

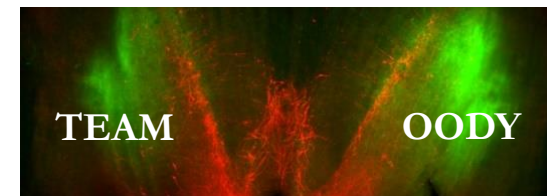
Can understanding the brain help with Mental Health Conditions?

(alcohol addiction and anxiety)

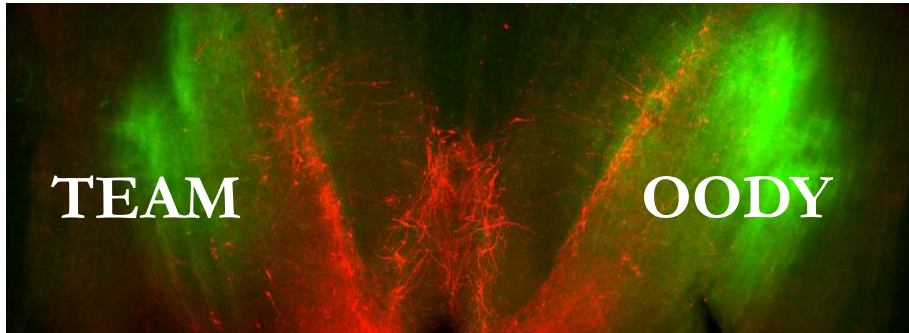


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R01 AA024109, P60 AA007611

Please Feel Free to Ask Questions

Any Time

Even Now

Disease Burden of Mental Health Conditions

Disease Burden of Mental Health Conditions

The Indiana Behavioral Health Commission

STUDIED THE COST OF **UNTREATED MENTAL ILLNESS**
IN INDIANA AND ESTIMATES

\$4.2 BILLION
ANNUALLY

INDIANA BEHAVIORAL HEALTH COMMISSION
ADVOCACY TOOLKIT

INDIANA
COUNCIL
of Community Mental Health Centers, Inc.

MIHA
Mental Health
of Indiana

NAMI
National Alliance on Mental Illness
Indiana

Disease Burden of Mental Health Conditions

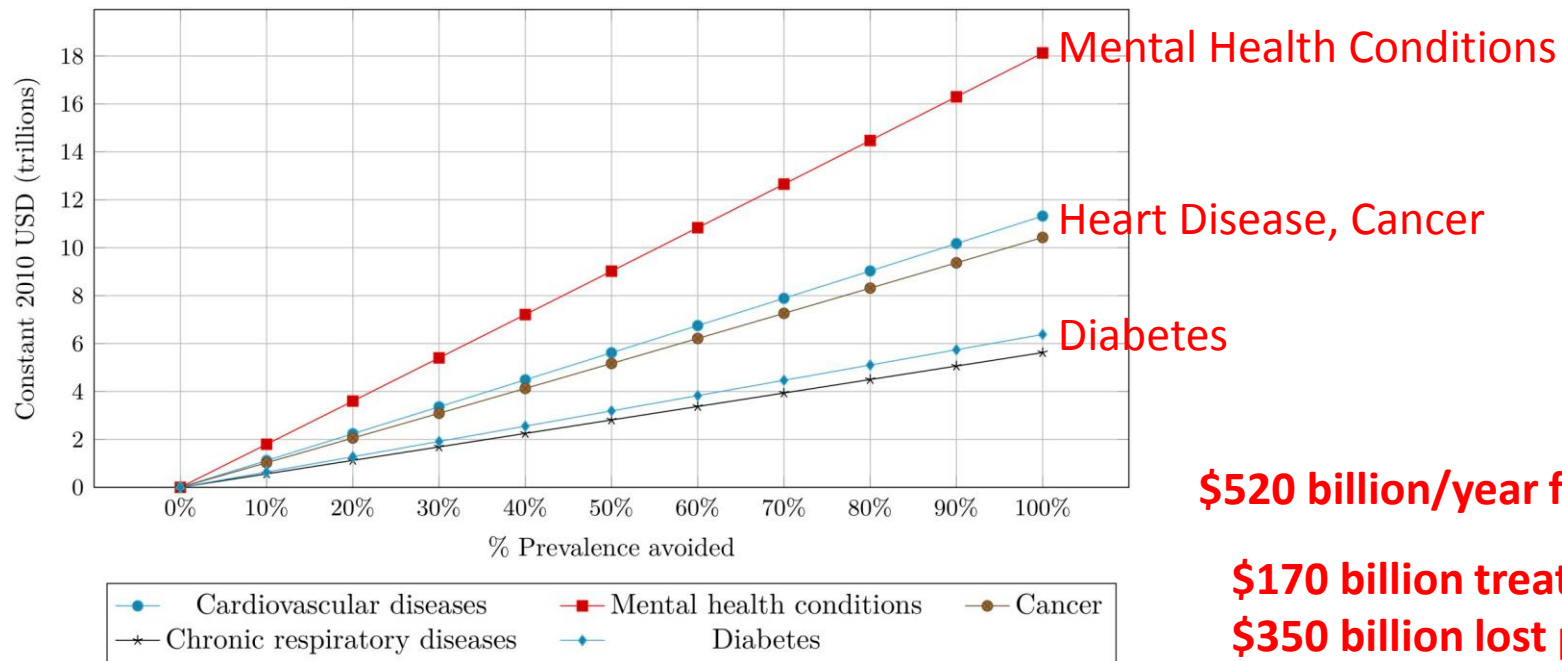
If the US spent \$150 billion across 15 years (\$10 billion/year) on depression and anxiety treatment

It would return \$700 billion (\$47 billion/year) across 15 years.

- \$300 billion for healthy life years (personal relief from disease burden)
- \$400 billion from greater economic productivity (~55% depression, ~45% anxiety)

Disease Burden of Mental Health Conditions

Disease Burden of Non-Communicable Conditions in the US



The Cost of Alcohol and Binging

The Cost of Alcohol and Binging

Alcohol Addiction (2013):

~\$250 billion, ~90,000 preventable deaths in US per year

(CDC 2014)

**The 1/7th of US adults that are
binge drinkers**

consume 3/4th of the cost



CDC, 2014

The Cost of Alcohol and Binging

Alcohol Addiction (2013):

~\$250 billion, ~90,000 preventable deaths in US per year

(CDC 2014)

Alcohol now Leading Cause of Death *(Esser et al. 2022)*

1 in 5 deaths for 20-49 yr old, 1 in 8 for 20-64 yr old

Covid: ~25-30% increase in drinking

~30-50% increase in Mental Health Conditions

(Many studies) (Kessler et al., 2022)

Sex-Specific Risks

- Women have nearly twice the risk of developing a mental health condition

(White et al., 2015; Grant et al., 2017; Grucza et al., 2018; Carvalho et al., 2019; Hasin et al., 2019; McKetta et al., 2019).

- Alcohol drinking in women has risen dramatically in recent decades
- Women can have greater alcohol problems, including mental health conditions

(Anglin et al., 1987; Piazza et al., 1989; Brady et al., 1999; Westermeyer et al., 2000; Lynch et al., 2002; Erol et al., 2015; Becker and Chartoff, 2016).

(1) A huge amount of need

(2) Help develop new treatments

(individual differences likely crucial)

(3) Decrease Stigma and Shame

(mental health condition as a brain disease)

(brains strengths and weaknesses)



Contents lists available at ScienceDirect

Addictive Behaviors Reports

journal homepage: www.elsevier.com/locate/abrep



Review

Addiction, cigarette smoking, and voluntary control of action: Do cigarette smokers lose their free will?



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University of Queensland, Australia
The Florida State University, USA

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Voluntary behavior

ABSTRACT

Opinions differ widely as to whether addicts lose the ability to control their behavior and employ free will. This article reviews empirical findings regarding multiple questions relevant to the issue of free will among addicted smokers: Is smoking voluntary behavior? Can people quit smoking? Why don't people quit smoking? Why do smokers relapse when they try to quit? Do addicted smokers suffer from irresistible cravings? Are there some people who cannot quit? Are there conditions that make resistance impossible? Why would they smoke knowing it can kill them? The evidence reviewed here seems most consistent with the view that smokers retain control over their actions but cannot easily stop having frequent desires to smoke.

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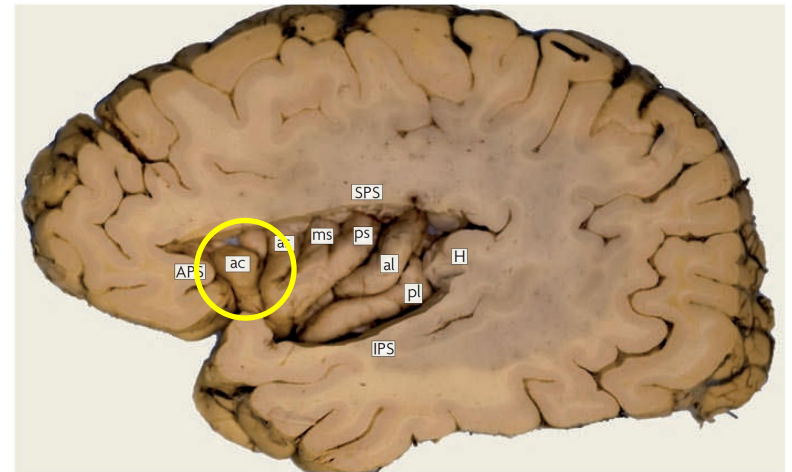
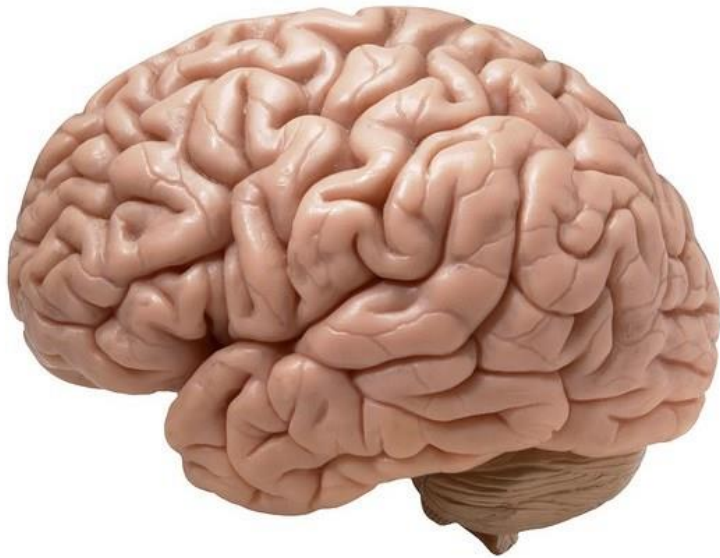


Figure 1 | **Anatomy of the insula.** A photograph of the left insular cortex of a human patient. For a

A Brain Area so powerful that sometimes a lesion there (a stroke) leads a smoker's body to forget that it's addicted



Brain

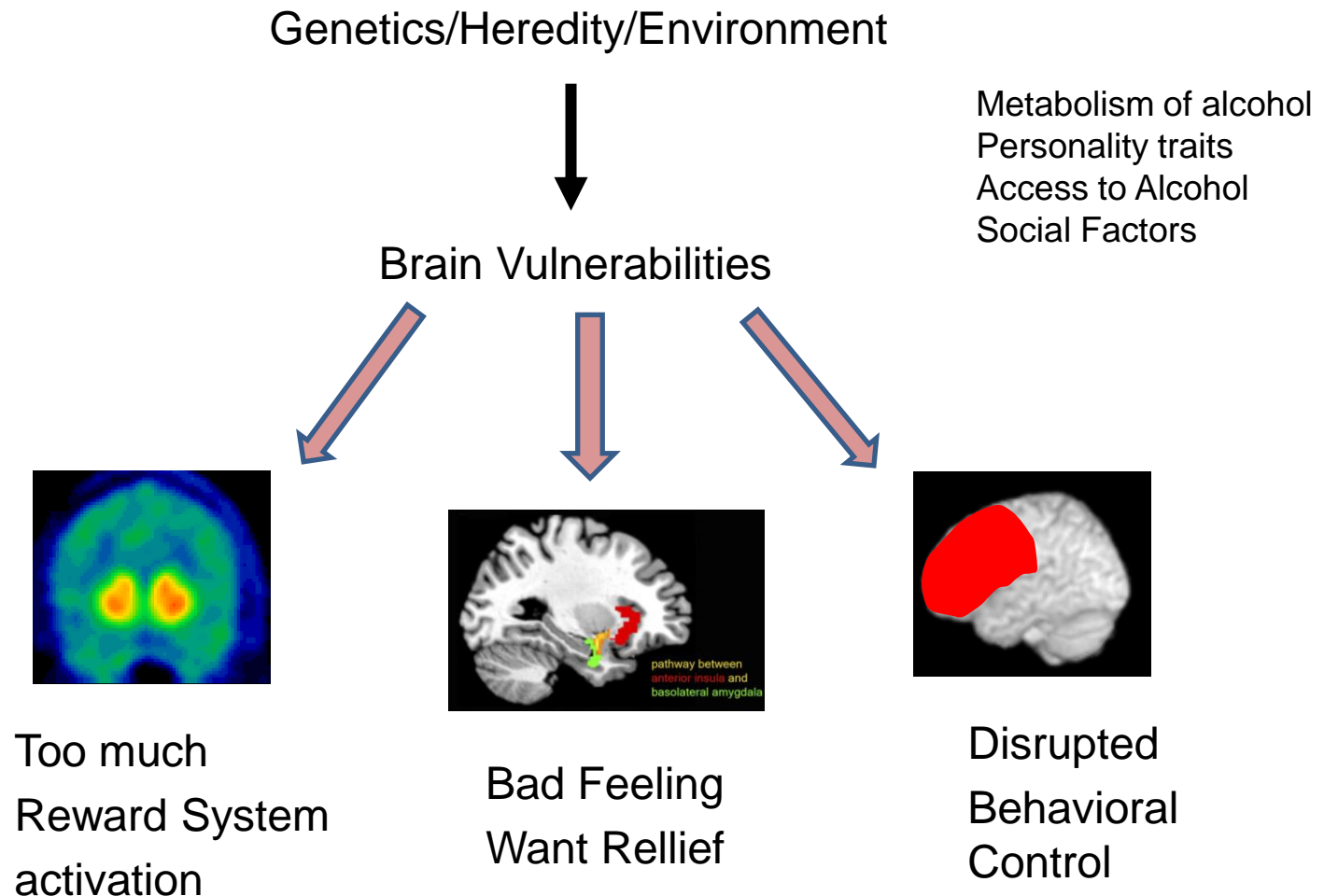
What leads to Problem Alcohol Drinking?

Genetics/Heredity/Environment



Metabolism of alcohol
Personality traits
Access to Alcohol
Social Factors

What leads to Problem Alcohol Drinking?

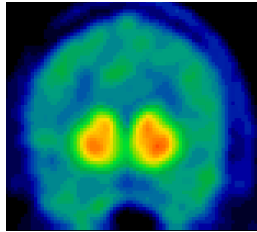
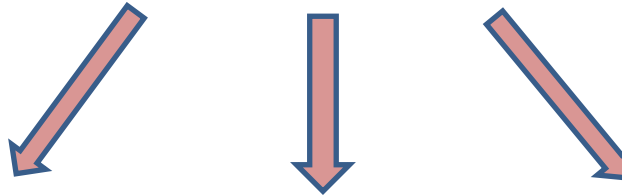


Neuroimaging: watching the brain, e.g. crave for alcohol

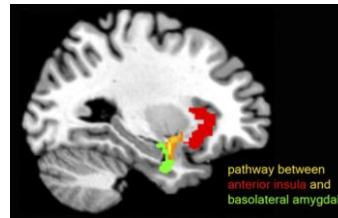
Genetics/Heredity/Environment



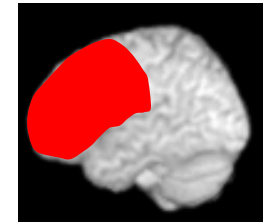
Brain Vulnerabilities



Too much
Reward System
activation

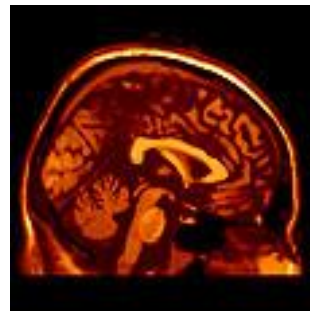
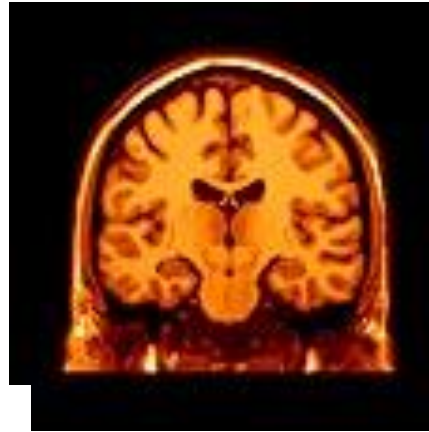
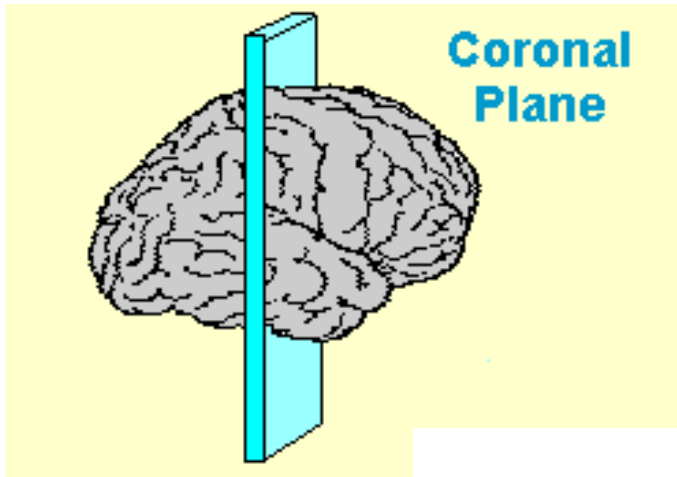


Bad Feeling
Want Relief



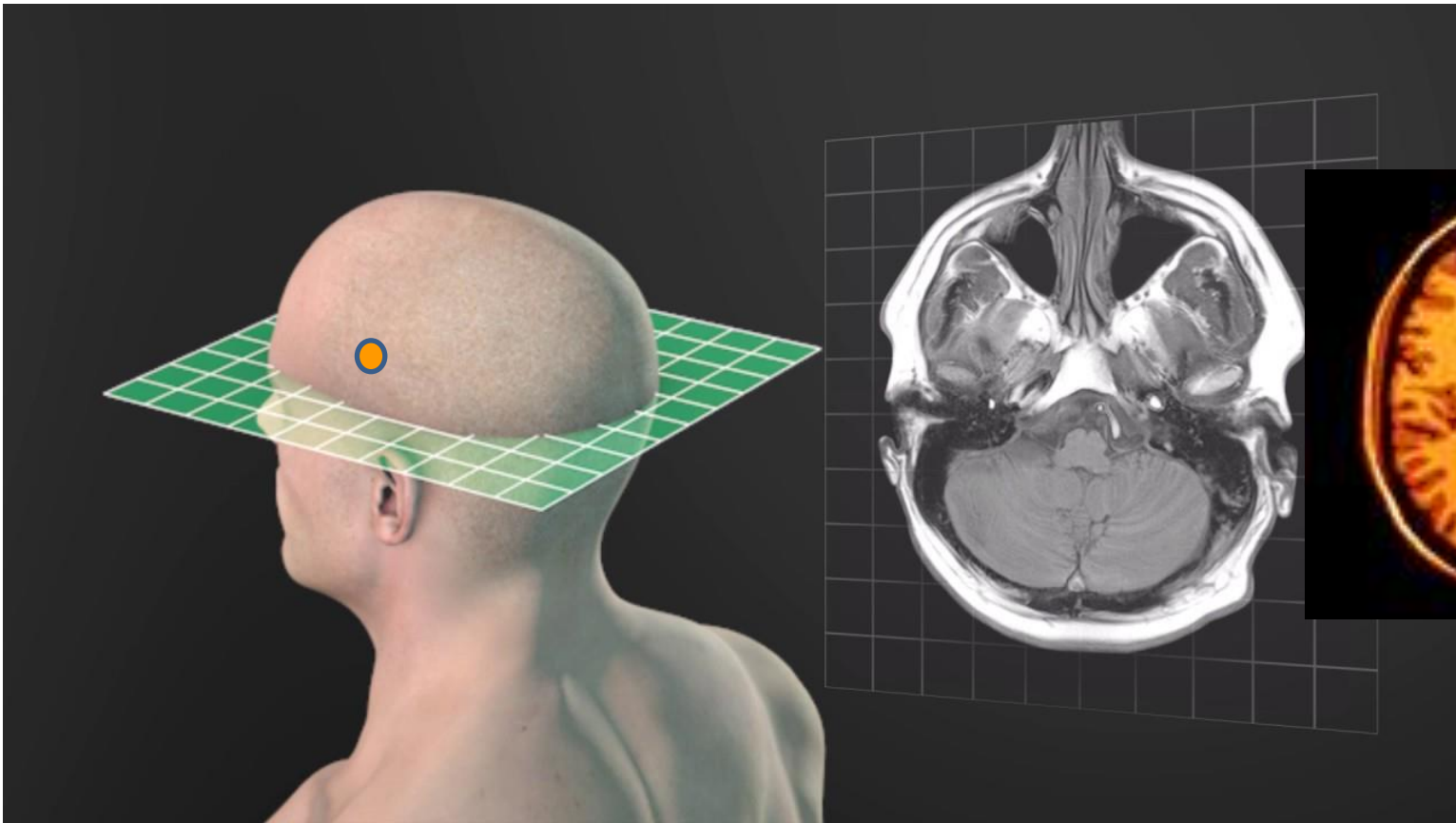
Disrupted
Behavioral
Control





from
<https://faculty.washington.edu/chudler/slice.html>

a neuroscience for kids site



3D4Medical channel...

<https://www.youtube.com/watch?v=2J8bDkALBic>

The AIC (anterior Insula cortex)

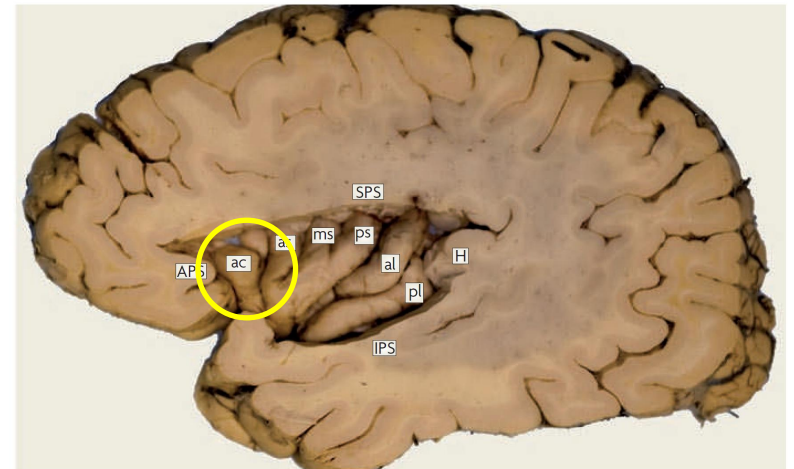
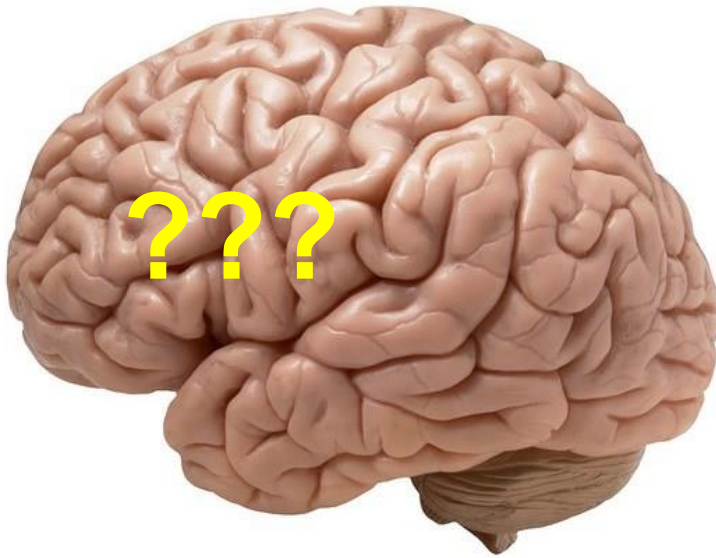


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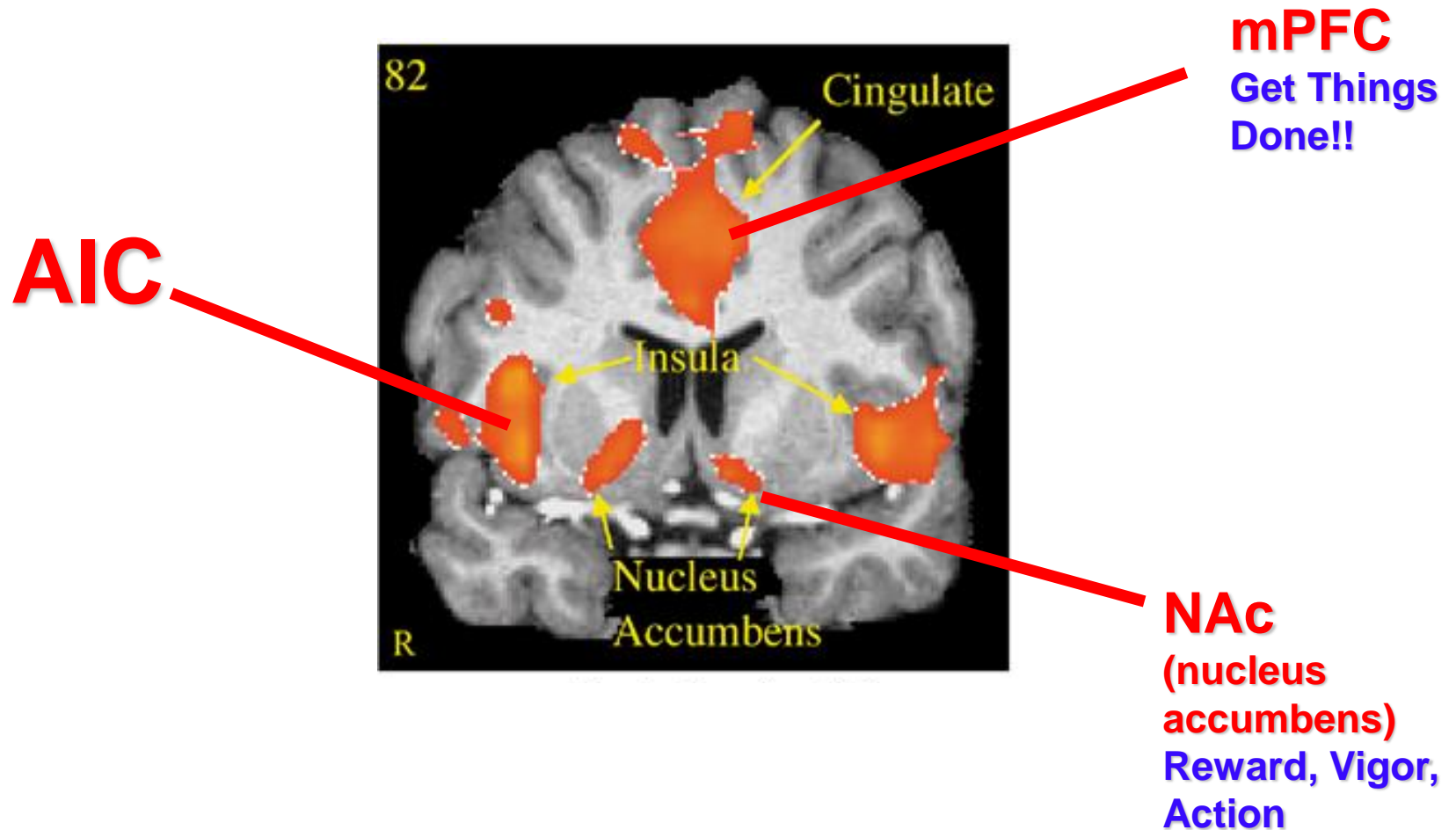
**If there is a challenge
It's usually because**

There's someone / something
really really important
That makes all the challenge worth it

The **IMPORTANCE SYSTEM!!**

Somewhere else says what is important

The importance system makes it happen



Anxiety in the moment:

Anxiety in the moment: more co-activation between AIC and amygdala

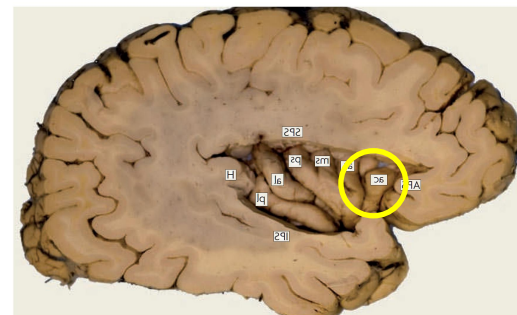
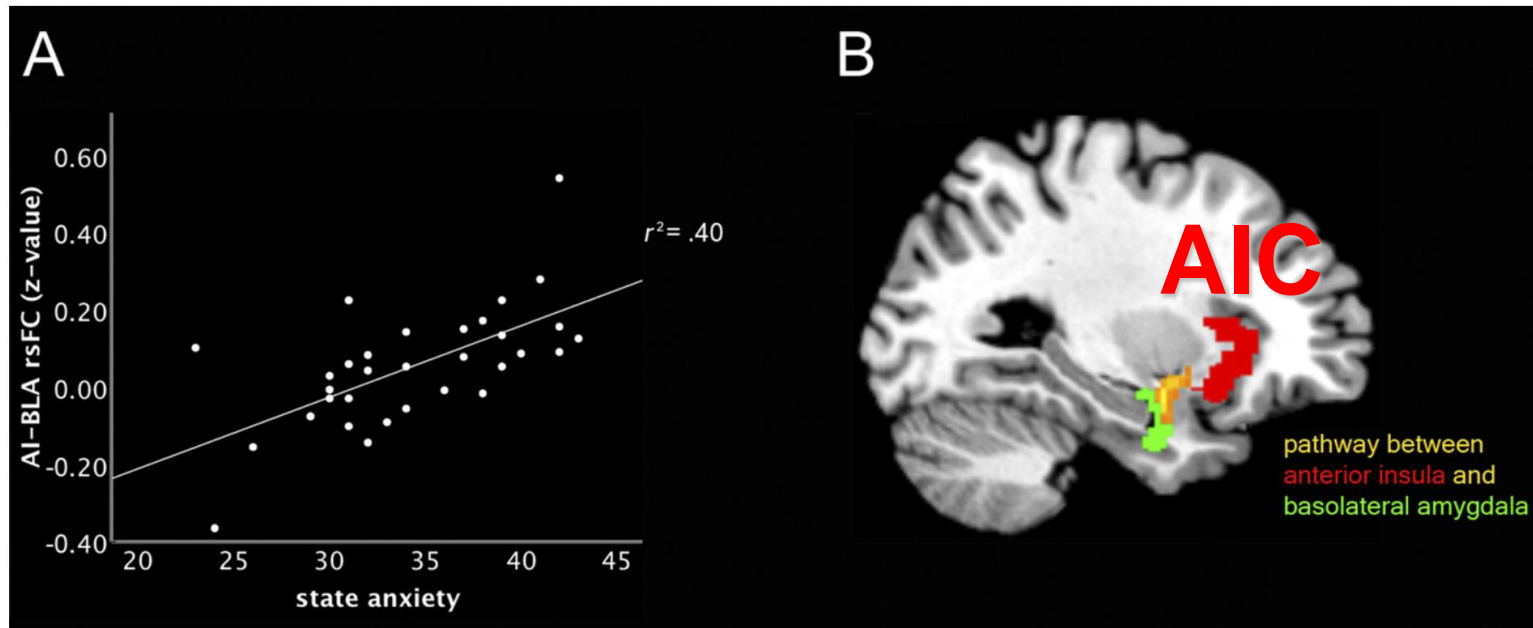
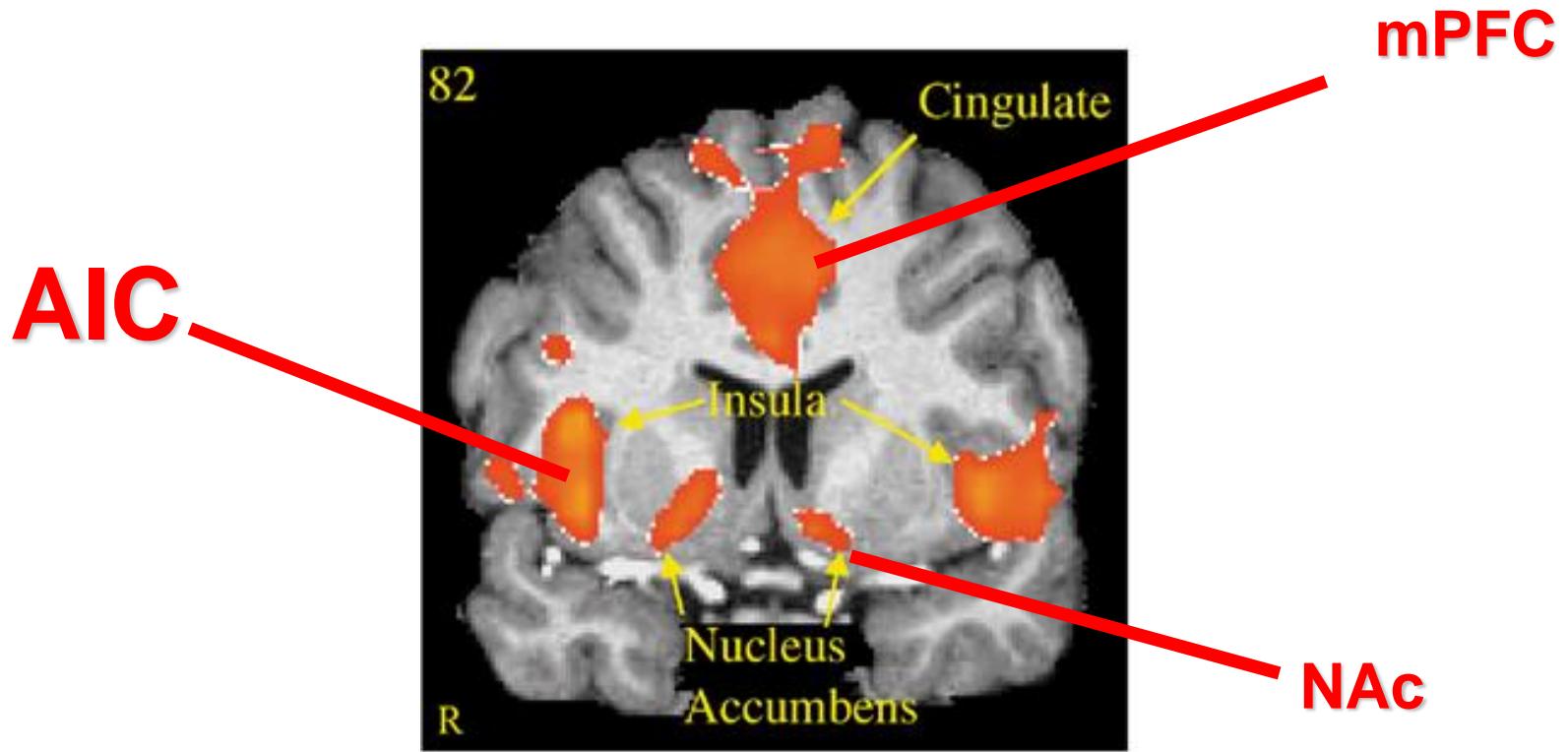


Figure 1 | Anatomy of the insula. A photograph of the left insular cortex of a human brain. For

Alcohol cues

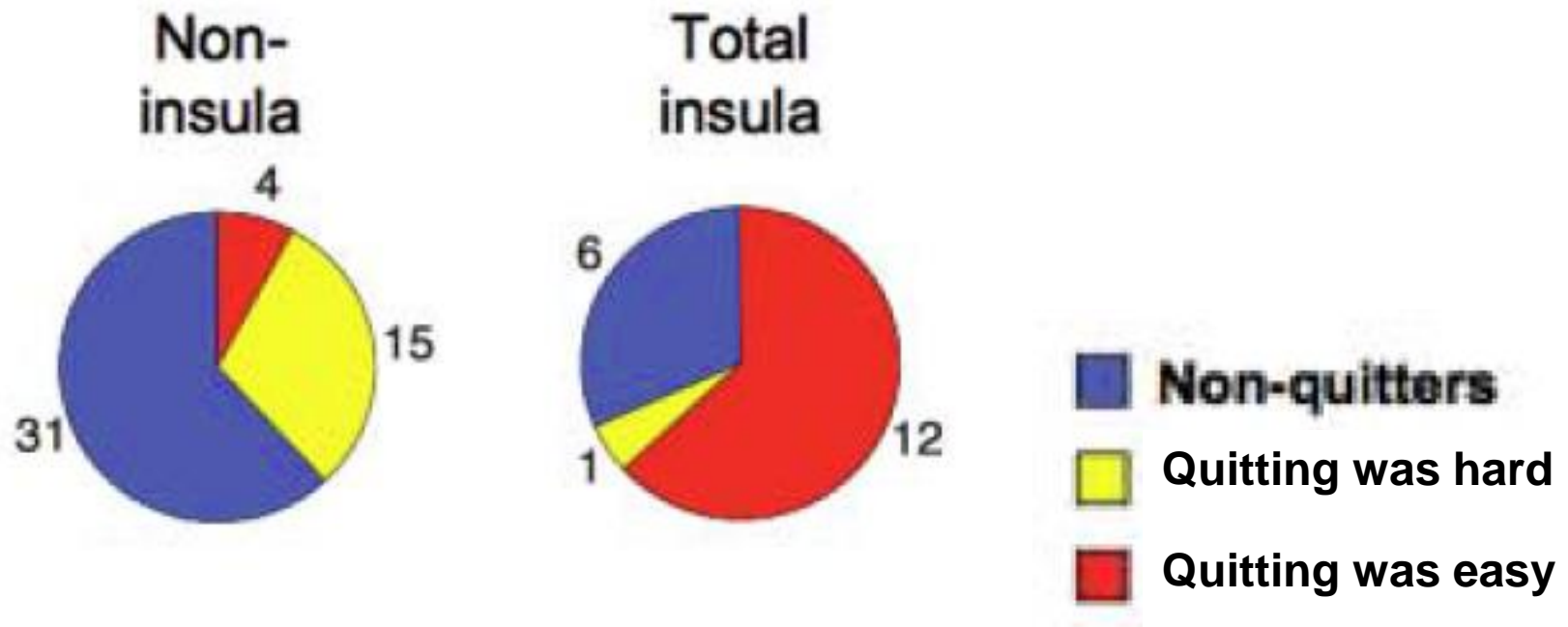
Activity predicts future intake and relapse



How powerful is this system?

Insula Stroke:

Give up smoking without effort



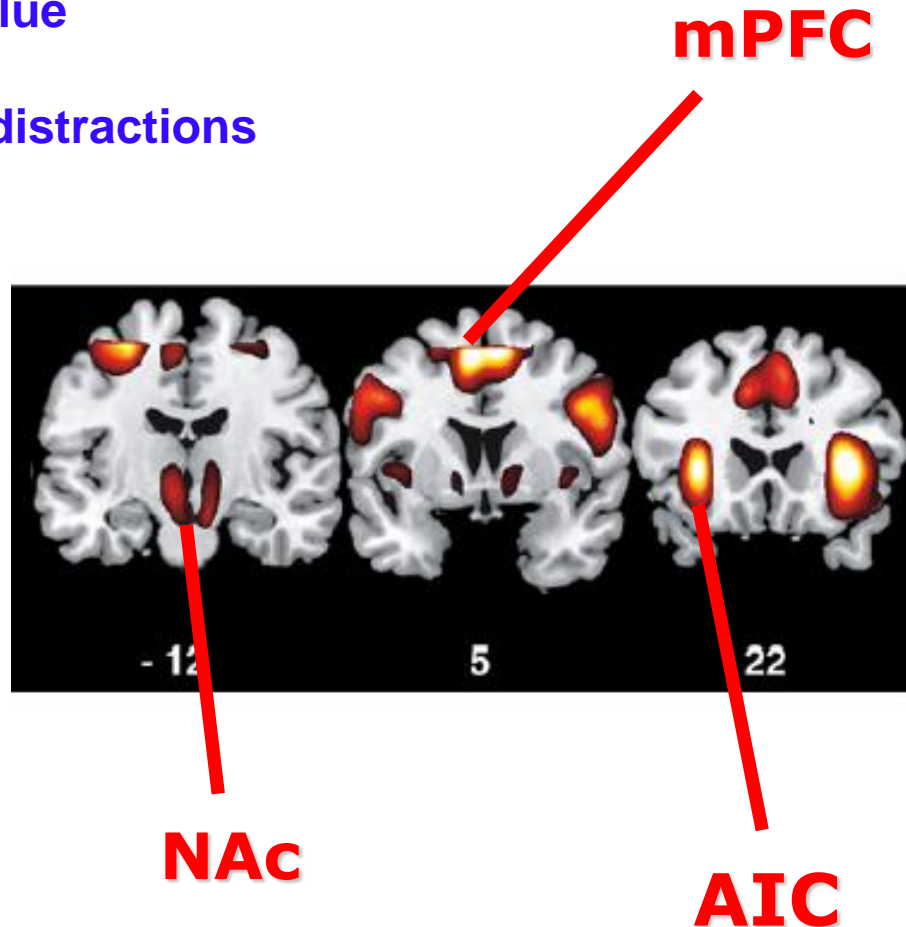
More AIC system activity when

Maintain attention when have

(1) high reward value

and

(2) Have to avoid distractions

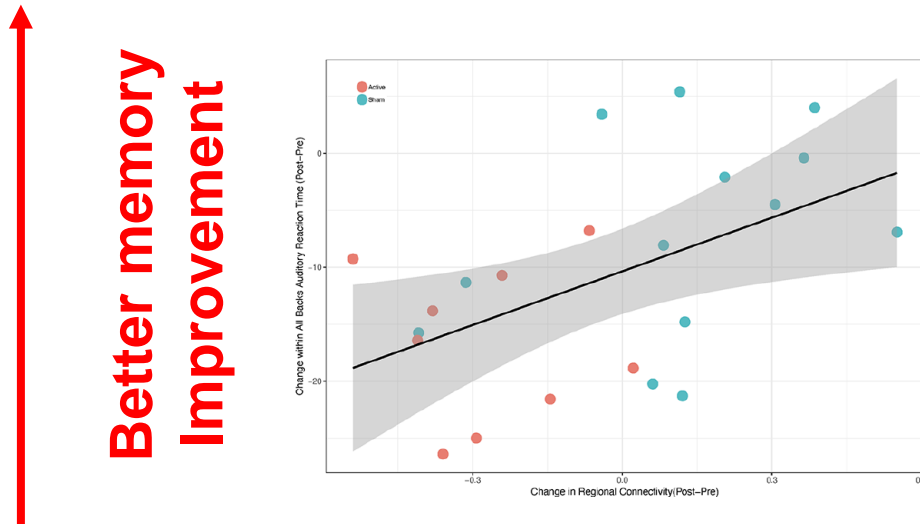


People with TBI have impaired working memory
(things fall out of our memory)

If we do Brain Stimulation of “mental control areas”

People with TBI have impaired working memory (things fall out of our memory)

If we do Brain Stimulation of “mental control areas”



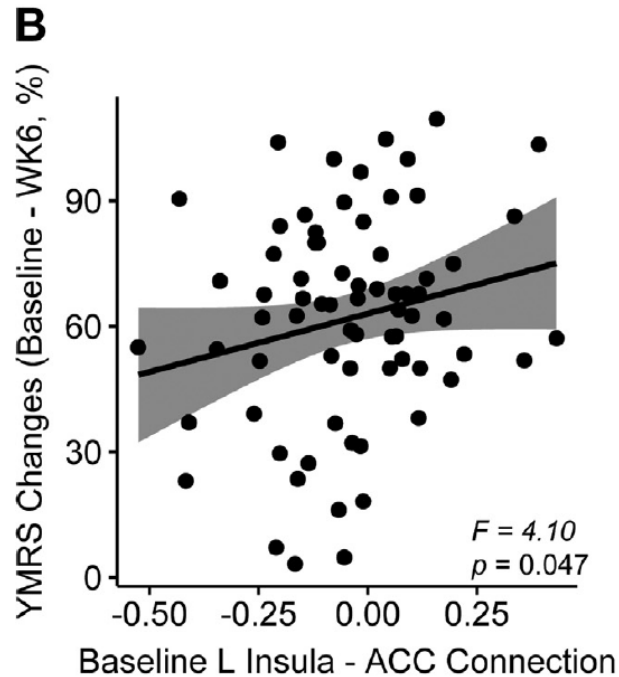
**Better memory
Improvement**

**More disconnection of mental control area
From the AIC**

Too much AIC hold on thinking and remembering areas,
If we break that link, memory gets better!!

Better response to drug treatment in youth with Bipolar Disorder?

Better Improvement

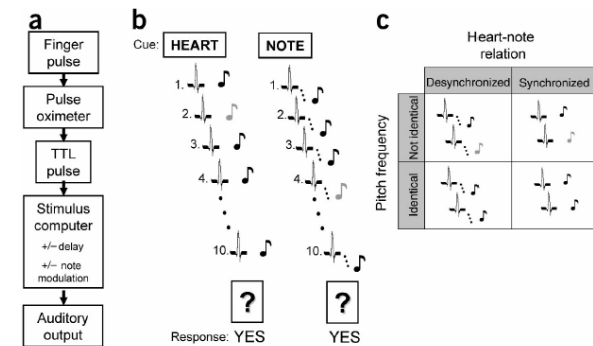


Better AIC connections



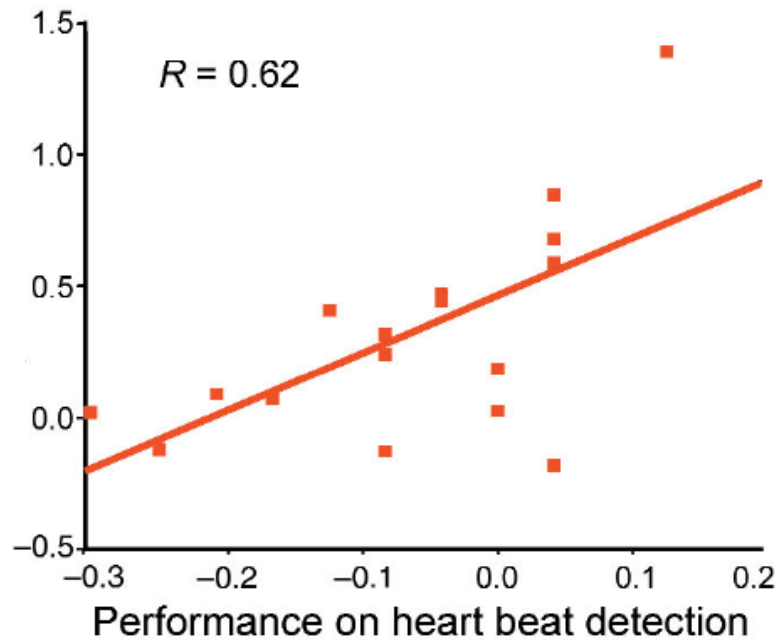
Steve Strakowski
IU Dept Psychiatry

A game: is my heartbeat in time with music rhythm?

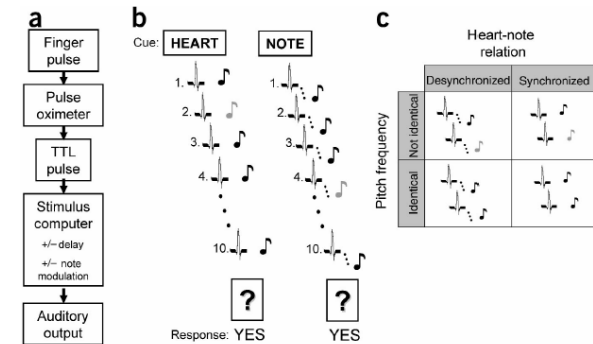


AIC is where you feels things (Generate and Experience “Feelings”)

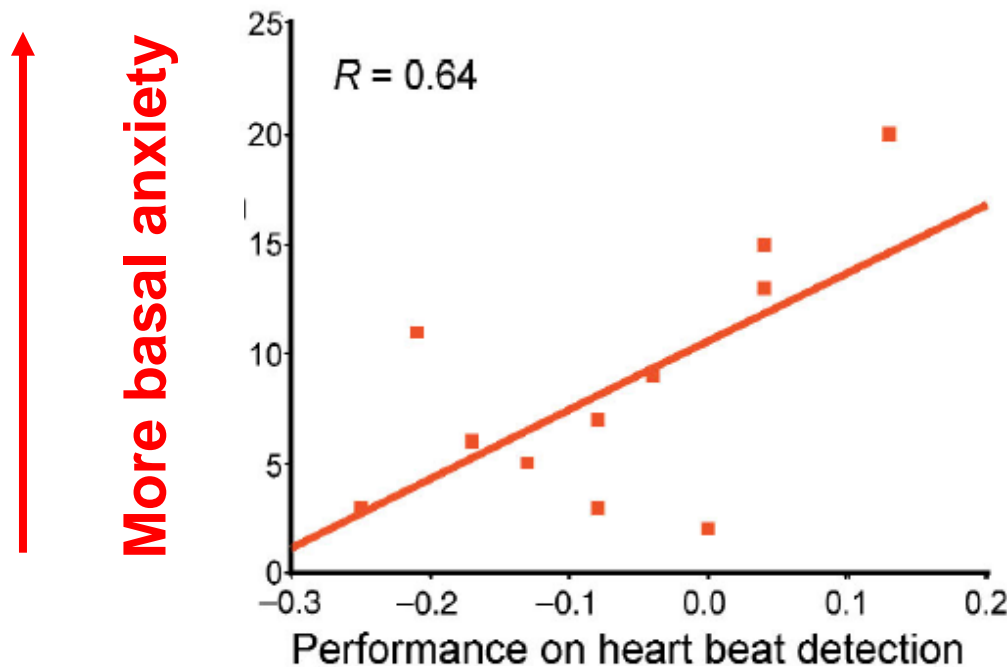
More AIC activity



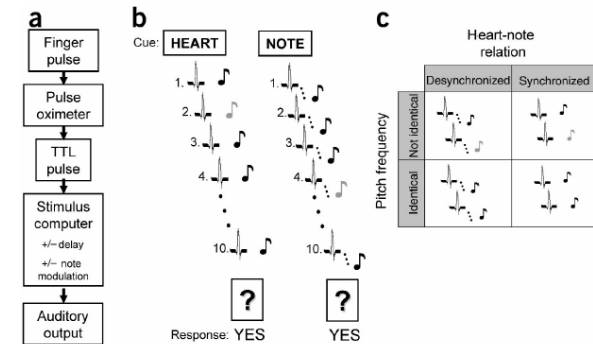
Better ability to feel body



Feel body better = more basal anxiety



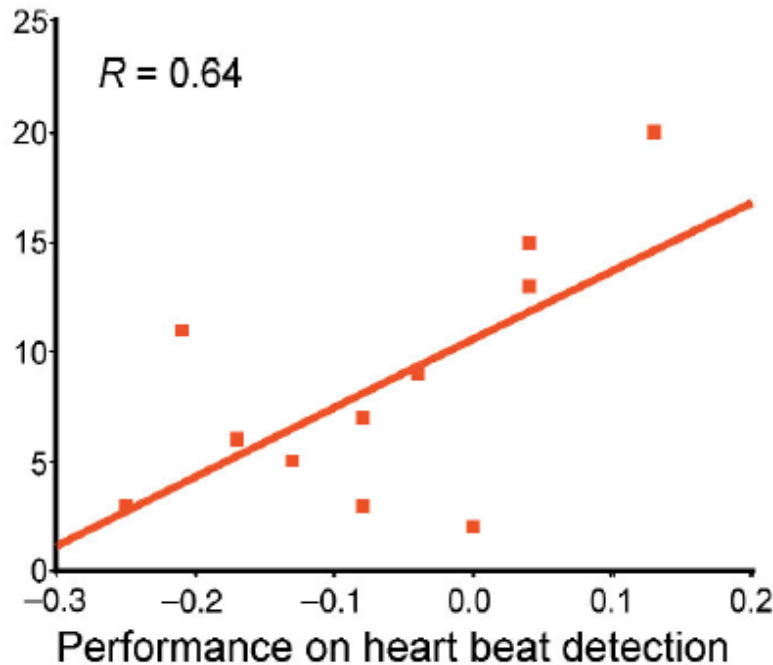
Better ability to feel body



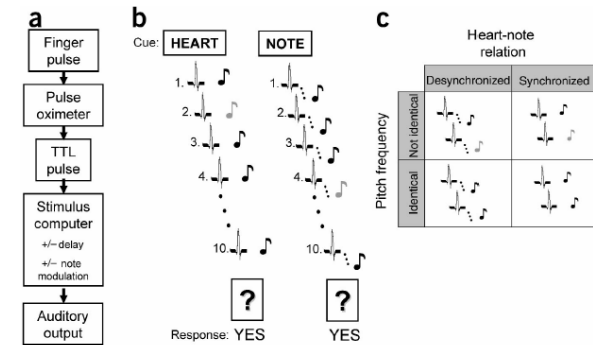
Awareness innately comes with some anxiety



More basal anxiety



Better ability to feel body



“Emotional Compromise”?

Brain can “sell us out”

“Emotional Compromise”?

Brain can “sell us out”

The brain will tolerate bad feelings (anxiety, depression)
if they are predictable!

Prevents strong fluctuations in feelings

(that could be even more debilitating).

Having moderate worry can prevent bigger changes in bad feelings

(including where relaxing feels scary)

proposes that individuals with generalized anxiety disorder (GAD) are hypersensitive to sharp upward shifts in negative emotion that typically accompany negative events, and use worry to maintain sustained intrapersonal negativity in an attempt to avoid these shifts. Although research shows that

While worry increases negative emotionality it also mutes further emotional reactivity to a stressor when compared to the worry period (e.g., Llera & Newman, 2010), no study has

AIC: Keep Calm and Carry On

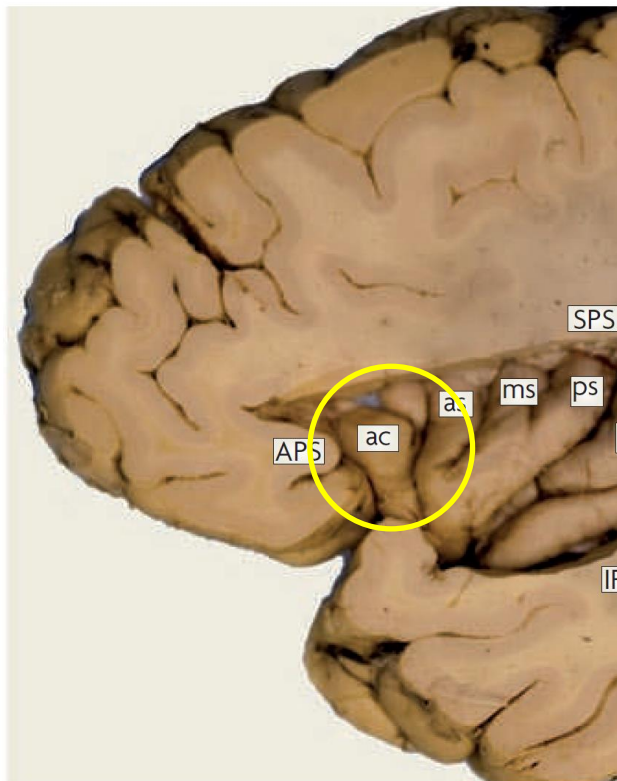


Figure 1 | **Anatomy of the insula.** A photograph of the left insular cortex of a human patient. For a

Problem Drinking

Compulsive alcohol drinking

Pardon Me, Officer, While I Finish My Beer



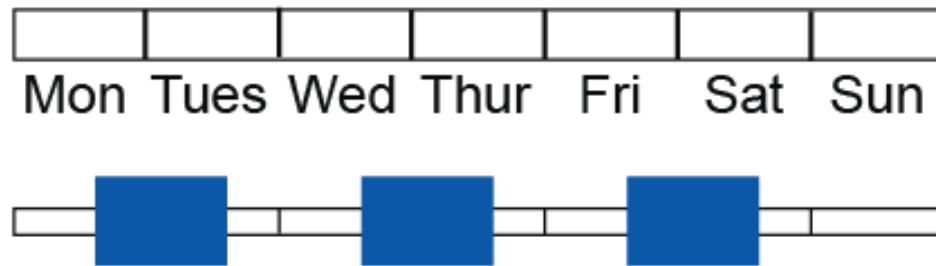
**Keep drinking despite
“Known” harms**

AIC circuitry and Compulsion-like Alcohol Drinking

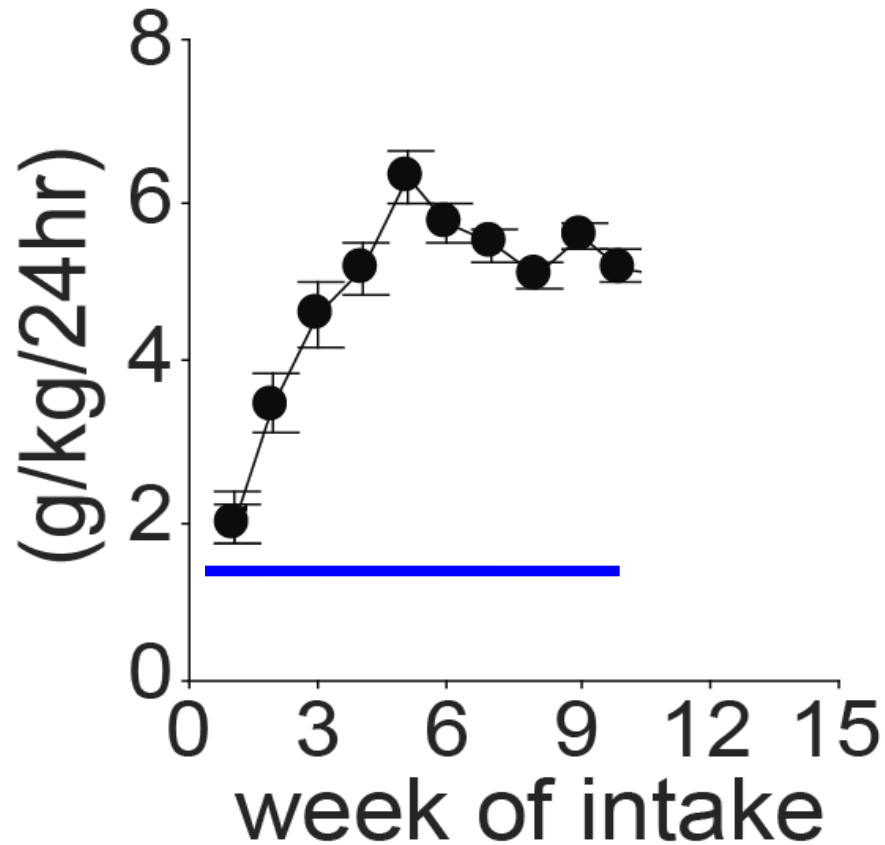


Rats get 24 hours alcohol Every other day

■ = 2-bottle choice for
20% alcohol or water

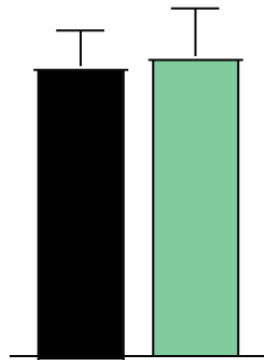


Rats learn to like to drink



**If the same brain circuit mediates
consequence-resistant alcohol drinking
in human and rats ...**

Inhibit AIC connection wires to where brain's adrenaline (noradrenaline) is made



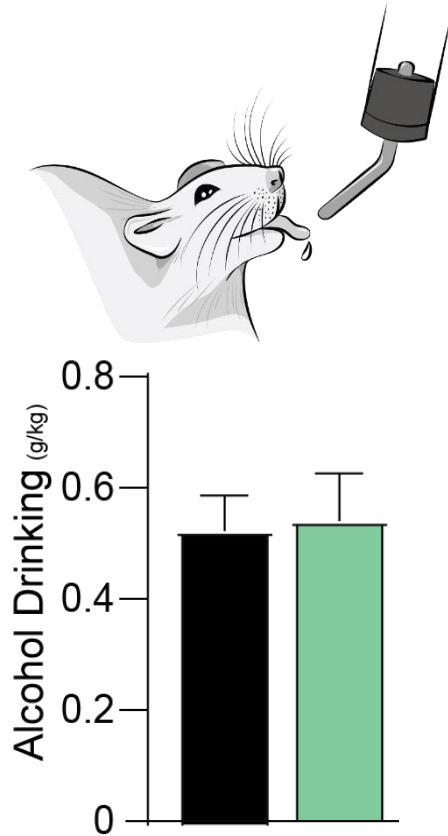
Brain area active

Brain area inhibited!!

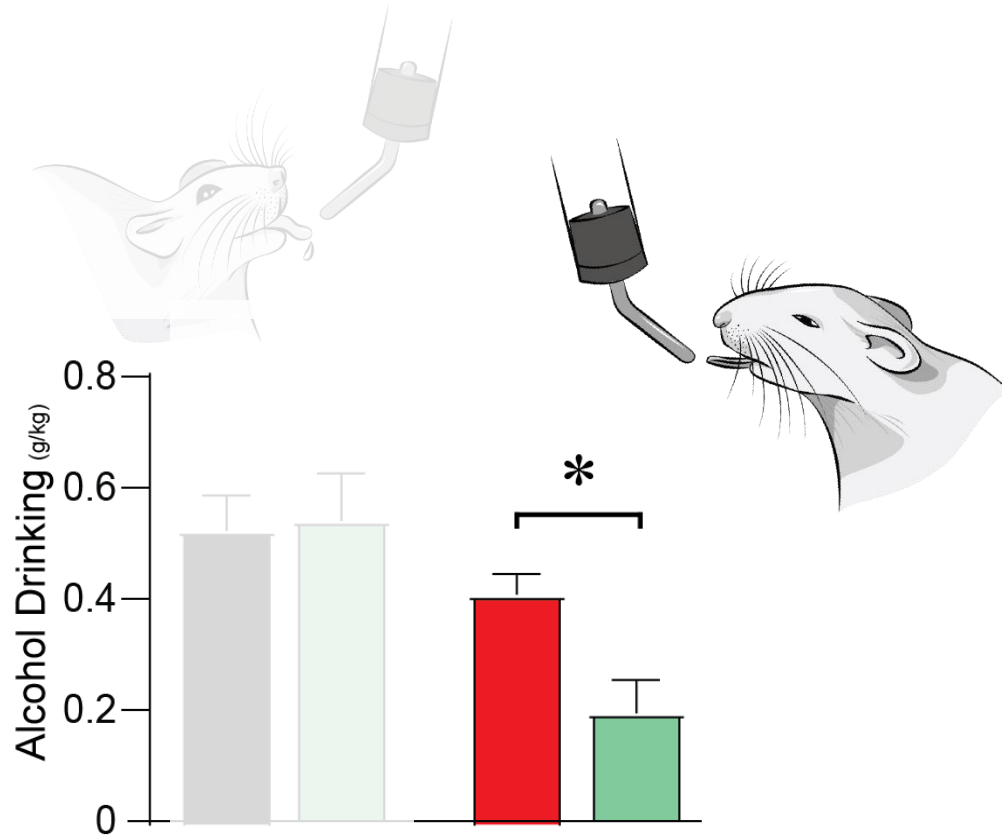
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Sergio, PhD



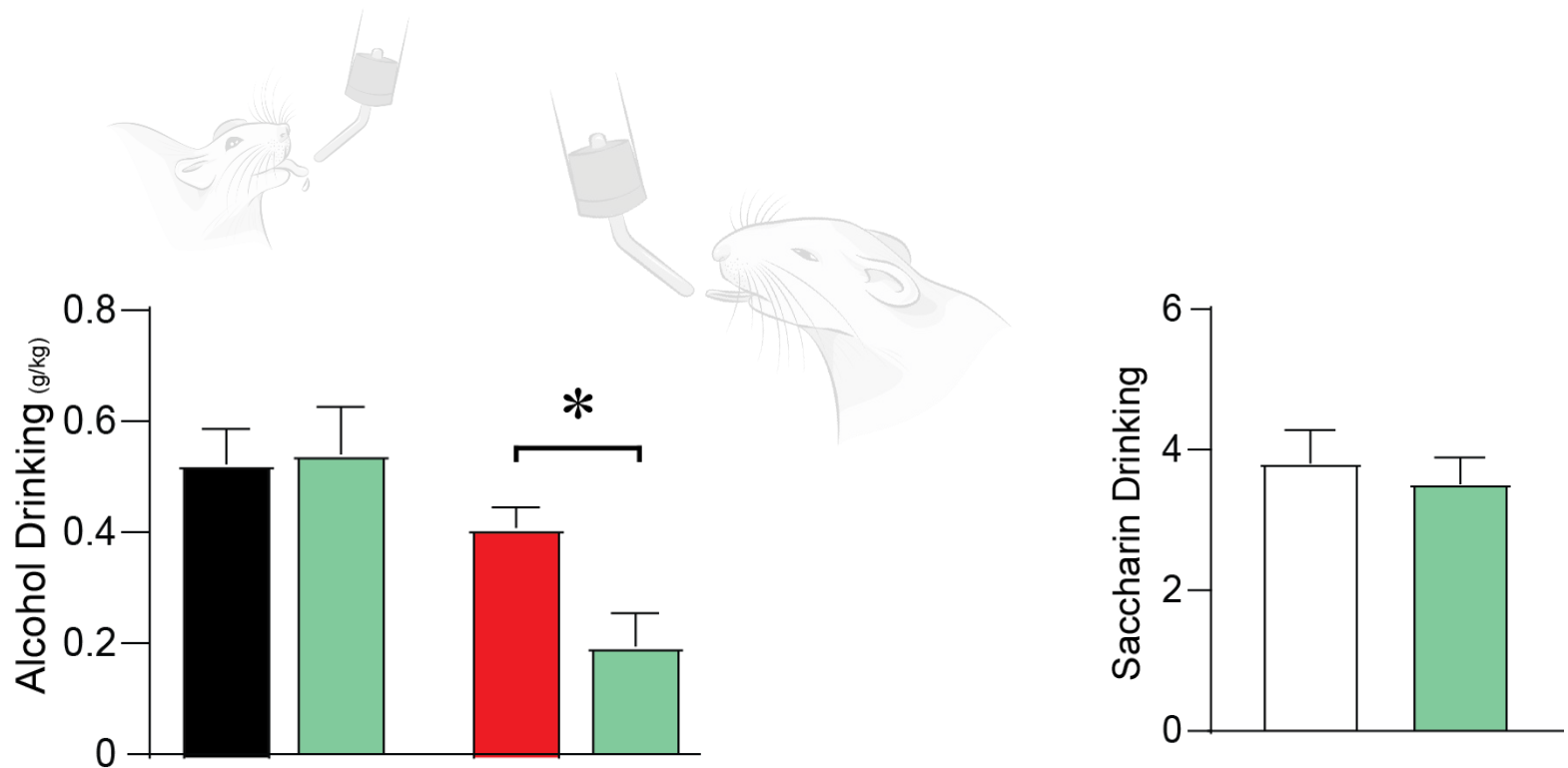
Inhibiting this brain connection: Does not impact “Regular” Drinking



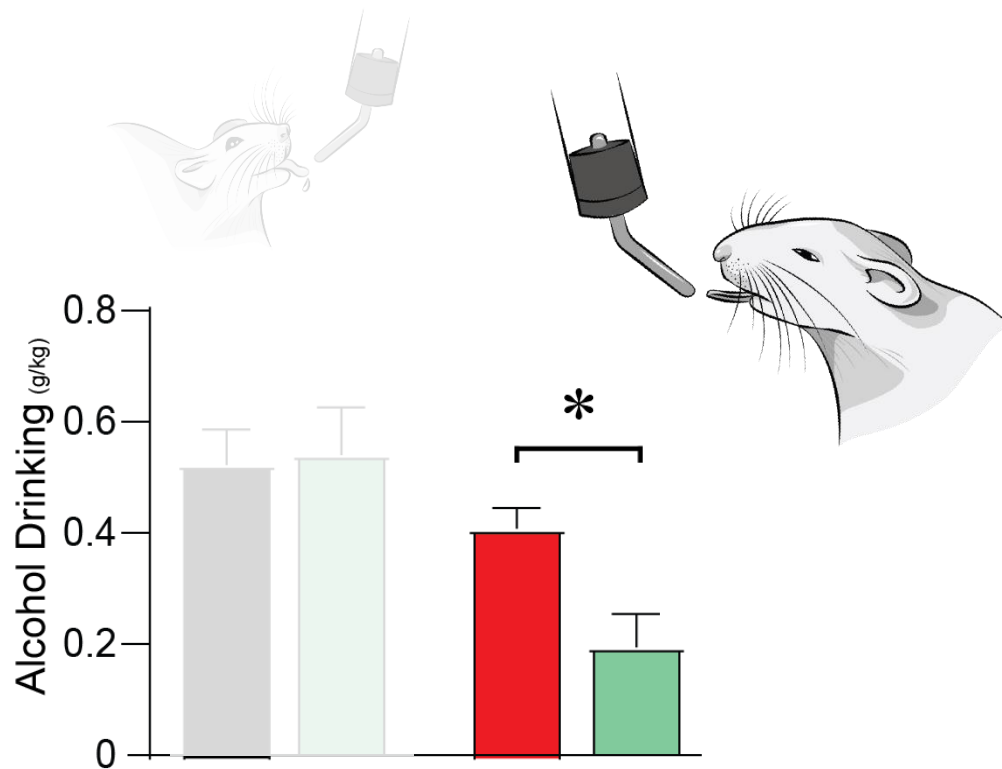
Inhibiting this brain connection: Strongly reduces compulsive drinking



Inhibiting this brain connection: Doesn't change sugar drinking



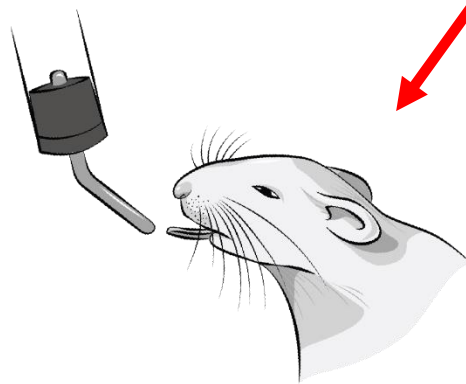
Why does the AIC system only drive Compulsive drinking?



No Conflict,
Happy striatum



Conflict Recruits
Cortical Circuits

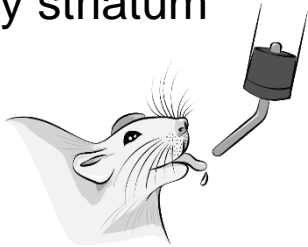


Different brain circuits drive
drinking
Depending on mindset
(conflicted or not)

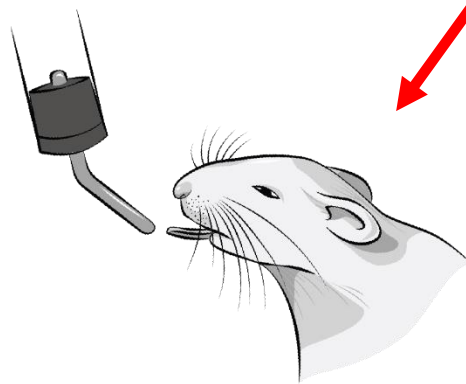
Which can literally change
from moment to moment

Does this pattern happen in humans?

Alcohol-Only,
No Conflict,
Happy striatum



Conflict Recruits
Cortical Circuits

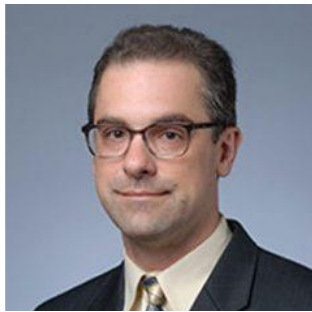


**The level of alcohol
People
Prefer to experience**

**The level of work
People will do
to get alcohol**



*Melissa Cyders
IU Dept Psychology*

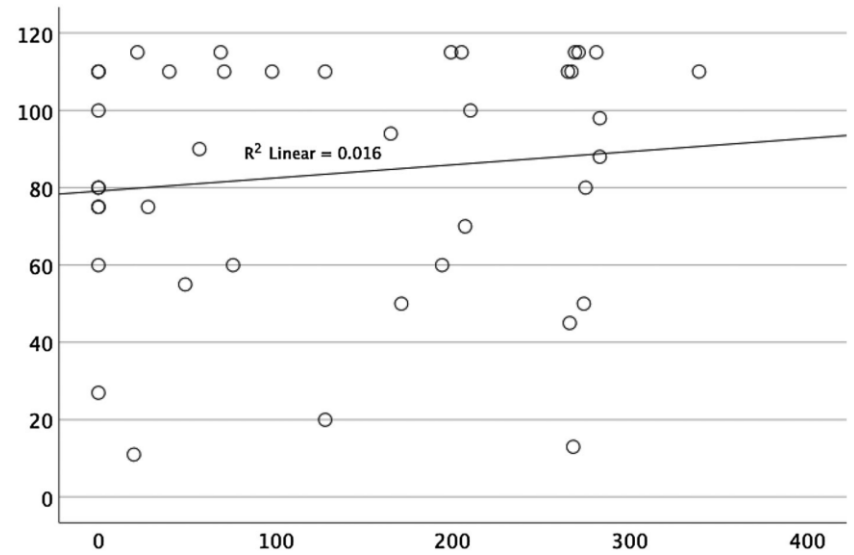


*Marty Plawecki
IU Dept Psychiatry*



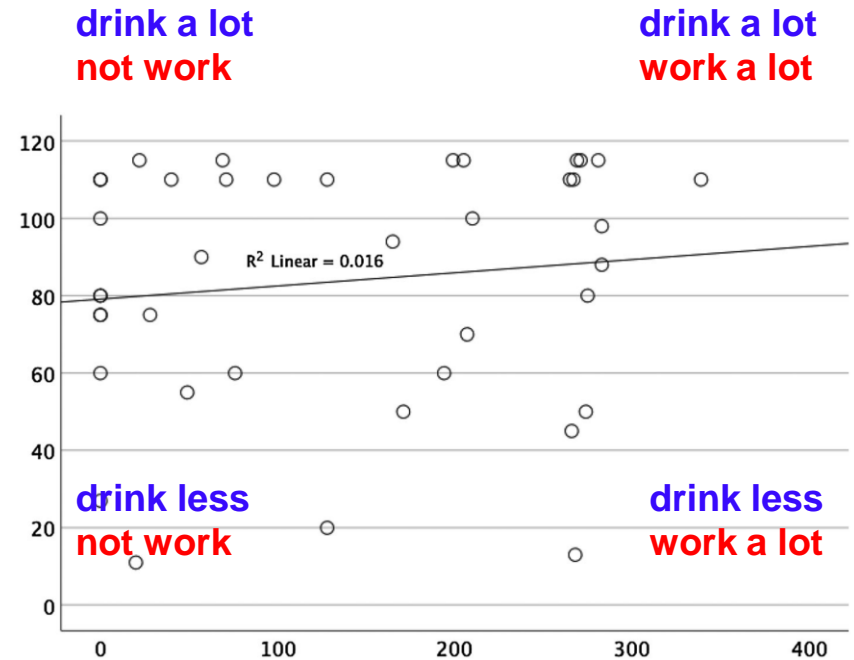
*Sean O'Connor
IU Dept Psychiatry
and Biomed. Engin.*

The level of alcohol People Prefer to experience



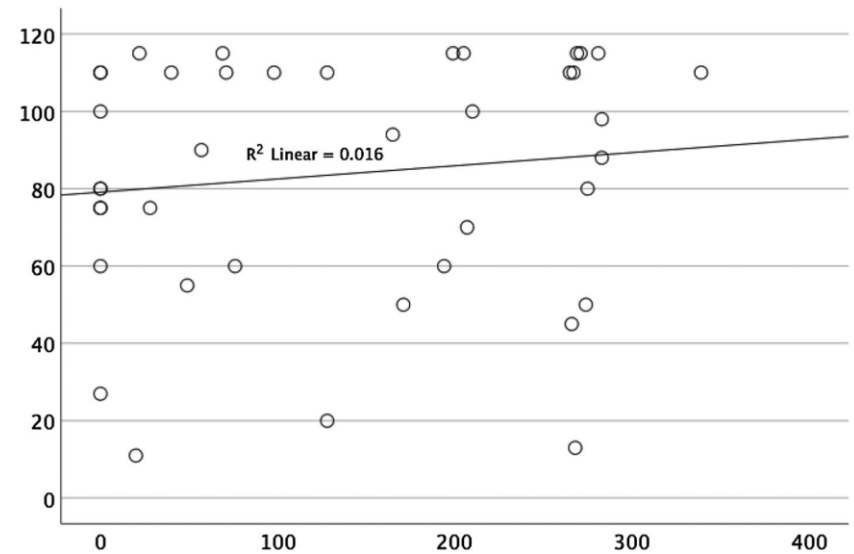
The level of work People will do to get alcohol

**The level of alcohol
People
Prefer to experience**



**The level of work
People will do
to get alcohol**

**Enjoying but
Not craving**



**Craving but
Not enjoying**

**Linked to disinhibition
Family risk of heavy drinking**

Two different brain pathways to “help you” have drinking problems

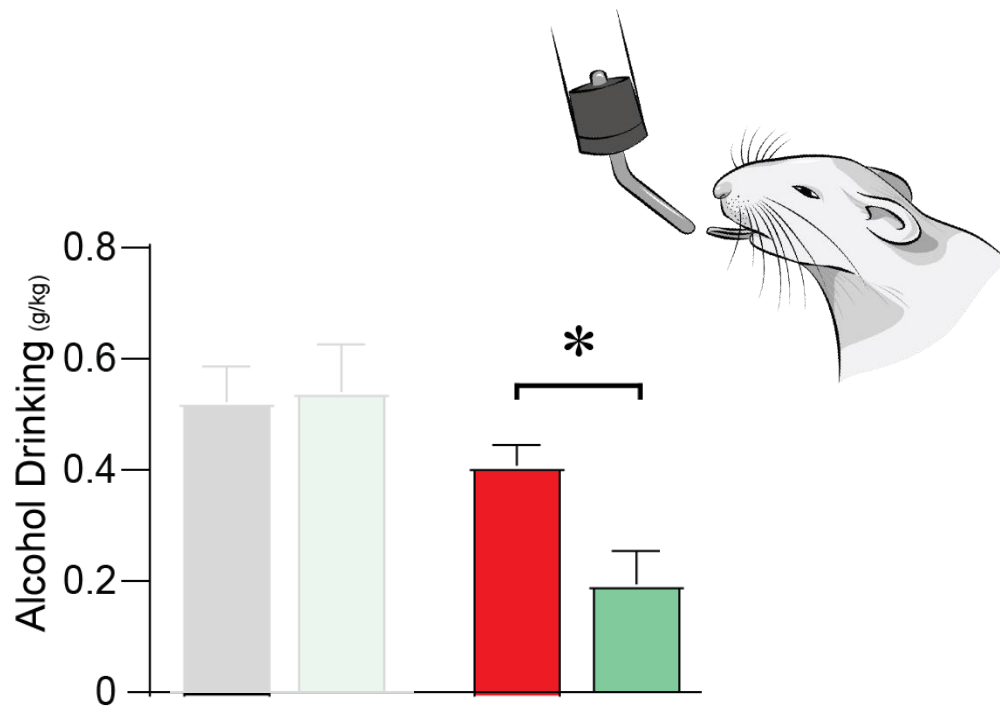
Binge drinking



Compulsive drinking (drink despite harm)



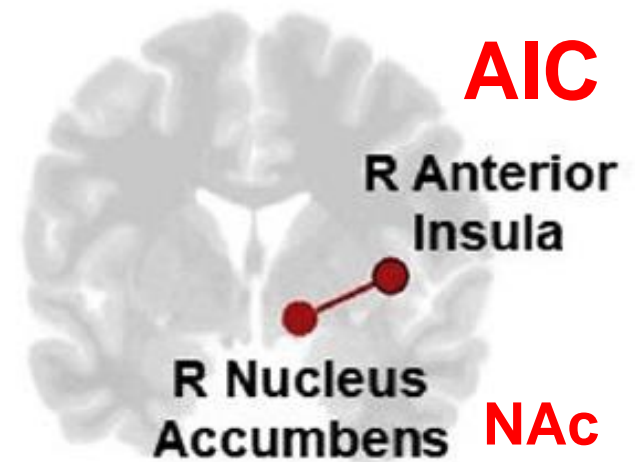
Does the AIC system only drive Compulsive drinking **in humans**?



Heavy Drinkers

More AIC-NAc connection correlates with

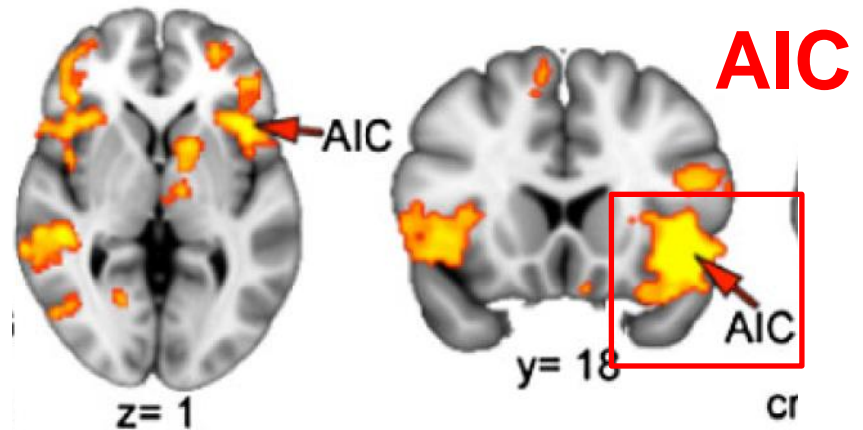
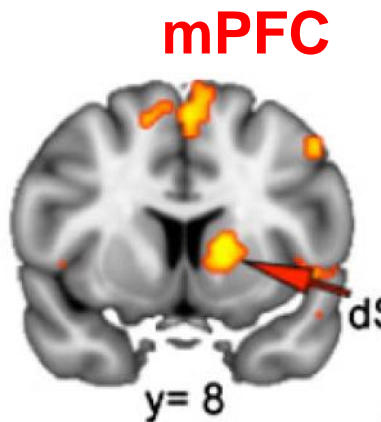
- more compulsive behavior
- greater self-reported compulsivity



Heavy Drinkers

AIC system

IMAGINING Alcohol drinking
Under “high-risk” situations



AIC system promotes Compulsive Action for Alcohol in Humans and Rats

Your brain selling you out:

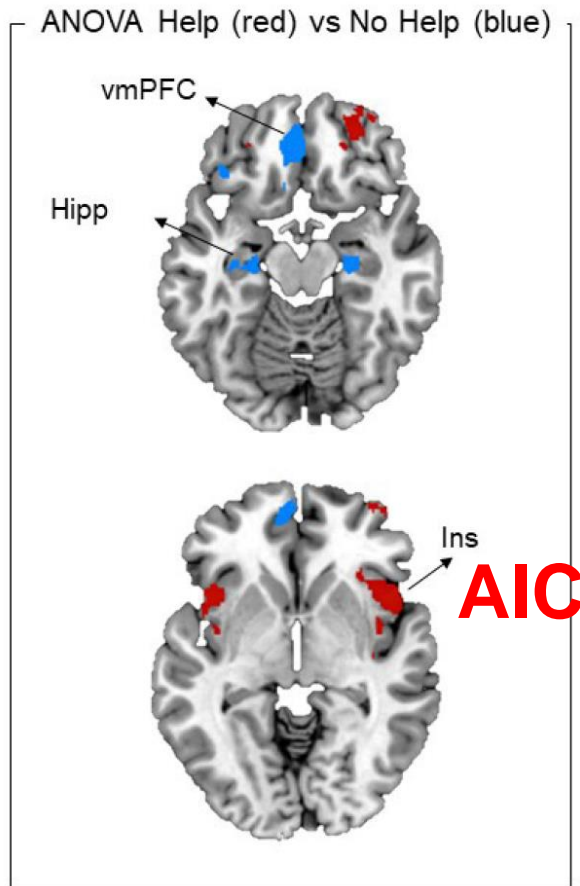
Ignoring bad consequences makes
things easier in the short term

But

AIC system and empathy / stigma

What is the AIC really all about?

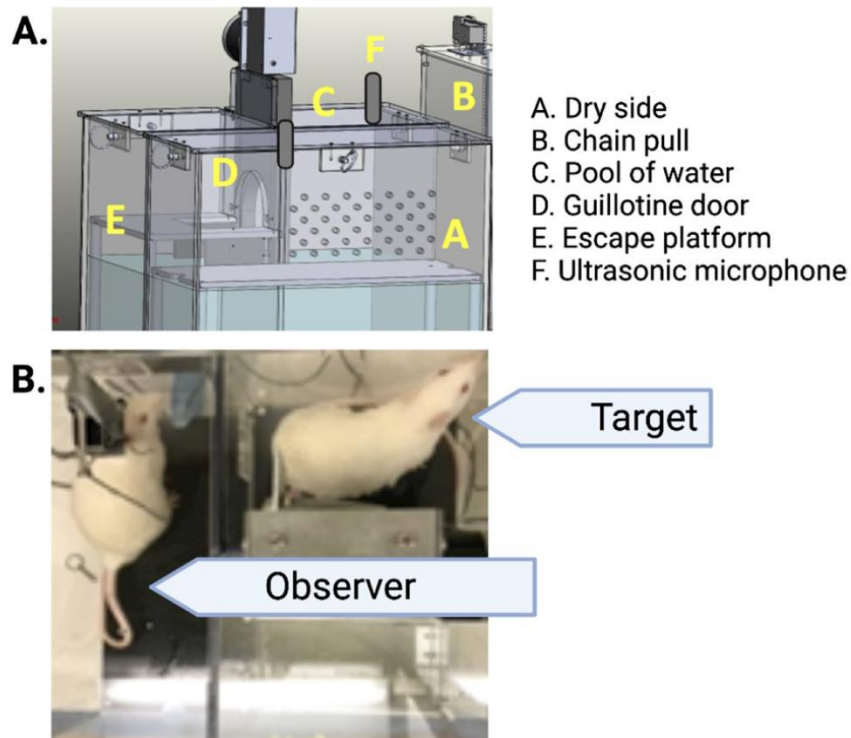
AIC and empathy in humans



Brain areas for the most basic
defense reflexes (AIC)
also mediate
empathy and helping

You feel bad
It drives you to help others

AIC and empathy in rats



AIC: For freeing a friend
in distress (Targeted Helping)

Not for the joy you feel
in a place where you hang out
with your friend (Social Reward)

Homeless person

got there by their own choices

got there beyond their control

Empathy
Cooperation

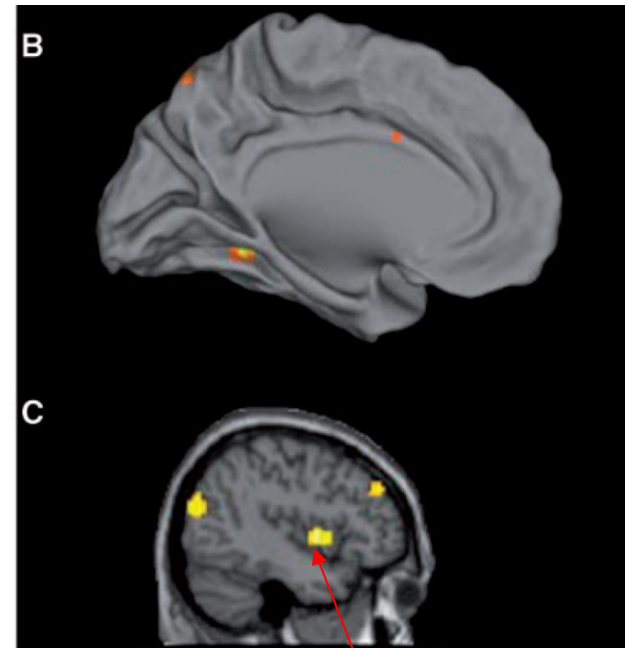
Homeless person

got there by their own choices

Top of mPFC



got there beyond their control



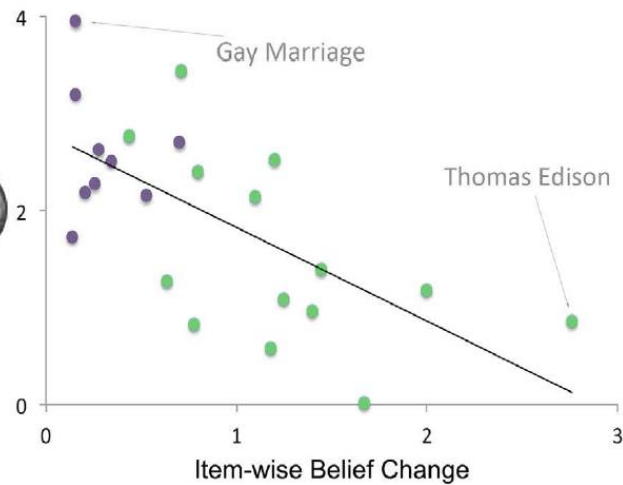
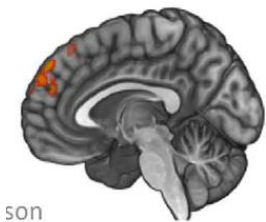
AIC!!!
Empathy
Cooperation

Beliefs threatened? More DMP means less belief change

Specific things
won't change belief on

mPFC

B



Beliefs threatened? More DMP AIC means less belief change

Specific things
won't change belief on

Overall resistance
to belief change

mPFC



AIC

amygdala

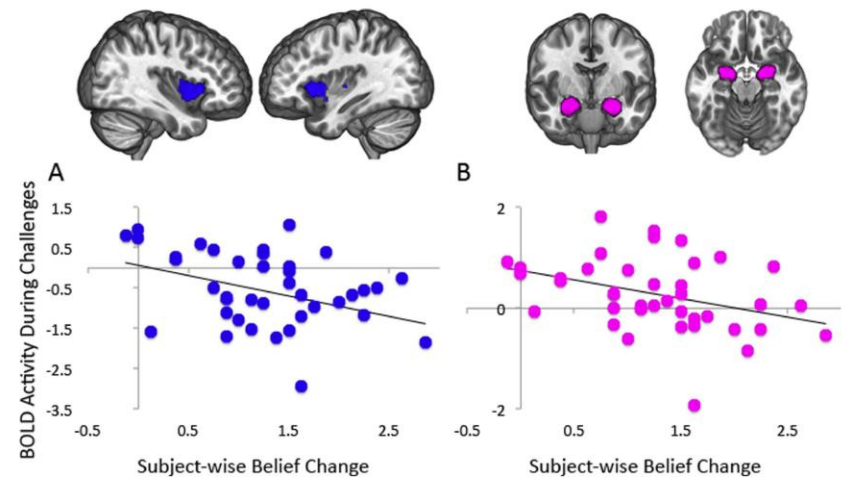


Figure 4. BOLD signal during challenges correlated with belief change across participants in (A) dorsal anterior insular cortex and (B) amygdala, from region of interest analysis.

AIC

Emotion

Attention

Self-control

Empathy

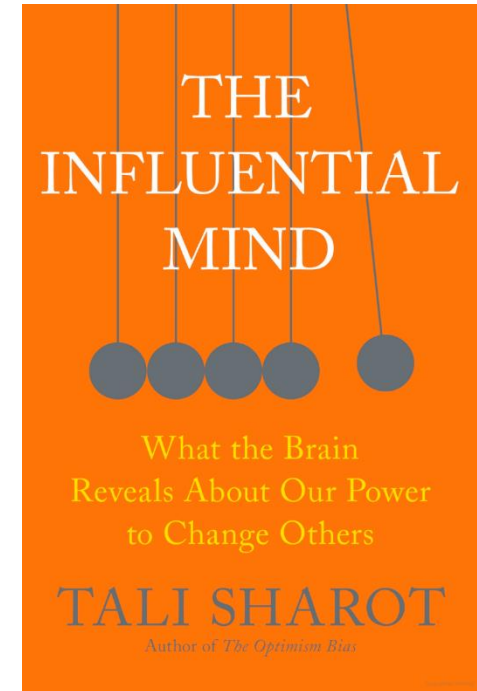
Cooperation

etc.

BUT

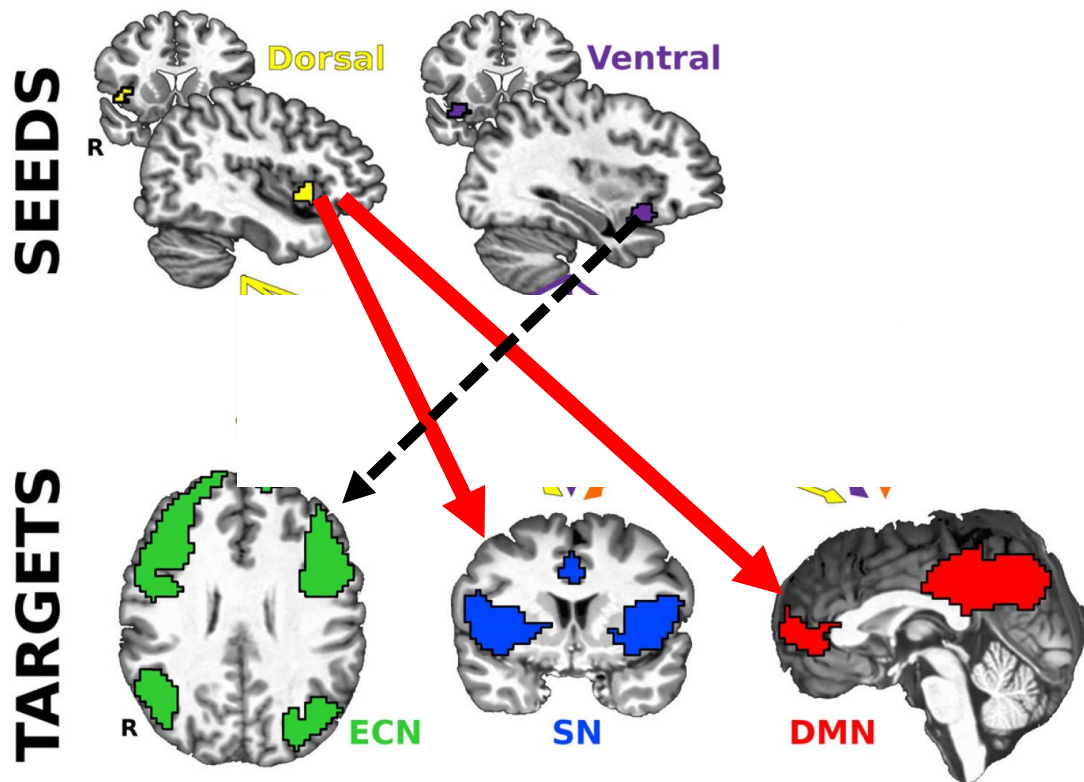
Can get defensive when
back is up against the
wall

Speak to the Heart



“Sharot reveals the critical role of emotion in influence, and the weakness of data.”

1-2 days since cigarette RIGHT SIDE AIC



Less Ventral AIC (emotion)
To Executive Control areas

More Dorsal AIC (control) to itself
And to High Value/Self Feeling Areas

The Will to Persevere Induced by Electrical Stimulation of the Human Cingulate Gyrus

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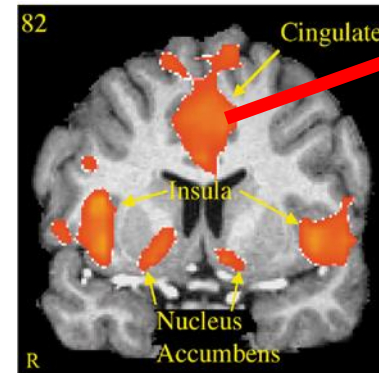
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- Get Things Done!!
- Flexibility

In the current study, we show that electrical charge delivery in the anterior midcingulate cortex (aMCC) elicits autonomic changes and the expectation of an imminent challenge coupled with a determined attitude to overcome it. Seed-based, resting-state connectivity analysis revealed that the site of stimulation in both patients was at the core of a large-scale distributed network linking aMCC to the frontoinsular and frontopolar as well as some subcortical regions. This report provides compelling,



go go go

Confidence, I can do it!
(feels good to do it)

LEFT AIC

**Positive yet
Vulnerable**

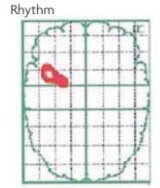
RIGHT AIC

**Harder
Things**

TOGETHER



Pleasant
music



Rhythm



Maternal
Affiliation

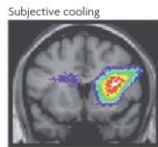
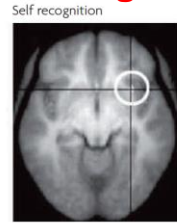


Happy
Voices



See or Make
a Smile

self-recognition



Cold



Heat
Pain



Feel
Heart
Beart

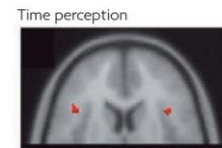
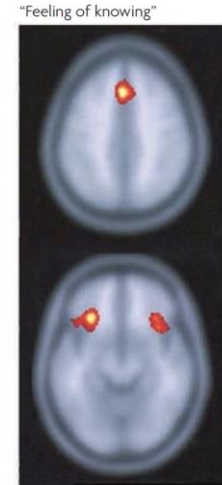
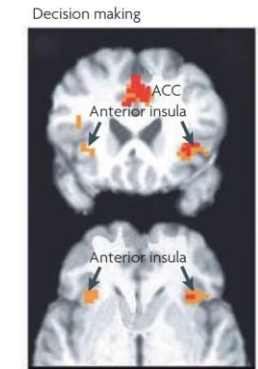
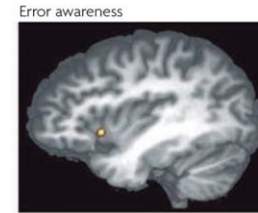


Learn
pain

**Choose to
Not Act
("free won't")**

**Moment of
Recognizing
("Aha!")**

**Decision
making**



**Feeling of
Knowing**

**Inspecting
(sustained
attention)**

**Time
Perception
(and
Distortions)**

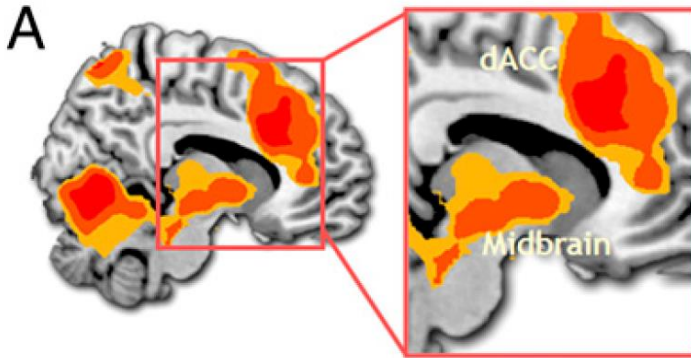
**Craving (lower)
1-2 hours after
Last Cigarette**

**Craving (higher)
1-2 days after
Last Cigarette**

**Most Singular Sense
of Self in the moment**

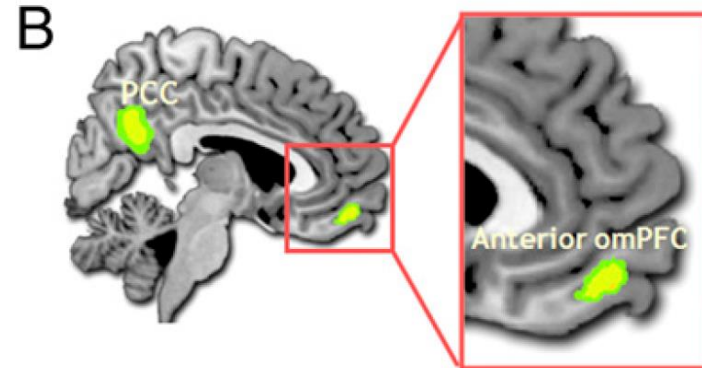
Fear

Spider moving
Towards foot



Safety

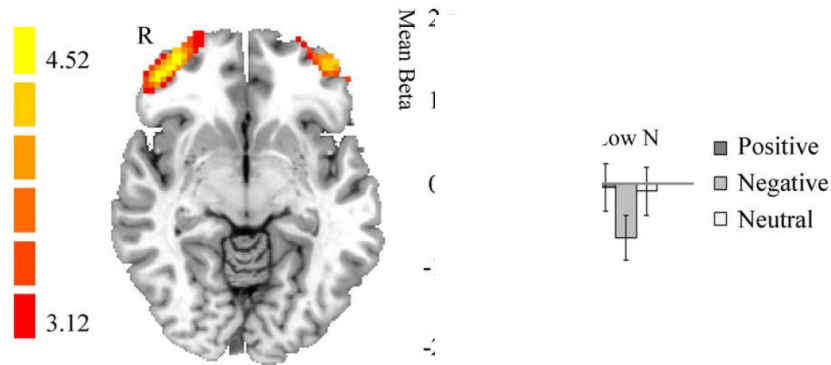
Spider moving
Away from foot



Self-Feeling Areas

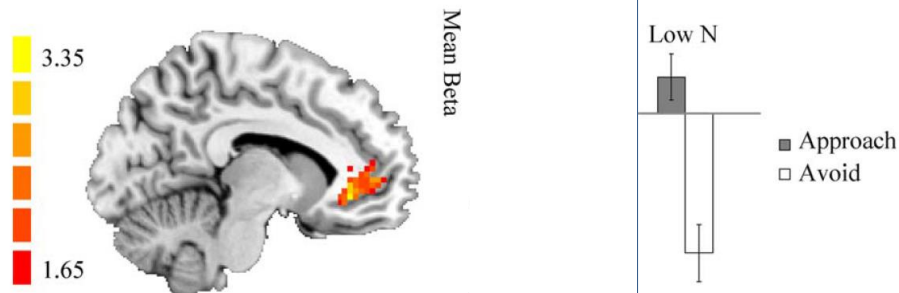
Not just have higher activity
levels that indicate Safety,
But embody the good feelings
(of safety, security, peace, etc)

A cousin of AIC: encodes potentially high-value events

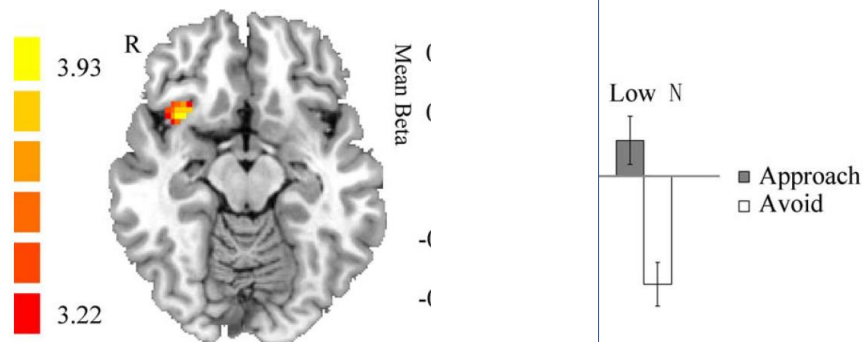


Seeing a Negative Emotional Image (“avoid”)

Self Feeling Area



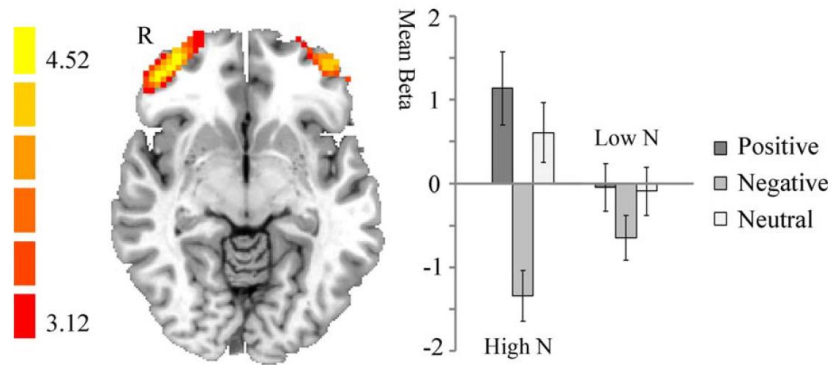
AIC



turns off
detaching attention from a negative
image?

turns off
detaching attention from a negative
image?

A cousin of AIC: encodes potentially high-value events

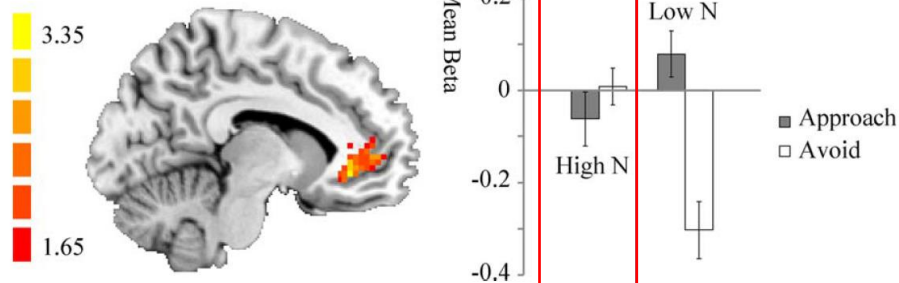


Higher Neuroticism (HN)

More impacted by both negative and positive emotion images.

Sends a **too-large signal** about events, rather than emotion disruption per se

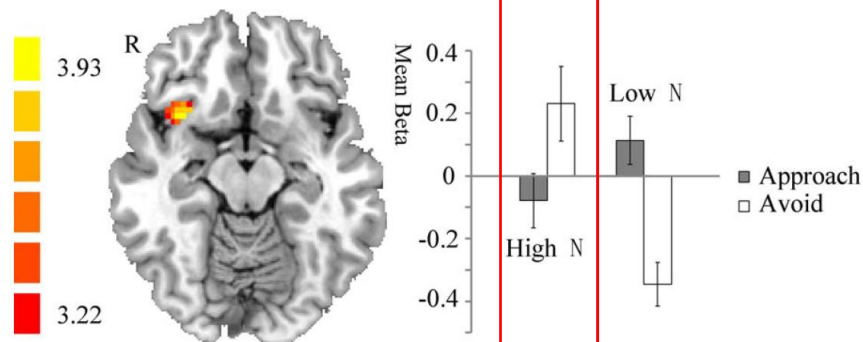
Self Feeling Areas



stays on

[Too much internalization makes disengagement harder?]

AIC



AIC activity actually bigger
Dysfunctional form of emotional regulation?

**Heavy drinkers:
greater AIC correlates with
less drinking** (and impulsivity)

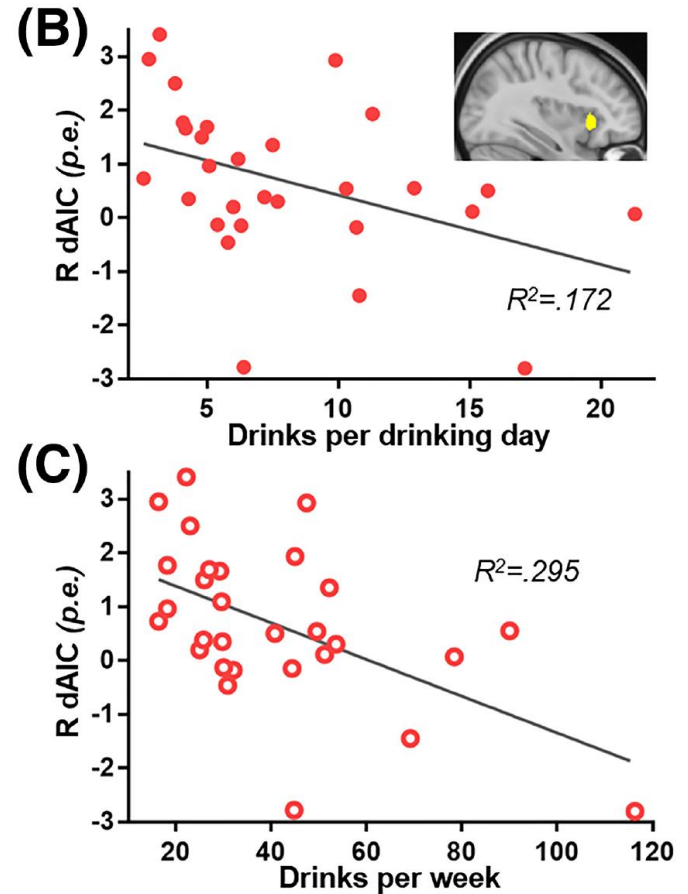
Better self control!!



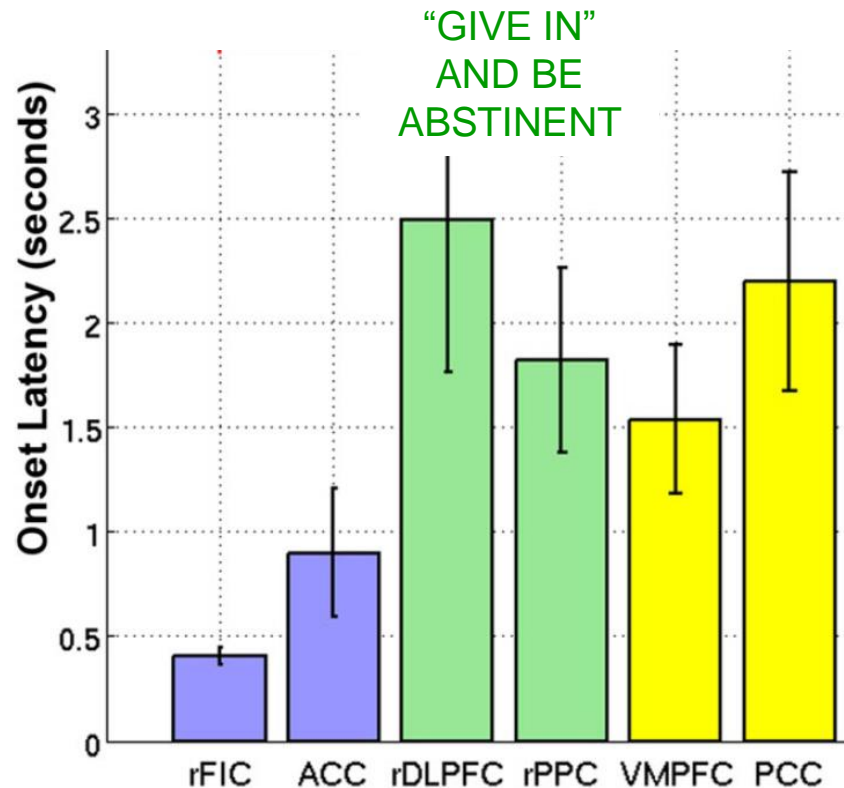
*Meredith Halcomb
IU Dept Radiology*



*Brandon Oberlin
IU Dept Psychiatry*



The aINS helps switch between
“Outside”
(Executive Control)
and
“Inside”
(Default Mode, one’s highest values).

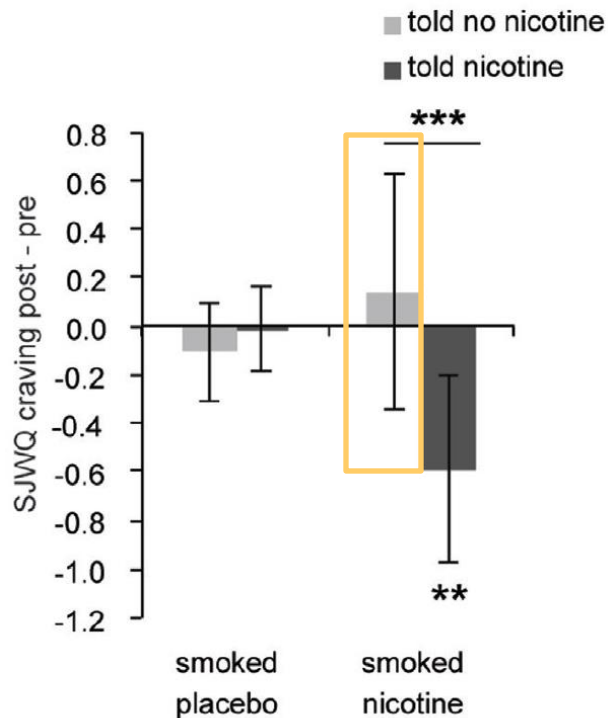


Ready to Ignore
Bad Things, for
Something
Very Worth It!!!

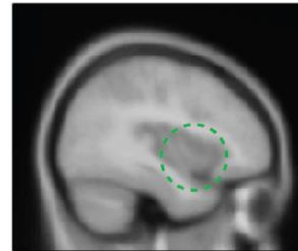
AIC and the power of expectation

If you smoke nicotine and believe there is nicotine, only then is AIC activated and craving reduced

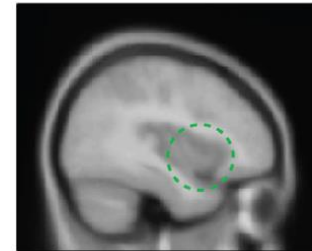
belief modulates change in
reported craving



told no nicotine, smoked placebo



told nicotine, smoked placebo



told no nicotine, smoked nicotine



told nicotine, smoked nicotine

