# Social Cognition: Vulnerable Networks Involved in FTD

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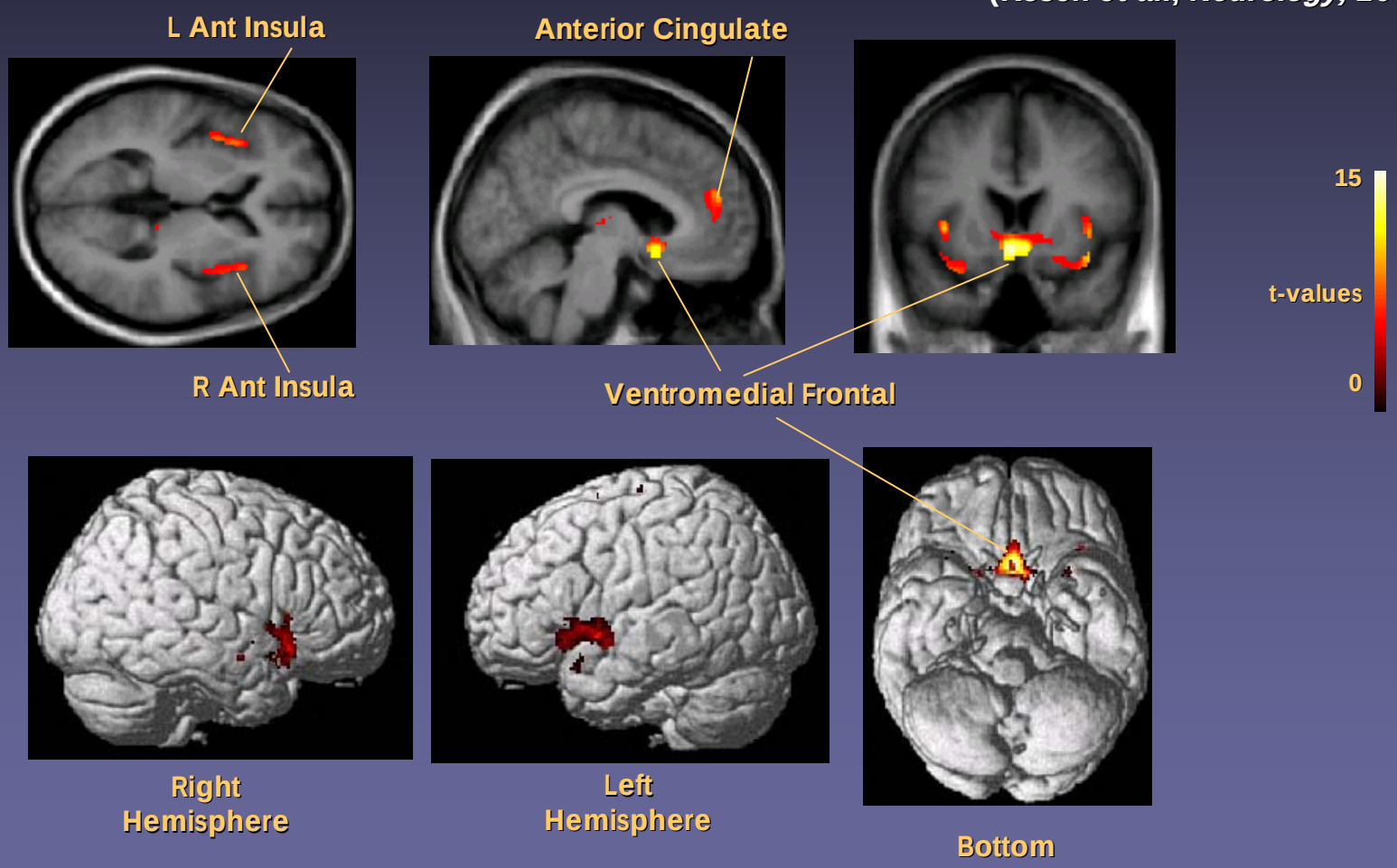
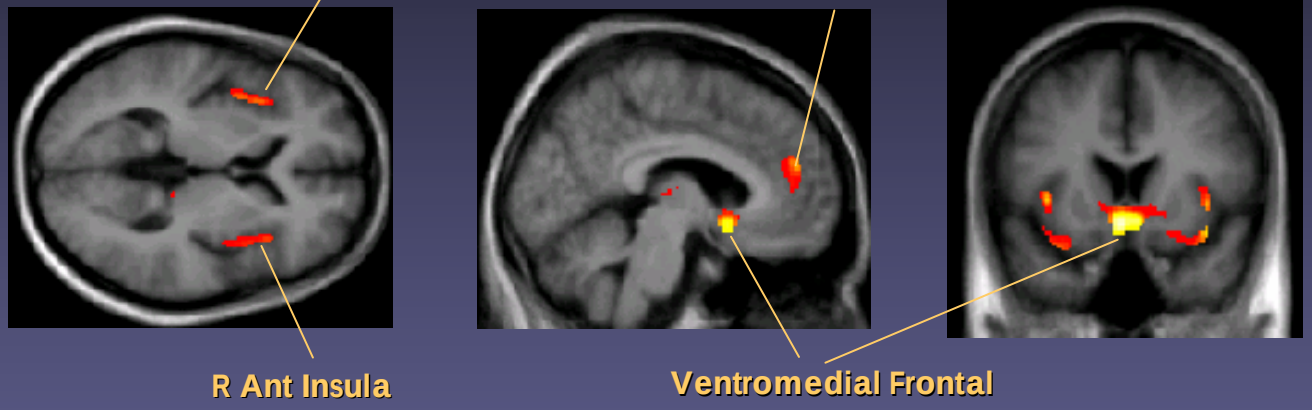
# Early FTLD

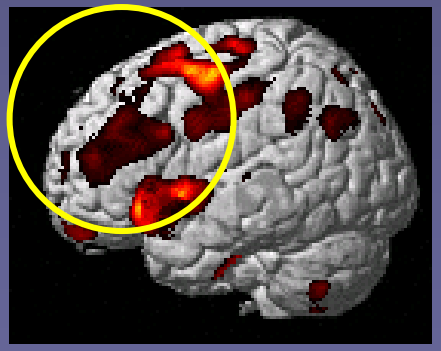
(Rosen et al., *Neurology,* 2002)



# Early Frontotemporal Dementia

(Rosen et al., *Neurology,* 2002)

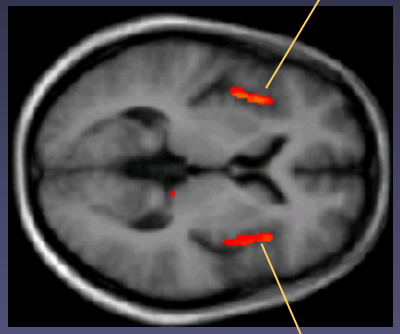


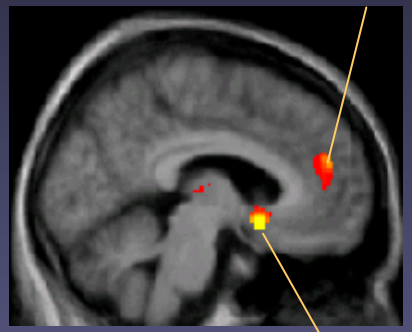



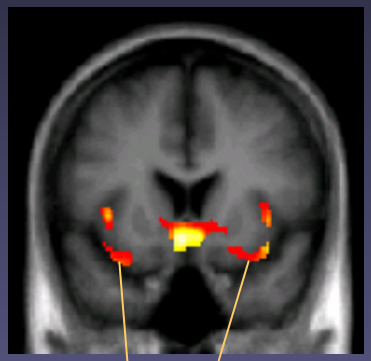
Dorsolateral frontal atrophy, corresponding to standard neuropsychological tests of executive functioning, occurs later in the course of FTD

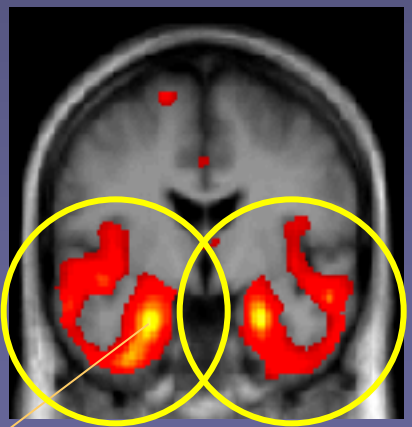
# Early Semantic Dementia

(Rosen et al., *Neurology,* 2002)




While SD is defined as a language disorder, a subset of patients initially present with unilateral right temporal disease

# Clinicopathologic Correlations

## Core Diagnostic Features – FTD

A. Insidious onset and gradual progression
B. Early decline in social interpersonal conduct
C. Early impairment in regulation of personal conduct
D. Early emotional blunting
E. Early loss of insight

## Supportive diagnostic features – SD

B. Behavioral disorder
    1. Loss of sympathy or empathy
    2. Narrowed preoccupations
    3. Financial parsimony

(Neary et al., 1998)

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# Assessment of social cognition is essential to early and accurate diagnosis

- Many neurodegenerative disease patients show behavioral changes, some of them social and emotional
- We need a sophisticated clinical understanding of the various profiles associated with all these diseases to improve our diagnostic accuracy in atypical or mixed cases – “personality change” is not specific enough to be useful
- These important behavioral symptoms have not been operationalized yet
  - Currently assessed qualitatively via clinical interviews
  - We need tests that are objective, standardized, repeatable

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# Measuring social cognition: empathy

## Interpersonal Reactivity Index (Davis, 1983)

- Perspective Taking:
  - "The patient believes there are two sides to every question and tries to look at them both."
- Empathic Concern:
  - "If the patient sees someone being taken advantage of, they feel protective towards them."

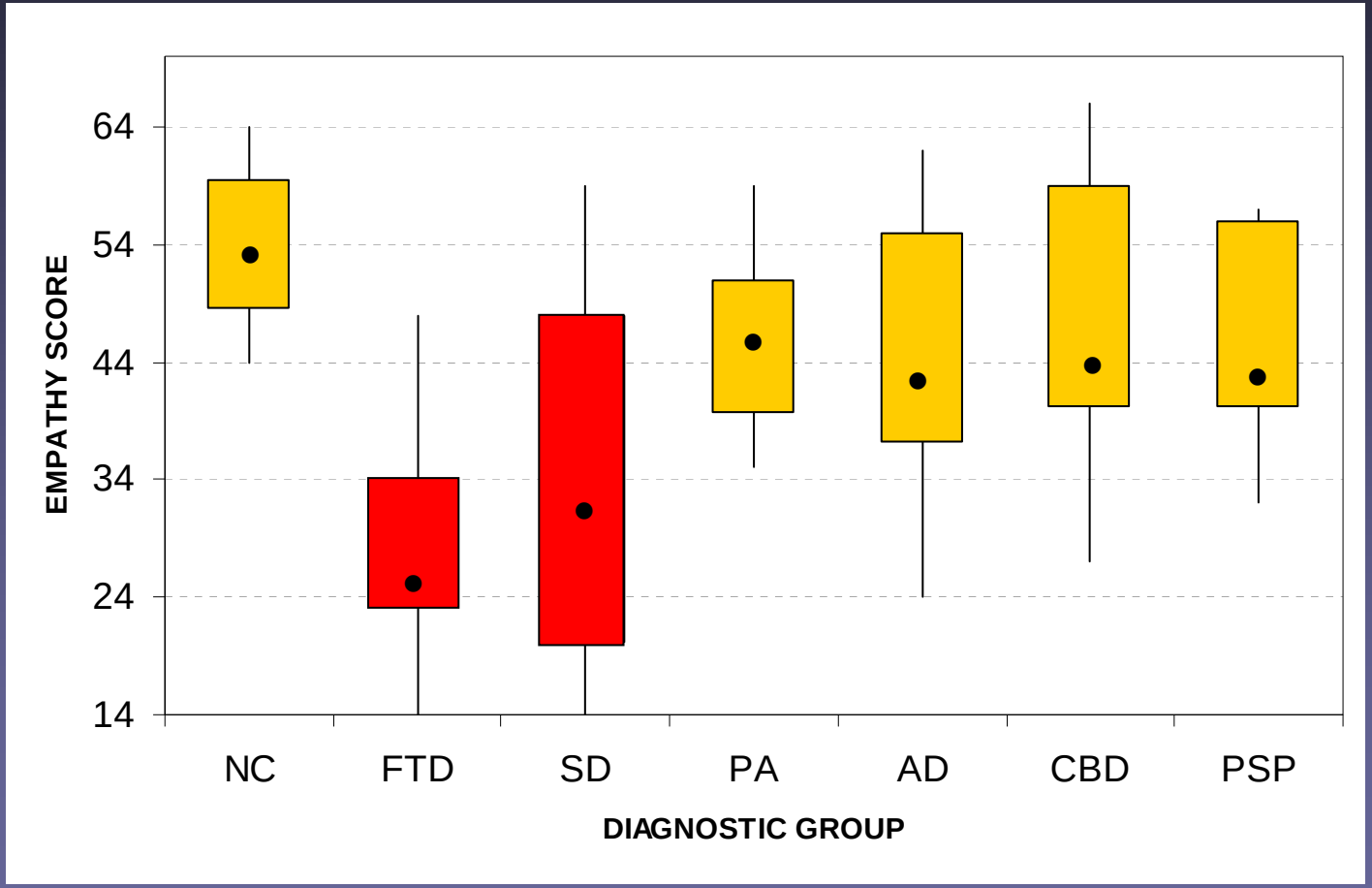
# Measuring social cognition: empathy

METHODS

- 123 patients from the UCSF Memory & Aging Center (30 FTD, 26 SD, 8 PNFA, 38 AD, 15 CBD, 6 PSP)
- Caregivers filled out IRI questionnaire evaluating patients' current level of empathy
- All patients underwent T1-weighted MP-RAGE MRI
- Voxel-based morphometry
  - Brain volumes analyzed using IRI scores as covariate of interest (continuous)
  - Controlling for age, sex, and total intracranial volume

(Rankin et al., Brain, 2006)

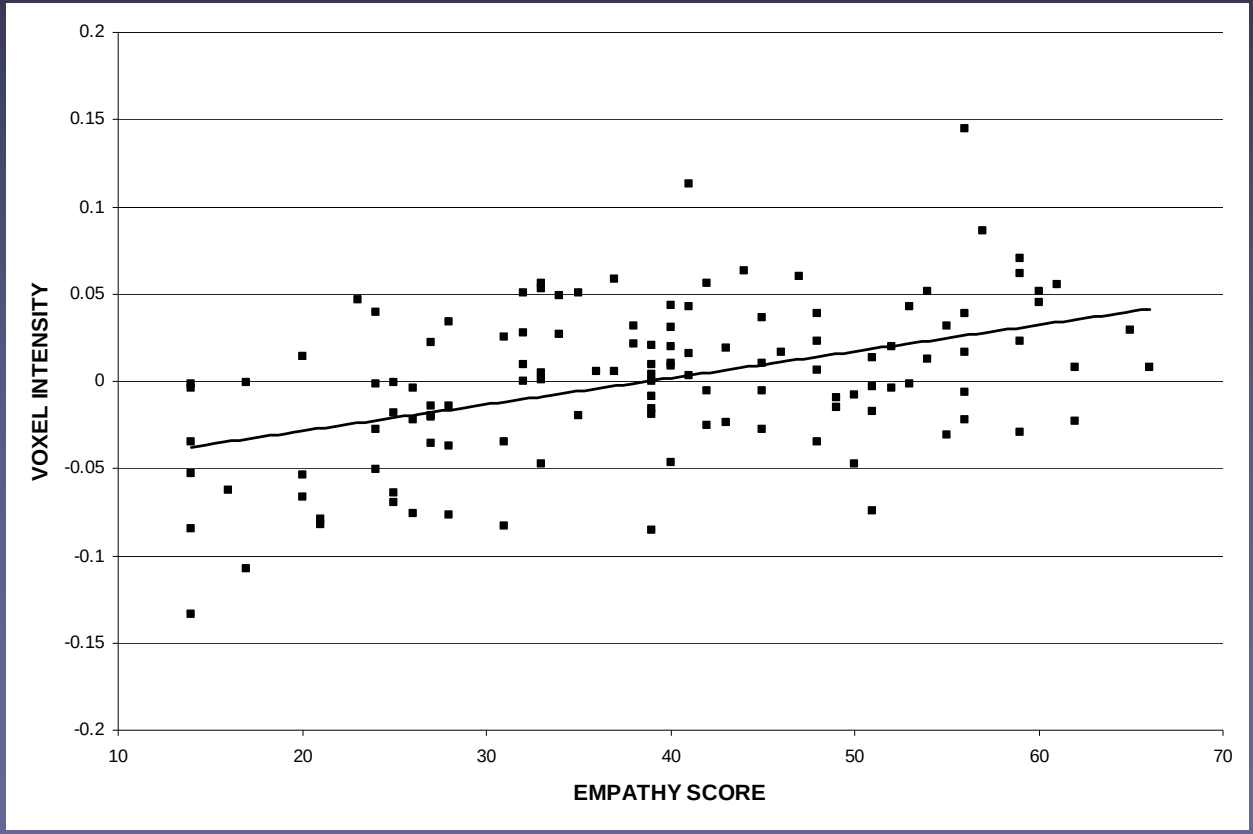
# Measuring social cognition: empathy




(Rankin et al., Brain, 2006)

# Measuring social cognition: empathy

Empathy score vs. volume at a sample voxel in the right temporal pole (58, 10, -33) adjusted for age, sex, and TIV




(Rankin et al., Brain, 2006)

# Regions where empathy score positively correlates with tissue density

(Analysis significant after FWE correction at p<0.05)

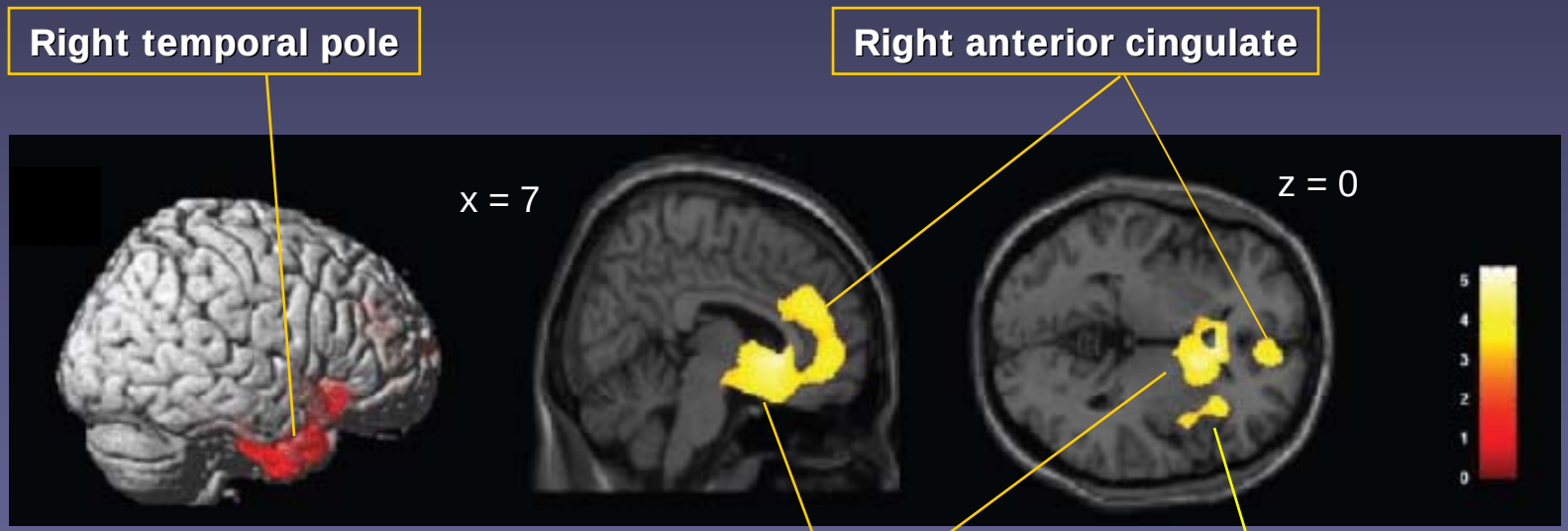
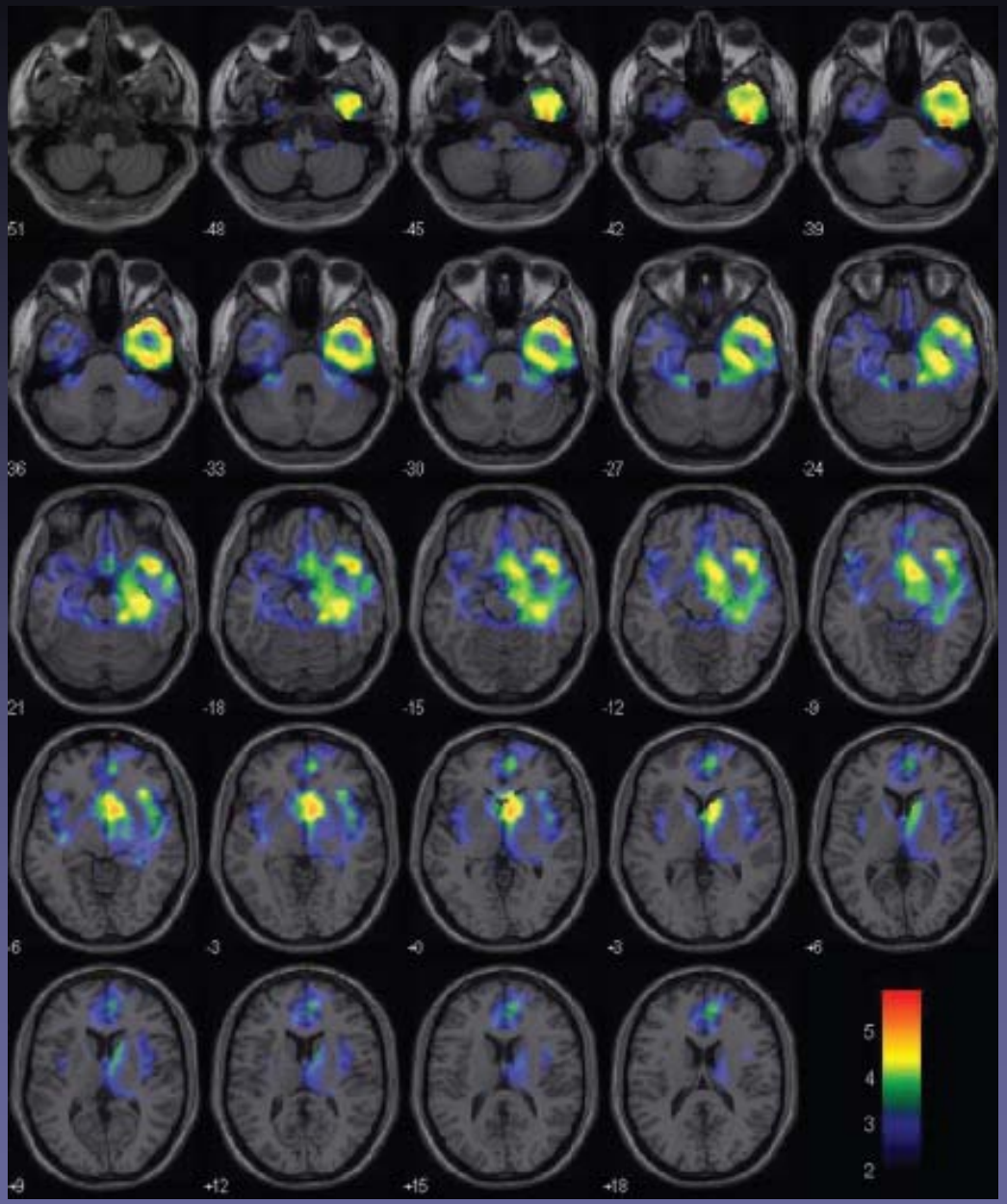



Figure threshold: p<0.001 uncorrected

(Rankin et al., Brain, 2006)




Only the right hemisphere appears to mediate empathy change in these patients

Unthresholded map:
$2.0 < T < 6.0$

(Rankin et al., Brain, 2006)

# Structural neuroanatomic correlates of empathy

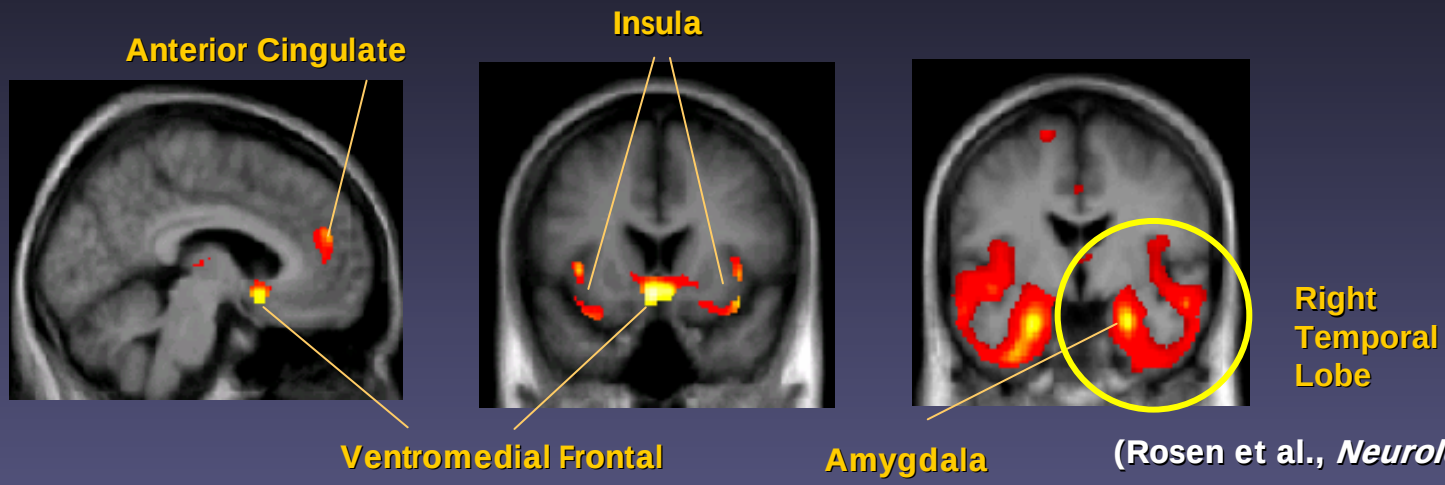
- Right temporal pole
  - "Transmodal association area" "acts as a gateway for binding. . .associations (such as name, voice, facial expression, posture, and private recollections)" (Mesulam, 1998)
  - Multimodal information is synthesized to create complex, personal symbolic representations

- Right postero-medial orbitofrontal cortex
  - May aid emotion recognition (Hornak, 1996, 2003)
  - Encodes reward value of 1º reinforcers (Kringelbach, 2004)
    - Visceral sensations accompanying emotional experience

# Structural neuroanatomic correlates of empathy

- Right caudate
  - Evaluation of reward expectancy from 1º reinforcers (Reynolds & Berridge, 2002)
  - Mixed findings re: facial emotion recognition, but is involved in emotional voice prosody recognition (Cancelliere & Kertesz, 1990)
    - may interpret stimuli with timing element
  - Imitating, but not merely observing, emotions (Carr, 2004)
- Right nucleus accumbens (?)
  - activity increases with both
    - emotional intensity, and
    - self-relatedness (Phan, 2005)

# Early FTLD




(Rosen et al., *Neurology,* 2002)

# Our study


(Rankin et al., *Brain*, 2006)

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(Neary et al., 1998)

# Measuring social cognition:
## social self-monitoring

The ability to adapt one's behavior based on (usually indirect or implicit) feedback from others

### The Revised Self-Monitoring Scale (RSMS)

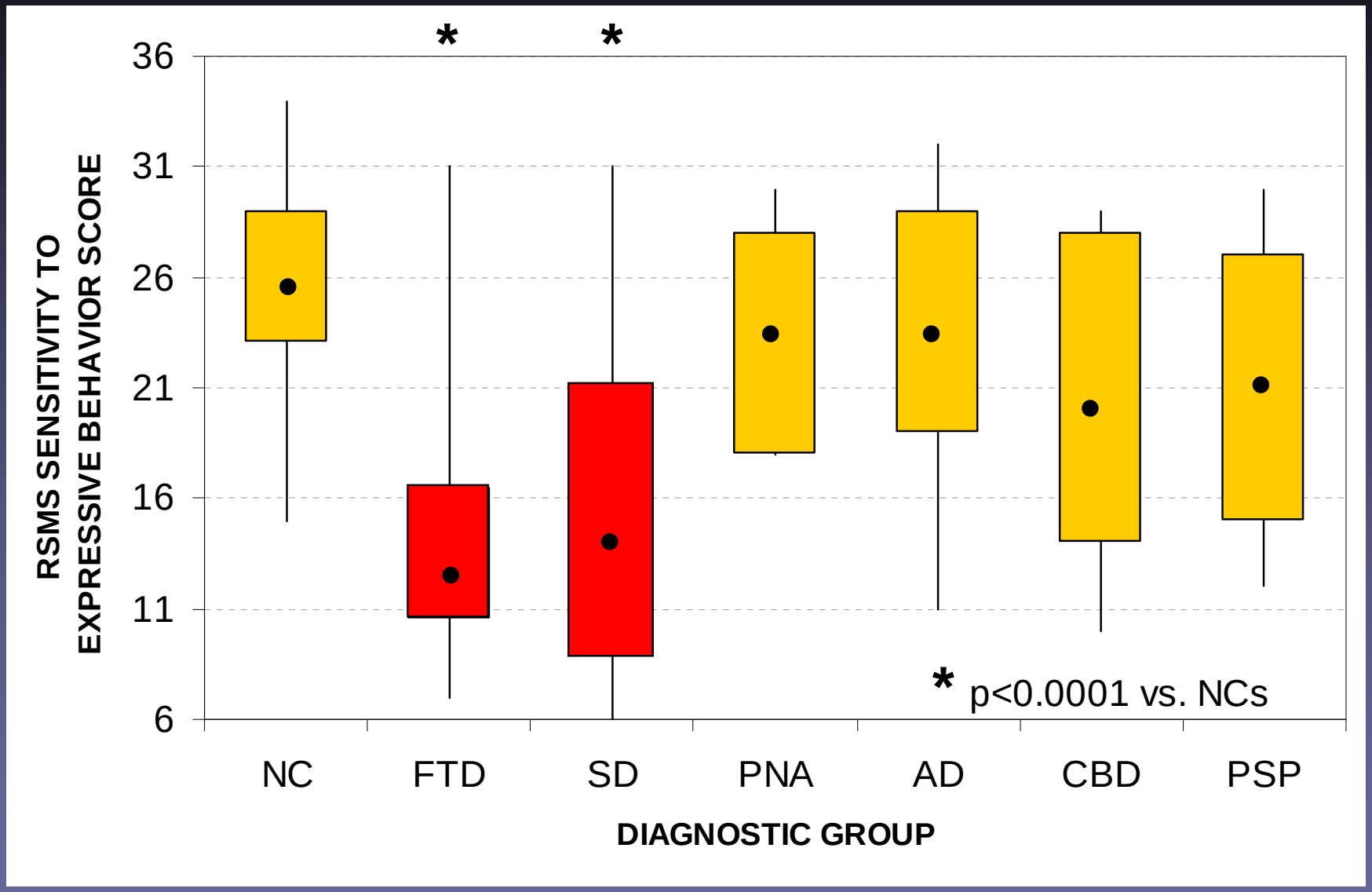
- "The patient can usually tell when others consider a joke to be in bad taste, even though they may laugh convincingly."
- "The patient can usually tell when he or she has said something inappropriate by reading it in the listener's eyes."

(Lennox & Wolfe, 1984)

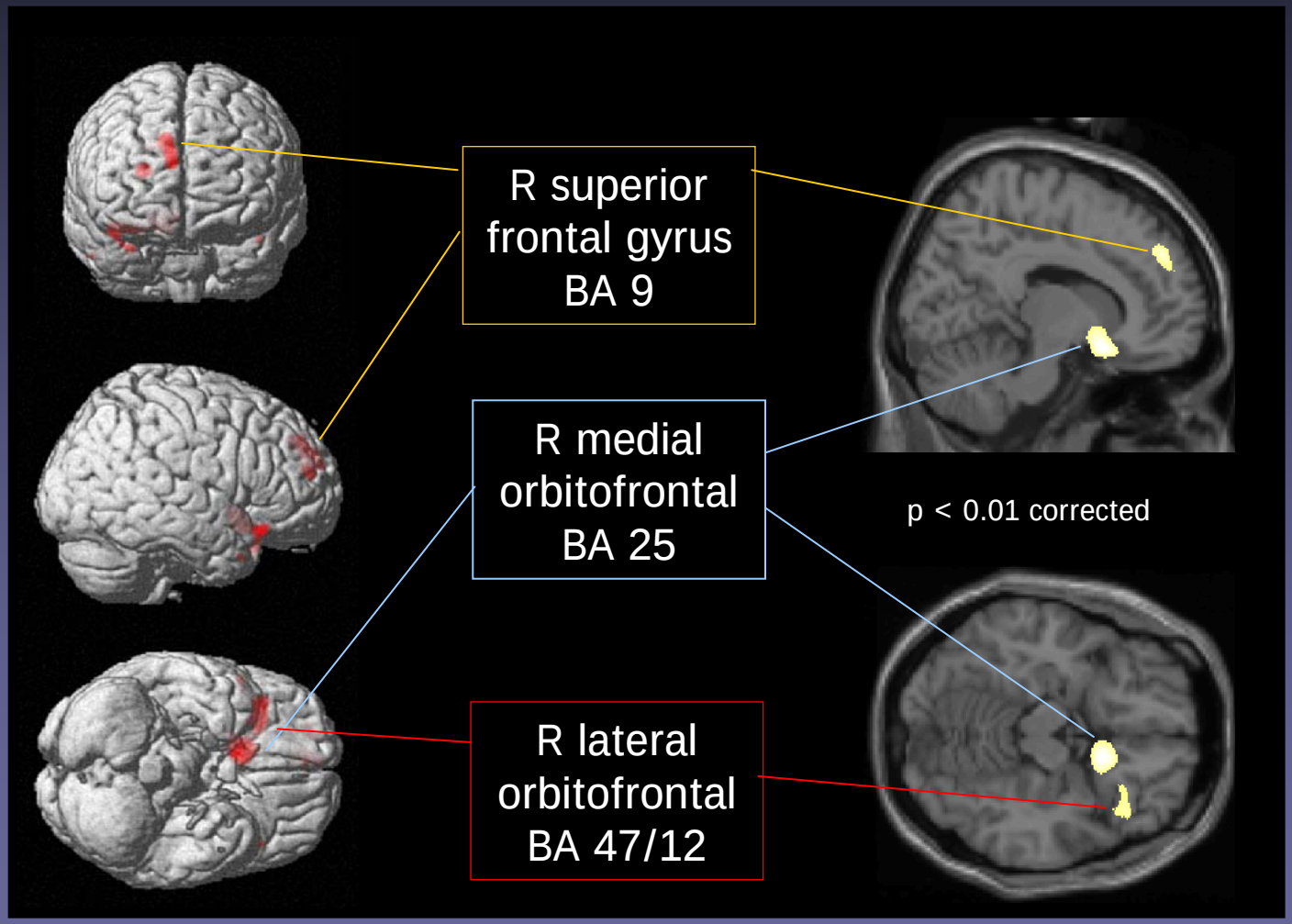
# Measuring social cognition: social self-monitoring

METHODS

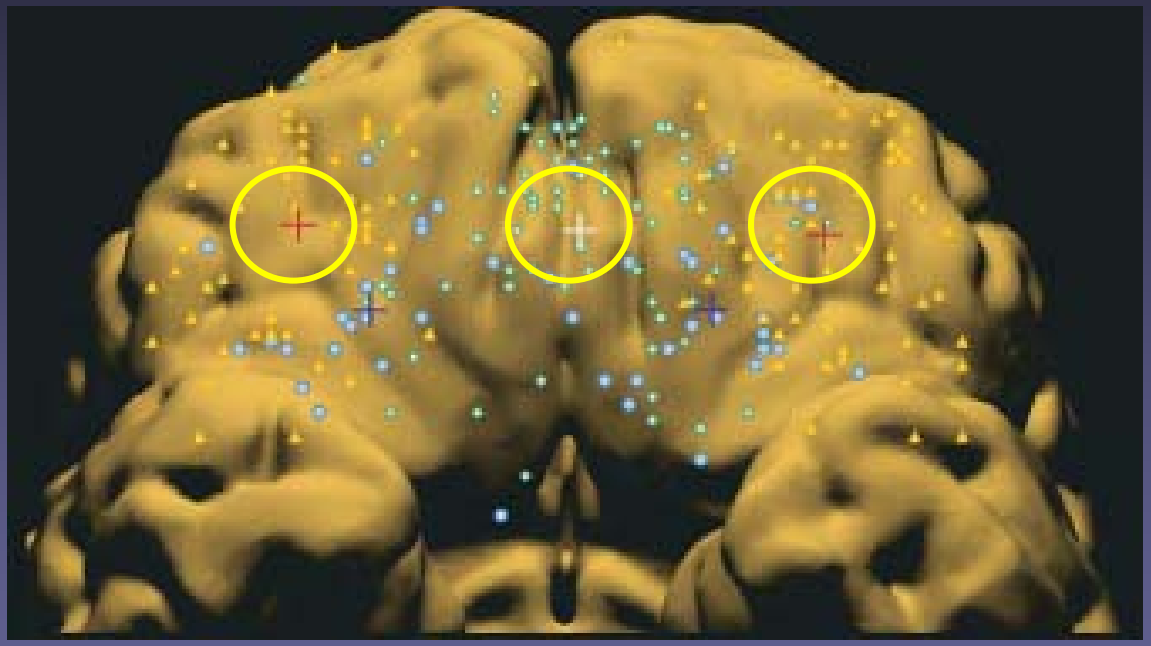
- 69 patients from a neurology clinic specializing in neurodegenerative diseases (FTD, SD, PNFA, AD, CBD, PSP)
- Caregivers filled out RSMS questionnaire evaluating the sensitivity of the patient to social feedback about his or her behavior
- All patients underwent T1-weighted MP-RAGE MRI
- Voxel-based morphometry
  - Brain volumes analyzed using RSMS scores as covariate of interest (continuous) controlling for age, sex, & TIV

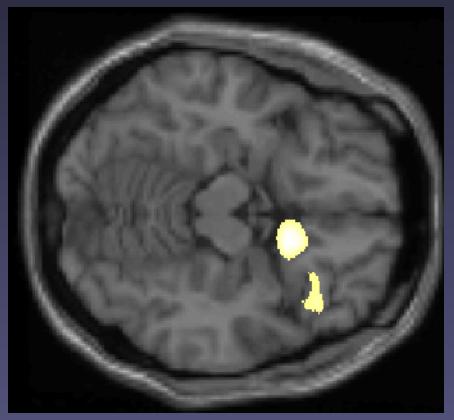

RSMS SENSITIVITY TO EXPRESSIVE BEHAVIOR SCORE
36
31
26
21
16
11
6
*
*
* p<0.0001 vs. NCs
NC
FTD
SD
PNA
AD
CBD
PSP
DIAGNOSTIC GROUP

# Regions where social self-monitoring score positively correlates with tissue density



# Social self-monitoring:
## medial vs. lateral orbitofrontal cortex





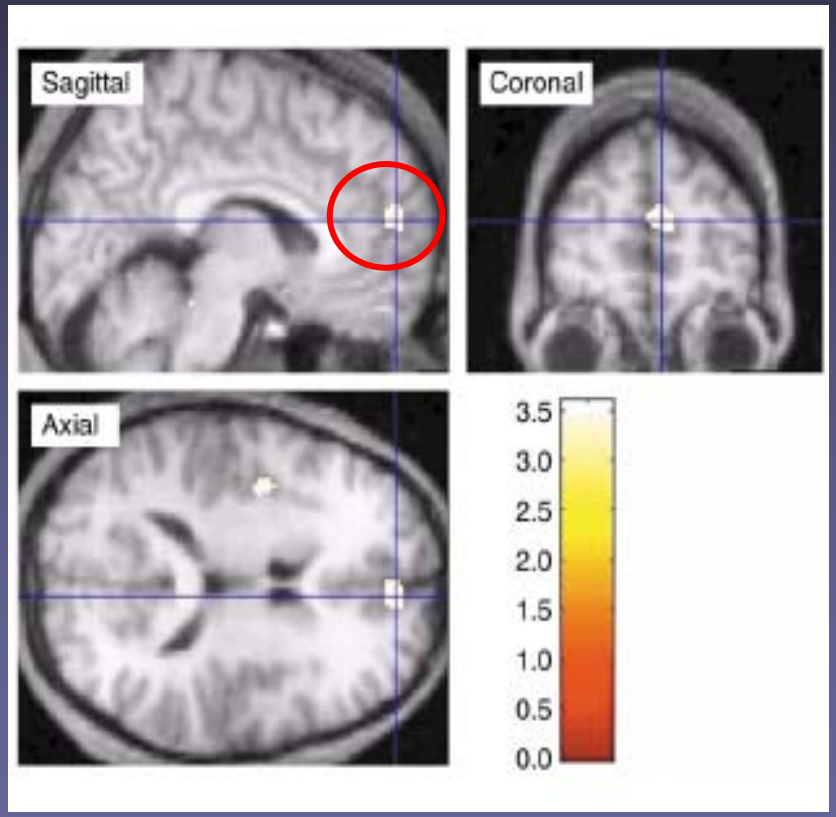
Our study

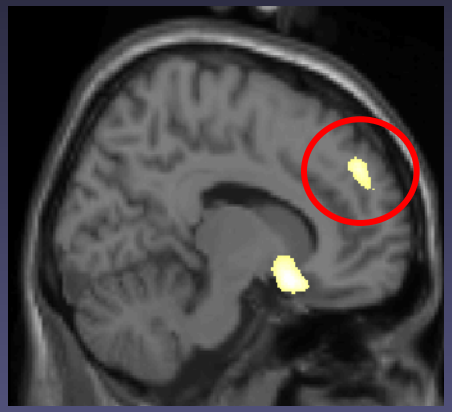
(Kringelbach & Rolls 2004 meta-analysis)

+ monitoring reward value
+ punishers leading to change in behavior

# Social self-monitoring: dorsomedial frontal cortex

(Gallagher & Frith review, 2003)



Our study

- Inferring others' intentions
- Imagining others' knowledge or feelings (Decety & Jackson review, 2004)

# Social self-monitoring: dorsomedial frontal cortex

## Perspective Taking (social set shifting?):

- separate your perspective/the other's perspective/the facts of the situation, and hold all three perspectives simultaneously ("triadic attention"?; Saxe, 2006)
- keep track of the "owner" of various mental states originating in self and other
- only understanding others' social intentions, not general (non-social) intentionality (Walter, 2004)

# Neuroanatomic correlates of social self-monitoring

## Kringelbach & Rolls, 2003: Social Response Reversal (fMRI)

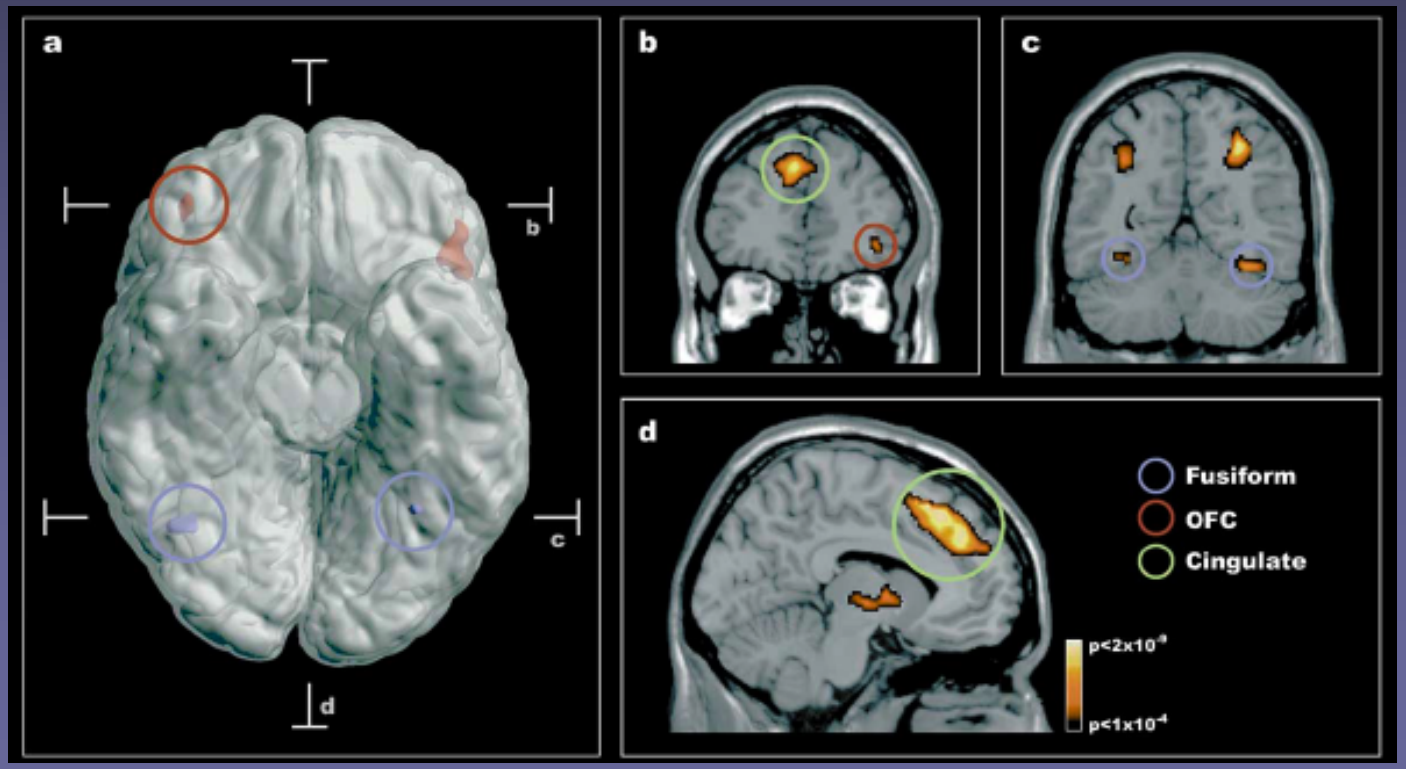
acquisition trials

reversal trials

# Neuroanatomic correlates of social self-monitoring

## Kringelbach & Rolls, 2003: Social Response Reversal (fMRI)

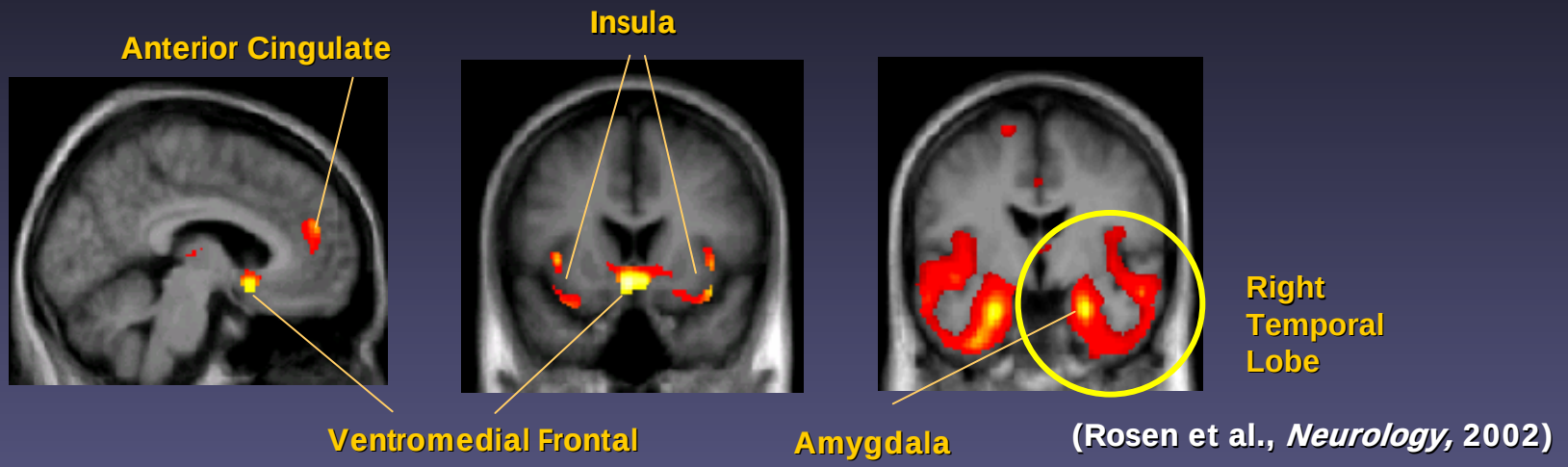
Areas showing increased activation when subjects change their behavior based on feedback from another's angry facial expression



# Elements of social cognition

- Warmth/empathy
- Comprehension of emotional stimuli
- Comprehension of situational stimuli
- Adherence to social norms
- Social decisionmaking
- Social perspective taking
- Dominance/assertiveness
- Self-awareness

# Early diagnosis ➔ early treatment




(Rosen et al., *Neurology,* 2002)

- To measure function in these brain regions, we must use social and emotional tests
- Without such tests, we will not be able to identify these patients early in the disease course
- As disease-modifying treatments become available, early diagnosis will be essential to timely intervention

# Early diagnosis ➔ early treatment

## Predominantly right temporal lobe FTLD patients:

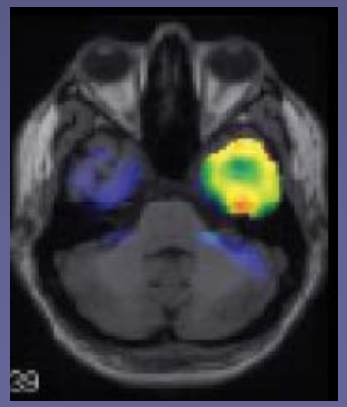
- Not initially recognized based on language or other cognitive symptoms
- Most likely subtype of FTLD to be mistaken for psychiatric or personality pathology; most resistant to assessment and care
- Temporal lobe FTLD patients more likely to have ubiquitin positive neuropathology

Right Temporal Lobe

Amygdala

(Rosen et al., *Neurology,* 2002)

VBM of empathy



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