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Cognitive Neuroscience of Thought
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Future directions and practical applications in the study of thought

So far in the course

Different aspects and forms of human thought

- goal-directed
- emotional
- spontaneous

Paradigms for study of thought

- task based (both neuroimaging and behavioral)
- observational

Today

Introduce a possible novel way of hypothesis testing in cognitive neuroscience

Using real-time fMRI to train modulation of brain activation

Examine some possible clinical applications

- real-time fMRI
- the role of thought processes in psychiatric disorders

Discuss the future directions in the study of thought and its practical applications

Rostrolateral Prefrontal Cortex (RLPFC)

• Meta-cognitive, introspective thought processes

(Christoff & Gabrieli, 2000; Christoff et al., 2001, 2003)

• Processing hierarchy of goals

(Christoff & Burgess et al., 2000;

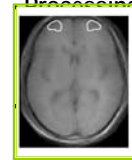
Christoff & Gabrieli, 2002; Ramnani & Owen, 2005)

• Establishing "episodic retrieval mode"

(Christoff & Gabrieli, 2000; Rugg & Wilding, 2000)

• Establishing "task set"

(Sakai & Passingham, 2003)



Theories of RLPFC functions

Seemingly disparate

Majority agree on one thing

RLPFC recruitment is determined by internal mental processes much more than by external task-related stimuli

Difficulties in testing theories of RLPFC

Paucity of relevant finding from animal studies

Uniquely human mental processes

Weak relationship between activation and external task-related stimuli

Driven by internal mental processes

Using task-based paradigms may not be sufficient for hypothesis testing

Real-time fMRI

Novel approach as an alternative to task-driven hypothesis testing

Real-time fMRI

Novel approach as an alternative to task-driven hypothesis testing

Traditional fMRI

Scanning → Analysis → Results

several hours to several months

Real-time fMRI

Novel approach as an alternative to task-driven hypothesis testing

Scanning → Analysis → Results

Performed simultaneously

Results can be observed by the person being scanned

(deCharms et al., 2004, 2005; Weiskopf et al., 2003, 2005; Posse et al. 2001, 2003)

Real-time fMRI

Novel approach as an alternative to task-driven hypothesis testing

Subjects control their own internal mental processes, while observing the effect on activation

Test if a particular internal mental process can be used to modulate RLPFC activation

Hypothesized cognitive process

Meta-cognitive awareness
(Christoff et al., 2003)

Specific predictions

Activation in RLPFC will

- ↑ with awareness of one's own internal thoughts
- ↓ with awareness of external perceptions and sensations

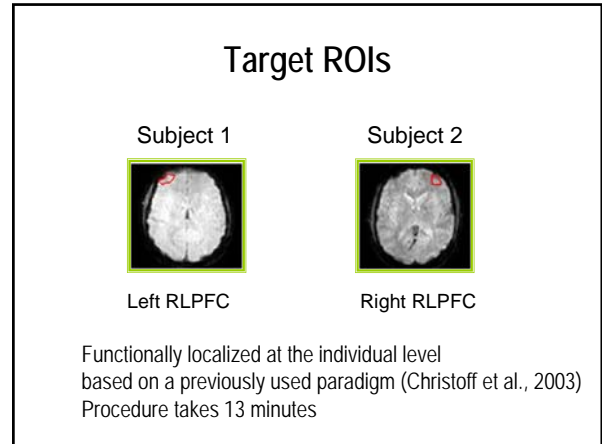
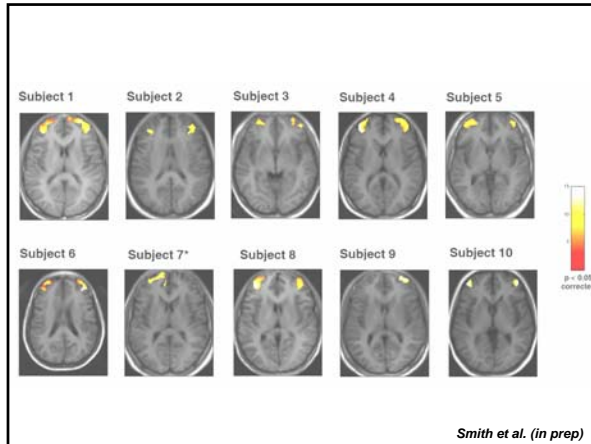
Modulation of RLPFC will improve with real-time fMRI training

Target ROIs

Subject 1 Subject 2

Left RLPFC Right RLPFC

Functionally localized at the individual level based on a previously used paradigm (Christoff et al., 2003)
Procedure takes 13 minutes



Briefing prior to training

Experimental question
"Whether people can learn to modulate activation in their RL PFC"

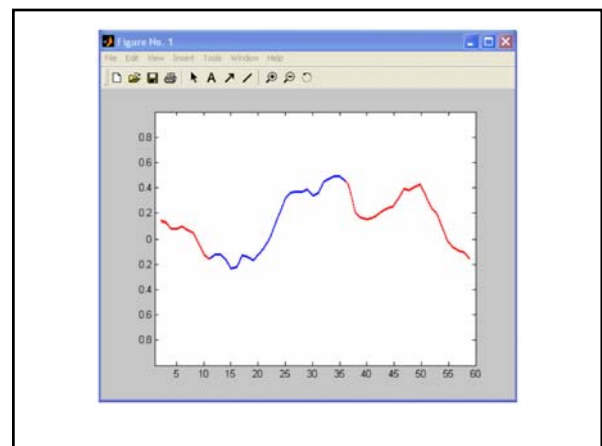
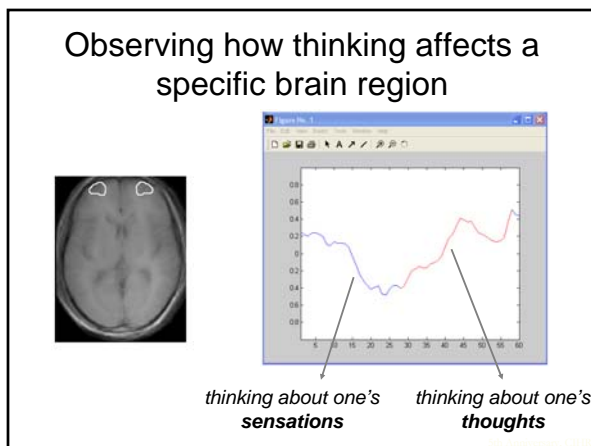
Putative functions of RL PFC
"Activated when people engage in introspective thought or when attention turns internally towards one's own thoughts"

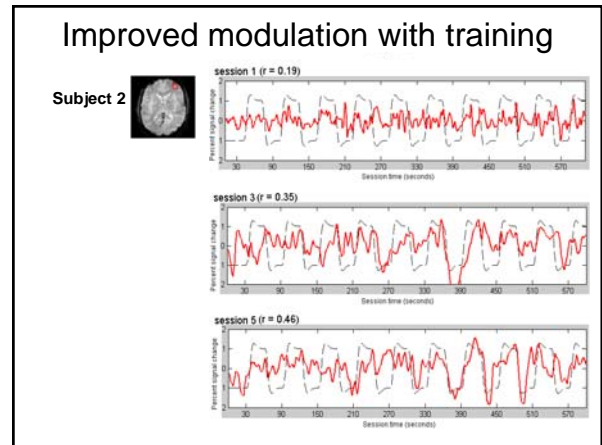
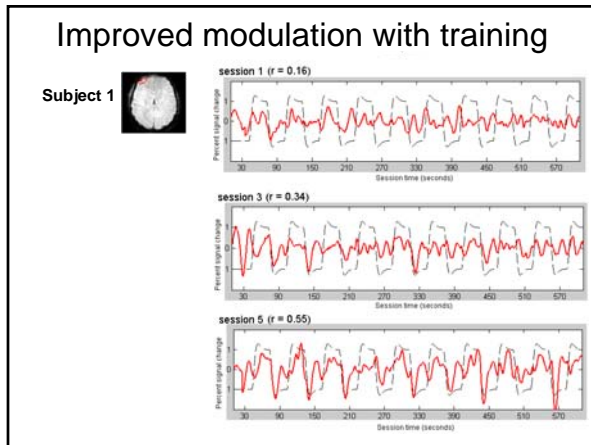
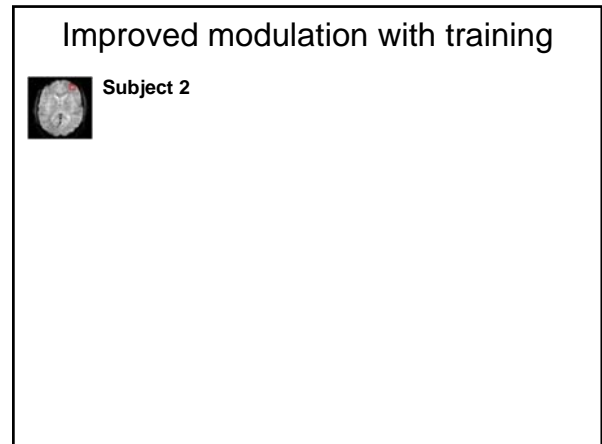
Instructions for real-time fMRI training

Try to modulate the level of RL PFC activation

Try to bring the activation up
becoming aware your own internal thoughts and mental processes

Try to bring the activation down
becoming aware of external perceptions and sensations





Improved modulation of RLPFC achieved in the course of 5 scanning sessions (total 50 minutes)

Activation in RLPFC more spatially localized and stronger with longer training

Potential for further improvement with longer duration of training

Theoretical Implications

Support to the hypothesis for a link between RLPFC and meta-cognitive awareness

Feasibility of real-time fMRI for hypothesis testing in higher order regions of the cortex

Especially for regions linked to internal task-unrelated mental processes

Clinical Applications

Chronic pain (deCharms et al, 2005)

- targeted the anterior cingulate cortex
- decreased ongoing level of chronic pain after real-time fMRI training

Depression

- target RLPFC
- improve control over meta-cognitive awareness
- help detect and change negative thought patterns (Segal, Williams & Teasdale, 2002)

Other potential targets

- subgenual cingulate (Mayberg, 2005)

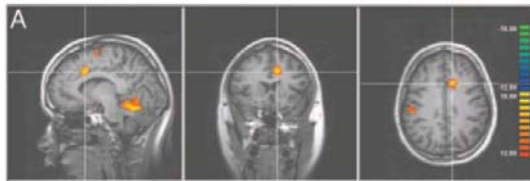
Clinical Applications

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- targeted the anterior cingulate cortex

Chronic pain

anterior cingulate cortex (ACC)
involved in pain perception and regulation
decrease in the ongoing level of chronic pain after real-time fMRI training



deCharms et al. (2005) PNAS

Clinical Applications

Chronic pain (deCharms et al, 2005)


- targeted the anterior cingulate cortex
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Depression

Thinking ↔ *Moods and Emotions*




Thinking ↔ *Moods and Emotions*



Depression

- An illness that affects thoughts, feelings, behavior and overall health
- Sufferers feel sad or down for long periods of time




Symptoms

Thoughts: guilt, hopelessness, worthlessness, indecisiveness, low concentration, suicide

Emotions: sadness, loneliness, irritability, anger

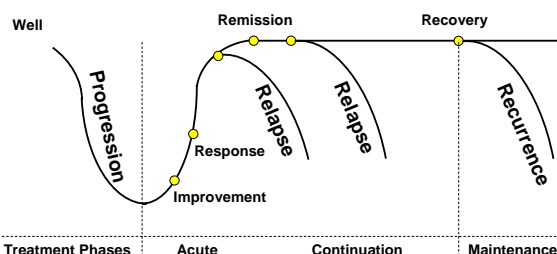
Physical: changes in weight and sleep patterns
 loss of energy or agitation



Prevalence

- 10-25 percent of women and 5-12 percent of men will likely become depressed in their life
- the first major depression occurs most often in mid to late twenties

Course and Outcome



Kupfer DJ (1991) *J Clinical Psychiatry*

Causes of depression

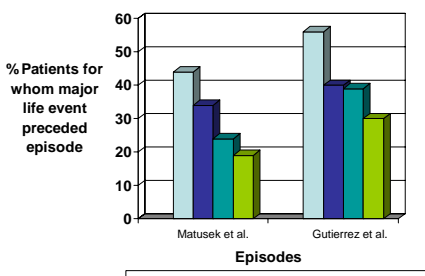
No single cause, instead combination of things

Traumatic events, stress, low self esteem, and physical illness can contribute

Stress is the leading cause for first episodes, but...

In recurrent depression, stress becomes less important

Stress and recurrent depression

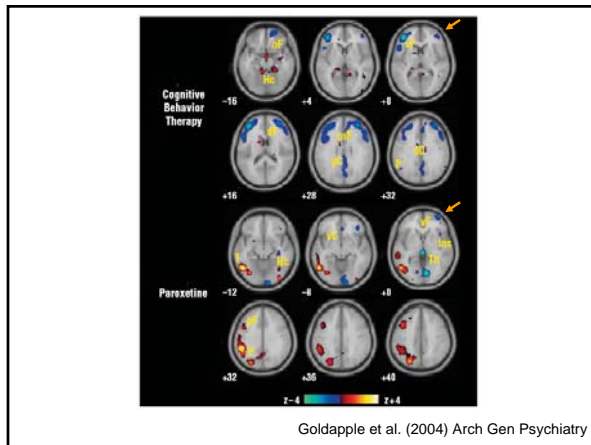
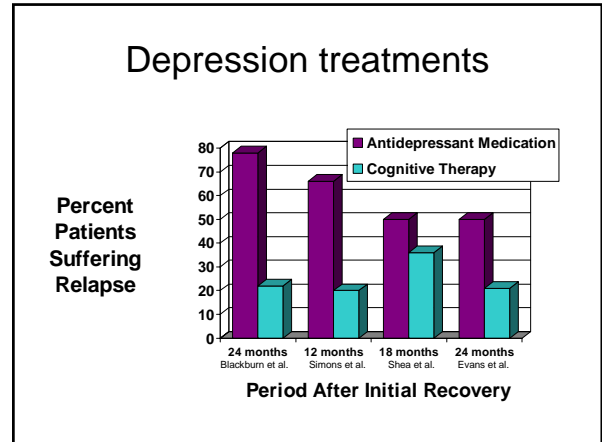


Study	First	Second	Third	Fourth
Matussek et al.	~45%	~35%	~25%	~20%
Gutierrez et al.	~55%	~40%	~35%	~30%

Depression treatments

Antidepressant medication
 often can achieve at least some improvement

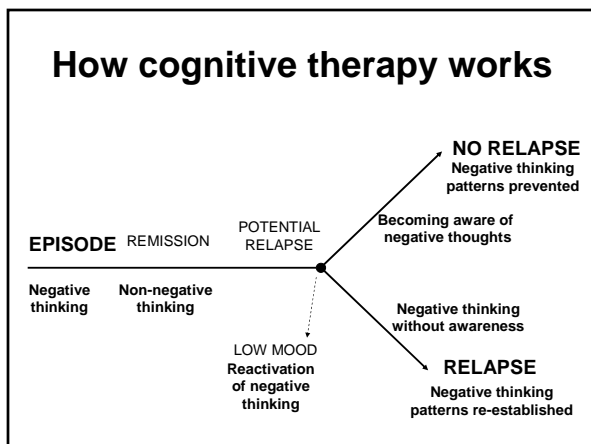
Cognitive therapy
 produces longer lasting effects



How cognitive therapy works

It teaches patients to

- observe and question their thoughts
- prevent automatic thinking patterns
- become aware of their own negative thoughts, especially when in low mood



Observing our thoughts

Introspectively
 analyzing ourselves; meditating

Communicating
 talking or writing about our thoughts



Observing our thoughts

Introspectively

analyzing ourselves; meditating

Communicating

talking or writing about our thoughts

Observing our thoughts

Introspectively

analyzing ourselves; meditating

Communicating

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Watching how our brain thinks

using functional magnetic resonance (fMRI)

Applications for treatment

Depression

help patients observe their thought processes

train awareness of thoughts

change undesirable thinking patterns

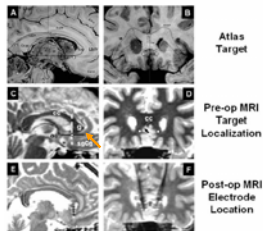
Possible target region: RLPFC

Other potential target regions

subgenual cingulate

metabolically overactive
in depression

deep brain stimulation
implant to chronically
reduce activity
dramatic improvement
in treatment resistant
depression



Mayberg et al. (2005) Neuron

medial prefrontal cortex

involved in emotional self-reflection

Applications for treatment

Depression

Anxiety

ADHD

Phobias

Phobias

CBT is an effective psychotherapeutic approach for reducing the symptoms of specific phobias

therapy consists of a combination of

- exposure-based treatment to the phobogenic stimuli (e.g., spiders)
- education for changing negative cognitive misattributions related to these stimuli

Brain correlates of phobia

Subjects suffering from spider phobia were scanned, before and after CBT, while viewing film excerpts of

- living spiders (activation task), or
- living butterflies (reference task)

Subject selection

- DSM criteria for phobia
- after piloting
- those who reported intense but tolerable fear in response to the spider films

Paquette et al. (2003) NeuroImage

Cognitive Behavioral therapy

4 consecutive weeks, 3-hour intensive group session once a week

Week 1: gradually exposed to an exercise book containing 50 color pictures of spiders.

Week 2: gradually exposed to film excerpts of living spiders (that were also used in the study)

Self-exposure homework, with the exercise book and the videotape, given between each session.

Week 3: exposed to real spiders

Week 4: subjects were asked to touch a tarantula

Paquette et al. (2003) NeuroImage

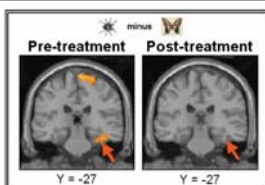
After therapy, all subjects were able to touch, without reporting fear reactions (behaviorally and cognitively)

- the entire series of pictures depicting spiders
- the TV screen showing living spiders
- the real spiders

fMRI procedure

- block design
- 30 s long blocks (spiders in captivity or butterflies in nature)
- blocks were separated by resting periods of 15 s of blue screen

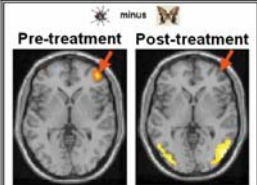
Paquette et al. (2003) NeuroImage



Parahippocampus (BA36)

automatic reactivation of the contextual fear memory that led to the development of avoidance behavior and the maintenance of spider phobia

- control subjects activated visual association cortex (BA 19) and right inferior temporal gyrus (BA 37), but not these areas



Rostrolateral PFC (BA10)

metacognitive strategies aimed at self-regulating the fear triggered by the spider film excerpts

Paquette et al. (2003) NeuroImage

Final thoughts and thought...

Theories of thought only useful if practical applications are found

Possibilities include

- clinical practice
- education
- social policy making
- crisis management and solution
- many others...