

Neural pathways in gambling and cocaine use disorders: commonalities and differences from a neuroimaging study

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Background

- Neurobiological theories of addiction and emerging neuroimaging evidence implicate *prefrontal striatal pathways involved in processing reward and stress*, in both gambling and substance use disorders.
- Gambling disorders and SUDs show partial overlaps in
 - DSM-V diagnostic criteria
 - Treatment (MI, CBT, nalmefene, naltrexone)
 - Aetiology and course
 - Comorbidity
 - Genetic overlap
 - Vulnerability

Common vulnerabilities in gambling and other SUDs

A family study of pathological gambling[☆]

Donald W. Black^{a,*}, Patrick O. Monahan^b, M'Hamed Temkit^b, Martha Shaw^a

2006

Table 4
Lifetime prevalence of psychiatric disorders in FDRs

Number (%) with	Proband diagnosis		Odds ratio (95% CI)	P value
	PG (n = 193)	Control (n = 142)		
Mood disorders				
Major depression	51 (26.4)	26 (18.3)	2.03 (0.88, 4.66)	0.10
Dysthymia	1 (0.01)	2 (0.01)	0.45 (0.12, 1.67)	0.23
Bipolar disorder	7 (5.8)	1 (0.01)	4.93 (0.57, 42.4)	0.11
Other mood disorder	2 (0.01)	1 (0.01)	3.78 (0.39, 49.8)	0.31
Any mood disorder	57 (29.5)	28 (19.7)	2.28 (0.96, 5.41)	0.06
Substance use disorders				
Alcohol abuse/dependence	56 (29.0)	18 (12.7)	5.09 (2.02, 12.81)	0.0006
Drug abuse/dependence	20 (10.3)	8 (5.6)	1.41 (0.50, 3.95)	0.51
Any substance use disorder	63 (32.7)	21 (14.8)	4.21 (1.91, 9.25)	0.0003
Anxiety disorders				
Panic disorder	11 (5.7)	6 (4.2)	2.17 (0.43, 10.93)	0.51
Agoraphobia ^a	4 (2.1)	0	3.76 (0.41, 179.2)	0.14
Social phobia ^a	0	4 (2.8)	0.14 (0.003, 1.31)	0.03
Specific phobia	3 (1.6)	5 (3.5)	0.80 (0.24, 2.68)	0.31
Posttraumatic stress disorder ^a	1 (0.01)	0	2.23 (0.18, 118.1)	0.51
Obsessive-compulsive disorder ^a	3 (1.6)	0	2.99 (0.29, 148.5)	0.26
Generalized anxiety disorder	14 (7.3)	8 (5.6)	1.67 (0.49, 5.67)	0.70
Any anxiety disorder	28 (14.5)	20 (14.1)	1.59 (0.66, 3.86)	0.97
Impulse control disorders				
Intermittent explosive disorder	1 (0.01)	2 (0.01)	0.36 (0.03, 4.06)	0.58
Compulsive buying	2 (0.01)	2 (0.01)	0.73 (0.10, 5.27)	1.00
Any non-PG impulse control disorder	3 (0.02)	2 (0.01)	1.10 (0.18, 6.70)	1.00
Eating disorder ^a	2 (0.01)	0	2.23 (0.18, 118.1)	0.51
Somatoform disorder	2 (0.01)	2 (0.01)	2.01 (0.29, 13.91)	0.48
Attention deficit hyperactivity disorder	5 (2.6)	4 (2.8)	1.32 (0.46, 3.81)	0.61
Antisocial personality disorder ^a	9 (4.7)	0	7.73 (1.07, 337.7)	0.01
Any mental disorder	103 (53.4)	57 (40.1)	2.71 (1.35, 5.45)	0.005

In a family study, family members of probands with PG were not only more likely to have a diagnosis of PG, but were also more likely to have SUD (OR=4.2)!

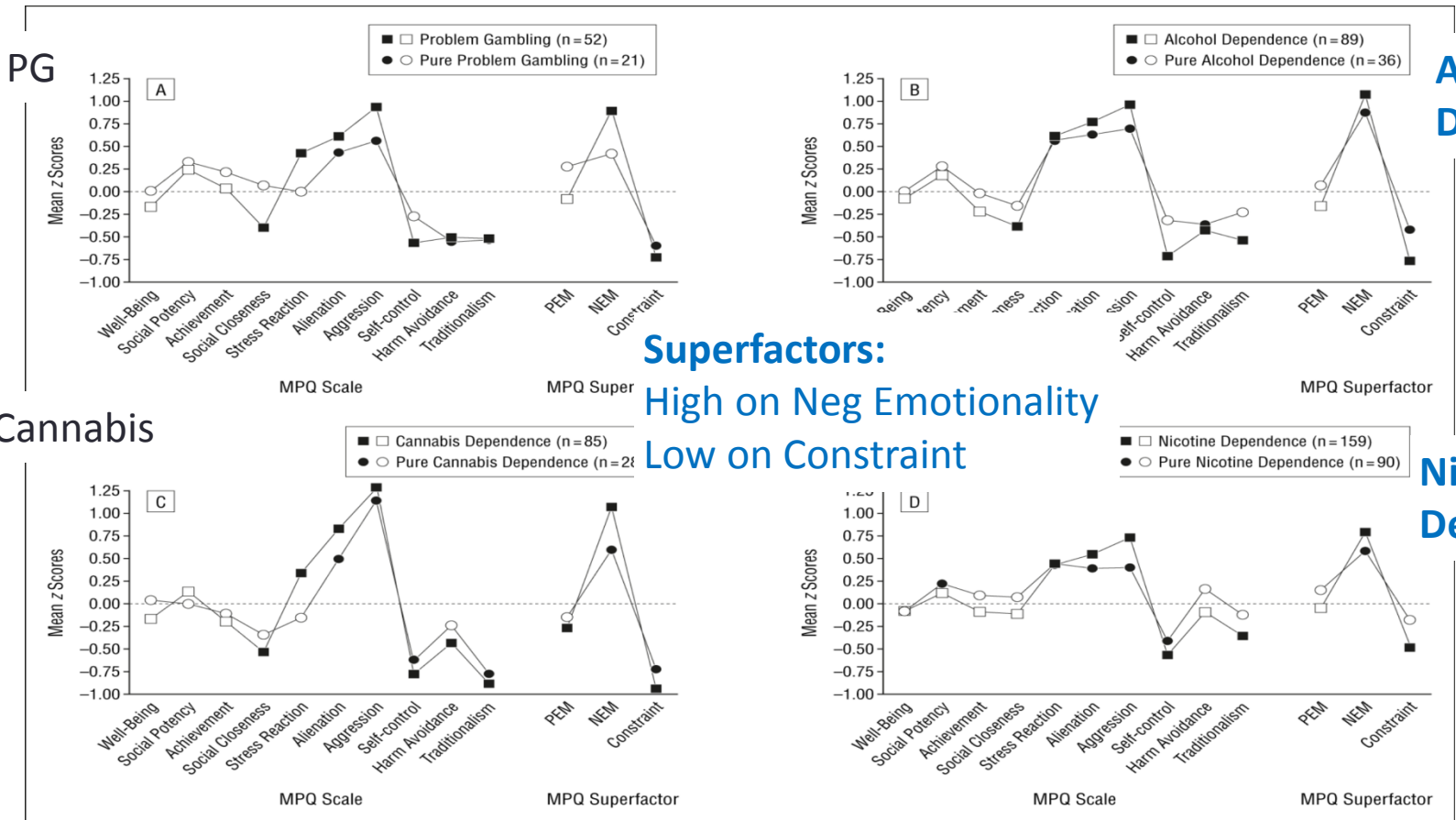
Personality and Problem Gambling

Archives Gen Psychiatry, 2005

A Prospective Study of a Birth Cohort of Young Adults

Wendy S. Slutske, PhD; Avshalom Caspi, PhD; Terrie E. Moffitt, PhD; Richie Poulton, PhD

High: Aggression Low: Self-control

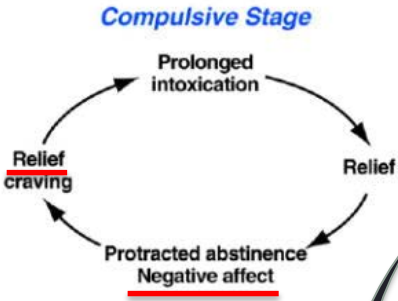
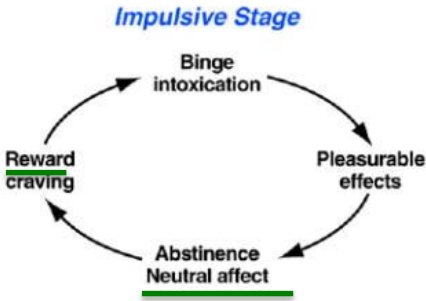
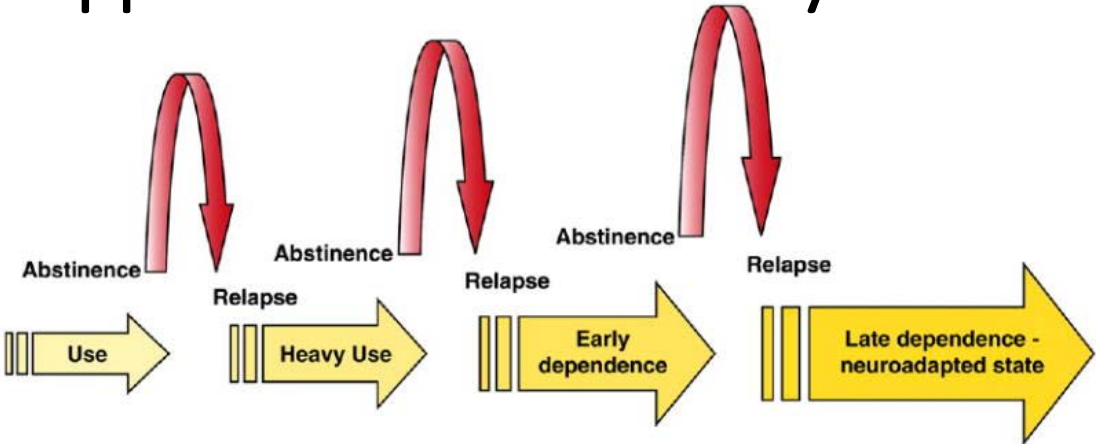


Superfactors:
High on Neg Emotionality
Low on Constraint

In this prospective community study the onset of PG and SUDs were associated with very similar premorbid personality profiles

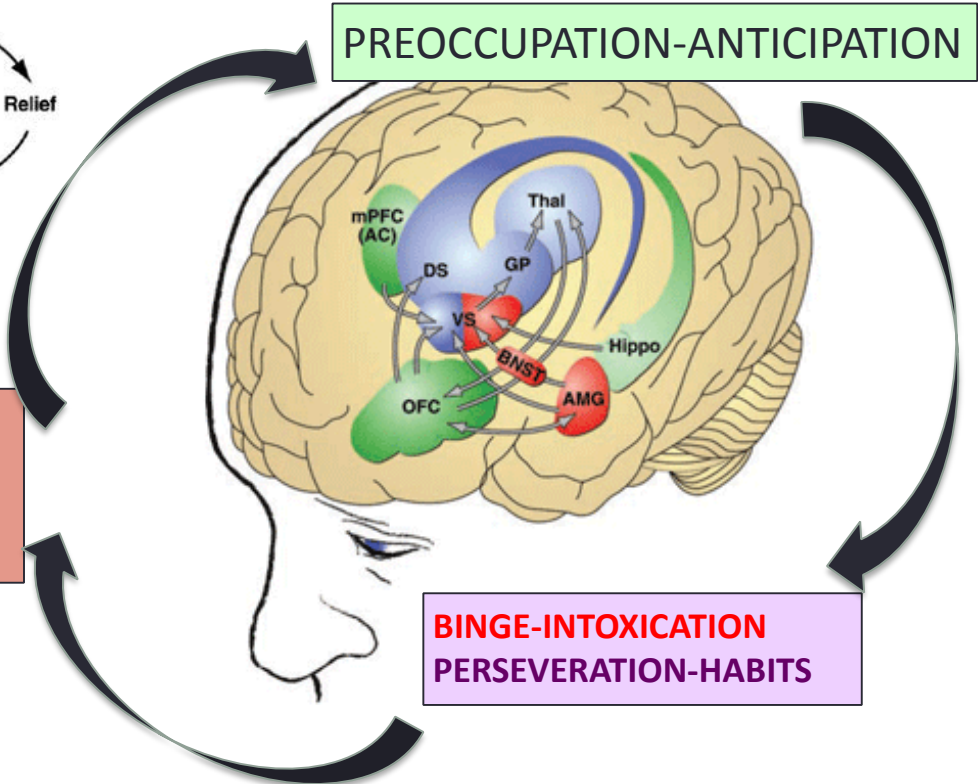
Opponent Process Theory

Stress model of addiction



Progression of addiction (Koob 2001, 2009)

WITHDRAWAL-
NEGATIVE
AFFECT



Impaired response inhibition and salience attribution I – RISA model (Goldstein & Volkow, 2002, 2011)

- Refers to several addiction related processes

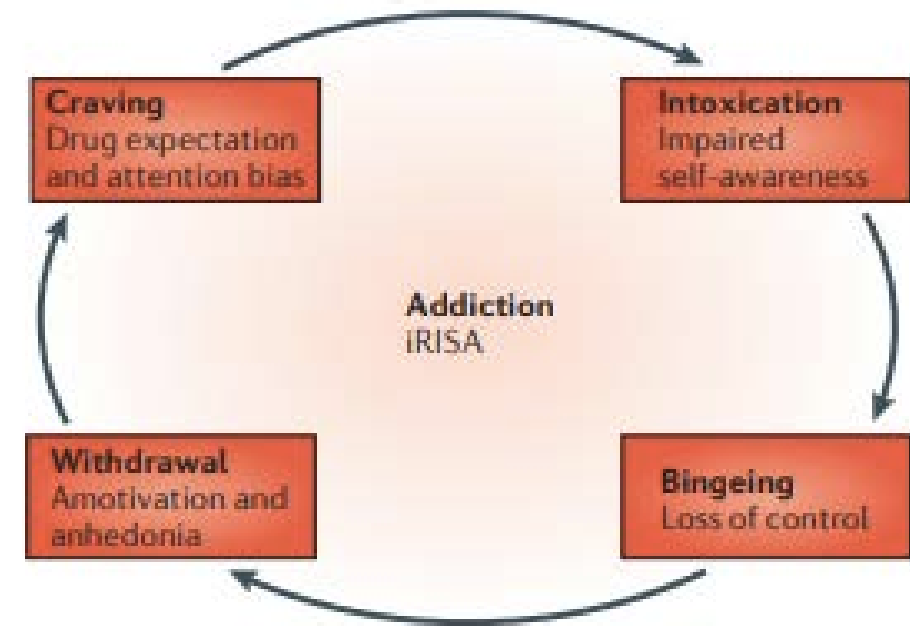


FIGURE FROM Goldstein, R. Z., & Volkow, N. D. (2011). Dysfunction of the prefrontal cortex in addiction: neuroimaging findings and clinical implications. *Nature reviews neuroscience*, 12(11), 652.

Evidence from functional neuroimaging (1)

- **Common alterations** in both gambling and cocaine users in the function of neural pathways implicated in cognitive processes that are aberrant in SUDs
- e.g., *mesolimbic dopamine pathways* ascribed to motivation and reward processing (i.e., nucleus accumbens, medial prefrontal areas)
- *corticostriatal pathways* implicated in decision making and hypersensitivity to substances / gambling (i.e., medial/orbito/dorsolateral prefrontal areas)
- *Other pathways* implicated in interoception (i.e., insula), craving (i.e., amygdala), habit forming (i.e., caudate, thalamus).
- **But...transient neural measures! Are the alterations persistent over time?**

Evidence from functional neuroimaging (2)

A minority of studies showed cocaine specific alterations in corticostriatal systems (i.e., anterior cingulate, thalamus and putamen).

This may be ascribed to essential differences between gambling disorders and SUDS:

- Uncertainty of winning
- Cognitive Distortions
- Role of “insensitivity” to losses
- **But...transient neural measures! Are the alterations persistent over time?**

Review

Reward pathway dysfunction in gambling disorder: A meta-analysis of functional magnetic resonance imaging studies

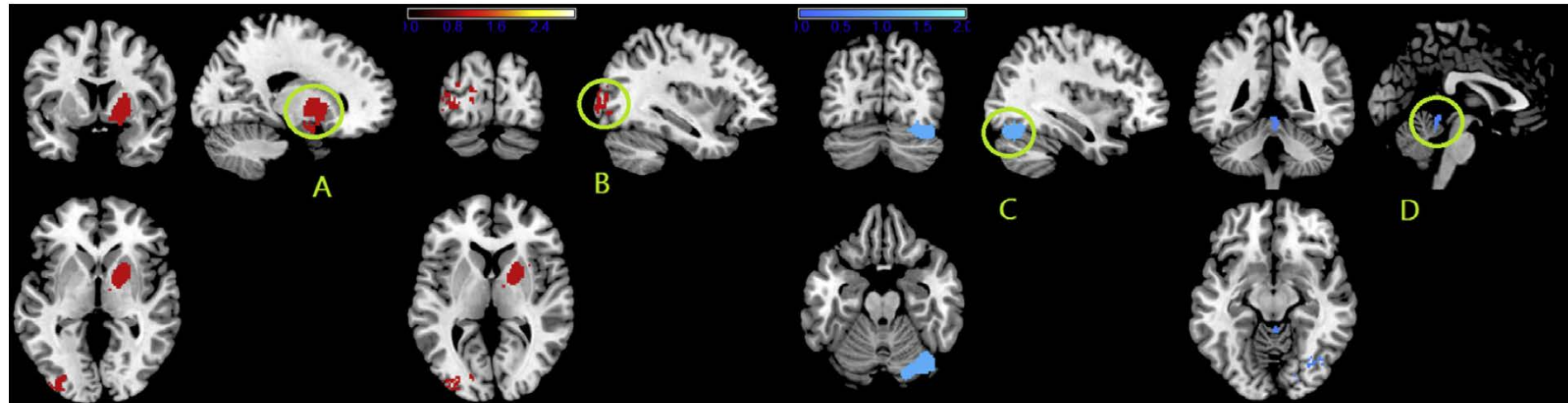


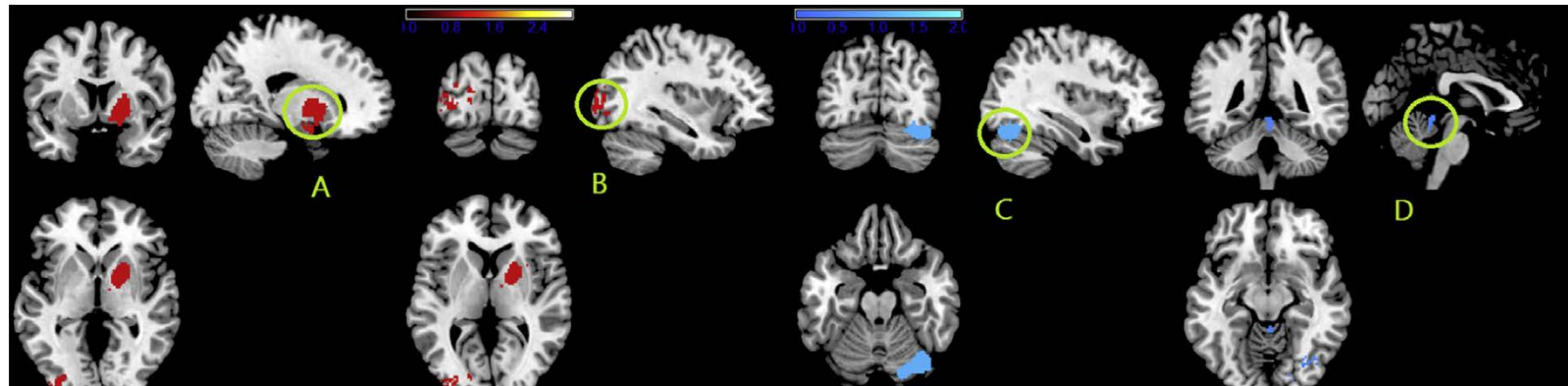
Fig. 2. Cognitive tasks brain response abnormalities in GD compared with HCs and meta-regression analyses. Patients with GD had significant hyperactivity in the right lentiform nucleus (red clusters: A), left middle occipital gyrus (red clusters: B), but deactivation in the bilateral cerebellum (blue clusters: C and D) compared with HCs in the

These results suggest dysfunction within the corticostriatal, mesolimbic dopamine and other pathways in GD

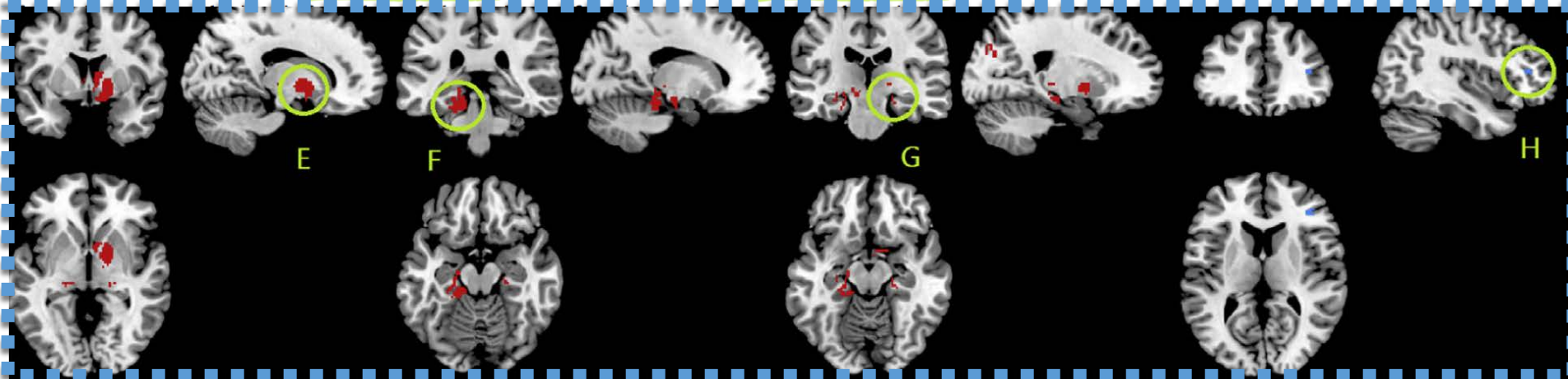


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meta-analyses. And the SOGS score of GD patients was positively correlated with activations in the right lentiform nucleus (red clusters: E), the bilateral parahippocampal gyrus (red clusters: F and G), but negatively correlated with activations in the right middle frontal gyrus (blue clusters: H) in the meta-regression analyses. (For interpretation



Research question: Are there common neuroanatomical alterations in gambling versus SUDs?

- First study to formally compare the neuroanatomy in gambling *versus* SUDs
- An ideal candidate SUD for comparison is cocaine use disorders, as it also heavily taxes the dopaminergic pathways

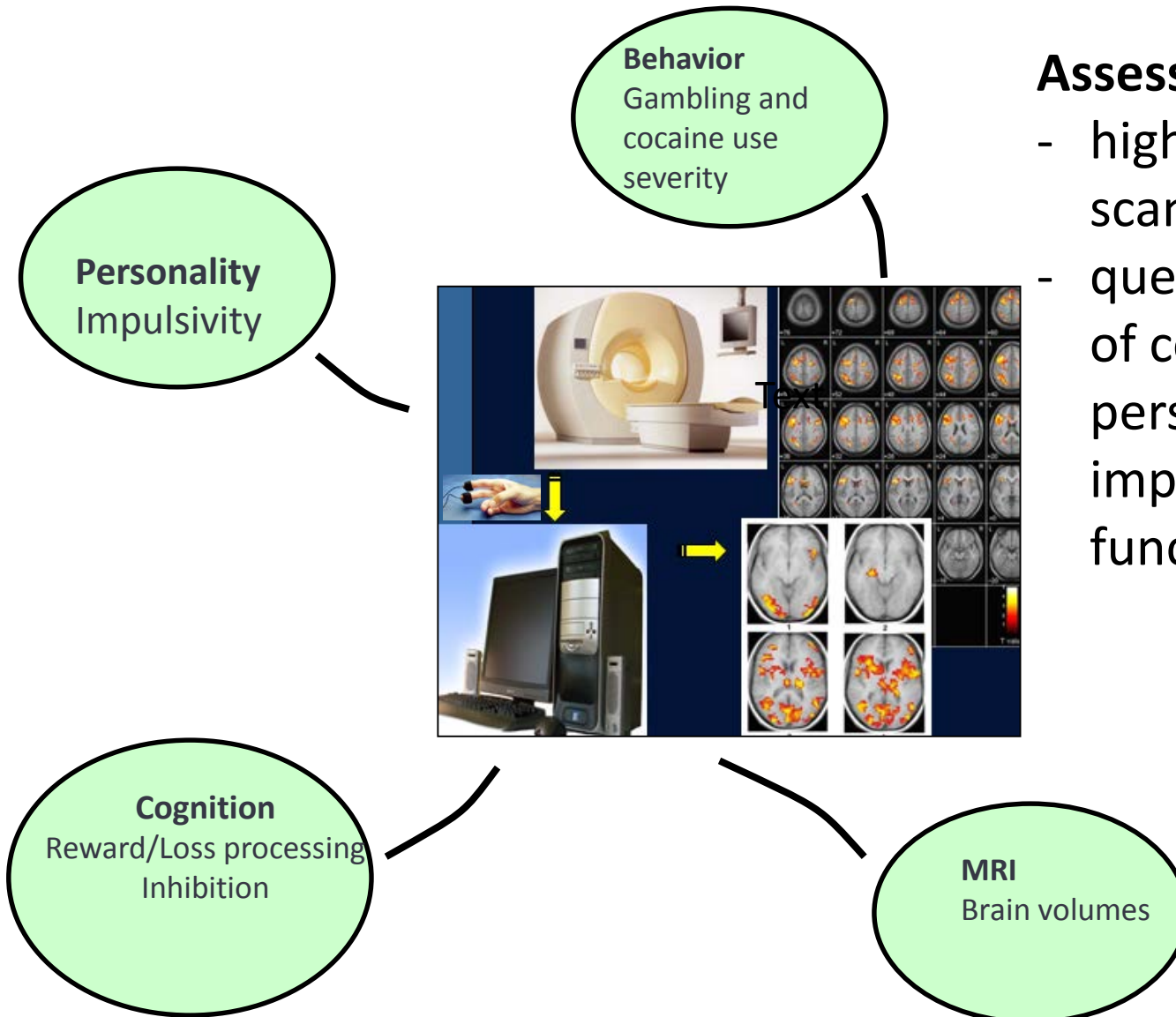
Hypotheses

Common (and dose-related) alterations in

- *mesolimbic dopamine pathways* ascribed to motivation and reward processing (i.e., nucleus accumbens, medial prefrontal areas)
- *corticostriatal pathways* implicated in decision making and hypersensitivity to substances / gambling (i.e., medial/orbito/dorsolateral prefrontal areas)
- *Other pathways* implicated in interoception (i.e., insula), craving (i.e., amygdala), habit forming (i.e., caudate, thalamus).

Methods

GROUP 1 - gambling disorders ($n=17$)
GROUP 2 - cocaine dependence ($n=19$)
GROUP 3 - controls; $n=21$).



Assessment

- high-resolution structural MRI scans
- questionnaires about the severity of cocaine use and gambling, personality and cognition (i.e., impulsivity, inhibition, executive function).

Both gamblers and cocaine users versus controls -> Lower volume of the inferior frontal gyrus (i.e., *inhibition and attentional control*)

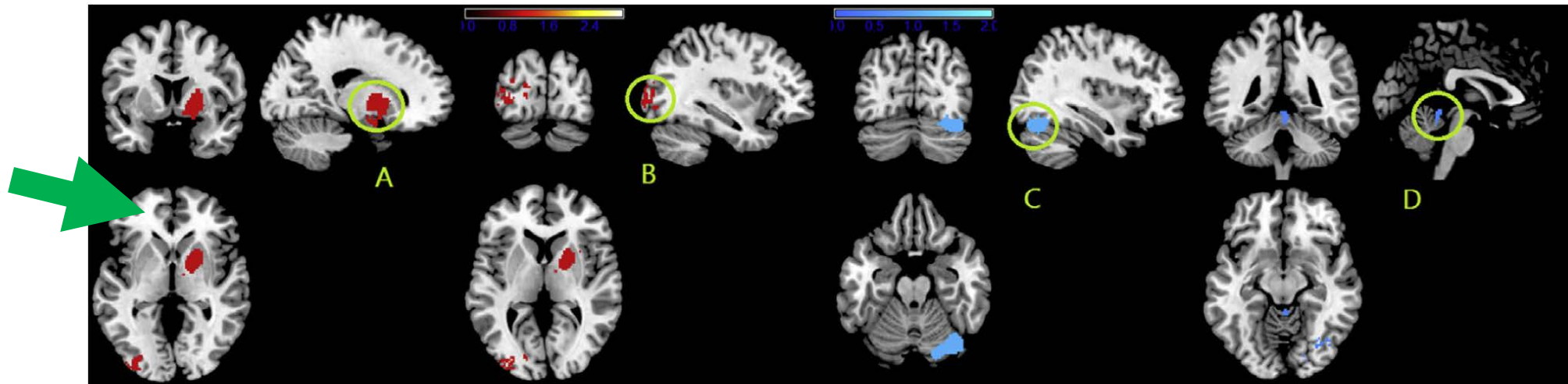


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Ya-jing Meng^{a,b,1}, Wei Deng^{a,b,1}, Hui-yao Wang^a, Wan-jun Guo^{a,b,*}, Tao Li^{a,b,**},
Chaw Lam^c, Xia Lin^{d,e,f}



- Gamblers versus controls** -> lower volume of
- prefrontal cortical pathways (i.e., rostral middle and superior frontal gyrus => *emotion regulation working memory*)
 - corpus callosum (i.e., connectivity between prefrontal regions -> *exec. control*).

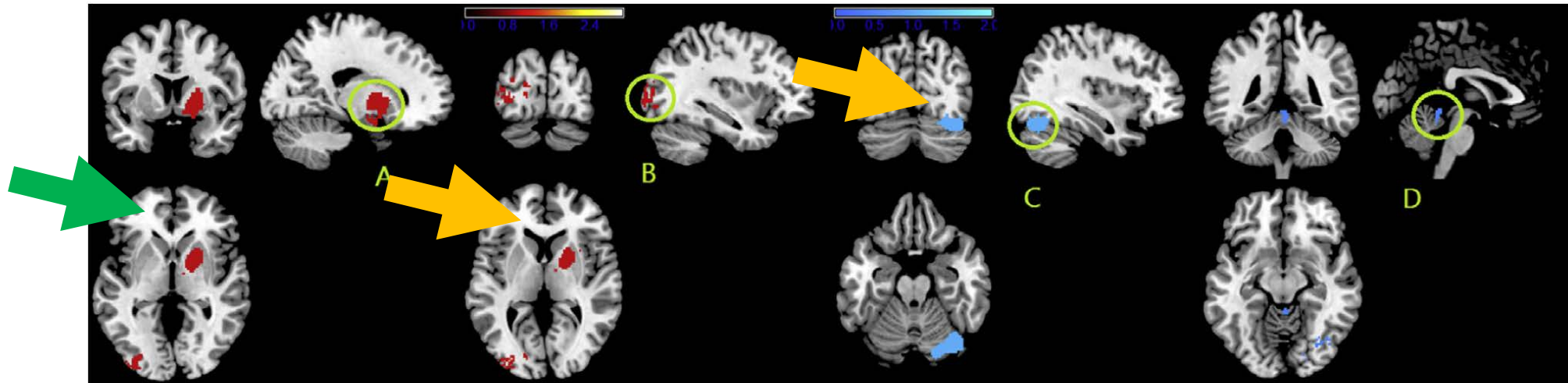


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gamblers and cocaine users : inferior frontal gyrus

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CrossMark

Gamblers versus cocaine users showed volumetric differences in **mesolimbic dopaminergic pathways** ascribed to *reward and motivation* (i.e., **nucleus accumbens, mOFC**) and **corpus callosum** (i.e., *executive functions*).

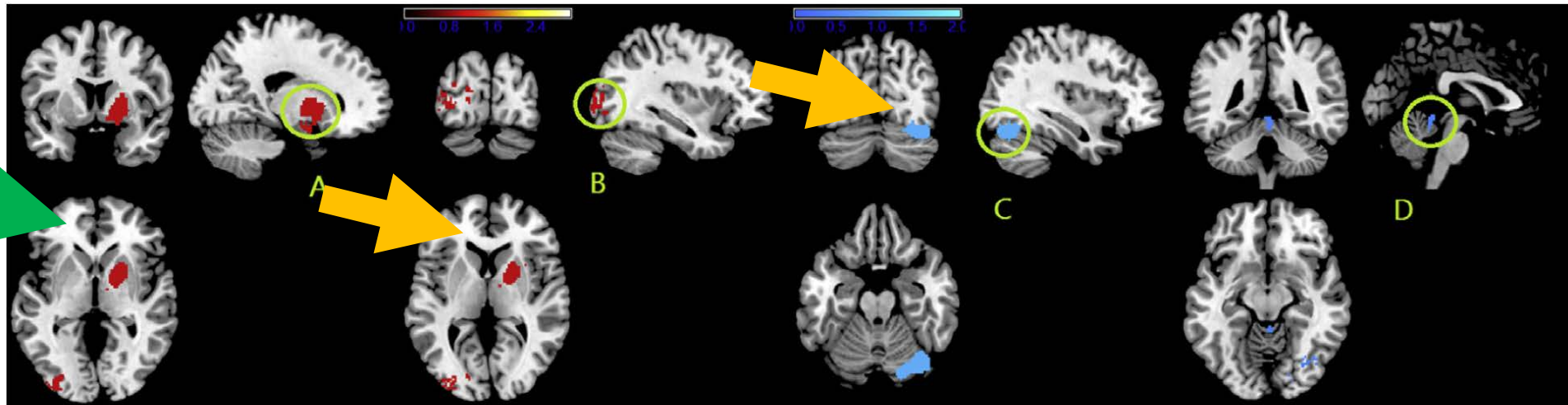


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gamblers and cocaine users :
inferior frontal
gyrus

gamblers:
prefrontal,
corpus callosum



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Brain behavior correlations, in cocaine group only

- ***Negative urgency*** ($\beta = .72, p < .01$), ***lack of premeditation*** ($\beta = -.70, p < .01$) and inhibition (D-KEFS CWIT scores; $\beta = -.74, p = .01$) predicted anterior **corpus callosum**.
- ***Severity of cocaine use*** ($\beta = .79, p = .02$) and ***inhibition*** (D-KEFS CWIT scores; $\beta = -.58, p = .05$) predict volumes of posterior **corpus callosum**.
- What drove neural alterations in gamblers?
- May explain group differences in corpus callosum, in cocaine versus gamblers

Summary of results

- **Both gamblers and cocaine users** versus controls -> Lower volume of the **inferior frontal gyrus** [*inhibition, attention*]
- **Gamblers versus controls** -> lower volume of **prefrontal cortical pathways** (i.e., rostral middle and superior frontal gyrus [*reward, motivation*]) and **corpus callosum** [*executive function*]
- **Gamblers versus cocaine users** showed volumetric differences in **mesolimbic dopaminergic pathways** ascribed to *reward and motivation* (i.e., nucleus accumbens, mOFC) and **corpus callosum** [*executive function*].

Conclusions

- Gambling disorders show neuroanatomical alterations that partially overlap with cocaine use disorders.
- Unclear what drives neural alteration in gamblers, future studies need to map gambling specific processes (i.e., uncertainty, insensitivity to losses)
- Cocaine users show alteration in additional brain regions that may reflect the neurotoxic effects of direct chronic cocaine exposure on dopaminergic pathways.