EXECUTIVE FUNCTIONS

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Executive Functions

• Theorized cognitive system that controls and manages other cognitive processes

• Handling novel situations outside the domain of some of our 'automatic' psychological processes
  – Situations that involve planning or decision making
  – Situations that involve error correction or troubleshooting
  – Situations where responses are not well-learned or contain novel sequences of actions
  – Dangerous or technically difficult situations.
  – Situations which require the overcoming of a strong habitual response or resisting temptation
Cognitive Control, Will-Power, Behavioral Regulation

• Fundamental executive capacity
• Goal-driven cognitive control or regulation of impulses, passions, cravings, and habits
• Behavioral changes critical for the prevention, management, and treatment of many important health conditions.
Cognitive Control

EMOTION

REWARD

MEMORY

DELAYED GRATIFICATION
Dual-Process Model

**Reflexic (X-System)**
- Automatic processes
- Fast operating
- Slow learning
- Phylogenetically older

**Reflective (C-System)**
- Controlled processes
- Slow operating
- Fast learning
- Phylogenetically newer
- Special cases & abstract concepts

Satpute & Lieberman *Brain Res* 2006
Can human behavior be influenced by modulation of the reflective system?

- Promote understanding of decision making
- Address uniquely human aspects of behavior
- Enhance cognitive control
- Translated to human disease

- Ethical debate
  - Steven & Pascual-Leone 2006
  - Canli et al. 2007
Right Lateral Prefrontal Cortex & Inhibition

- Wisonsin Card Sorting Test
- Go/No-Go & Stop Signal Paradigms
- Task-set switching

Aron & Poldrack, 2005

Nakahara et al, 2002
Ultimatum Game

Proposer

Responder

16

4

Fairness • Equity

Reciprocity

Self-interest

Altruistic Punishment

- People reject low offers even if stake levels are as high as three months’ income
- Rejection rates up to 80% for offers below 25% of the available money
fMRI Study

- Anterior insula & DLPFC activated when responders decide whether to accept or reject an unfair offer

- DLPFC more strongly activated when subjects face unfair offers compared to when they face fair offers

Sanfey et al. Science 2003
Role of the Lateral PFC

• Involved in the control of the emotional impulse to reject unfair offers; cognitive control of the emotional impulse associated with fairness goals (Sanfey et al.)

• Involved in the inhibition of selfish impulses
  – Note that emotional forces may be associated with selfish impulses as well as with fairness goals - consistent with dual systems approaches
  – Need to inhibit self-centered impulse in order to enable “morally appropriate” behavior
Predictions for Disruption of Lateral PFC

- If Lateral PFC exerts cognitive control for suppression of fairness impulses:
  - reduce the acceptance rate of unfair offers

- If Lateral PFC suppresses selfish impulses:
  - increase the acceptance rate for unfair offers
Ultimatum Game

Acceptance rate for the 16/4 offer in the human offer condition

Perceived unfairness of the 16/4 offer in the human offer condition

Reaction time for accepted 16/4 offer in the human offer condition

Ultimatum Game

Proposer

Self-interest  Fairness  Equity  Reciprocity

+  +  +  +

+  +  +/-  -

Ultimatum Game

• Social interaction often involves the simultaneous interaction of many subjects.
• In experiments examining altruistic behaviors it is important that subjects interact only once with many different partners.
• The absence of interaction partners during the experiment may raise suspicion among the subjects and may change their behaviors.
• The best implementation of social interactions is the simultaneous presence of all subjects during the experiment.

Knoch et al. *Cerebral Cortex* 07
Ultimatum Game

(a) Acceptance rate (%)
- Sham
- Cathodal tDCS

(b) Fairness judgment
- Sham
- Cathodal tDCS

Knoch et al. Cerebral Cortex 07
Ultimatum Game Experiments:
It is possible to modify response without altering the fairness judgment.

Suppression of the RIGHT Lateral PFC leads to an increase in acceptance rate for unfair offers.

The Lateral PFC (right) suppresses self-centered impulses.

Control of self-centered behavior is critical to suitably balance risk taking impulses. Is the role of the lateral PFC demonstrable in a risk task?
Decisions over time

- Impulsive / Fast Decisions: Affective mechanism ($\beta$ areas): heavily values the present
- Reflective Decisions: Deliberative mechanism ($\delta$ areas): over time considerations

McClure et al., Science 2004
Risk Task

Level of Risk

Points: 100

80
20

Balance of Reward

Risk Task

Knoch et al. *J Neurosci* 2006
Risk Task

Points Earned

Choice of Low Risk Option

Knoch et al. *J Neurosci* 2006
Suppression of the right lateral PFC leads to increased risk taking behavior.

Lateral PFC (right) suppresses impulsive, self-centered behavior.

Is it possible to decrease risk-taking behavior by increasing activity in the lateral PFC?

- Cathode  Anode +

Right Lateral PFC

5 min

Risk Task

Transcranial direct current stimulation

Level of Risk
Balance of Reward

Points: 100
90 10

Points: 10
90 10

Cathode Anode +

Right Lateral PFC
Increasing activity in the RIGHT lateral PFC decreases risk taking behavior.

Lateral PFC (right) suppressive impulsive, self-centered behavior.

What happens in circumstances when the balance of risk is unknown?

Is the level of activity in the right lateral PFC the critical variable, or the relative balance between left and right?
Balloon Analog Risk Task

Bilateral tDCS

Unilateral tDCS

Noninvasive modulation of Right Prefrontal activity can modify unique human traits of altruistic behavior and control of self-motivated impulses

- Hedonic desires
- Risk-taking impulses

(Right) Lateral Prefrontal Cortex

Self-centered behavior
Right Lat PFC Failure

- Impulsive, self-centered behavior with disregard to cultural & social convention
  - Traumatic brain injury
  - Frontal dementia
  - Mood Disorders
  - Sociopathic personality behavior
  - Borderline personality disorder
  - Addictive behavior
    - Cocaine
    - Nicotine
    - Pathological gambling
  - Eating disorders - Obesity
Cue-Provoked Nicotine Craving

Exposure 1:
Smoking movie and cigarette manipulation

T0: Baseline

T1: Assessment after exposure

Anode + - Cathode

Stimulation (tDCS) for 20 minutes

Exposure 2:
Smoking movie and cigarette manipulation

T2: Assessment after tDCS

Exposure 3:
Smoking movie and cigarette manipulation

T3: Final assessment

Cue-Provoked Nicotine Craving

Cue-Provoked Alcohol Craving

Exposure 1: Alcohol movie

T0: Baseline

Stimulation (tDCS) for 20 minutes

T1: Assessment after exposure

Anode + Cathode

Exposure 2: Alcohol movie

T2: Assessment after tDCS

T3: Final assessment

Boggio et al. Drugs an Alcohol Dependence (2008)
Cue-Provoked Alcohol Craving

Boggio et al. *Drugs an Alcohol Dependence* (2008)
Right PF rTMS in Cocaine Craving

Obesity

- Homeostatic Control
- Reward Gratification
- Elaborate Behavior Cultural & Social Messages

HUMANS

Right Prefrontal Cortex

Alonso & Pascual-Leone JAMA 2007
Right Brain Hypothesis of Obesity

Interactions of Reflective and Reflexive Eating Pathways

- Cognition
- Prefrontal Cortex
- Other Association Cortices

Homeostasis
- Hypothalamus
- Brainstem

Reward
- Limbic Structures
- Paralimbic Structures

Food Intake

Periphery
- Neural Signals (Vagal, Other)
- Hormonal Mediators
- Gastrointestinal Peptides
- Insulin
- Adipose Tissue Peptides

Reflective Eating
- Cognition

Reflexive Eating
- Homeostasis
- Reward

Cross Section of the Brain

- Prefrontal Cortex
- Cingulate Cortex
- Striatum
- Insular Cortex
- Amygdala
- Hippocampus
- Parahippocampal Region

Right Prefrontal Cortex

Alonso & Pascual-Leone JAMA 2007
Brain responses to subliminal presentation of food predict obesity risk
Brain responses to subliminal presentation of food predict obesity risk

Forced Choice Recognition Task

![Graph](image.png)
Brain responses to subliminal presentation of food predict obesity risk

Subliminal HI>LO
$r = 0.575; p = 0.013$
Daily Fiber Intake

% of total food weight

Daily Energy Expenditure

Kcal

Frequency of breakfast away

Episodes per month

Right DLPFC activation

Parameter Estimates

- FHO+
- FHO-
Obese show different pattern of brain activity.
Region of interest (ROI) analysis

Right DLPFC activation

Parameter Estimates

p=0.019

p=0.047

-0.9
-0.7
-0.5
-0.3
-0.1
0.1
0.3
0.5

-0.1
-0.05
0.05
0.1
0.15
0.2
0.25
0.3
0.35

-0.1
-0.05
0.05
0.1
0.15
0.2
0.25
0.3
0.35

-0.1
-0.05
0.05
0.1
0.15

-0.1
-0.05
0.05
0.1
0.15

-0.1
-0.05
0.05
0.1
0.15

-0.1
-0.05
0.05
0.1
0.15

-0.1
-0.05
0.05
0.1
0.15

FHO+
FHO-
OB/Bed
Changes in Right DLPFC activation
IOWA GAMBLING TASK

Iowa Gambling Test

Previous Total: 2800
Current Total: 2600

Gain: +50
Loss: -250

Points: 540

Collect $50
Click Here to Pump up the Balloon
Total $50
$6.50
Food craving

Assessment pre-cue, pre-tDCS

Assessment post-cue, pre-tDCS

20 minutes 2 mA tDCS

Assessment pre-cue, post-tDCS

Assessment post-cue, post-tDCS

- anodal L DLFPC, cathodal R DLPFC
- anodal R DLPFC, cathodal L DLPFC
- sham

VAS on craving:
- urge to eat
- food appearance
- food smell

VAS on mood

food movie &
eye tracker,
food exposure

food movie &
eye tracker,
food exposure,
invitation to eat

VAS on craving:
+ food taste
+ ingested calories

VAS on mood

Fregni et al. Appetite 2008
Anodal stimulation over the R DLPFC reduces food craving

Fregni et al. *Appetite* 2008
Anodal stimulation over the R DLPFC reduces ingested calories as libitum

Fregni et al. Appetite 2008
Anodal stimulation over the R DLPFC reduces fixation time on food

Fixation on food items during movie

Fregni et al. *Appetite* 2008
Conclusions

• Lateral Prefrontal Cortex (right)
  – Exerts a ‘repressive’ control onto self-centered behaviors / impulses
  – Switch between reflexic and reflective modes of operation

• Translational (Clinical) Cognitive Neuroscience
  Insights from Cognitive Neuroscience can be translated into clinical applications addressing uniquely human aspects of behavior

• Noninvasive Brain Stimulation offers a unique methodology to study and modulate causal brain-behavior relations