Pain Center

Yes or No?

Park Jun Hyeok
Lee Jaejun
Jule Brenningmeyer

The dorsal posterior insula subserves
a fundamental role in human pain
(Segerdahl et al. 2015)

hypothesis

regions showing a significant coupling
between absolute cerebral blood flow (CBF)
and the intensity of tonic pain experienced
would be well suited to be candidate
pain-specific brain regions.

baseline (7 min): before capsaicin was applied to the lower right leg region

pain onset (21 min): immediately after capsaicin application

pain peak (7 min): peak of the capsaicin pain experience

…

habituation (7 min): image the late pain state

rekindle (7 min): application of a warming water bottle to the site of capsaicin application

relief (7 min): application of a cooling water bottle to the site of capsaicin application
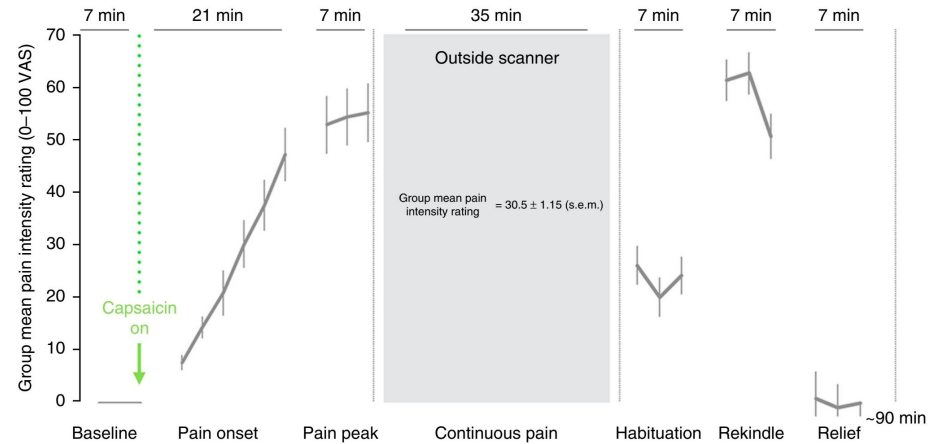

Figure shows the group mean tonic pain intensity ratings over time. Results confirm that the manipulation of the pain state was robust and consistent across participants.

Voxels with supra-threshold activation are shown in red. The only significant positive correlation between absolute CBF changes and pain ratings within subjects was observed in the **contralateral dpIns.** (**contralateral dpIns** showed a strong correlation between absolute CBF and pain ratings.)

(linear regression, mixed effects, z > 2.3, P < 0.01)

a

R   L

y = −20

5

2.3

x = −34

Contralateral hemisphere   z = 18

The correlation plotted in **Figure b.**
A plot of the group mean tonic pain ratings versus the absolute CBF in the contralateral dpIns.

b

Group mean CBF
(ml per 100 g per 60 s)

Group mean pain intensity rating
(0–100 VAS)

*dpIns (dorsal posterior insula)

c
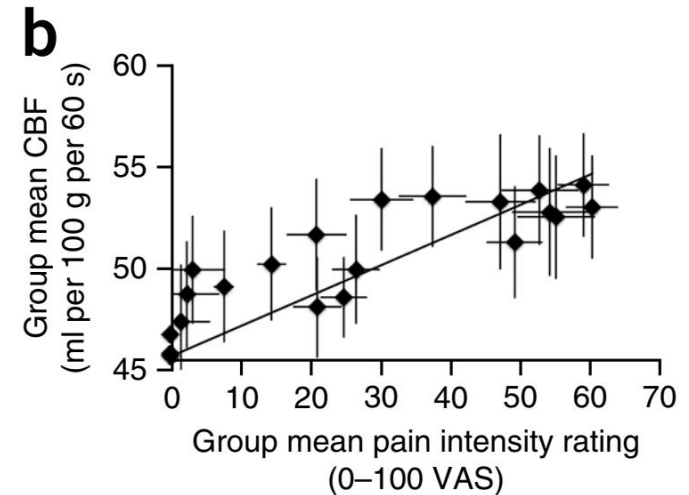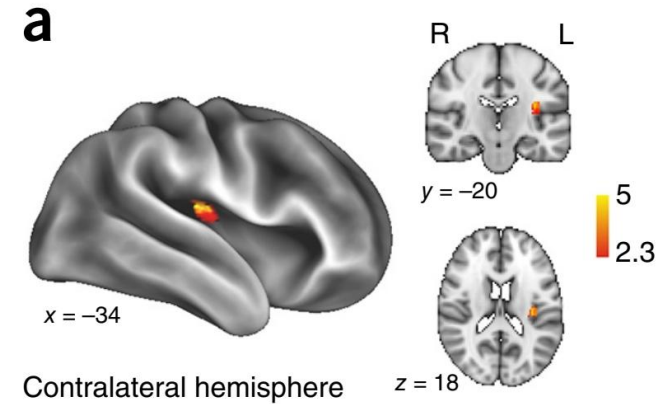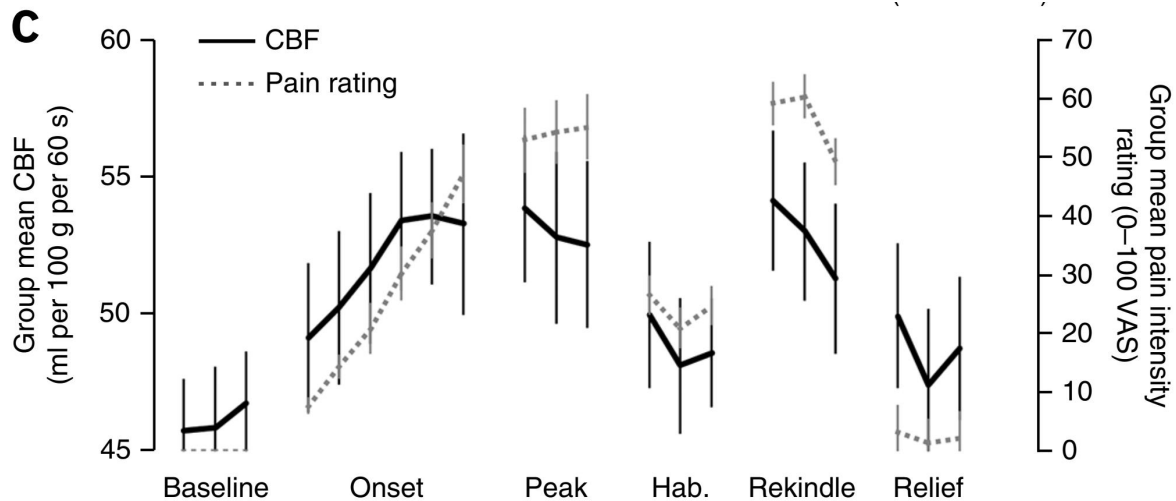
Group mean absolute CBF extracted from the peak contralateral dpIns cluster alongside the ongoing pain intensity ratings. Error bars represent the standard error of the means.

Previous work, tract tracing studies in monkeys has defined a nociceptive-specific cortical representation of incoming sensory stimuli that is modality, intensity and location specific. **This is in a subregion of the dpIns.**

a somatotopy for nociceptive inputs in **the posterior insula** exists for cutaneous and intramuscular stimuli; intra-cortical recordings in epilepsy patients show that electrical stimulation of this region **triggers pain** at specific body sites and lesions here **alter pain experiences**.

<u>Conclusion</u>
a subsection of **the posterior insula** is both anatomically and functionally well suited to serve a primary and fundamental role in **pain processing**

Matthew D. Lieberman[1] and Naomi I. Eisenberger

Department of Psychology, University of California, Los Angeles, CA 90095-1563

"The dorsal anterior cingulate cortex is selective for pain : Results from large-scale reverse inference"

Contents

Introduction

> dACC(Dorsal anterior cingulate cortex) activation
observed in many different studies of 'pain, executive control, conflict monitoring and salience processing'
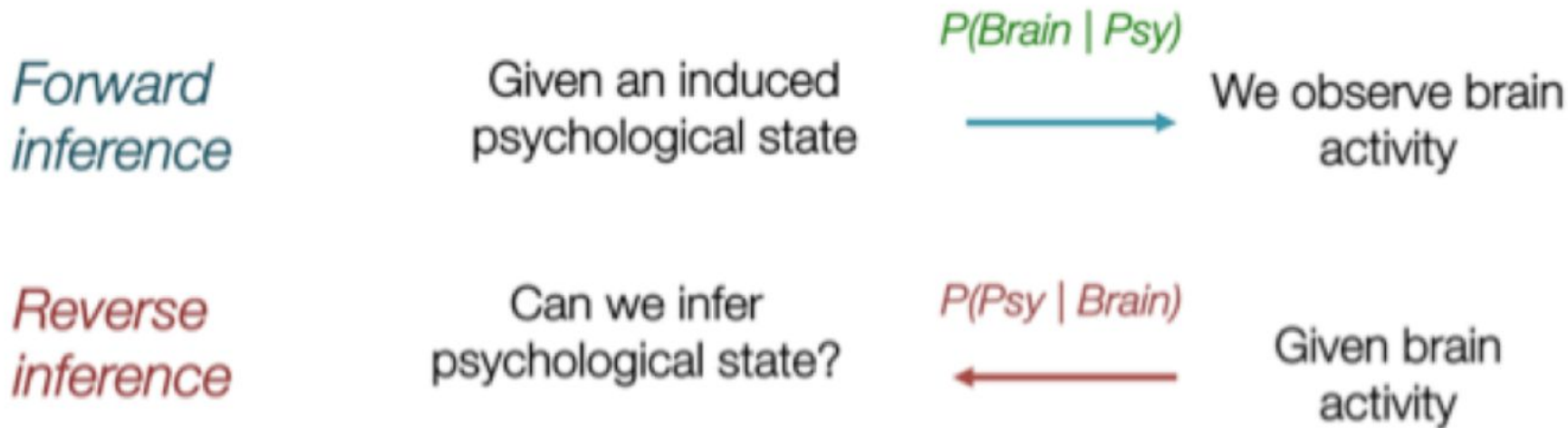→ Difficult to interpret dACC's specific psychological function

> Neurosynth (Neurosynth.org)

- an automated brainmapping database (of over 10,000 fMRI studies)
- Using Bayesian classifier, able to identify which psychological processes were likely to have been invoked when activity in a particular brain region was present (across 10,903 studies in the database)

Introduction

Forward inference — Given an induced psychological state — $P(Brain \mid Psy)$ → We observe brain activity

Reverse inference — Can we infer psychological state? ← $P(Psy \mid Brain)$ — Given brain activity

→ Best psychological description of dACC function : **Pain**

Step 1: Locating the dACC

A: Anatomical outlines of
   dACC, Supplementary motor area(SMA),
   and Presupplementary motor area(pre-SMA)

- Close alignment between anatomically defined
  and Neurosynth-derived boundaries
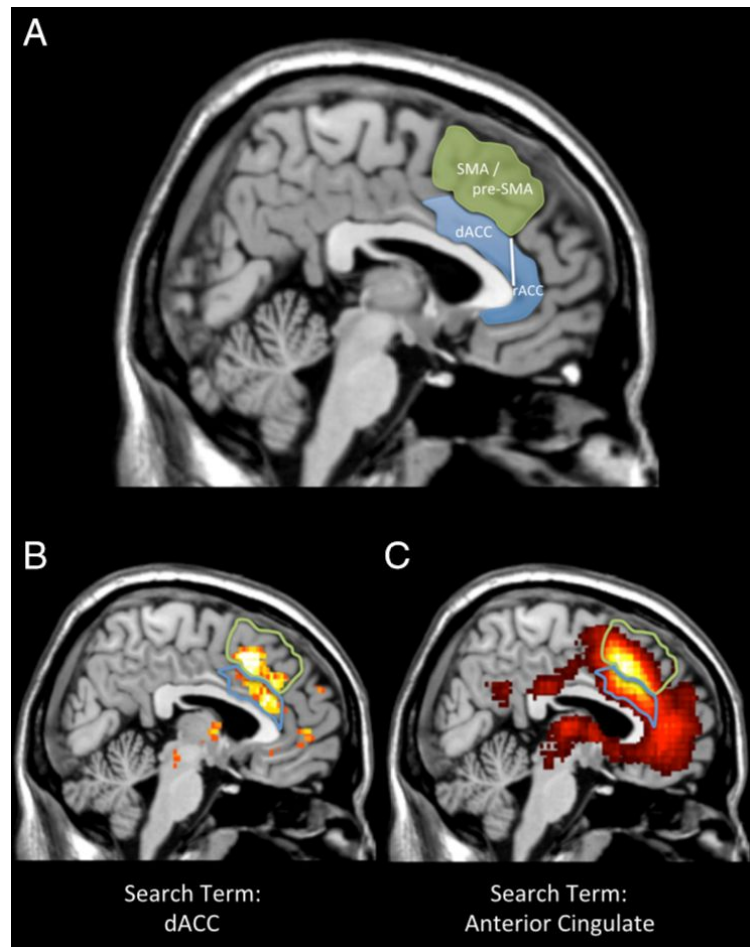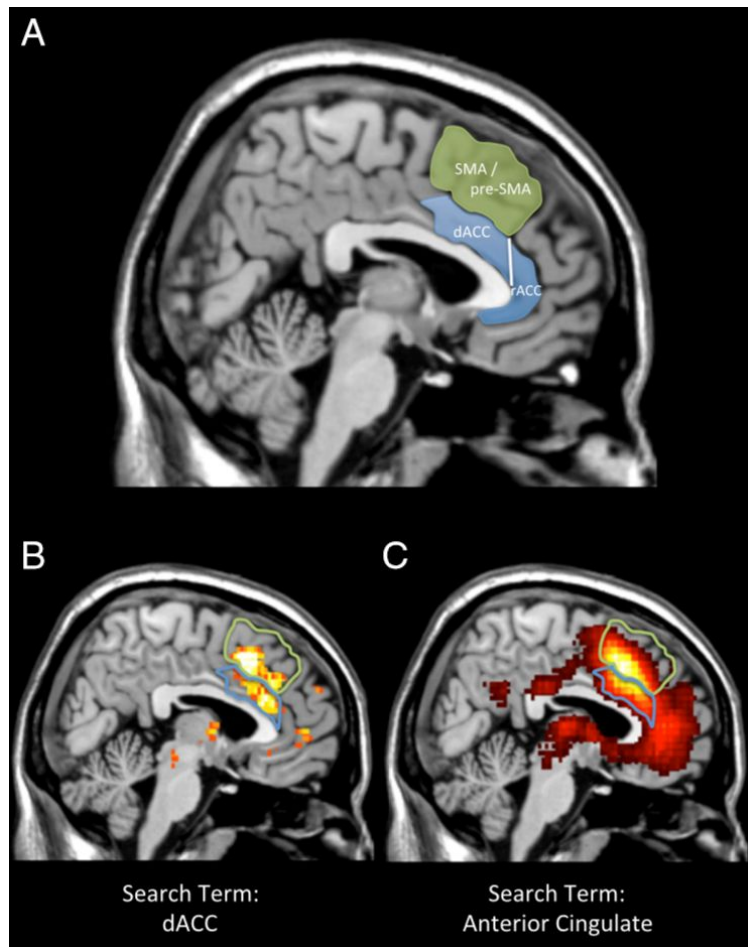
Step 1: Locating the dACC

Forward Inference analysis

B: Active regions of term "dACC"

C: Active regions of term "Anterior Cingulate"

- Neuroimaging literature mislabeled the location of dACC
- Studies on dACC are more likely to be reporting SMA/pre-SMA activations

→ Misunderstanding/Disagreement of dACC functionality

Step 2: Forward Inference in the dACC

Standard problem with dACC activation
: Variety of different psychological processes

By using Neurosynth
- Some processes have modest footprint
("Working memory", "Effort", "Stop signal", "Stroop",
"Salience", "Auditory", "Tactile")

→ In general, still various psychological tasks
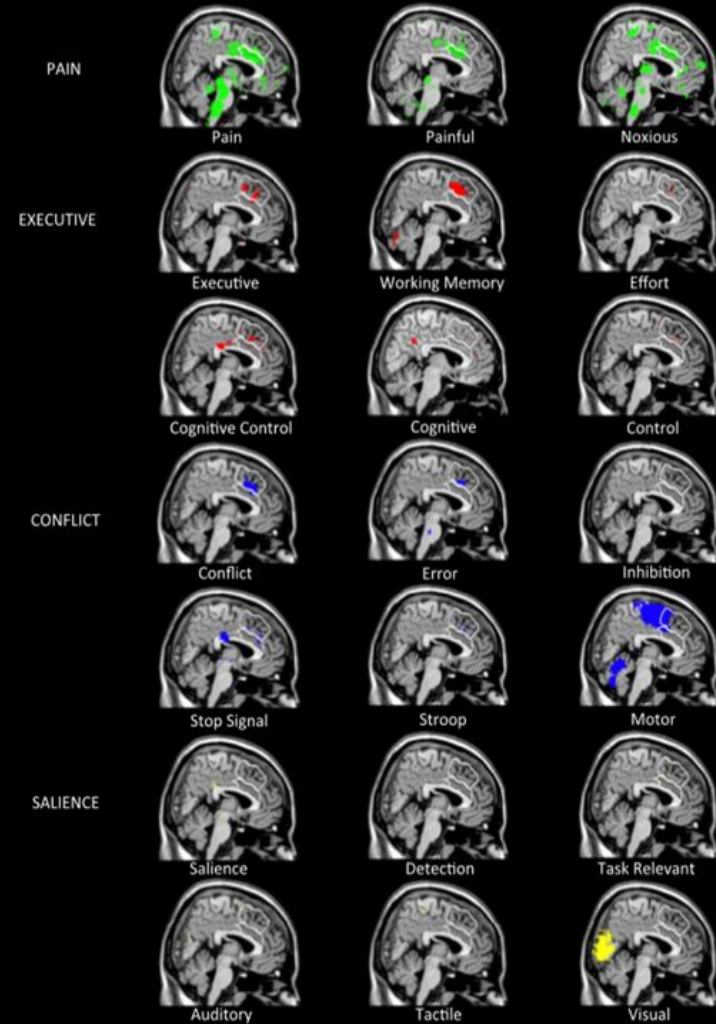activate dACC
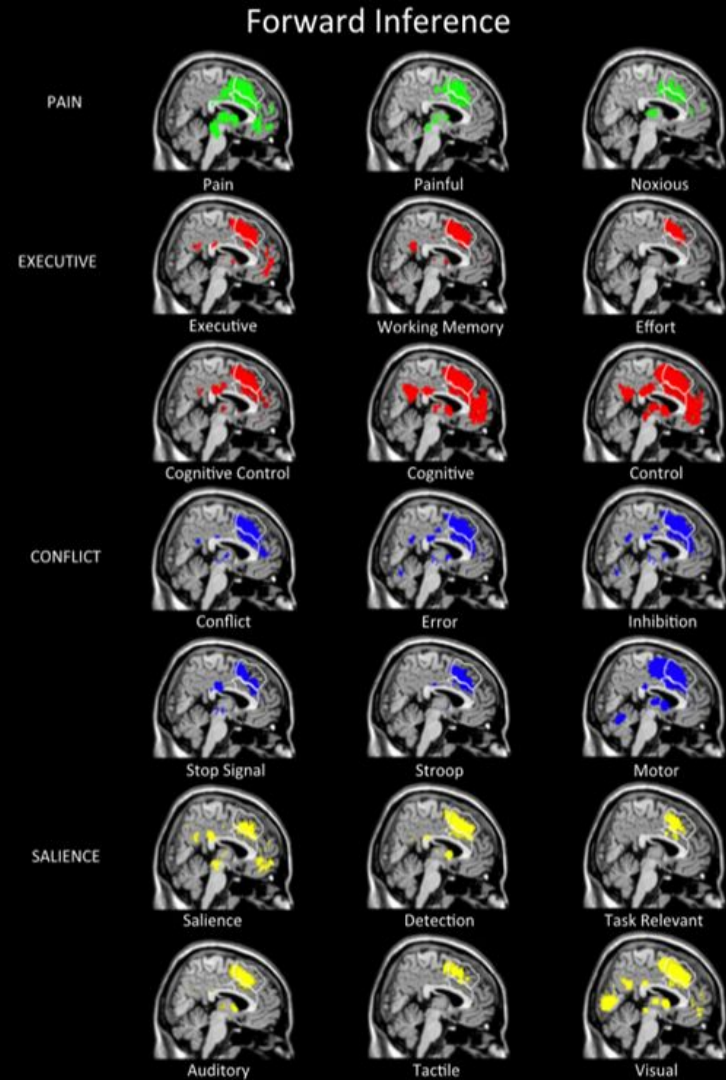
Step 3: Reverse Inference in the dACC

- The only psychological phenomenon that can be reliably inferred given the presence of dACC activity is **Pain**
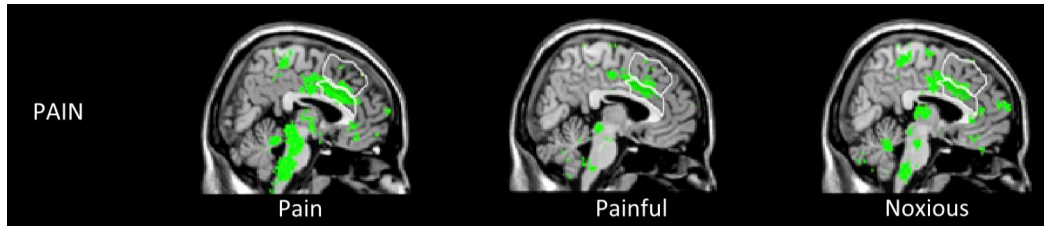
Comparison of reverse inference effects throughout the dACC

A: plotting the posterior probabilities at 8 different foci for each of the four terms.

Bayesian prior normed to 0.5, threshold: Z> 3,1, P <0,001 , "ns" means not significant

➜ posterior probabilities of pain is in 7 out of 8 foci significant higher

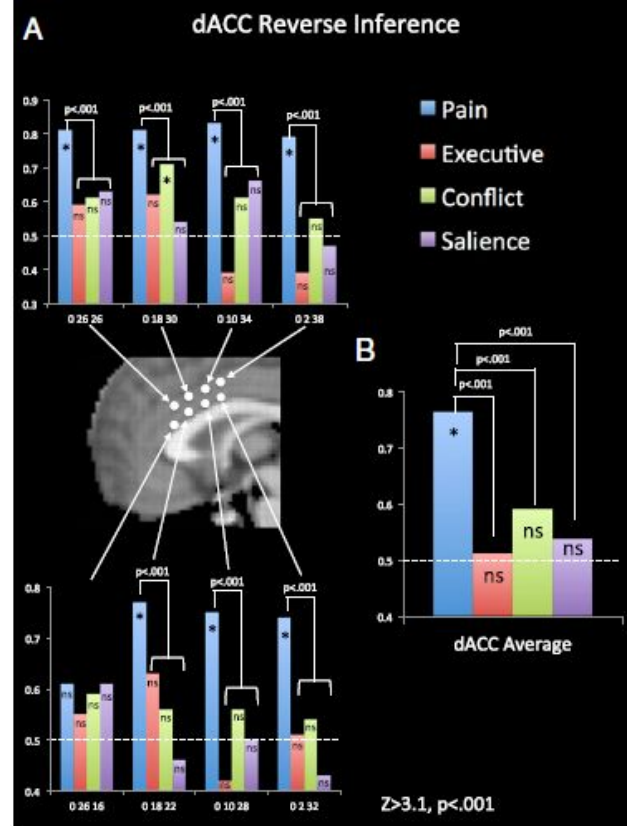➜ dACC activity in 7 out of 8 foci can be attributed to pain

Fig. 5. Comparison of reverse inference effects throughout the dACC. (*A*) Plotted posterior probabilities from Neurosynth reverse inference maps for pain, executive, conflict, and salience processes at eight foci on the midline of dACC. MNI coordinates are listed on the bar graphs. The dashed lines at 0.50 indicate the null hypothesis (i.e., no reverse inference evidence). All starred bars (*) had Z-scores of ≥3.1, P < 0.001, and "ns" indicates not significant at this threshold. For each location where "pain" was a reliable reverse inference term, "pain" was also a significantly stronger reverse inference term than all other terms (P < 0.001). (*B*) The average posterior probabilities across the eight foci for pain, executive, conflict, and salience.

B: Plotting the average of the posterior probabilities for each psychological term across the eight foci in the dACC.

➔ Still just pain is significant

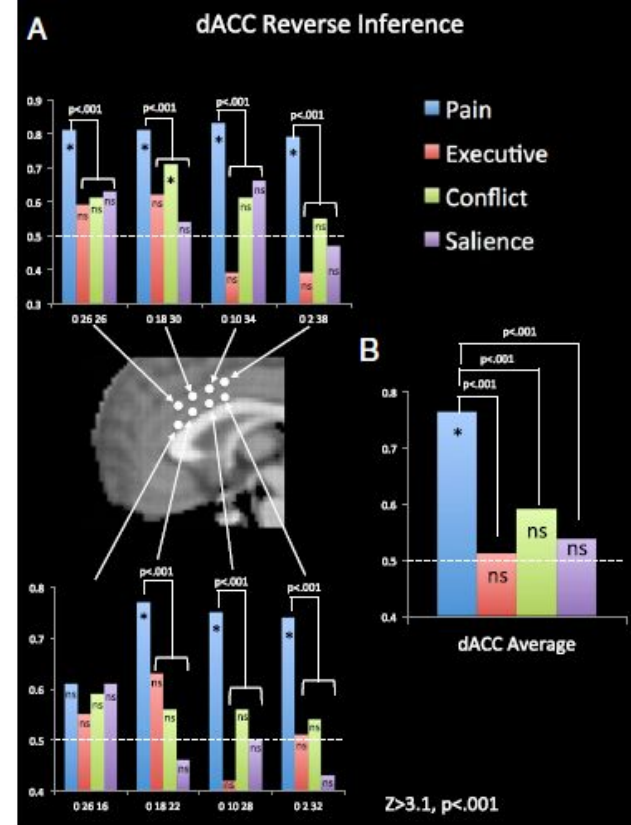**conclusion:** dACC is involved in pain processing

Fig. 5. Comparison of reverse inference effects throughout the dACC. (A) Plotted posterior probabilities from Neurosynth reverse inference maps for pain, executive, conflict, and salience processes at eight foci on the midline of dACC. MNI coordinates are listed on the bar graphs. The dashed lines at 0.50 indicate the null hypothesis (i.e., no reverse inference evidence). All starred bars (*) had Z-scores of ≥3.1, $P < 0.001$, and "ns" indicates not significant at this threshold. For each location where "pain" was a reliable reverse inference term, "pain" was also a significantly stronger reverse inference term than all other terms ($P < 0.001$). (B) The average posterior probabilities across the eight foci for pain, executive, conflict, and salience.

Arbitrary vs. Survival Goal Conflicts

- the most speculative aspect of the article
- The dACC is phylogenetically older than the SMA/pre-SMA
- In reverse inference maps the activity of dACC and SMA/pre-SMA points to psychological responses to goal conflicts, but they respond to qualitatively different forms of conflict
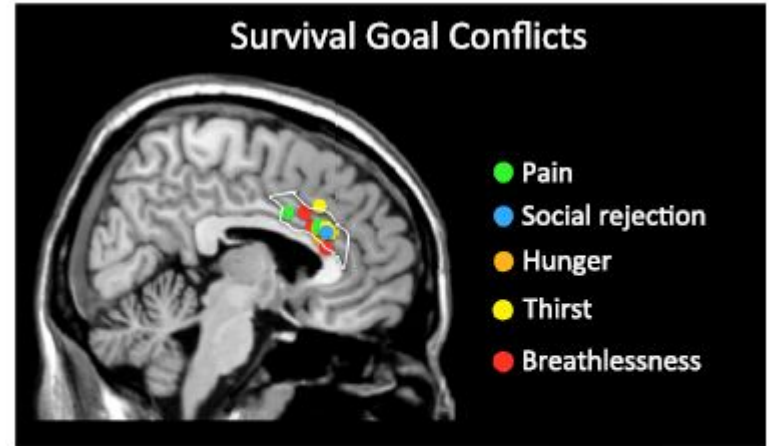

Survival Goal Conflicts

- Pain
- Social rejection
- Hunger
- Thirst
- Breathlessness

Fig. 6. Survival-relevant goal conflicts in the dACC. Several survival goal conflicts produce activations in the dACC. Pain foci were derived from the two strongest reverse inference effects from Neurosynth. Social rejection activation comes from a meta-analysis (34). Hunger (35), breathlessness (36–38), and thirst (39–41) foci all come from individual studies.

Arbitrary vs. Survival Goal Conflicts

- The dACC seems to play more of a role in permanent survival-relevant goal conflicts whereas the SMA plays more of a role in flexible temporary goal conflicts.
- it would be expected that, when other survival-relevant goals are threatened the dACC would be activated.
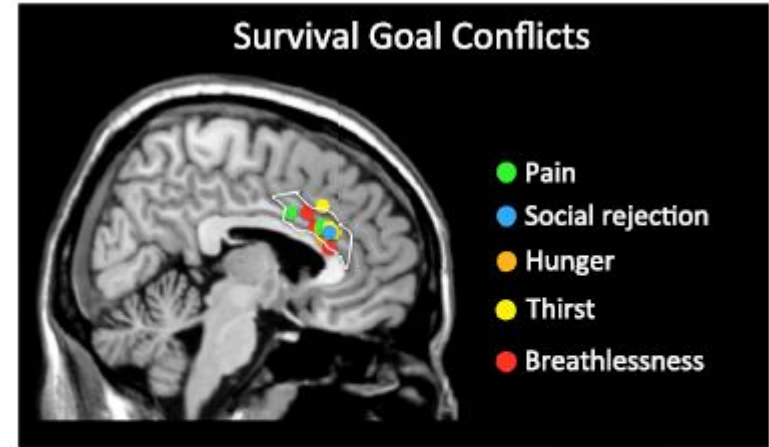

Fig. 6. Survival-relevant goal conflicts in the dACC. Several survival goal conflicts produce activations in the dACC. Pain foci were derived from the two strongest reverse inference effects from Neurosynth. Social rejection activation comes from a meta-analysis (34). Hunger (35), breathlessness (36–38), and thirst (39–41) foci all come from individual studies.

Limitations

- **Neurosynth: activations and deactivations will be treated the same way.**
➔ Creators provide robust quantitative reverse inference data.

- **Different terms have different base rates within Neurosynth. This can produce different strong reverse inference effects.**
➔ Neurosynth setts the Bayesian prior to 0.5 for every term in the database, so high frequency terms don't overwhelm rare terms in reverse inference analyses.

- **It is possible that more tightly defined constructs produce reverse inference effects more easily.**
➔ This does not affect the outcome, because loosely and tightly defined constructs failed to produce dACC reverse inference.

Conclusions

- Articles using the term "dACC" may be mistakenly labeling the SMA/pre-SMA as the dACC. (Step 1)
- Many tasks reliably activate the dACC. (Step 2)
- The best interpretation of dACC activity is in terms of pain processes. (Step 3)

➔ The clearest account of dACC function is, that it is selectively involved in pain-related processes.