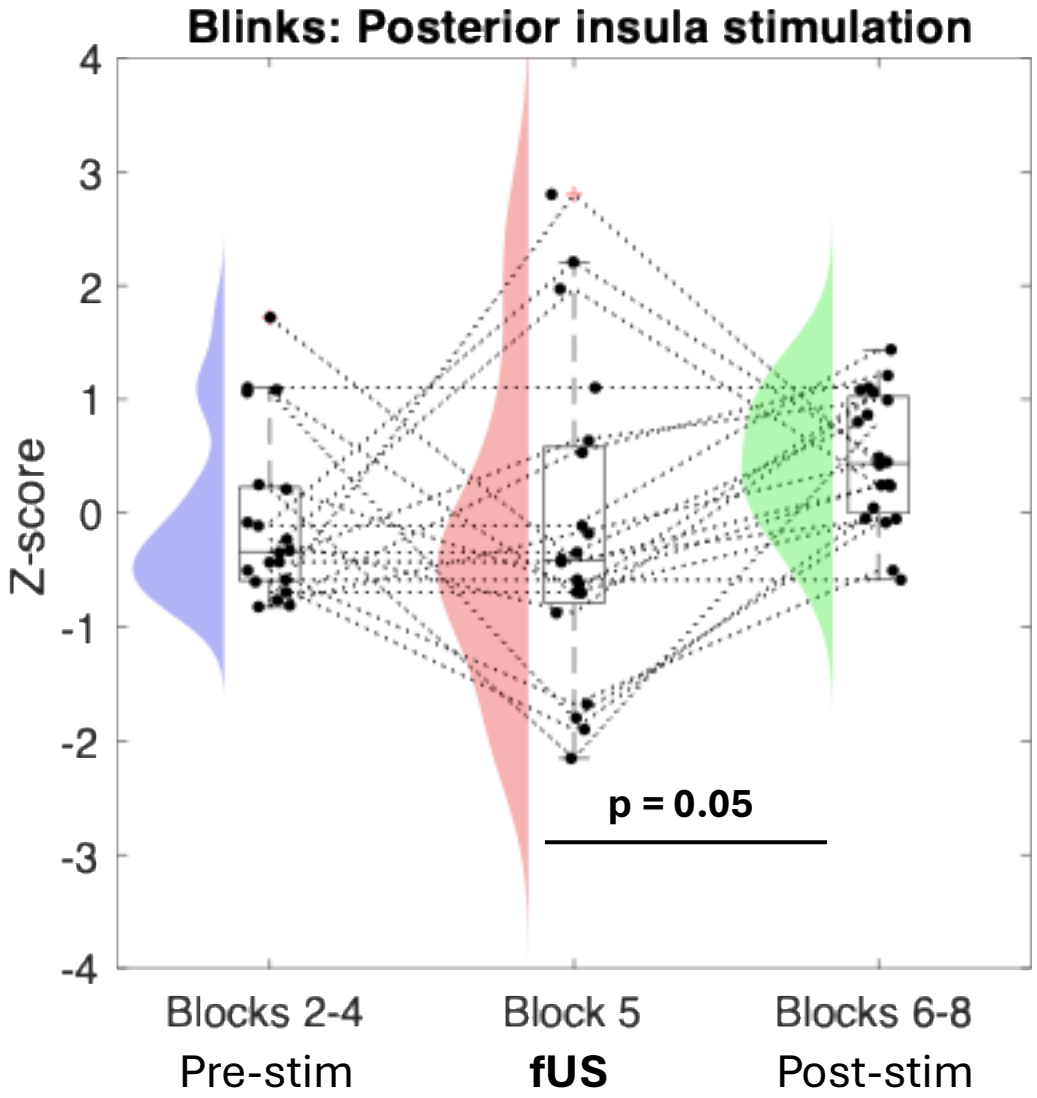
Results: escape blinks and urge estimates **during blink suppression**



- **Anterior insula fUS:** escape blinks **increase** at block 5 (only during fUS); $p < 0.05$
- **Posterior insula fUS:** escape blinks increase at block 8 and urge ratings increase at blocks 9 and 12 (i.e., 12 and 21 minutes after TUS); $p < 0.05$

Results: blinks occurring **during blink suppression blocks**





Summary

- The urge-to-blink increases during blink suppression, but is temporarily removed by ‘escape blinks’
- Blink suppression is associated with increased activation of **dorsal anterior insula**, mid-cingulate cortex, and supplementary motor area.
- Urge-to-blink severity ratings are linked to increased activity in the **ventral anterior insula** and **posterior insula.**
- We speculated that:
    1. Functional connections between insula and motor cingulate may contribute to the release of blinks in response to urges
    2. Anterior insula, along with inferior frontal cortex, motor cingulate and SMA may contribute to action suppression.
- fUS is effective in inducing behavioural changes in deep brain areas such as the insula.
- fUS delivered to the right anterior insula induced an increase in escape blinks during stimulation.
- fUS delivered to the right posterior insula induced an increase in escape blinks and urge ratings after stimulation had ceased.

Team members and research funding

Team members

Mairi Houlgreave

Kat Gialopsou

Cyril Atkinson-Clement

Caitlin Smith

Tourette Association of America

Awareness. Research. Support.

Tourettes action

PARKINSON'S UK

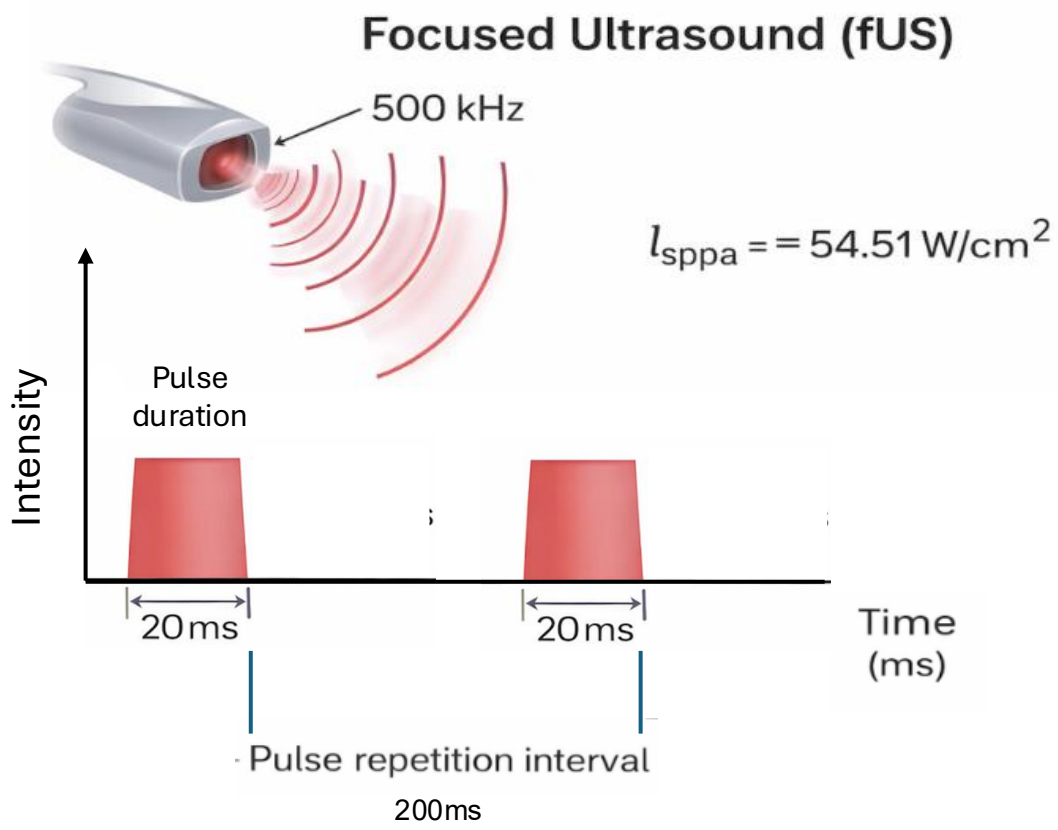
CHANGE ATTITUDES.
FIND A CURE.
JOIN US.

UKRI Medical Research Council

NHS National Institute for Health Research

Key fUS parameters

fUS stimulation protocol	
Parameter	**Value**
Central frequency	500kHz
Spatial peak pulse average intensity (Isppa)	54.51W/cm^2
Pulse duration	20ms
Pulse repetition interval	200ms
Pulse repetition frequency	**5Hz**
Duty cycle	**10%**
Total stimulation duration	**80s**



Duty cycle 10% (20ms / 200ms)

Total duration: 80 seconds