Neuro-cognitive systems underpinning antisocial behavior and the impact of maltreatment and substance abuse on their development

R.J.R. Blair
Center for Neurobehavioral Research

Talk plan

- **Boys Town and the mission of the Center for Neurobehavioral Research.**
- **Neuro-cognitive systems underpinning antisocial behavior**
  - **“Empathy”**
  - **Acute threat response**
  - **Response control**
  - **Reinforcement-based decision-making**

Boys Town

- Large residential treatment center in Omaha Nebraska.
- The residential center itself caters for approximately 400+ youth each year (40% female). Psychosocial focus to the intervention though considerable psychiatric input.
- In addition, there are a number of Boys Town centers around the USA, most of which see adolescents as outpatients (35,000+ patients per year)
- BT and local donor community invested in the Center for Neurobehavioral Research (CNR). The CNR launched properly in 2016. I moved from NIMH to run the CNR in late August 2016.

Boys Town sample (as of March 2017)

(40% female)

	%	N
DIAGNOSIS		
ADHD	42.6	52
ODD	37.7	46
CD	34.4	42
MDD	11.5	14
GAD	15.6	19
SAD	10.7	13
PTSD	9.02	11

The current situation

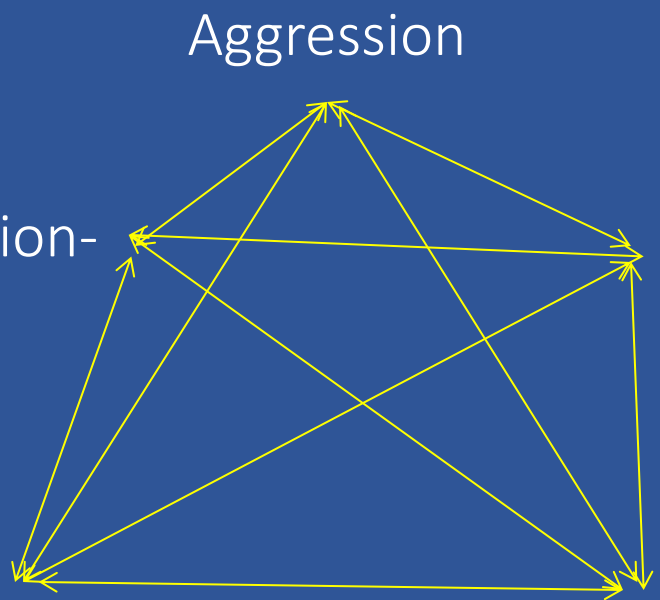
- Currently, all mental health diagnoses are driven by child and care-giver reports of the child's behavior.
- There is no other branch of medicine like this.

- Problems
  - How do we know what a person has?
  - How do we know when/if the intervention has been successful?

- **Brain level differences have significant implications for treatment**

Problem space

Acute threat response/
Response control/
Reinforcement-based decision-making



The goals of the CNR

- Identify neural signatures of healthy development
- Identify neural signatures related to atypical development
  - The impact of substance abuse
  - The impact of maltreatment
  - Neural signatures related to particular forms of psychopathology.
- Determine the extent to which the Boys Town intervention “normalizes” atypical brain signatures.
- Determine which brain level problems the Boys Town intervention works best for.
- Determine whether the identified neural signatures can be used diagnostically.

“Empathy”

The fearful expression: A signal of distress.

A healthy response to this distress cue involves an interruption in current behavior and learning the negative value of actions associated with this distress.

Callous Unemotional Traits

DSM-5 (low prosocial emotions)

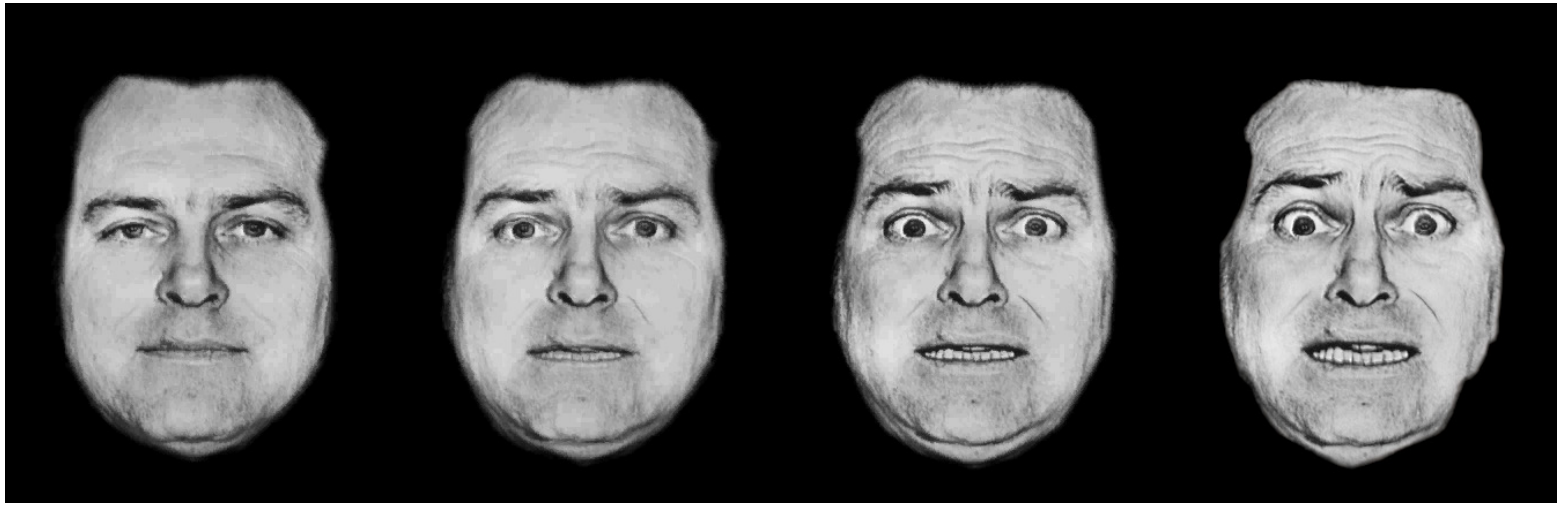
Lack of remorse or guilt

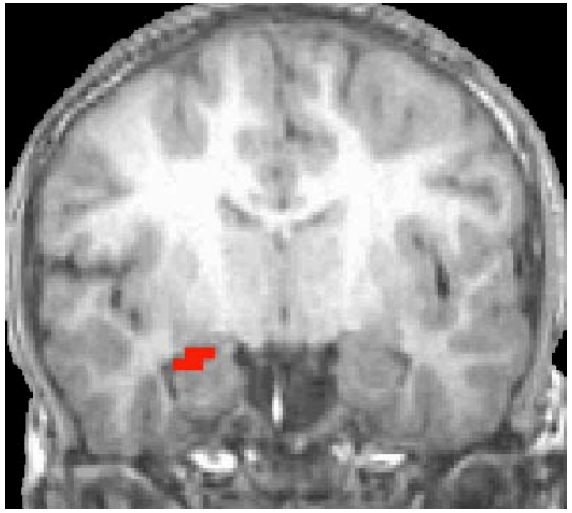
Callous-lack of empathy

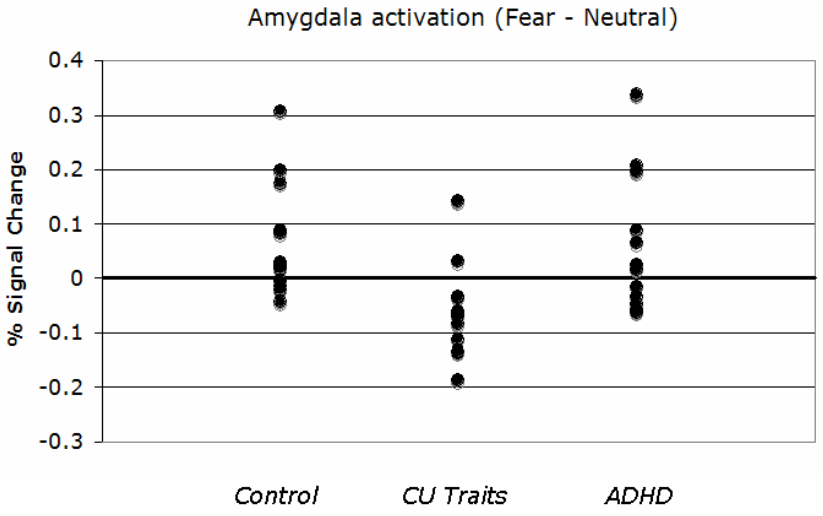
Unconcerned about performance

Shallow or deficient affect

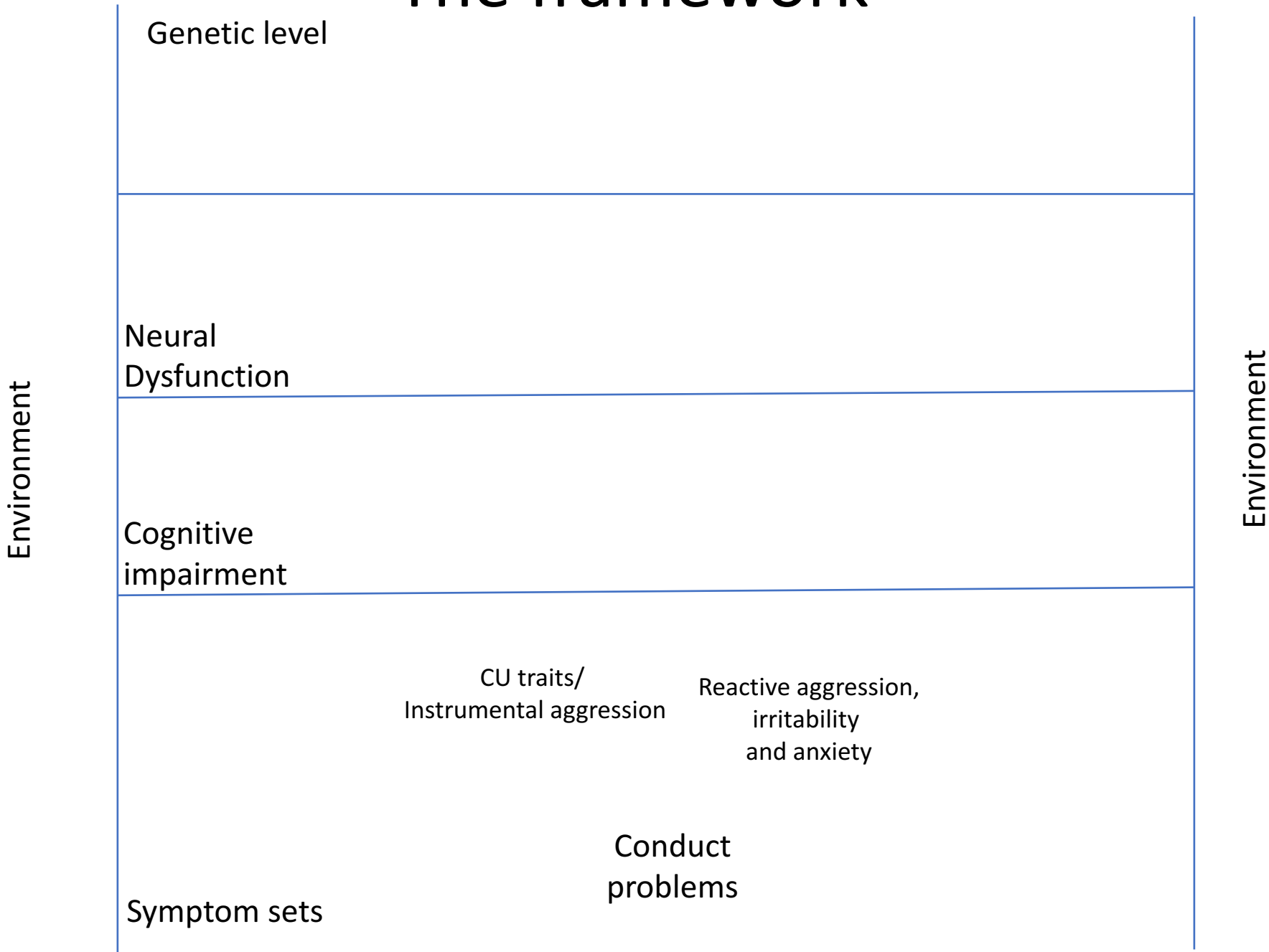
Empathy: The response to the distress of others. It is significantly reduced in those with conduct disorder and callous-unemotional traits (Marsh et al 2008).







The framework



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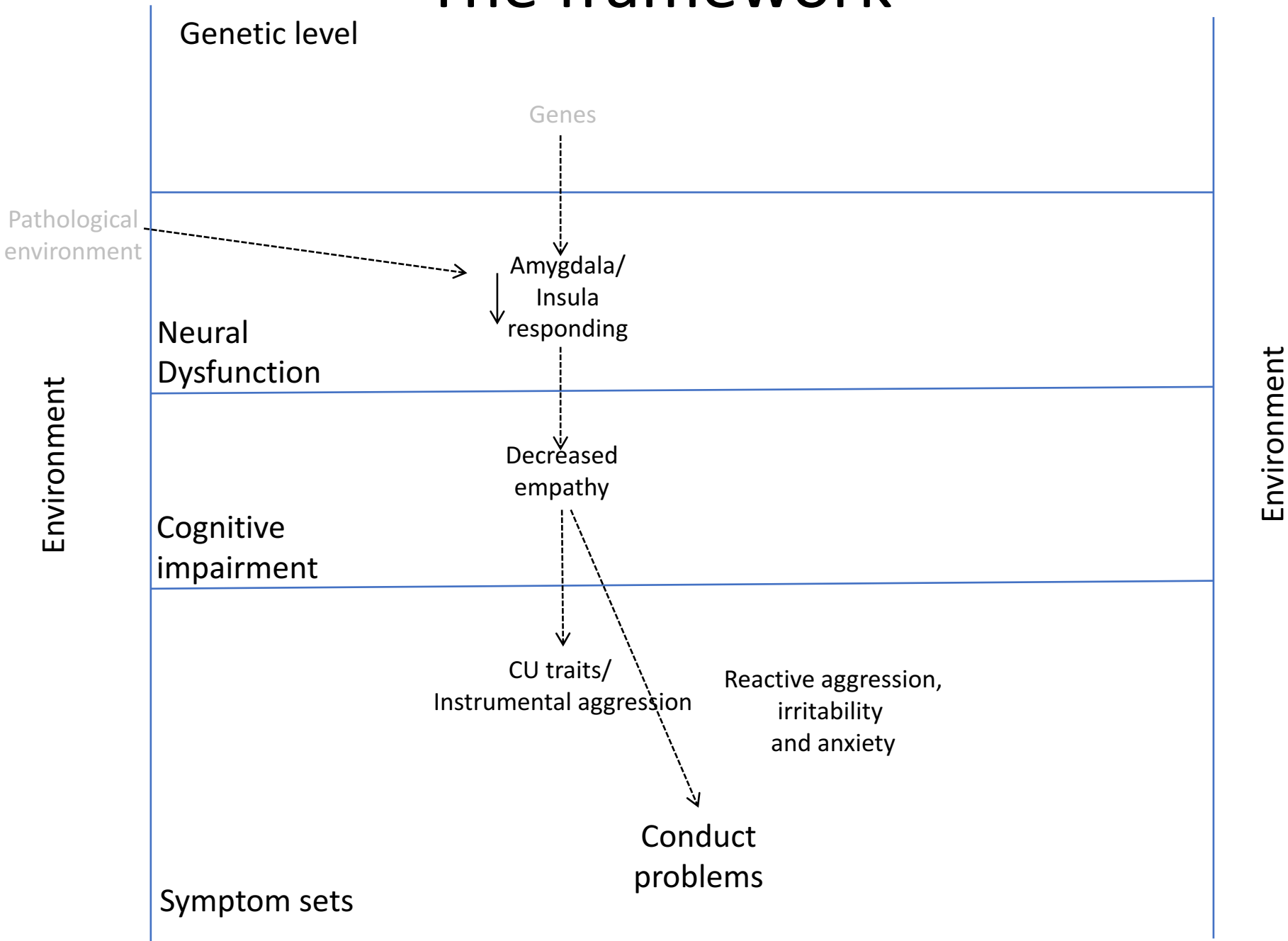
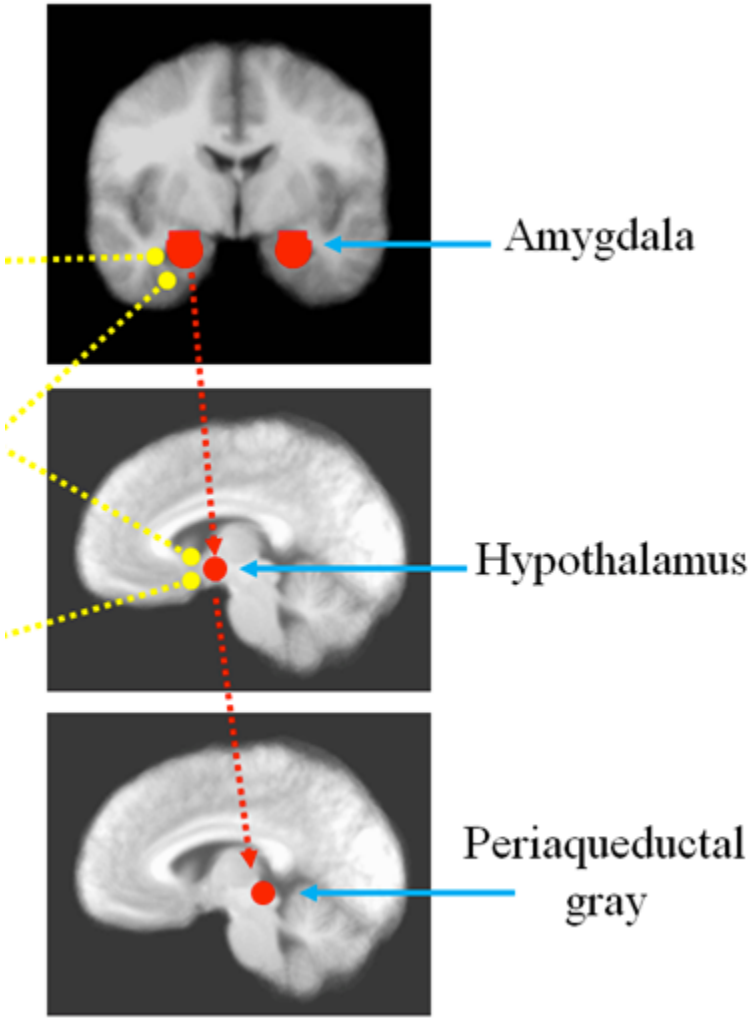
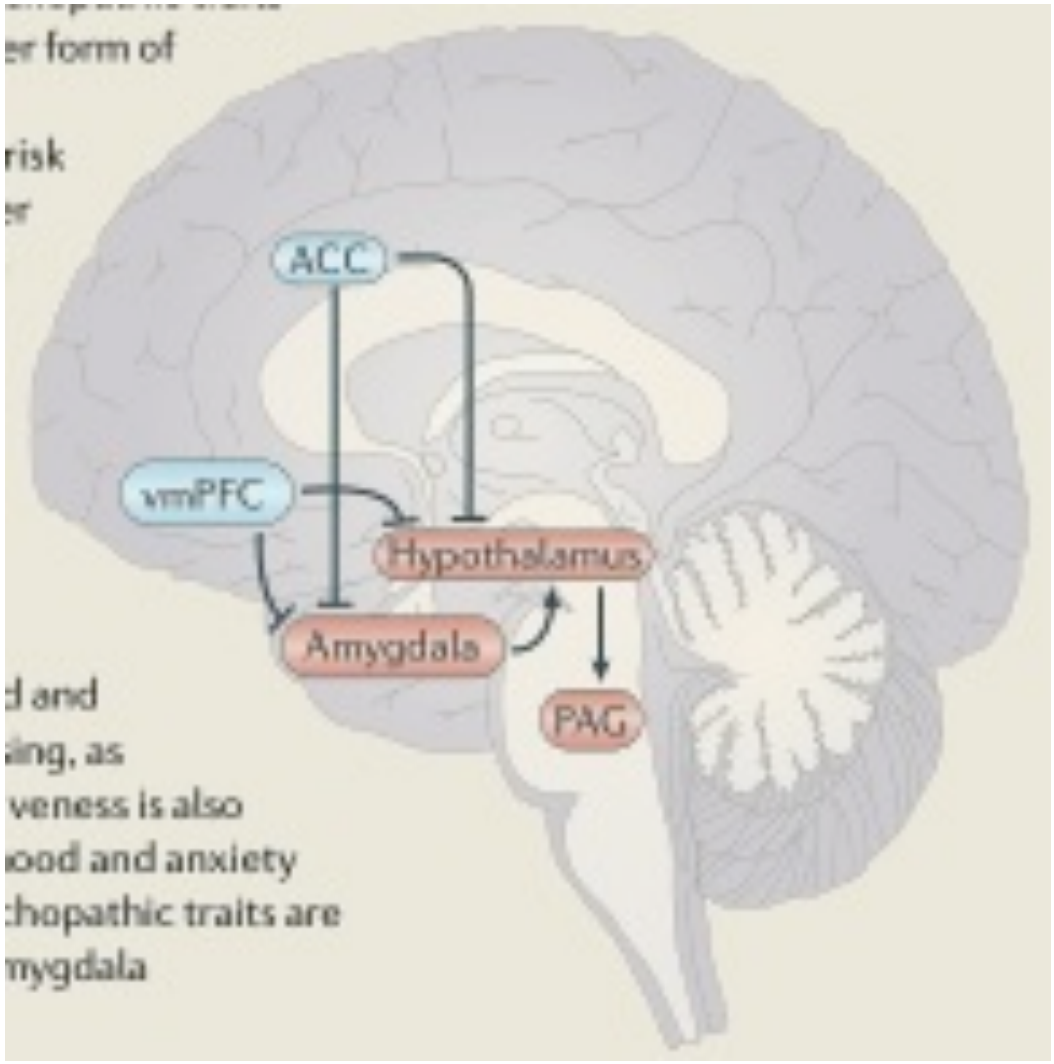
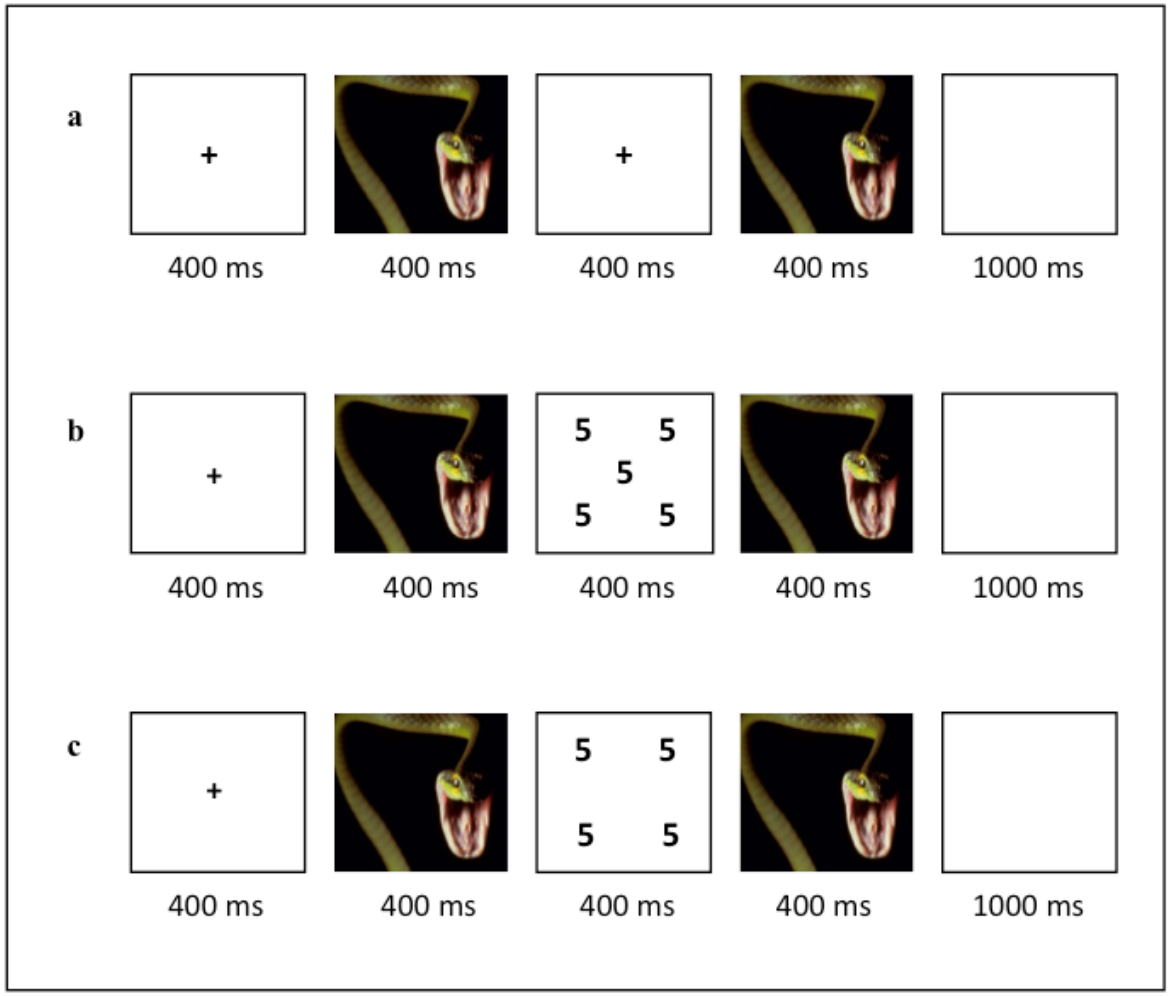


Acute Threat Response
(Blair, *Nature Neuroscience Reviews*, 2014; cf. 2004)

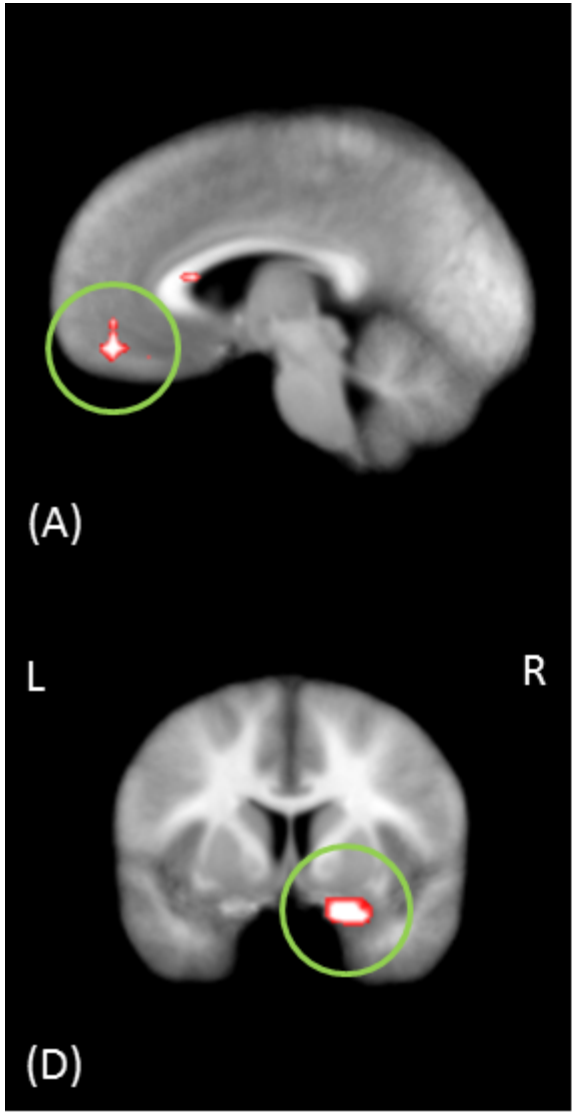


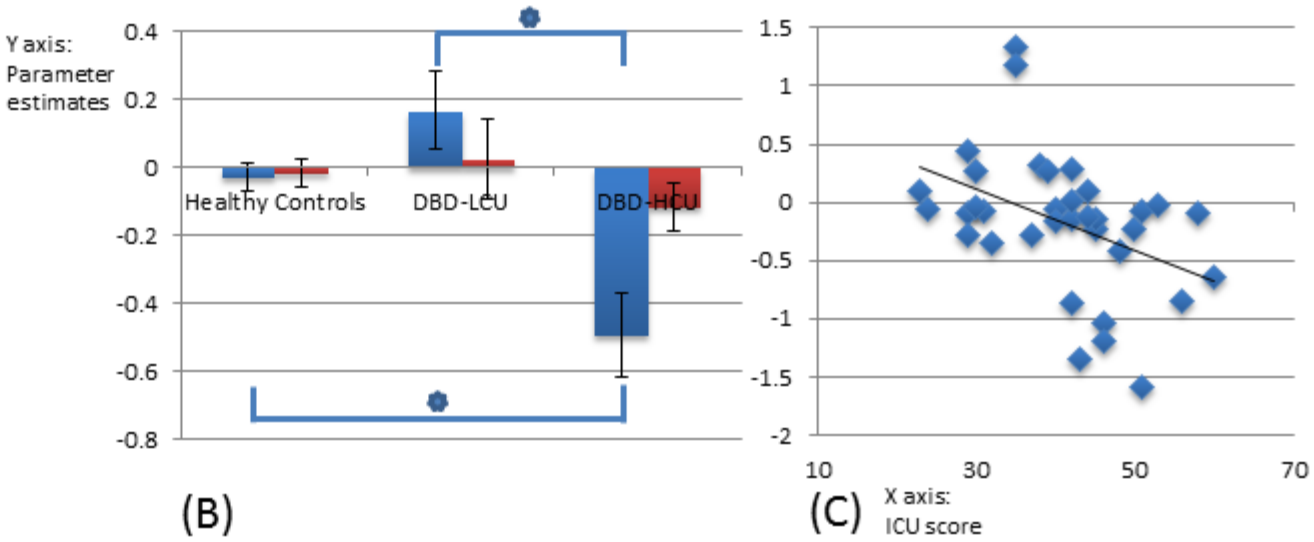


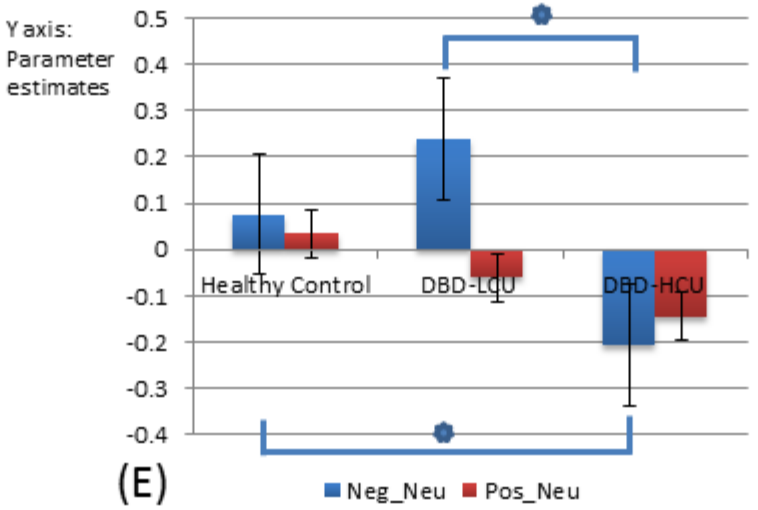
Affective Stroop (Blair KS et al 2007)



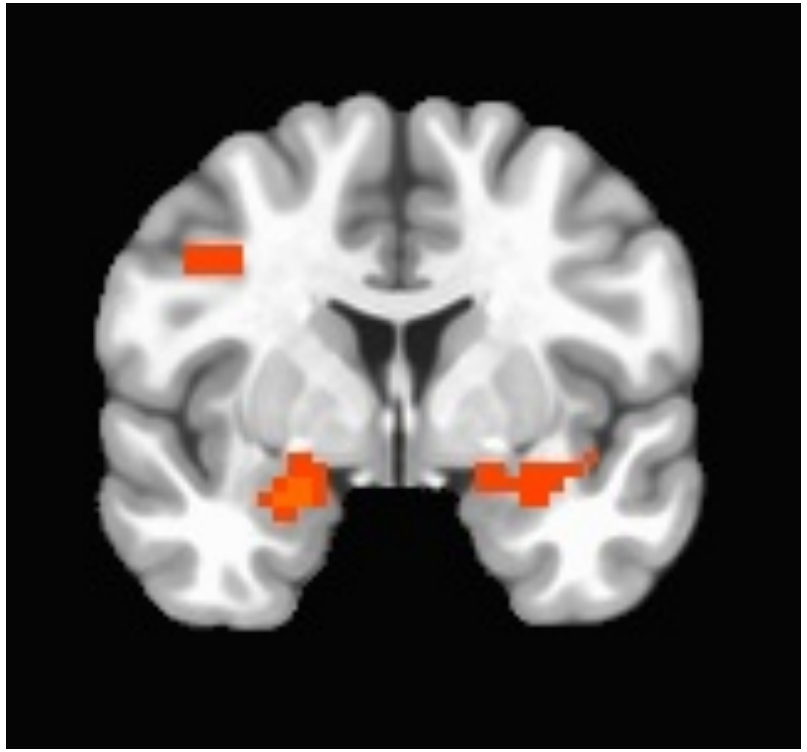
Hwang et al (2015)

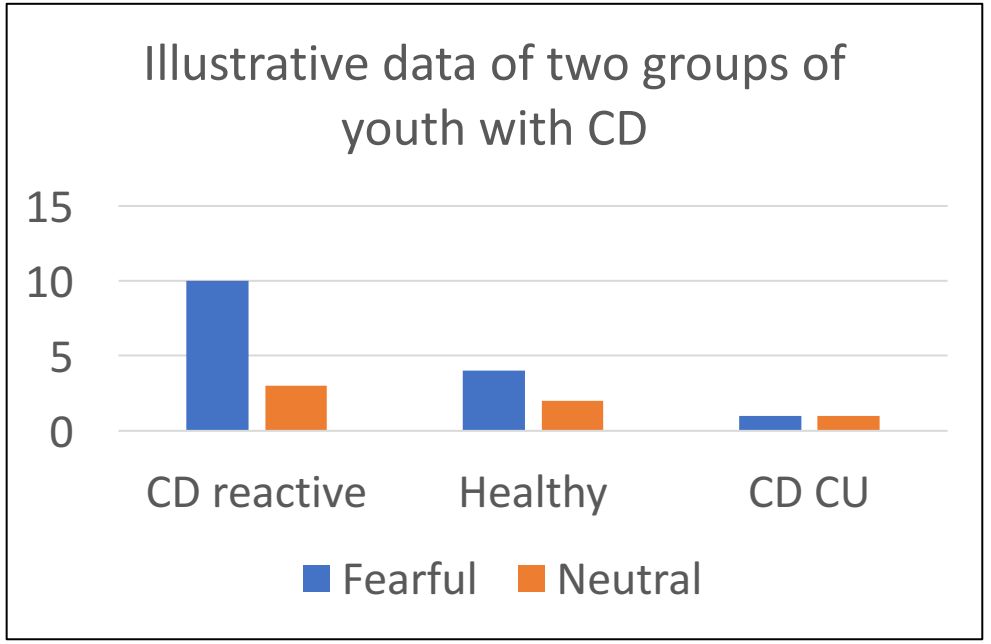






The case of Conduct Disorder



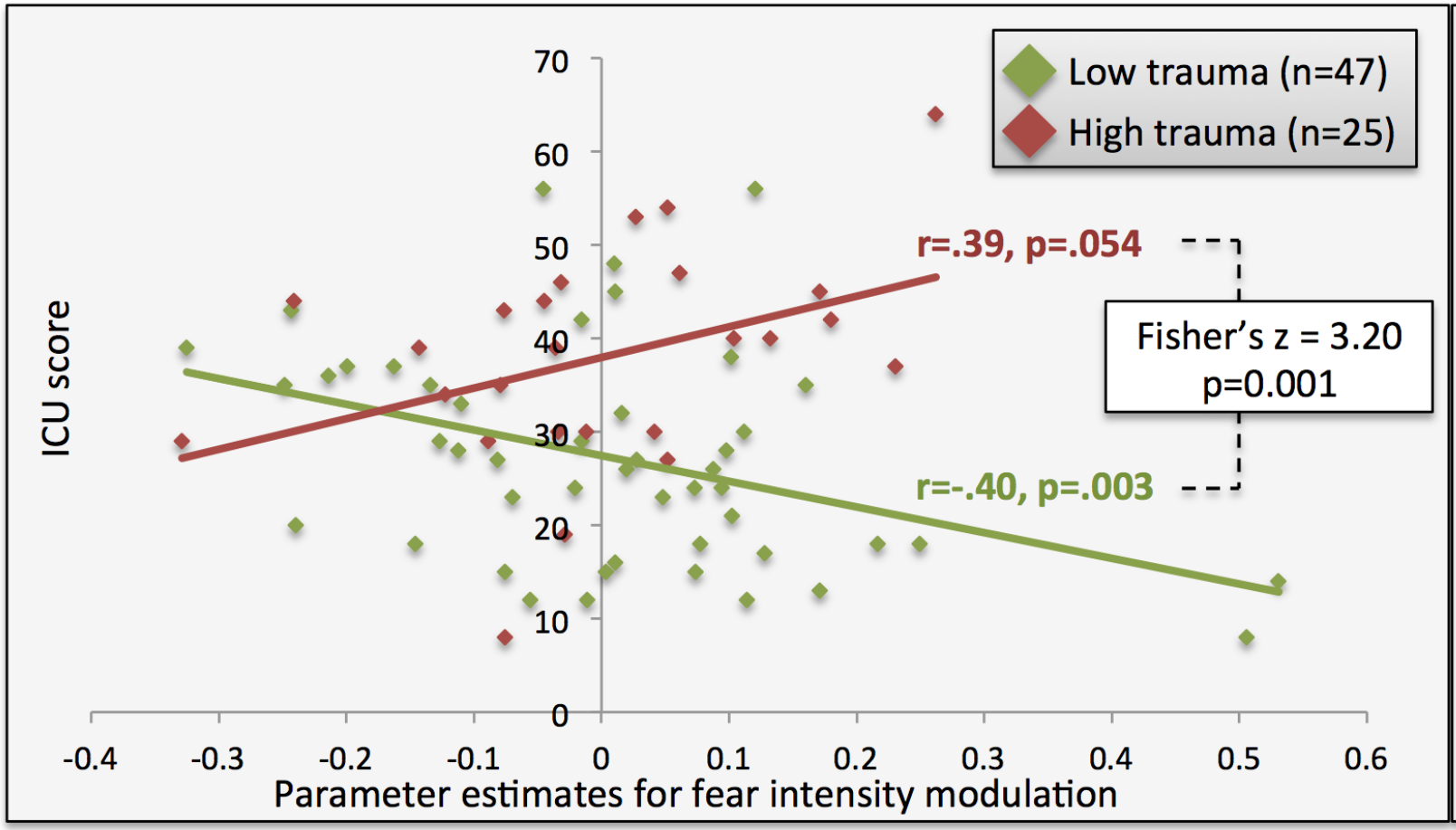


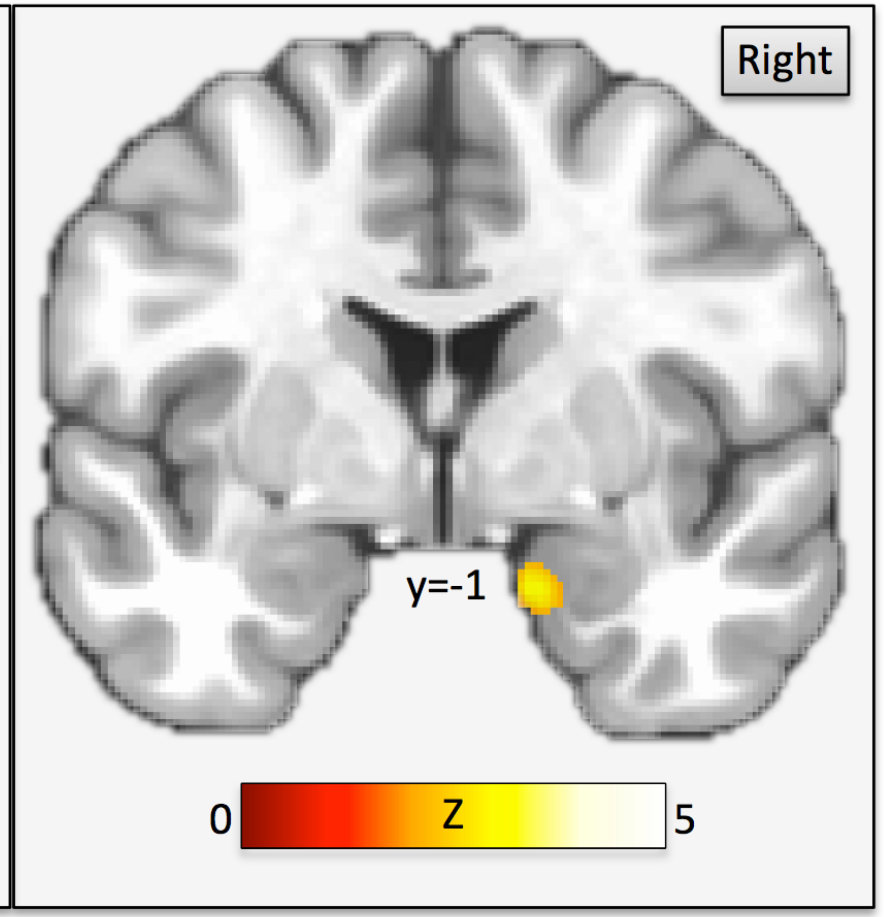
Why be concerned? Implications for treatment!

BUT!

The impact of maltreatment

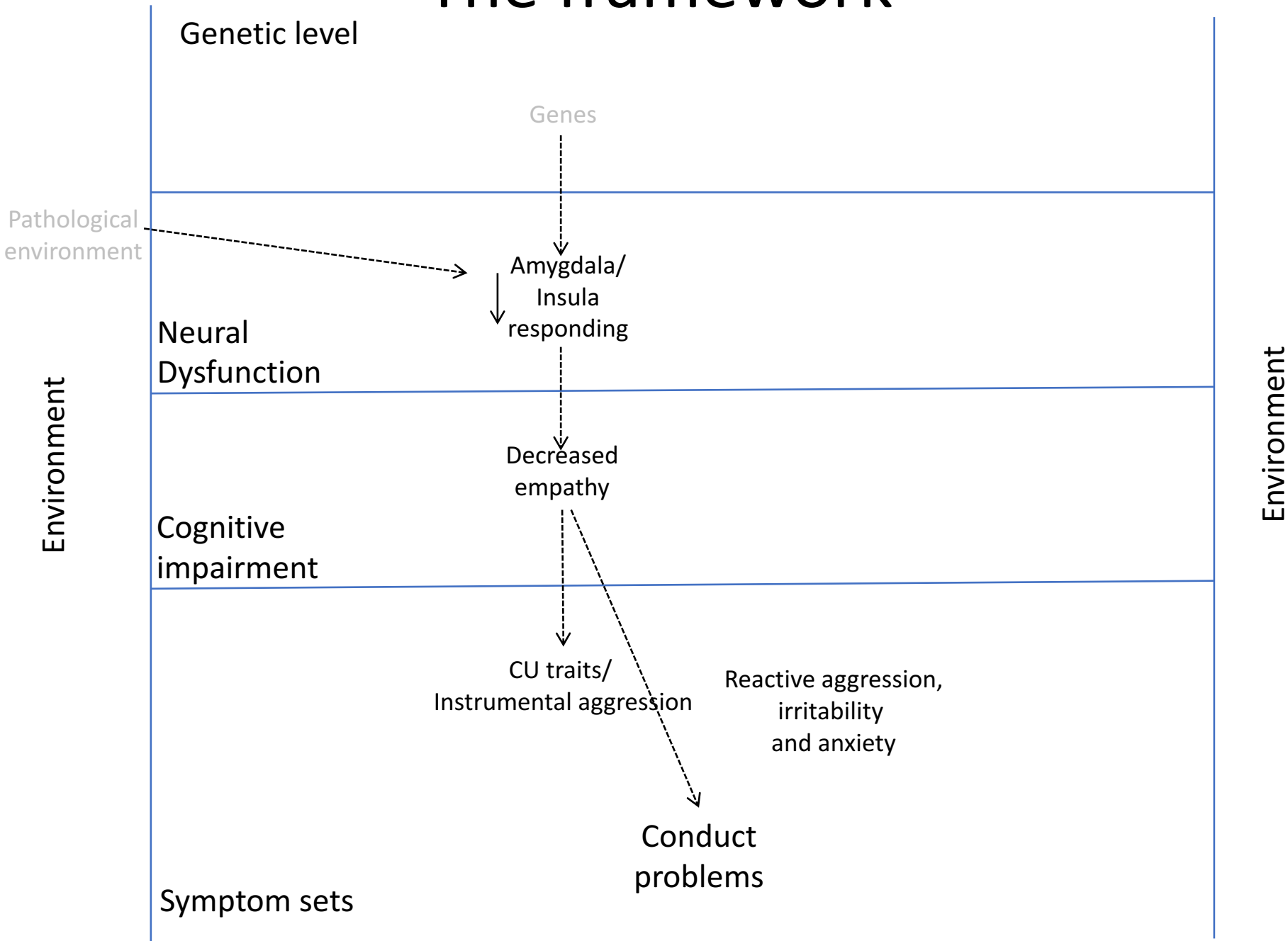
An interaction between CU-traits prior trauma on fear intensity modulated BOLD response in the right amygdala





Meffert et al. under revision

The framework



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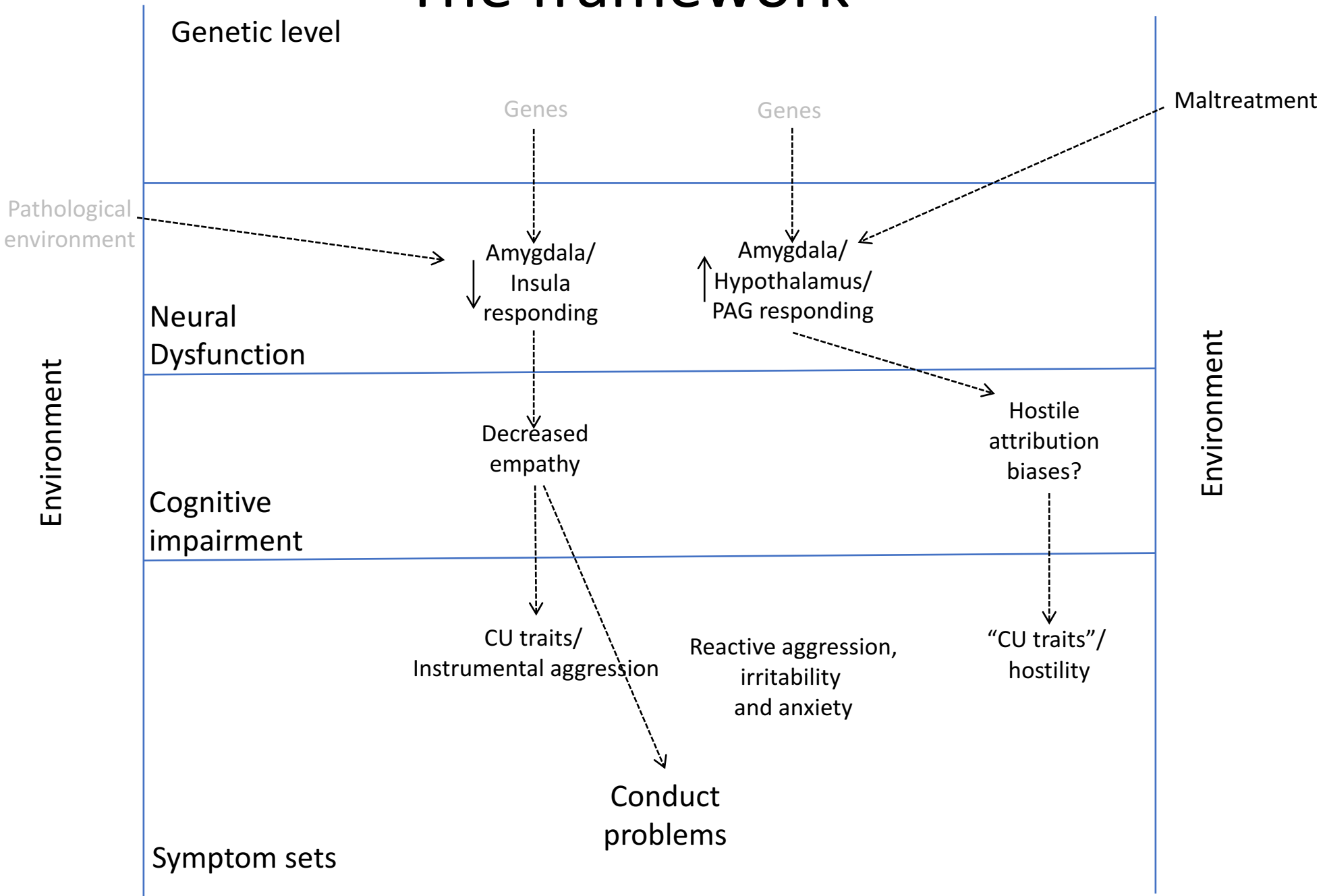

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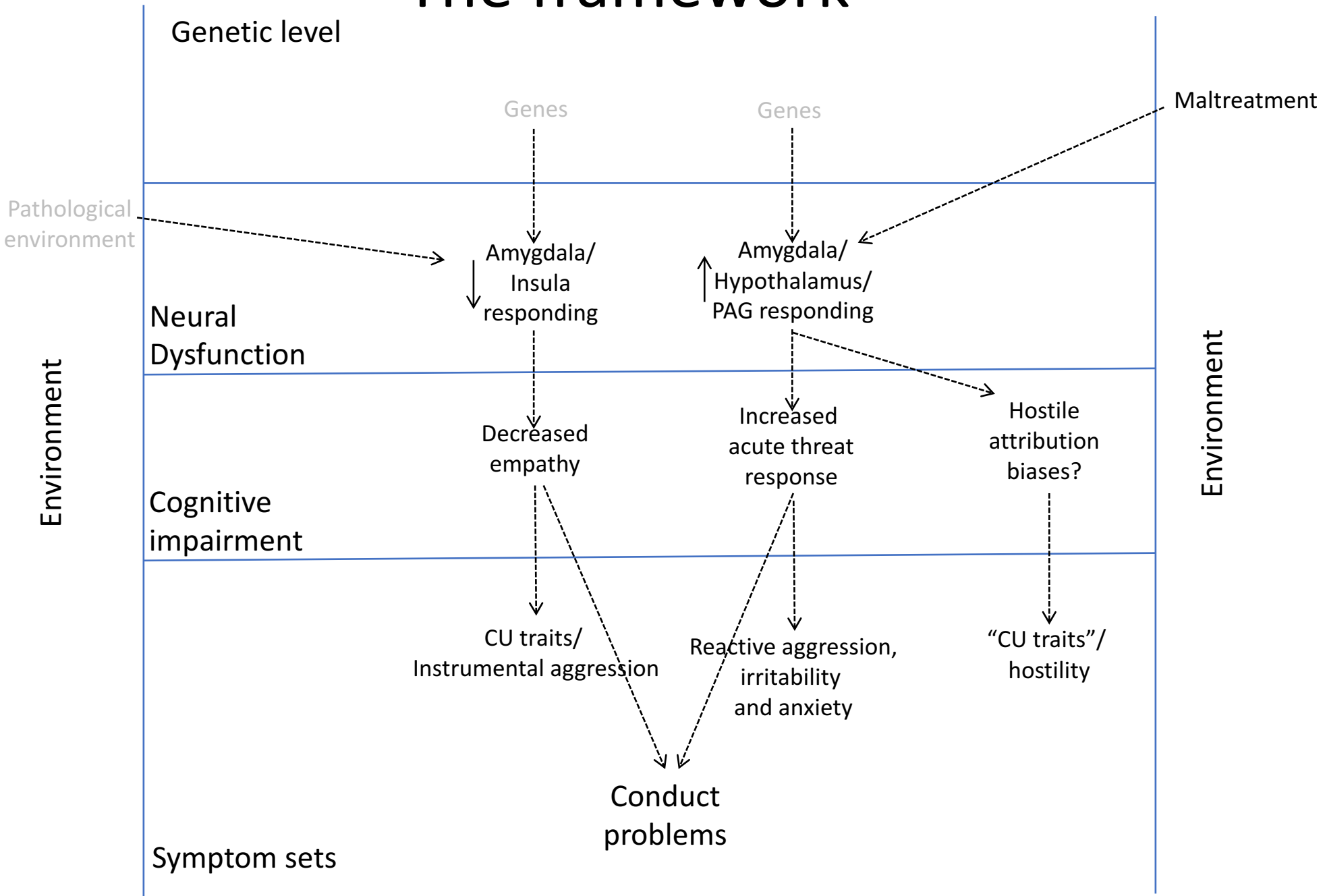
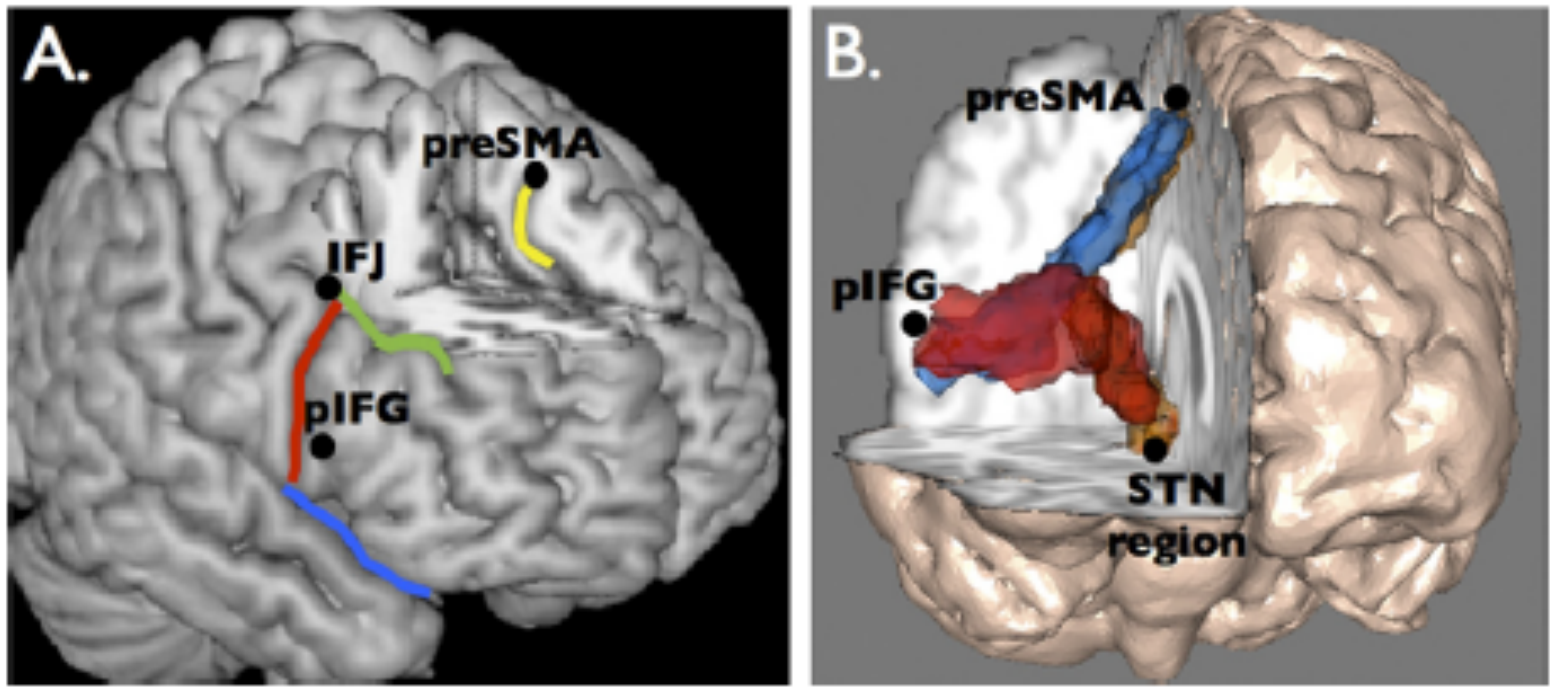


Response control Dysfunction

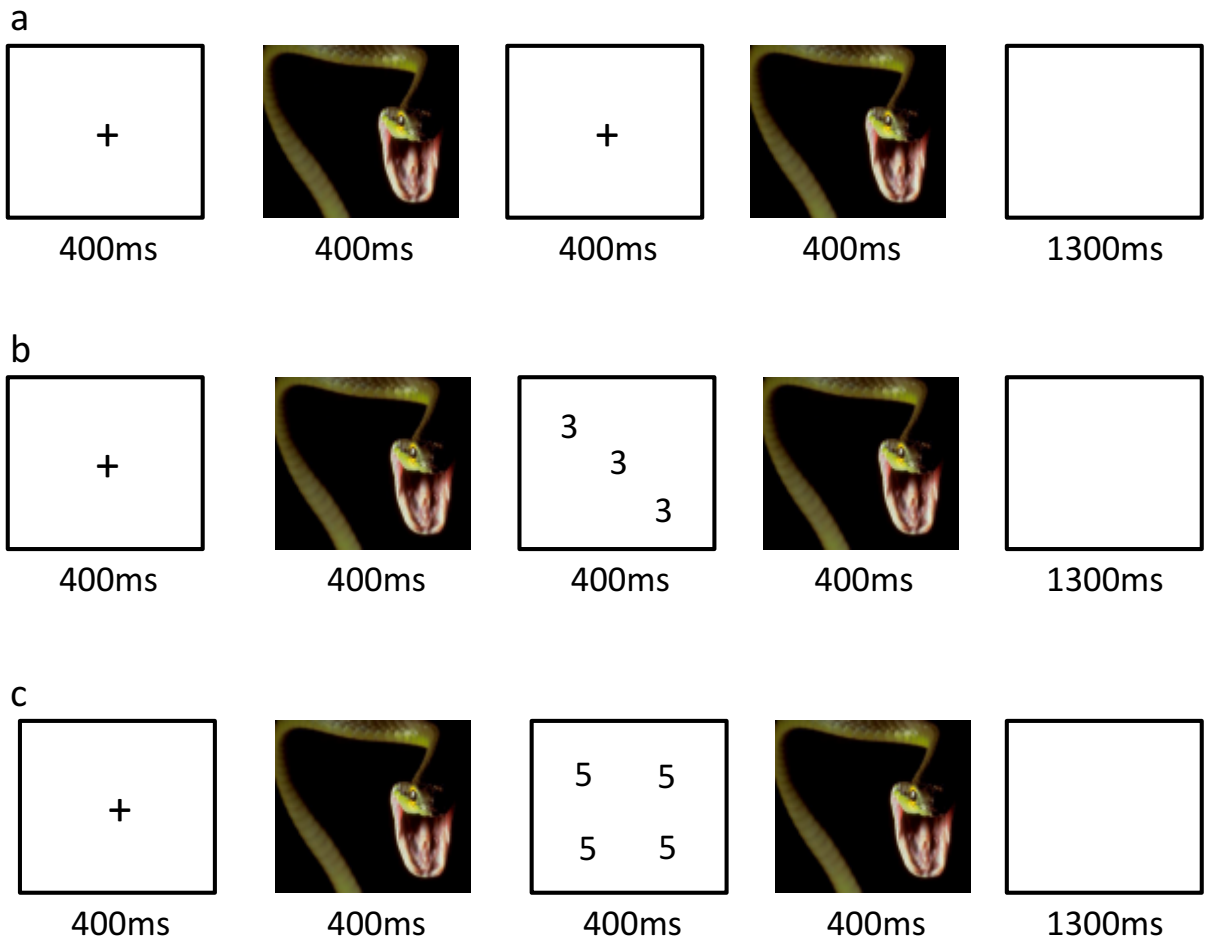
From Reactive to Proactive and Selective Control: Developing a Richer Model for Stopping Inappropriate Responses

Adam R. Aron

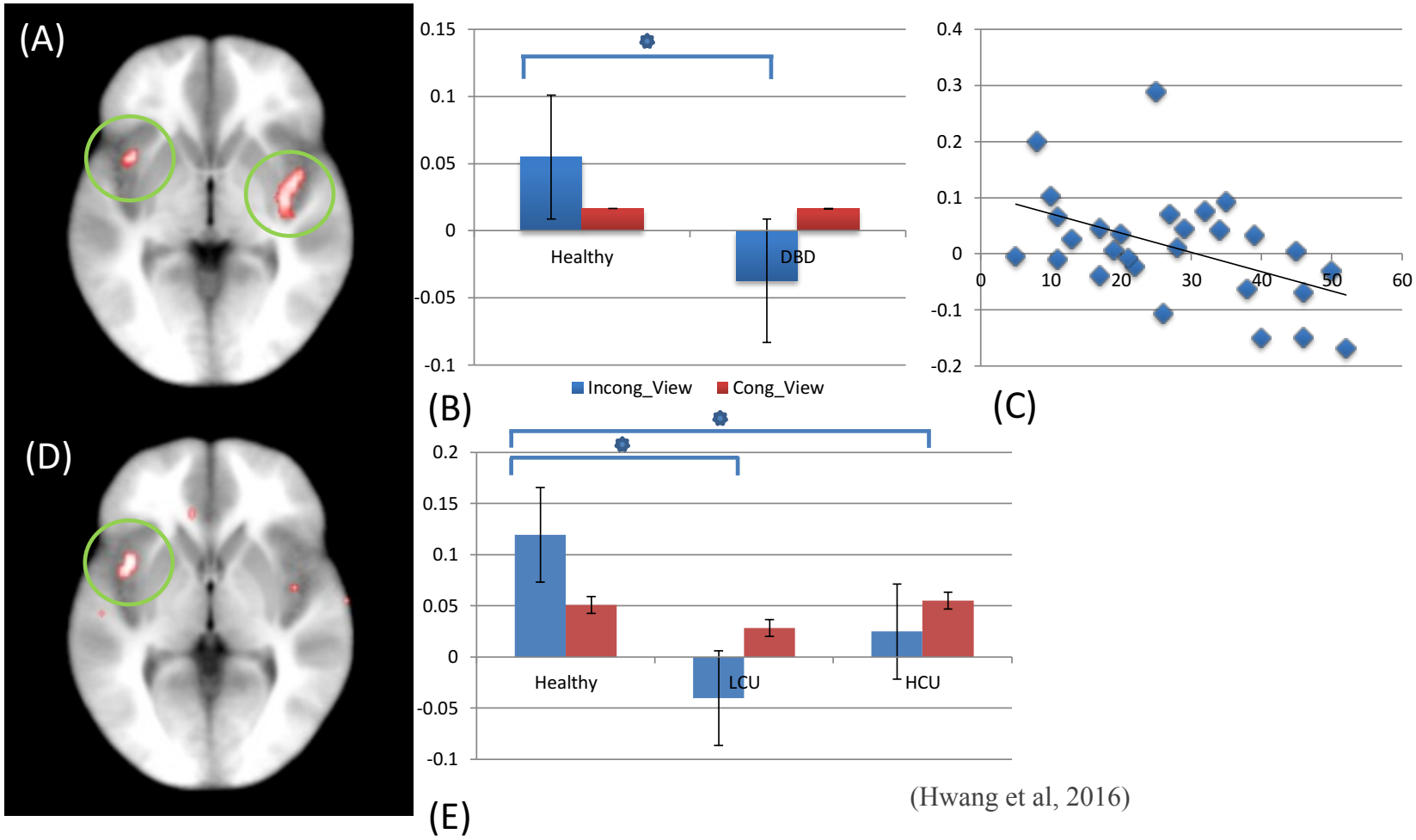


. The brain network for reactive stopping. **(A)** Regions that are critical for stopping in the standard stop signal paradigm. Two regions rontal cortex (IFC) are the inferior frontal junction (IFJ) and the posterior (p)IFG. The presupplementary motor area (preSMA) is in the med e matter tractography using diffusion tensor imaging reveals a three-way network in the right hemisphere between nodes that are action. Reprinted with permission from (31).

Affective Stroop Task (Blair et al., 2007)

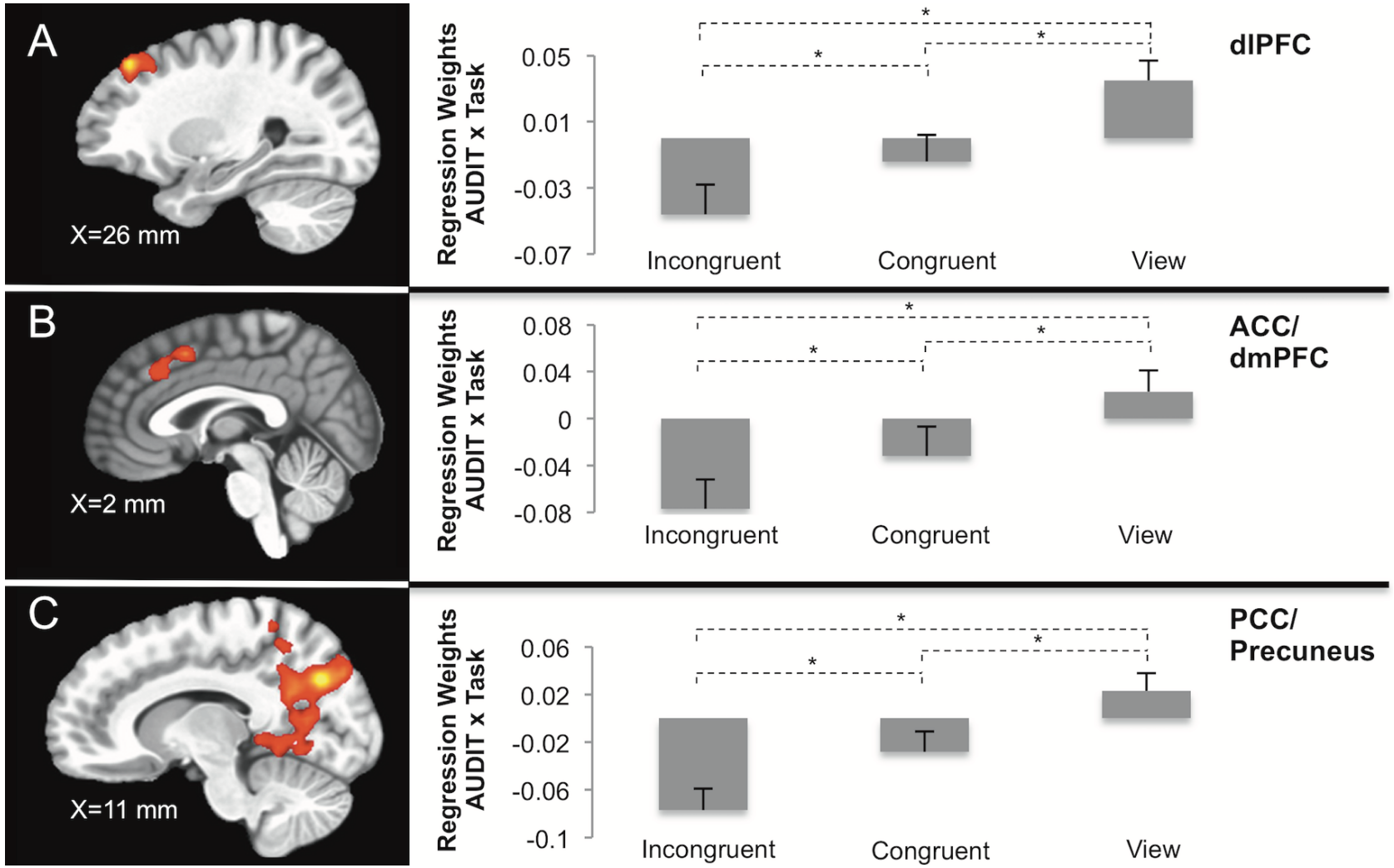


Decrease activation in insula in children/adolescents with DBD (N=35, HC=18) in presence of increased cognitive demand and its correlation with ADHD symptom severity (Hwang et al., 2015)



(Hwang et al, 2016)

Increasing alcohol abuse related problems are associated with increasingly compromised brain functioning



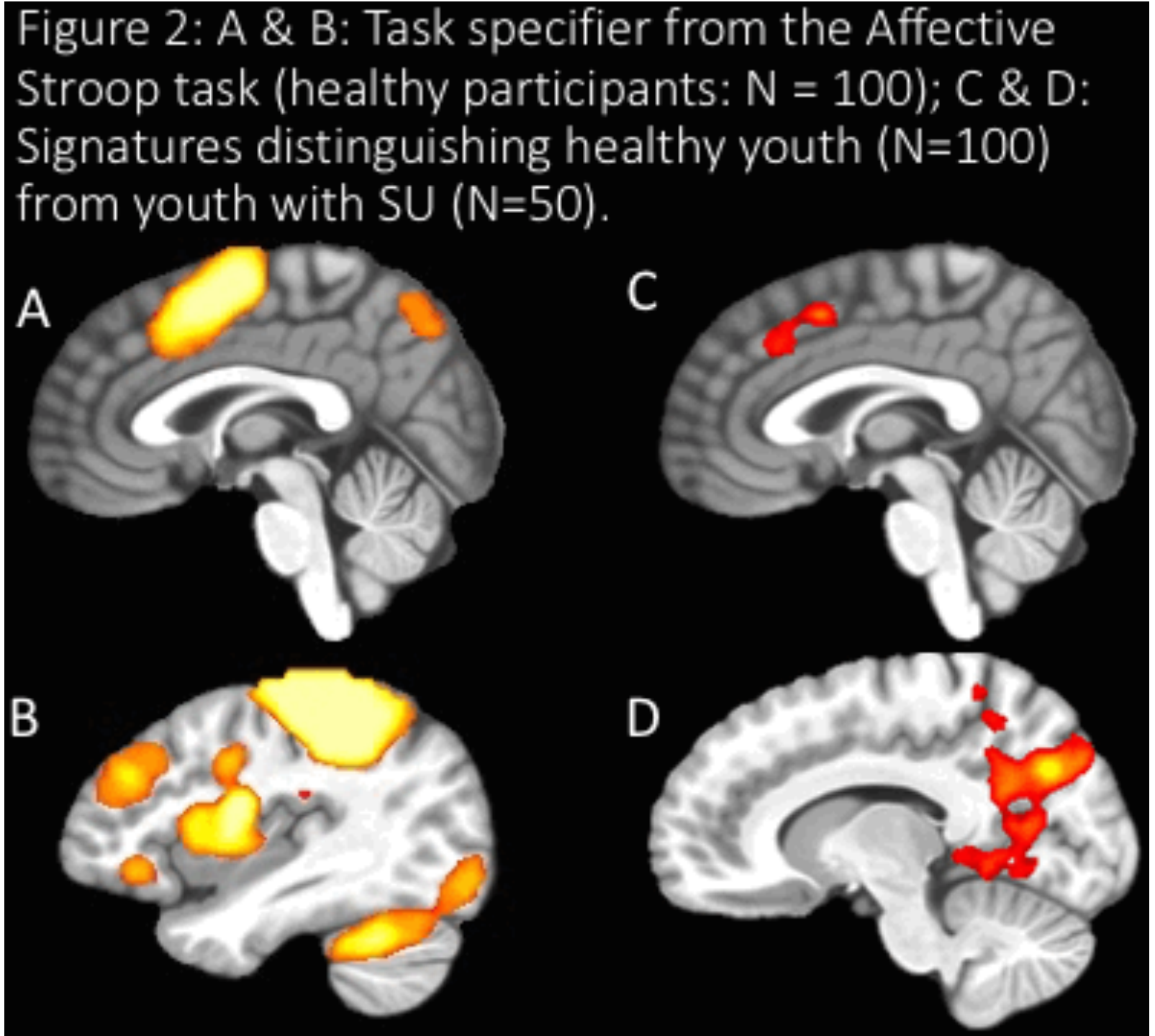
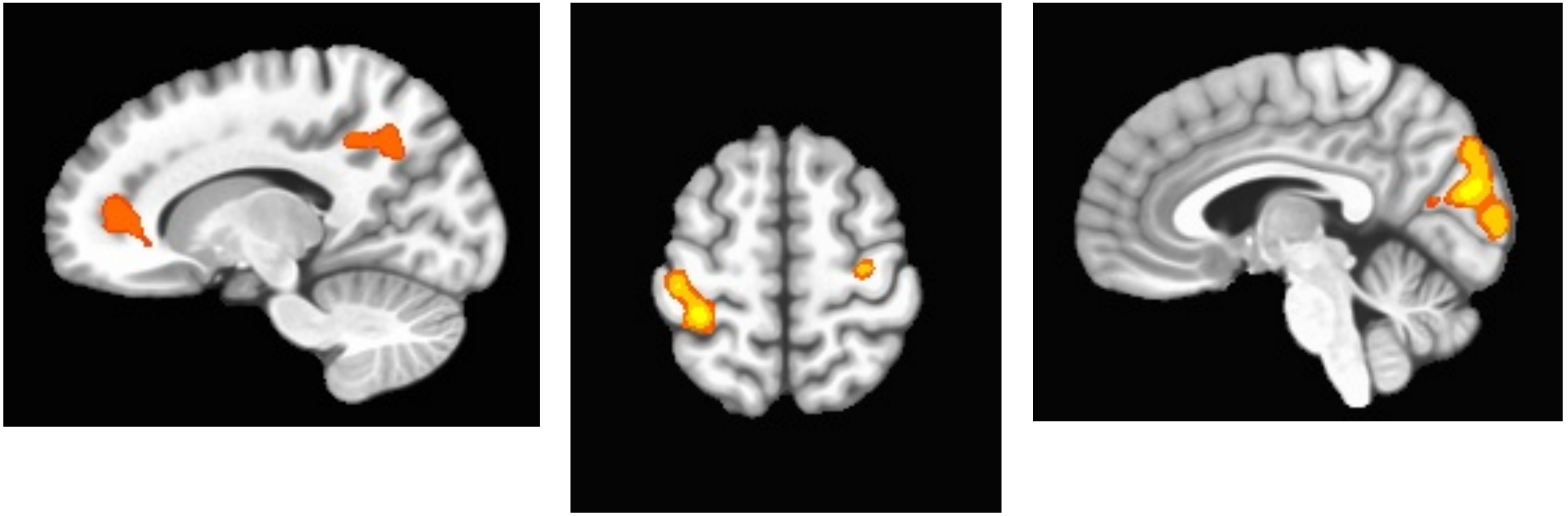


Figure 2: A & B: Task specifier from the Affective Stroop task (healthy participants: N = 100); C & D: Signatures distinguishing healthy youth (N=100) from youth with SU (N=50).
A
C
B
D

Response Control:

Increasing maltreatment – particularly sexual and emotional abuse - are associated with increasingly compromised brain functioning



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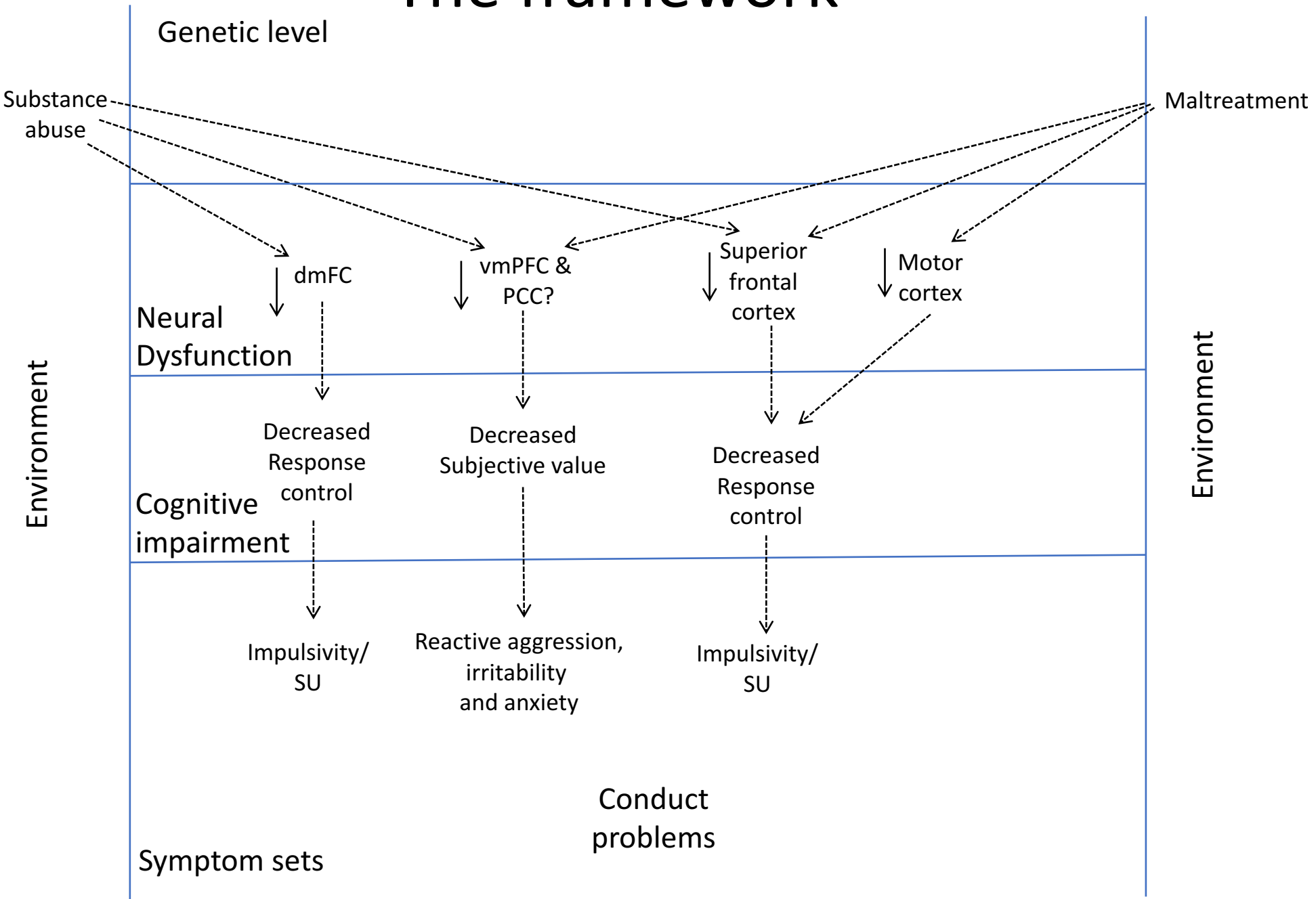

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- Ventromedial frontal cortex and expected value based choices
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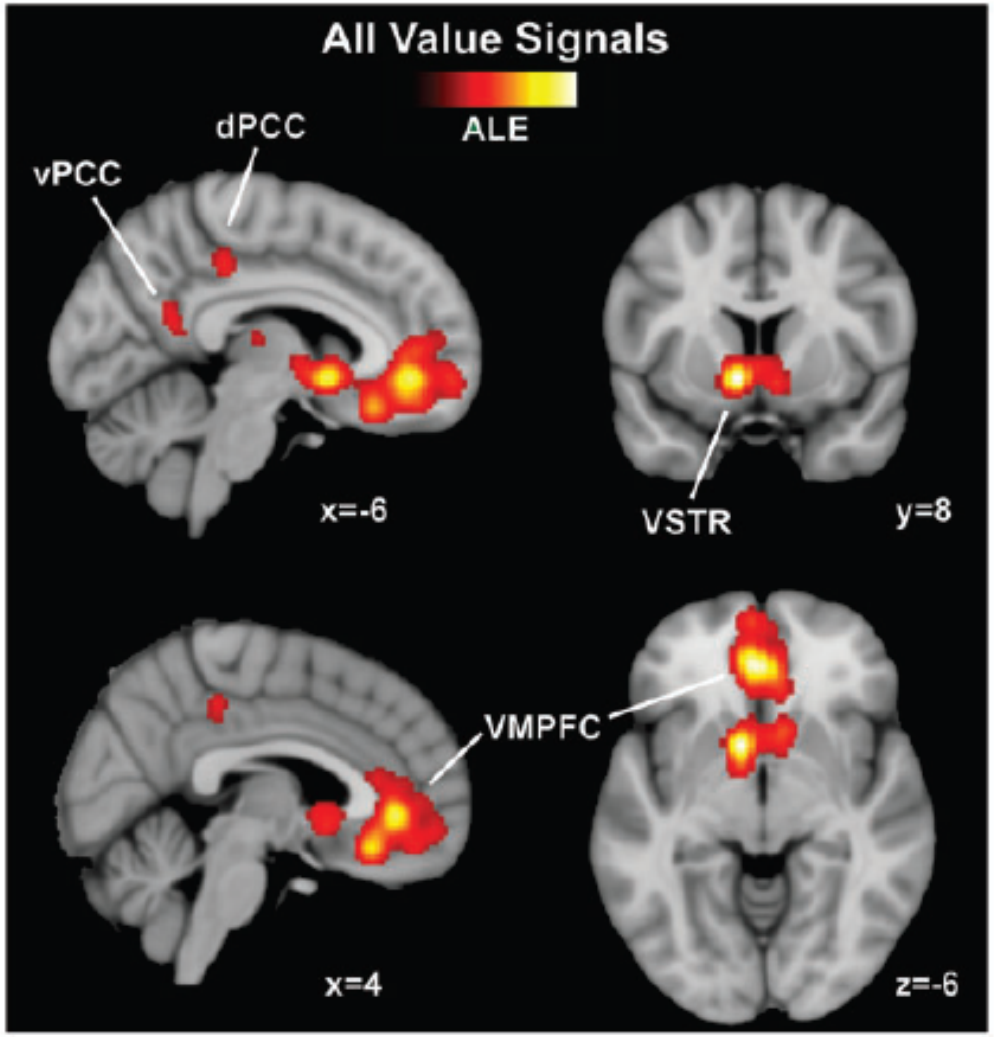
- Throughout consideration of impairments present in individuals with a diagnosis vs. impairments related to a specific symptom set.

Systems engaged in reward value: Clithero & Rangel (SCAN: 2014)



Striatum

Prediction error (PE) = The difference between the expected and received reinforcement:.

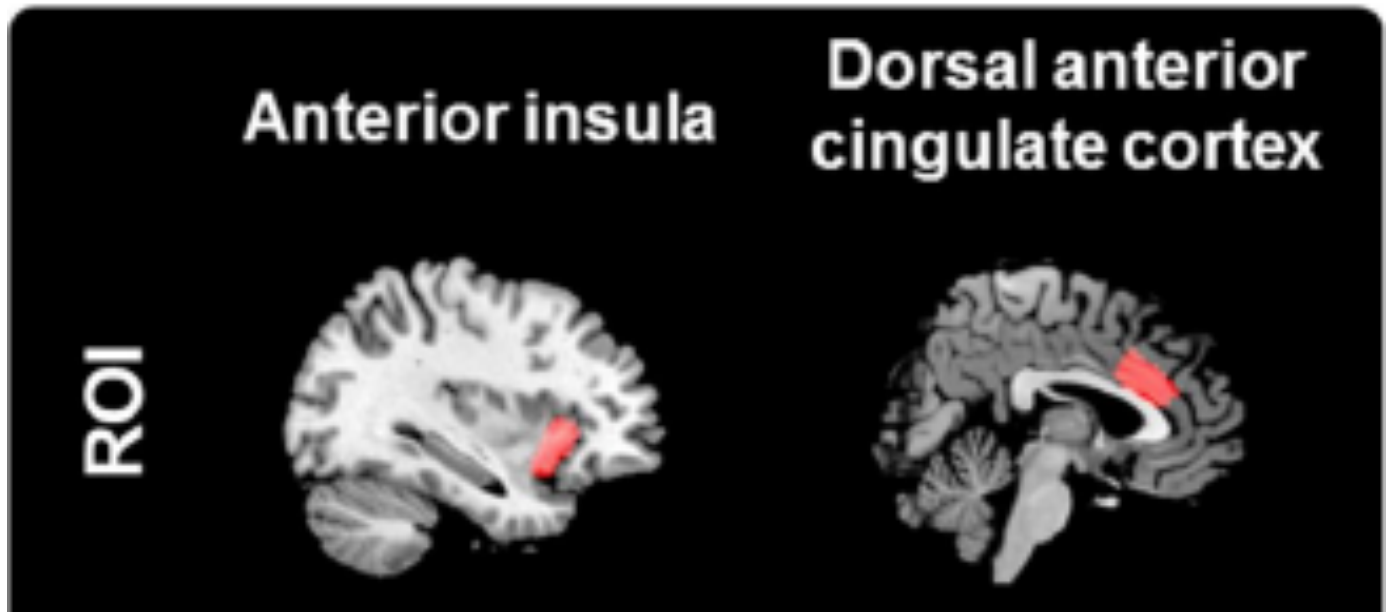
$$PE_{(t)} = F_{(t)} - EV_{(t)}$$

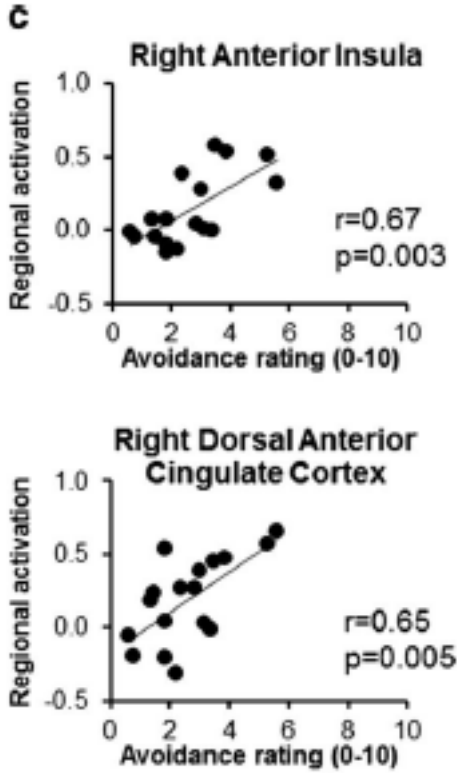
vmPFC

Expected value (EV) = The expected reinforcement if the action is undertaken:

$$EV_{(t)} = EV_{(t-1)} + (\alpha * PE_{(t-1)})$$

Systems engaged in avoidance (Lin et al, 2015)





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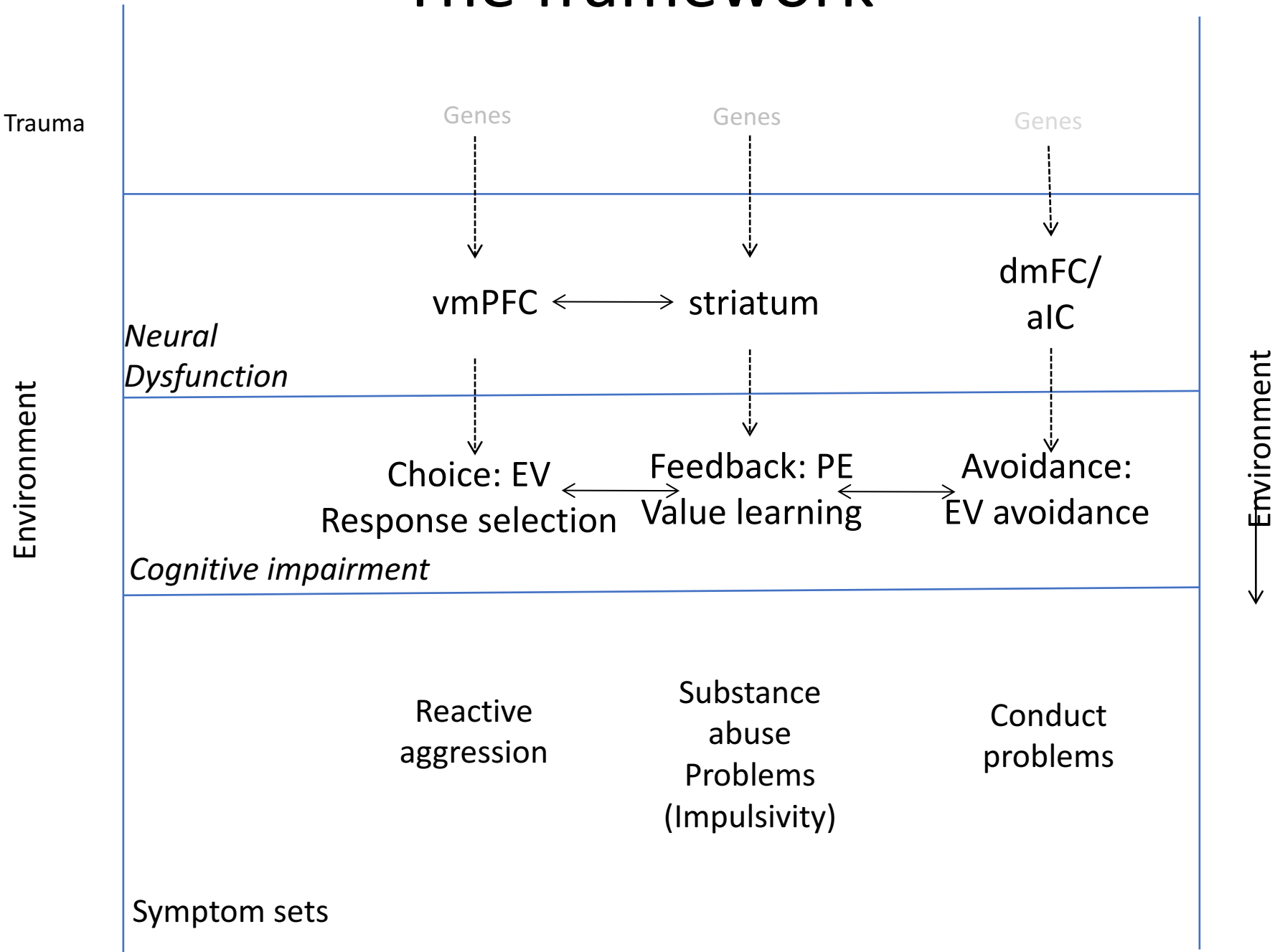

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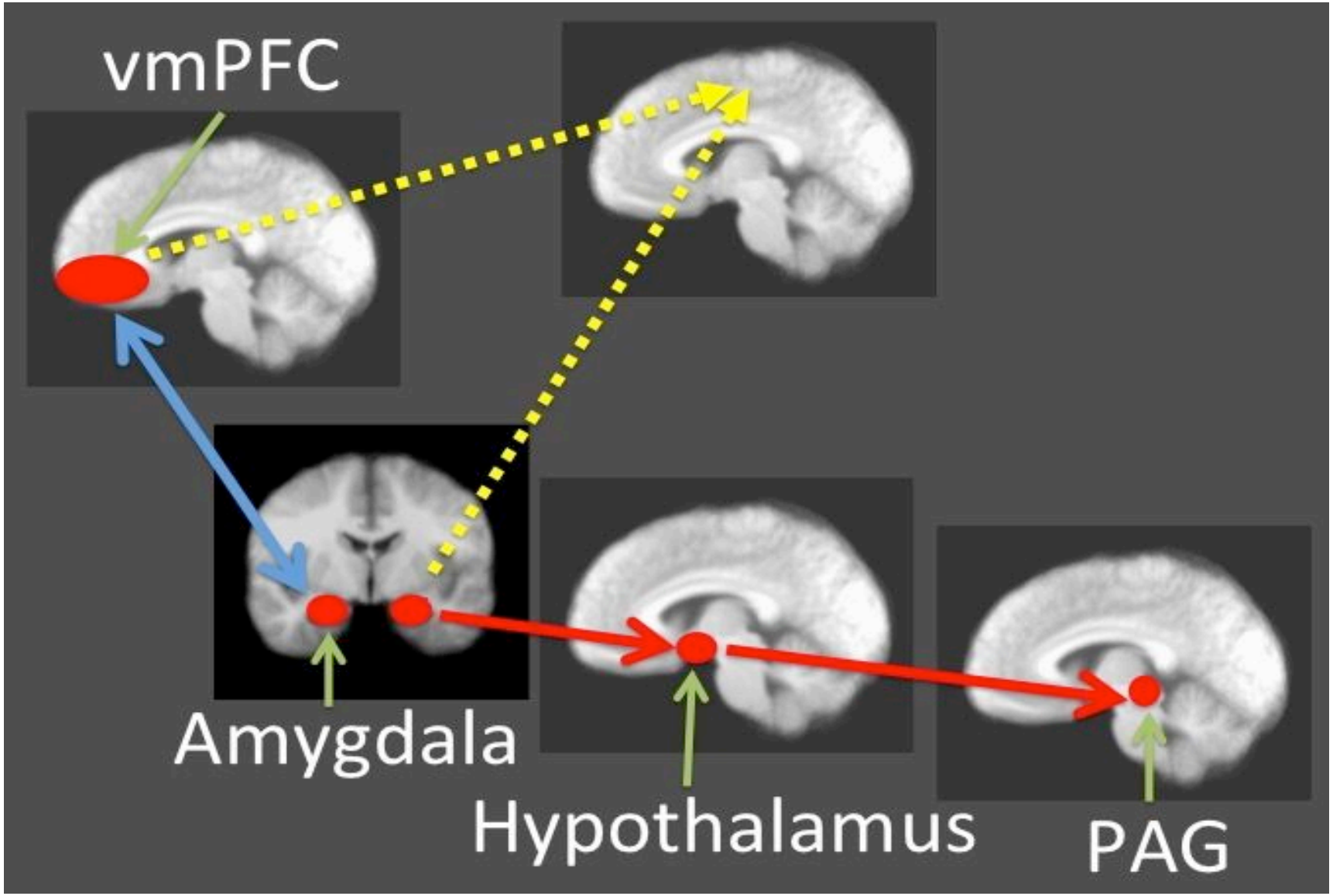
“Instrumental-reactive” Aggression



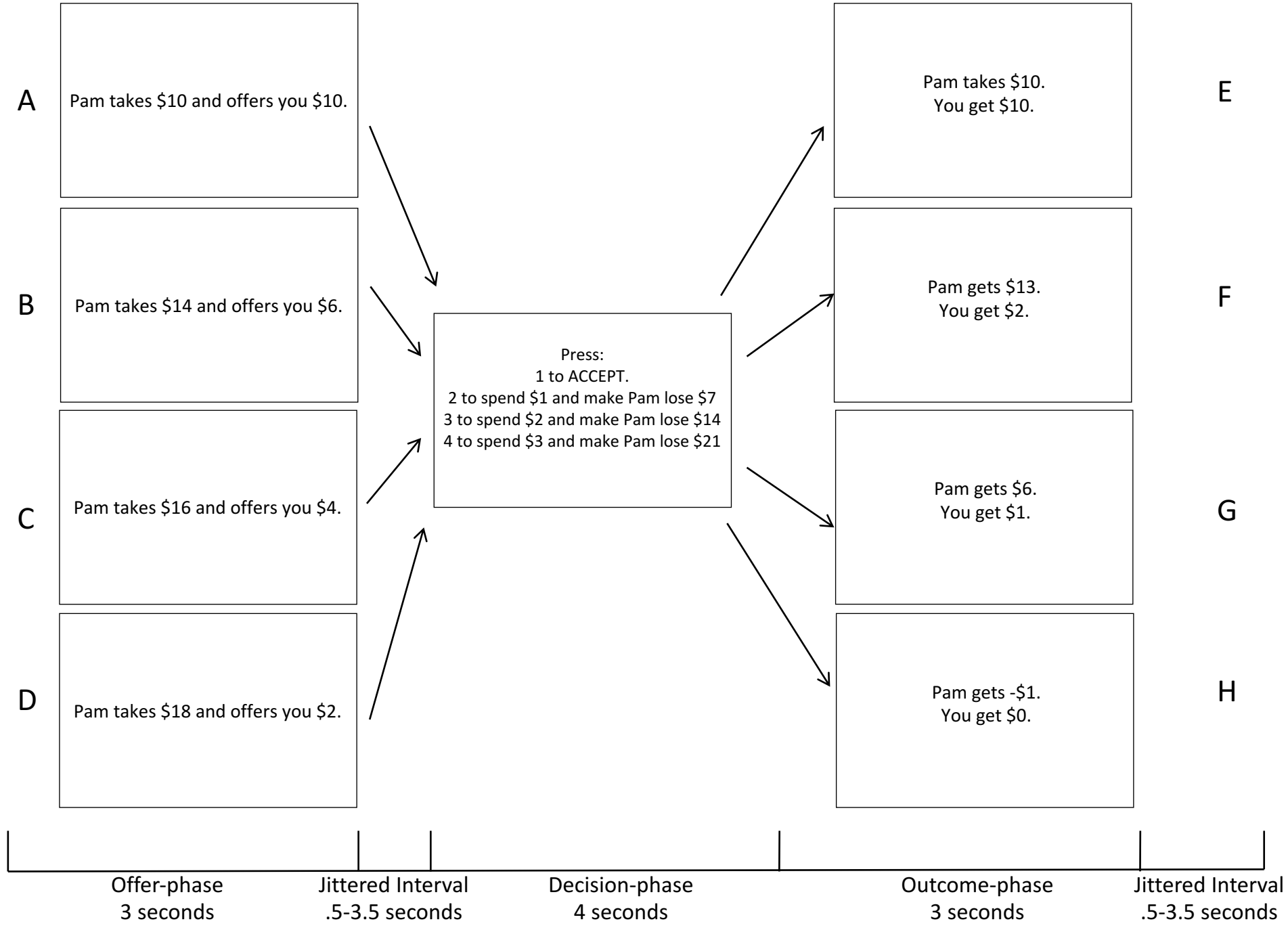
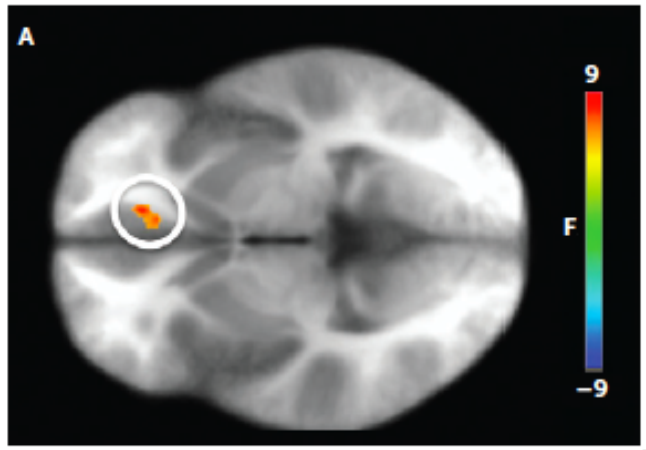
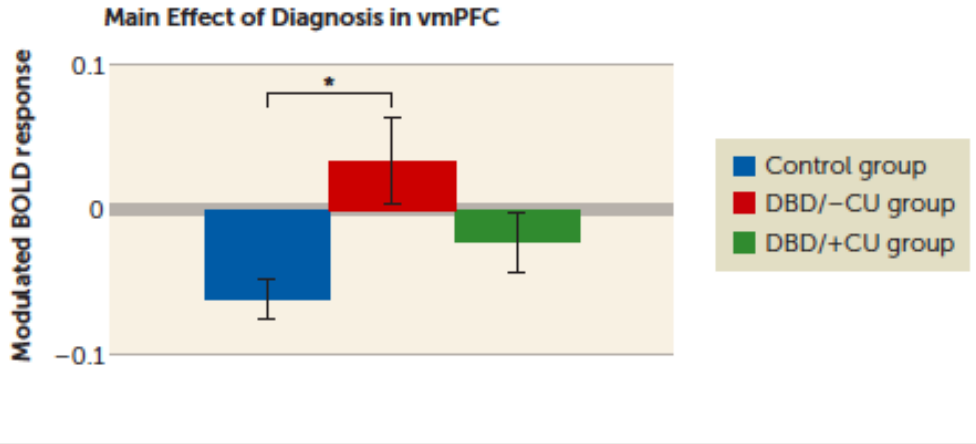
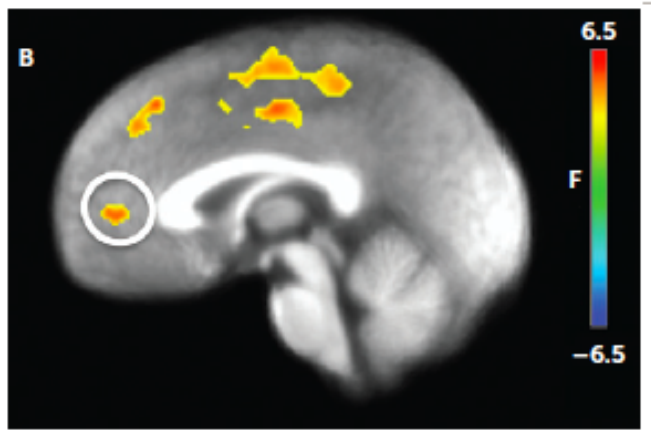
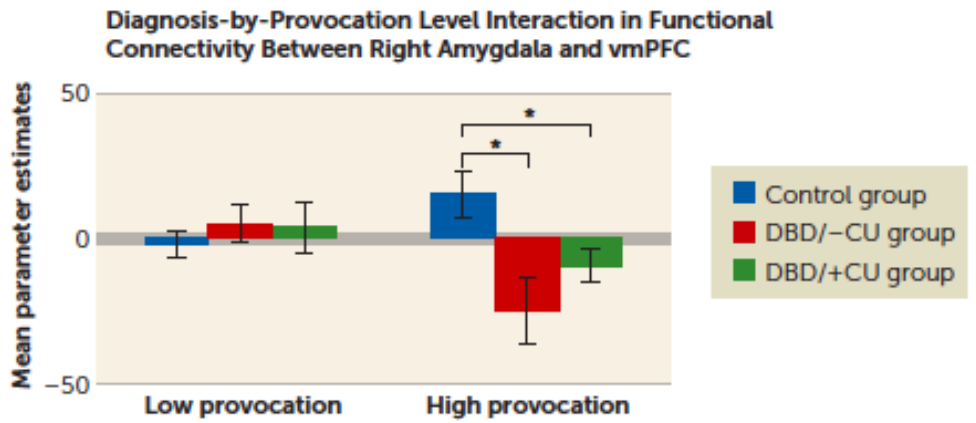

A
Pam takes $10 and offers you $10.
B
Pam takes $14 and offers you $6.
C
Pam takes $16 and offers you $4.
D
Pam takes $18 and offers you $2.
Press:
1 to ACCEPT.
2 to spend $1 and make Pam lose $7
3 to spend $2 and make Pam lose $14
4 to spend $3 and make Pam lose $21
Pam takes $10.
You get $10.
E
Pam gets $13.
You get $2.
F
Pam gets $6.
You get $1.
G
Pam gets -$1.
You get $0.
H
Offer-phase
3 seconds
Jittered Interval
.5-3.5 seconds
Decision-phase
4 seconds
Outcome-phase
3 seconds
Jittered Interval
.5-3.5 seconds

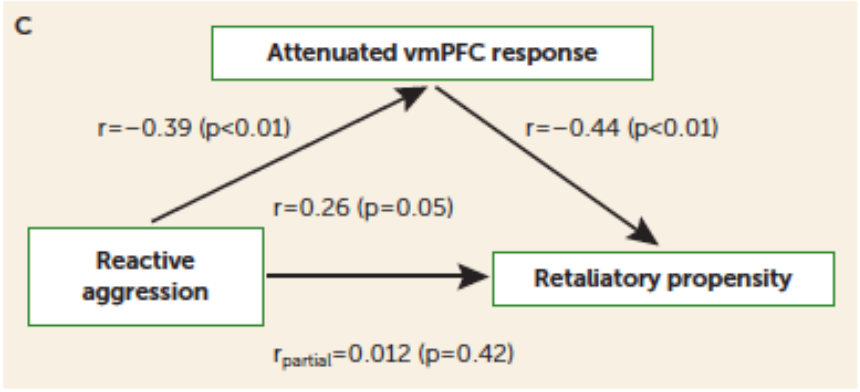
FIGURE 3. Group Differences in the Ventromedial Prefrontal Cortex Between Healthy Youths (N=28) and Youths With Disruptive Behavior Disorders and Low (N=15) or High (N=15) Levels of Callous-Unemotional Traits[a]

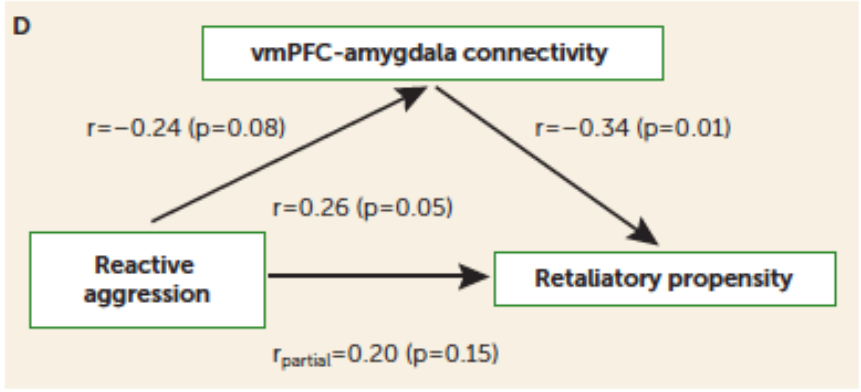




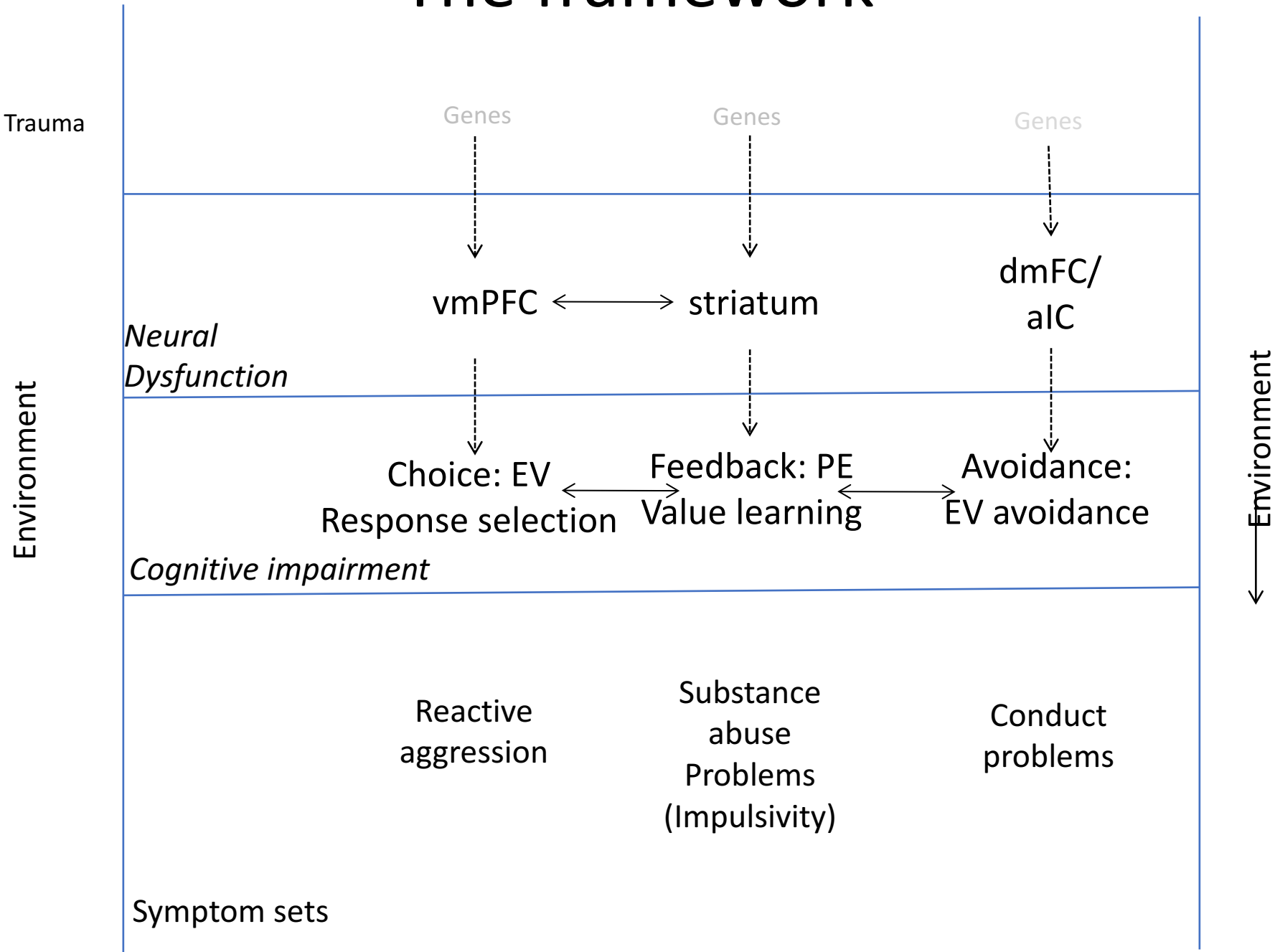








The framework



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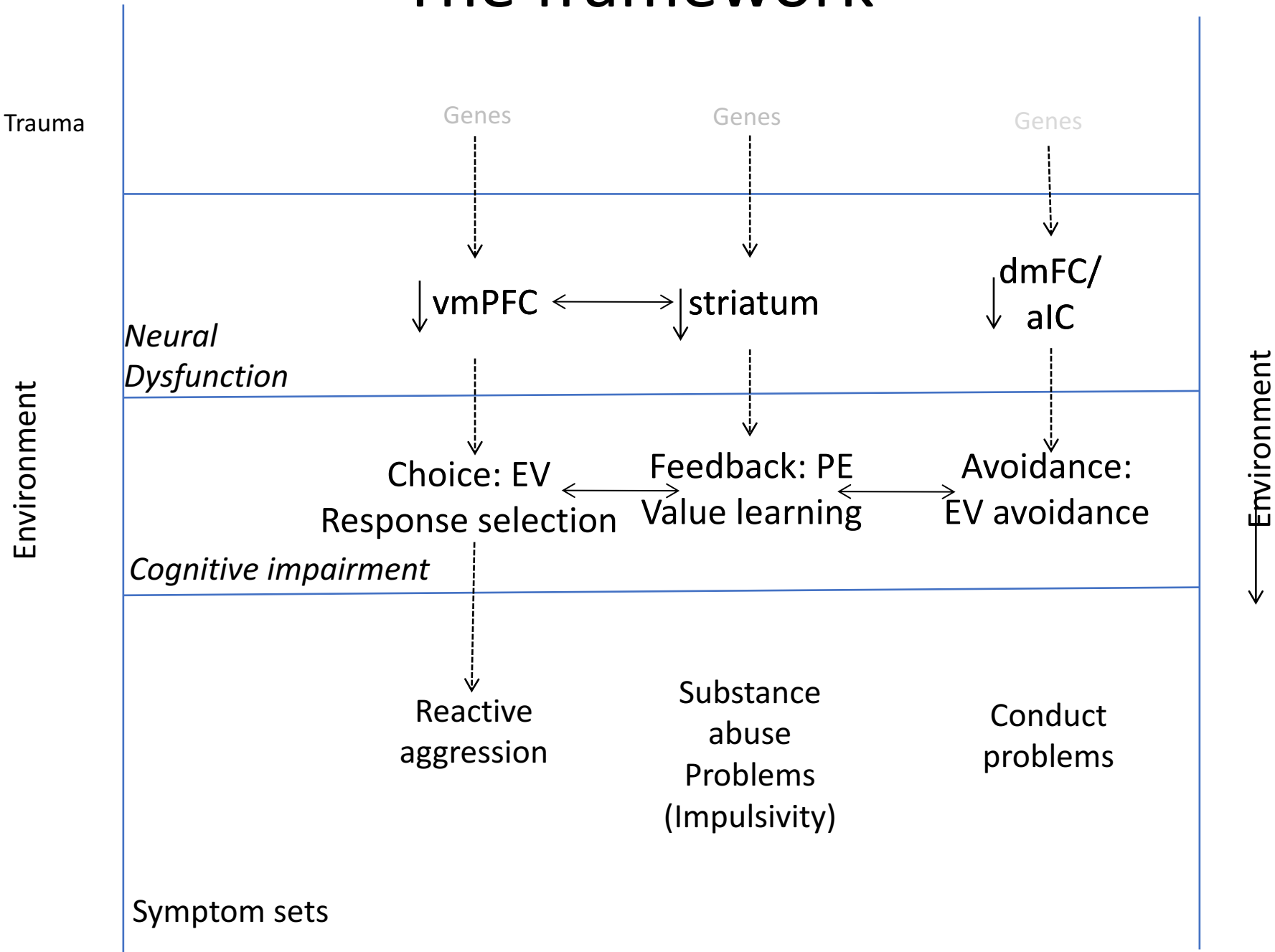

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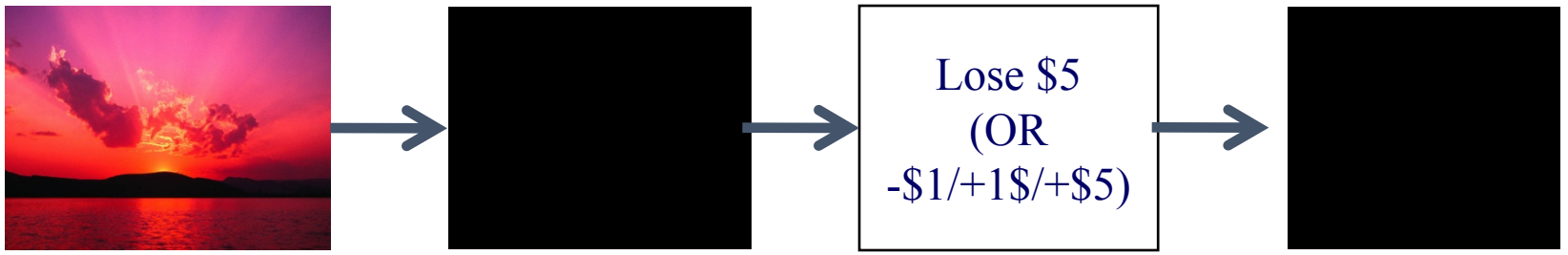
Passive avoidance learning (White et al, AJP)

"Early" study: Finger et al. AJP, 2011. Apparent signaling to early reinforcements within OFC and caudate .
Critical though to distinguish BOLD responses to cue from those to feedback.



1000ms 0 - 3000ms 1000ms 0 - 3000ms

Regressors for Chosen, Non-Chosen and Reward, Punishment were weighted according to learning theory: Rescorla-Wagner:
Prediction error for the current trial$_{(t)}$ equaled the feedback value for the current trial minus the expected value for the current trial.

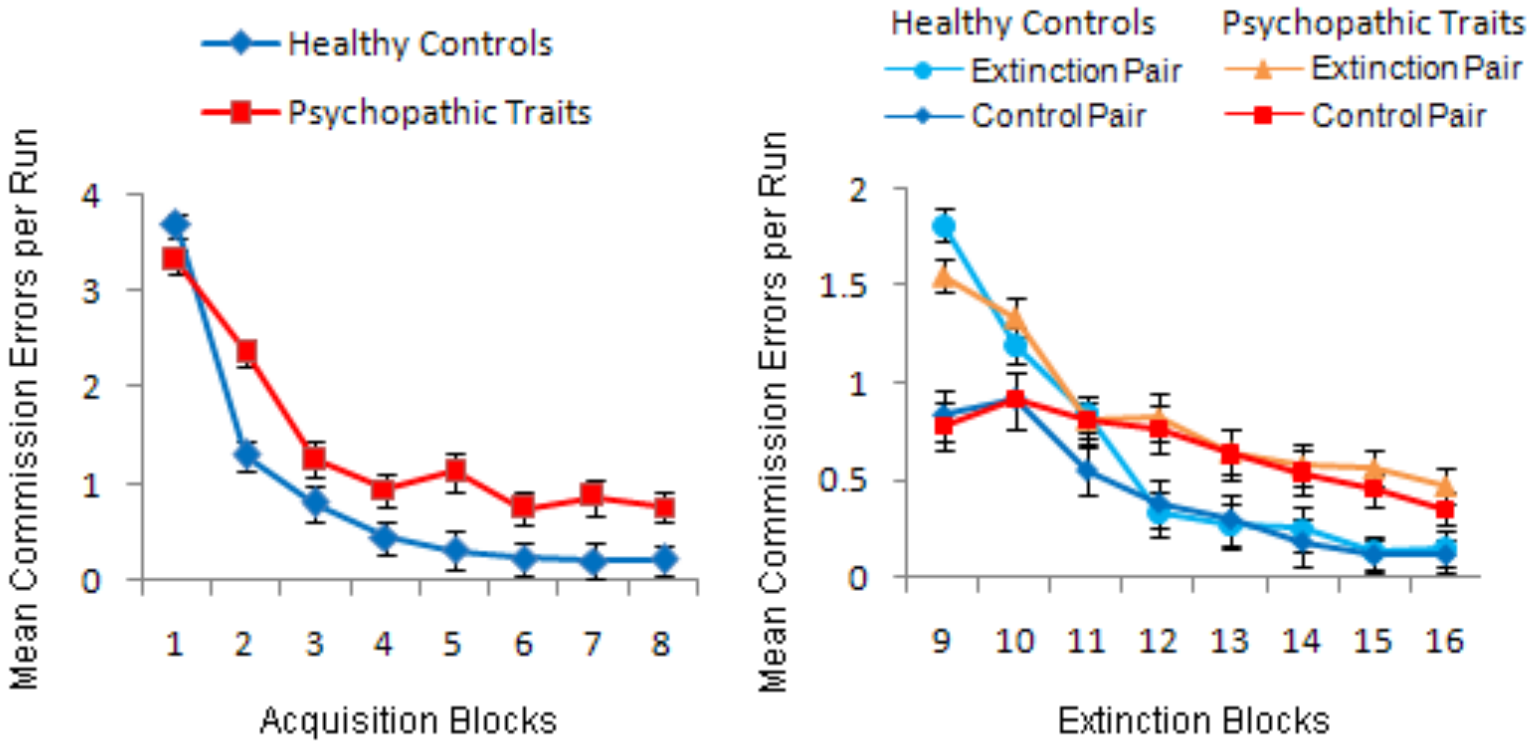
$$PE_{(t)} = F_{(t)} - EV_{(t)}$$

EV was calculated via the following formula:

$$EV_{(t)} = EV_{(t-1)} + (\alpha * PE_{(t-1)})$$

PA details; Impairment in CD

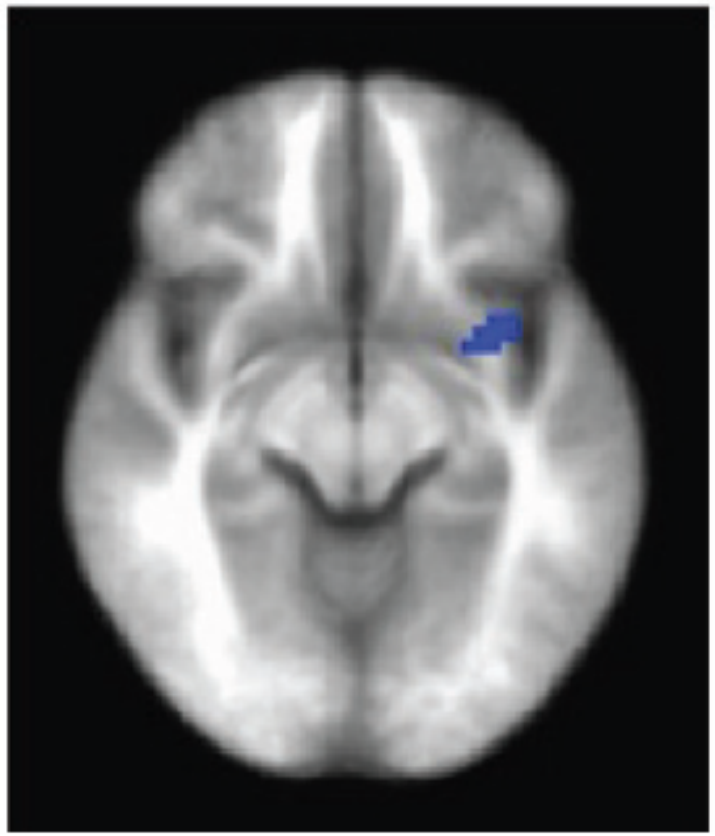
- Impairment in learning to avoid “bad” responses.

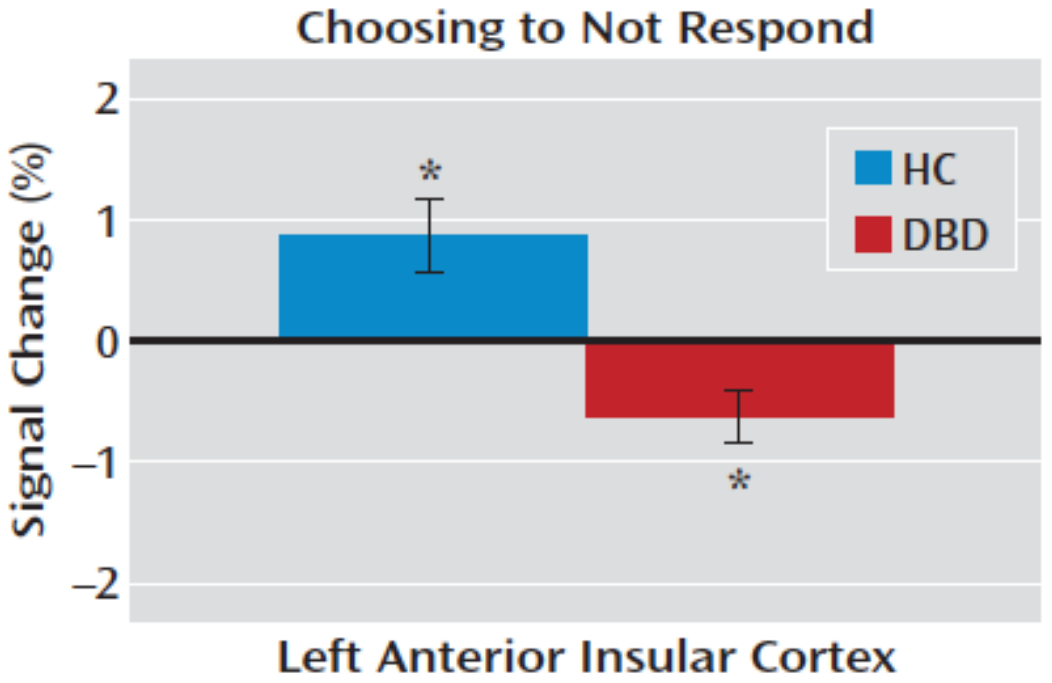


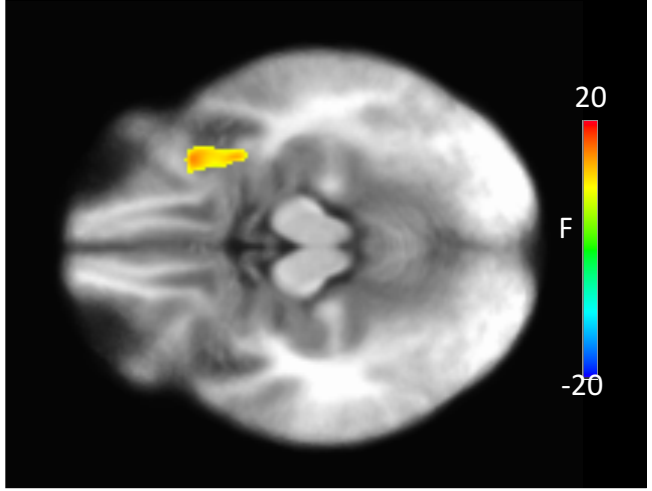
White et al (AJP: 2013)

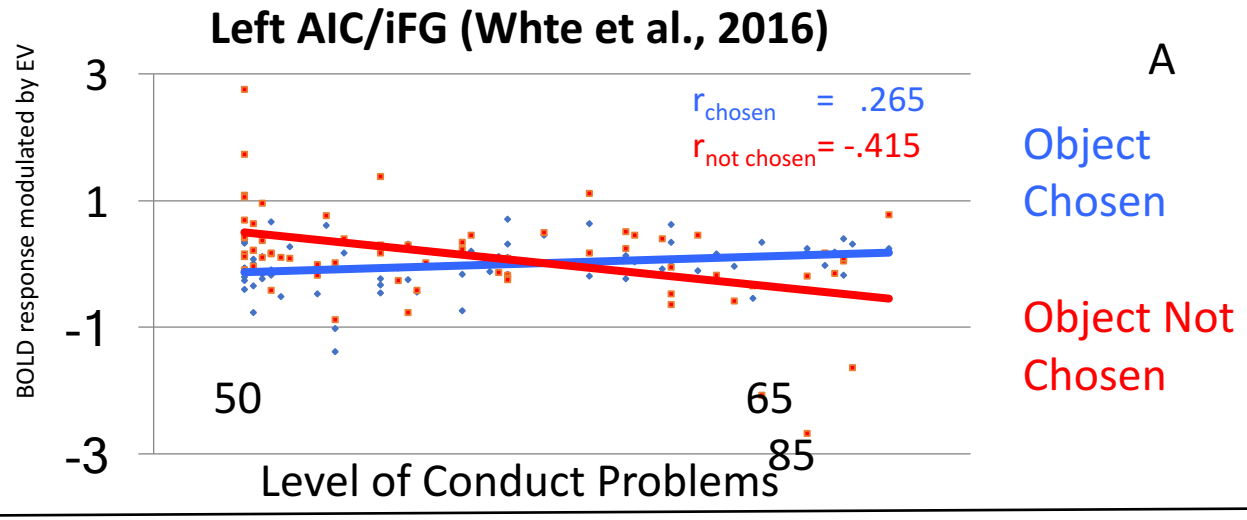
- Youth with DBD (N=20; 85% CD) and TD youth (N=18)
- Matched for age (DBD: 15.2, TD: 14.9) & gender (majority male)

White et al (2013: N=36): Avoidance responding







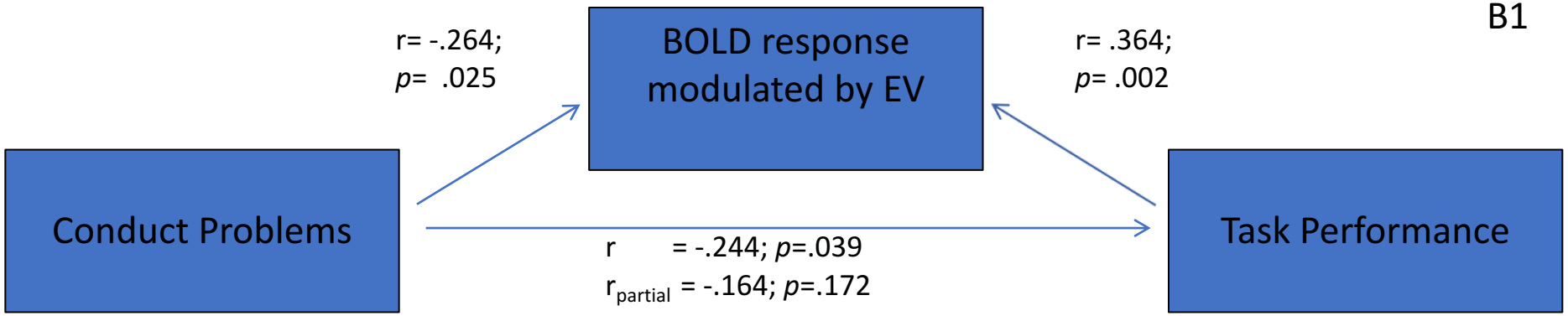


A

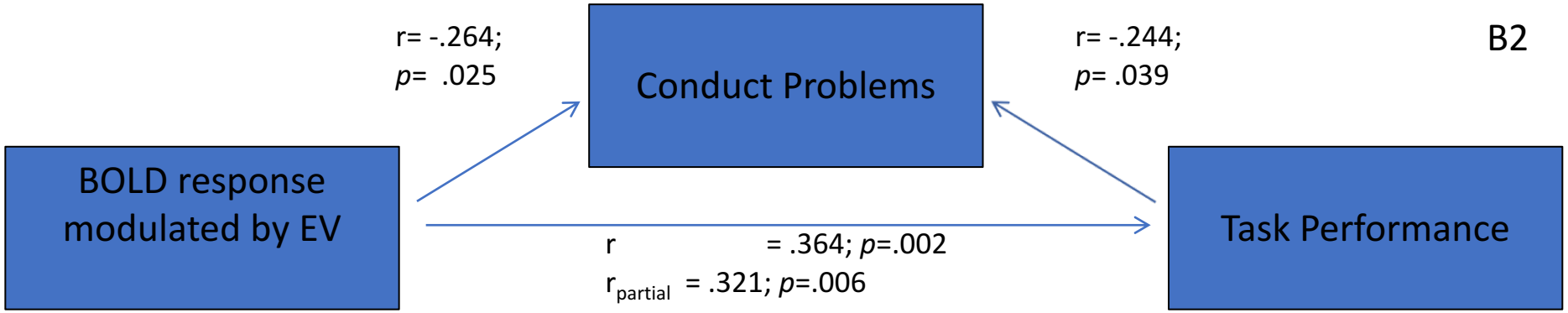
Object Chosen

Object Not Chosen

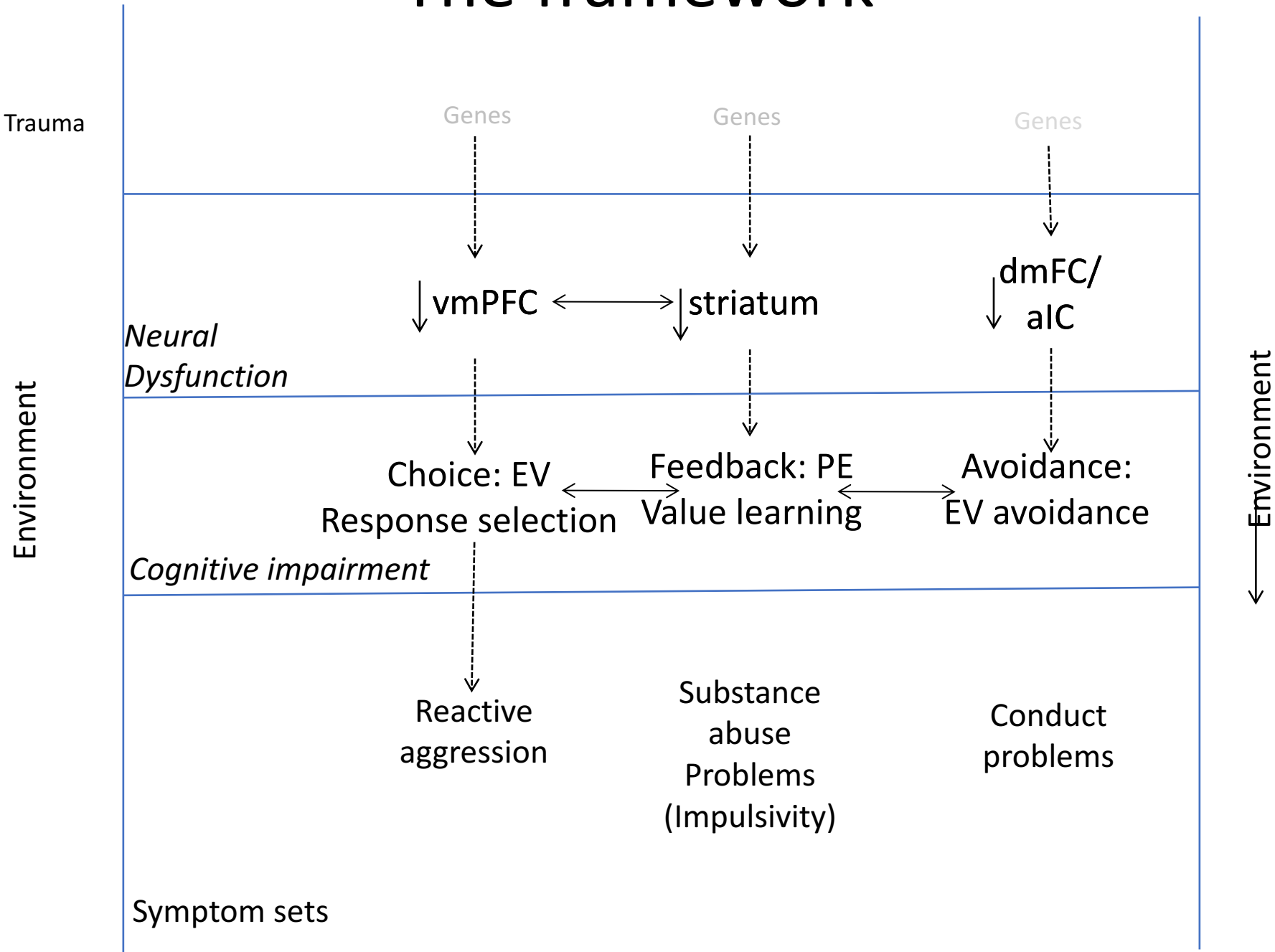
B1



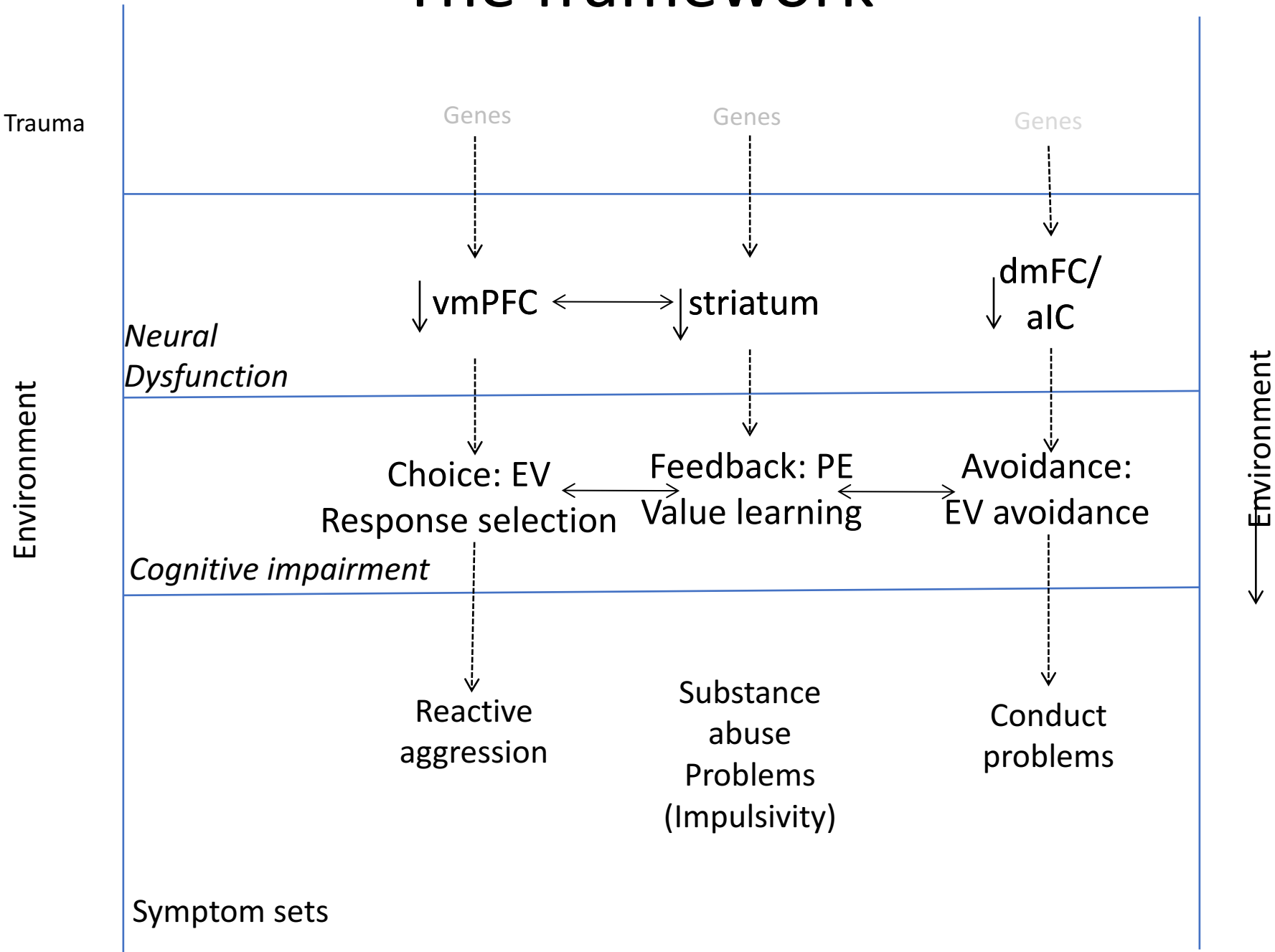
B2



The framework



The framework

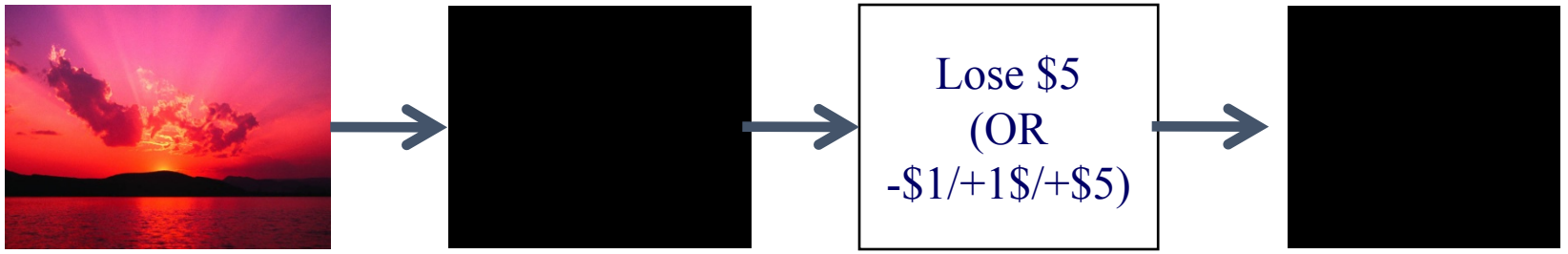


Talk plan

- **The problem space and basic framework**
- **Neural systems involved in approach and avoidance reinforcement-based decision-making.**
- **Ventromedial frontal cortex and expected value based choices**
- **Anterior insula cortex and expected value based avoidances**
- **Striatal involvement in prediction error signaling**
- **Throughout consideration of impairments present in individuals with a diagnosis vs. impairments related to a specific symptom set.**

Passive avoidance learning (White et al, AJP)

"Early" study: Finger et al. AJP, 2011. Apparent signaling to early reinforcements within OFC and caudate .
Critical though to distinguish BOLD responses to cue from those to feedback.



1000ms 0 - 3000ms 1000ms 0 - 3000ms

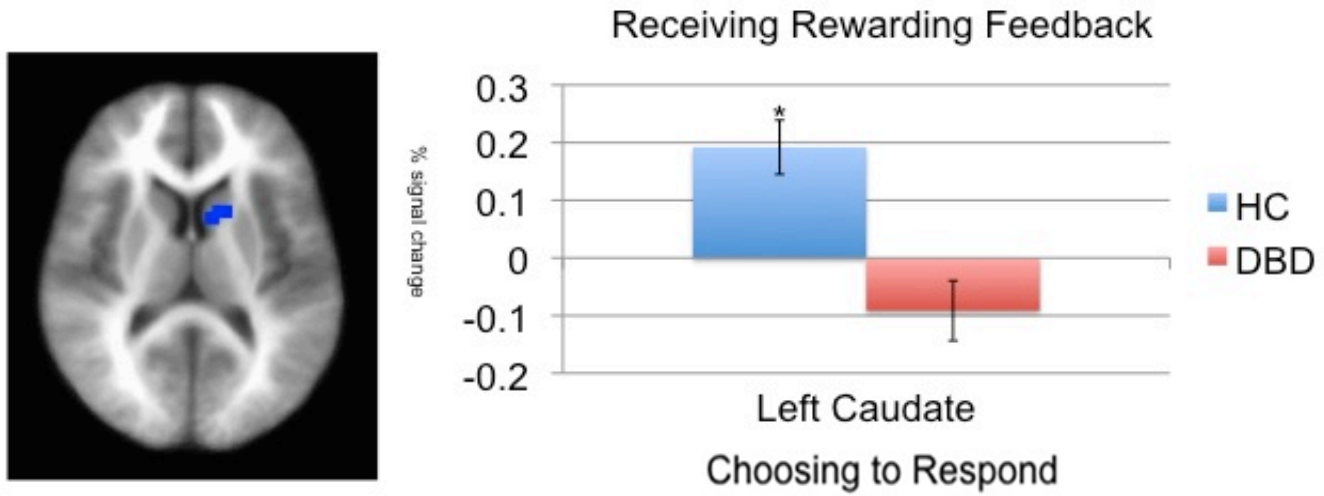
Regressors for Chosen, Non-Chosen and Reward, Punishment were weighted according to learning theory: Rescorla-Wagner:
Prediction error for the current trial$_{(t)}$ equaled the feedback value for the current trial minus the expected value for the current trial.

$$PE_{(t)} = F_{(t)} - EV_{(t)}$$

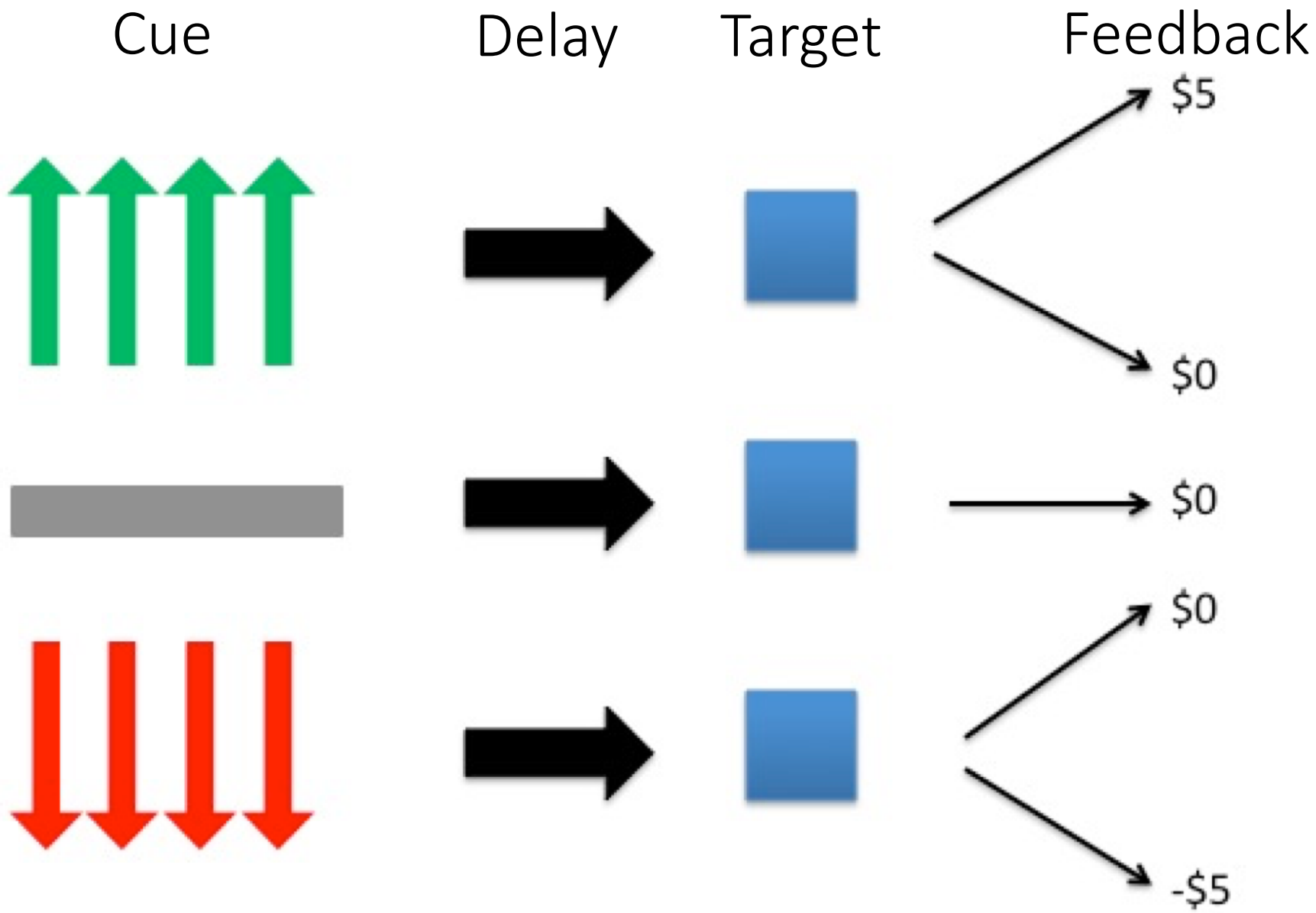
EV was calculated via the following formula:

$$EV_{(t)} = EV_{(t-1)} + (\alpha * PE_{(t-1)})$$

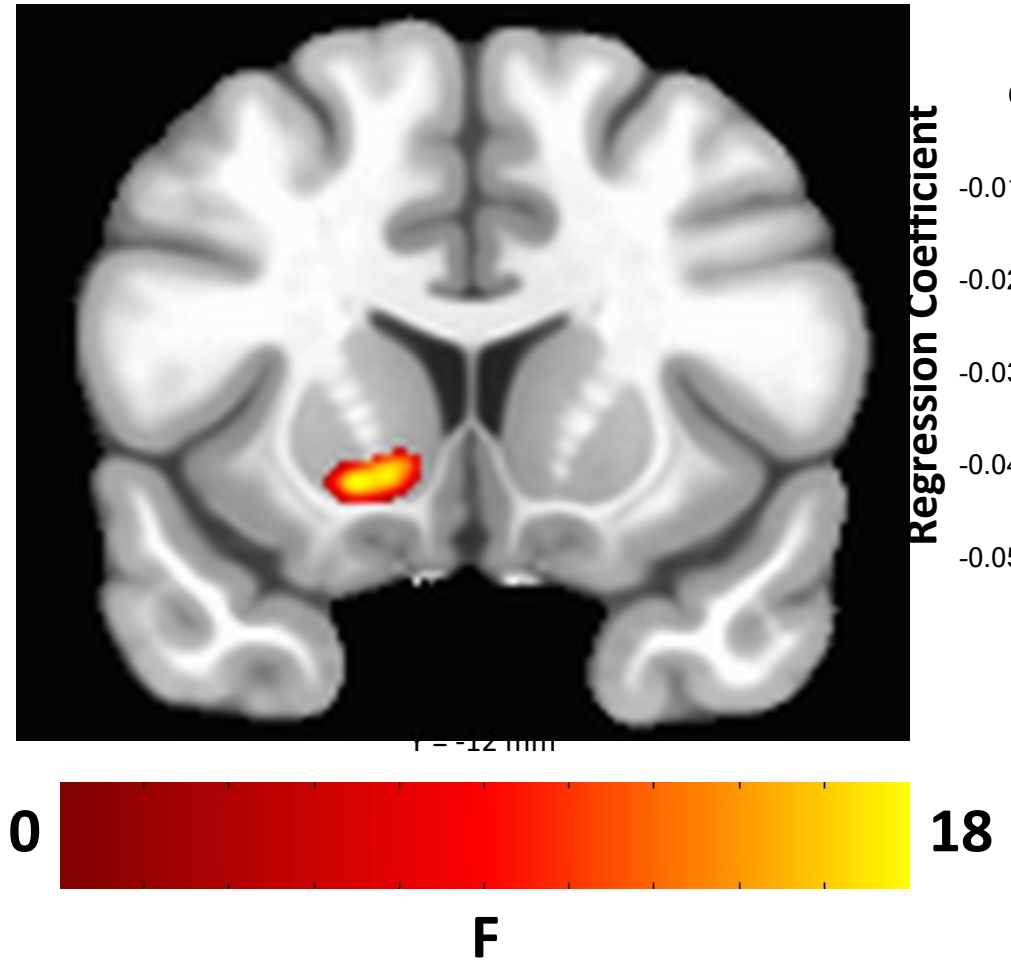
Reward prediction error response (White et al., AJP 2013)

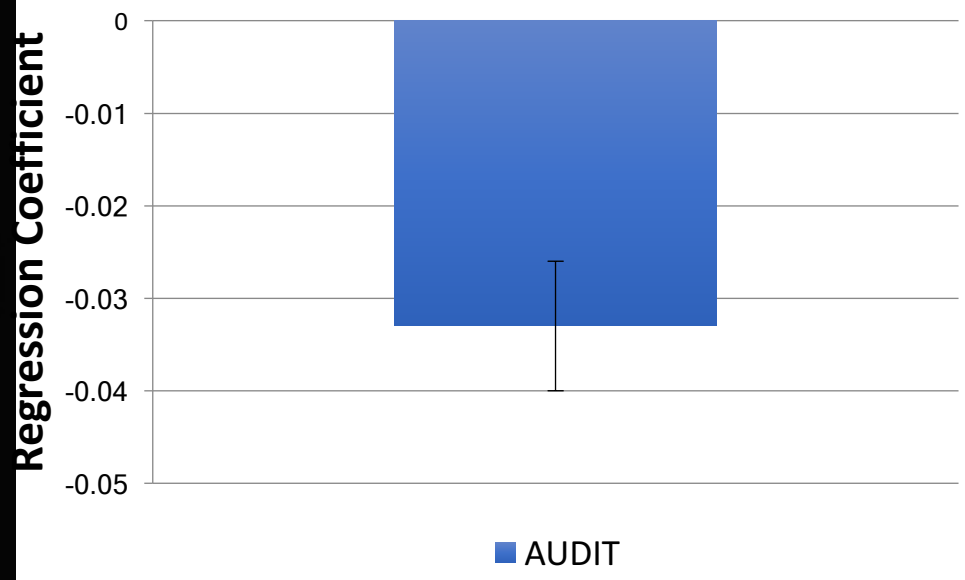


Monetary incentive delay task



Decreased striatal responses to reward associated with increased substance abuse (particularly alcohol abuse)





Gerin et al (2017)

- **Well characterized sample of youth with maltreatment and comparison individuals.**

- Profound impairment in PE signaling within striatum and vmPFC.

Reward processing:

Increasing maltreatment is associated with reduced reward responsiveness.

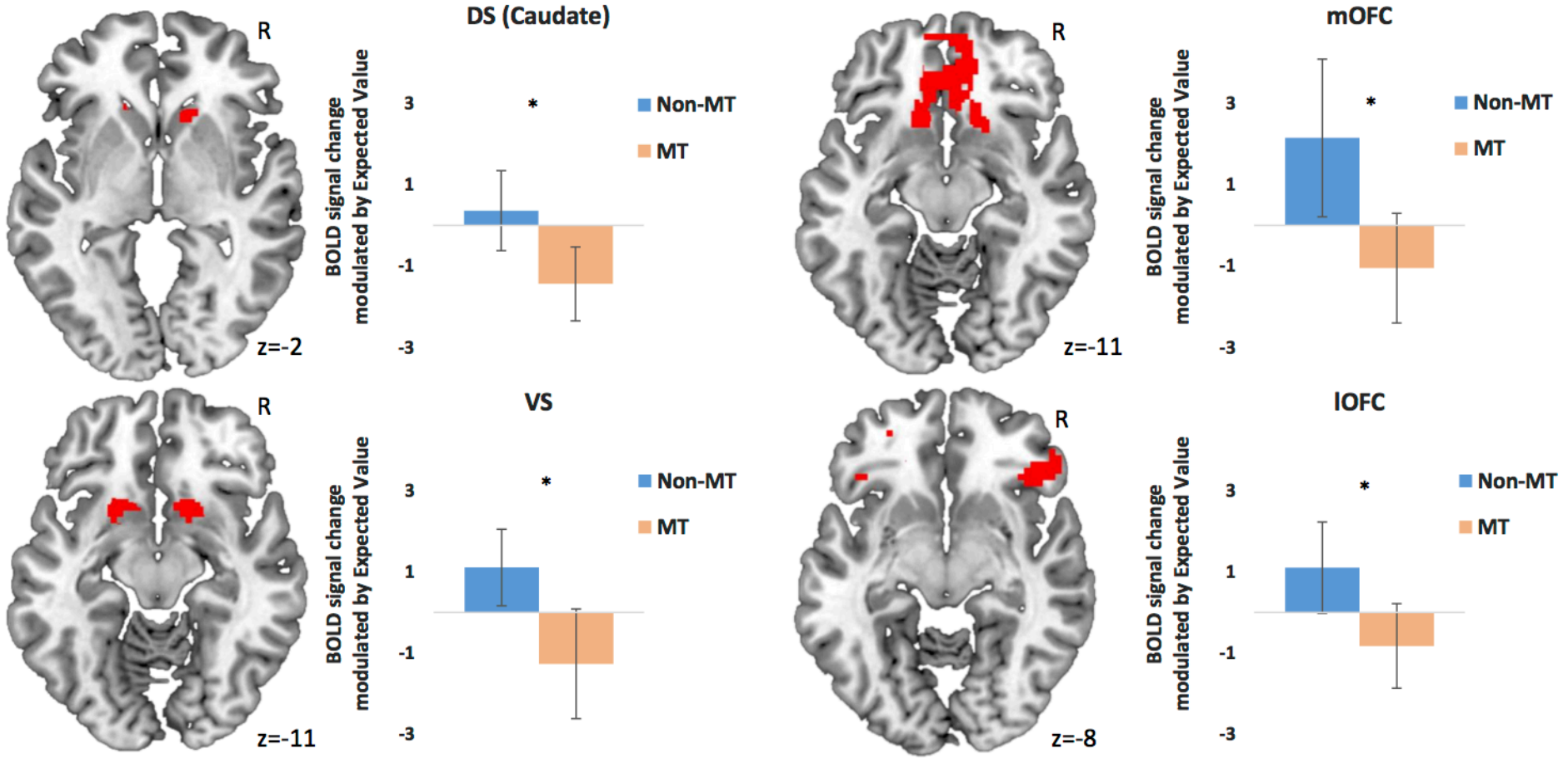
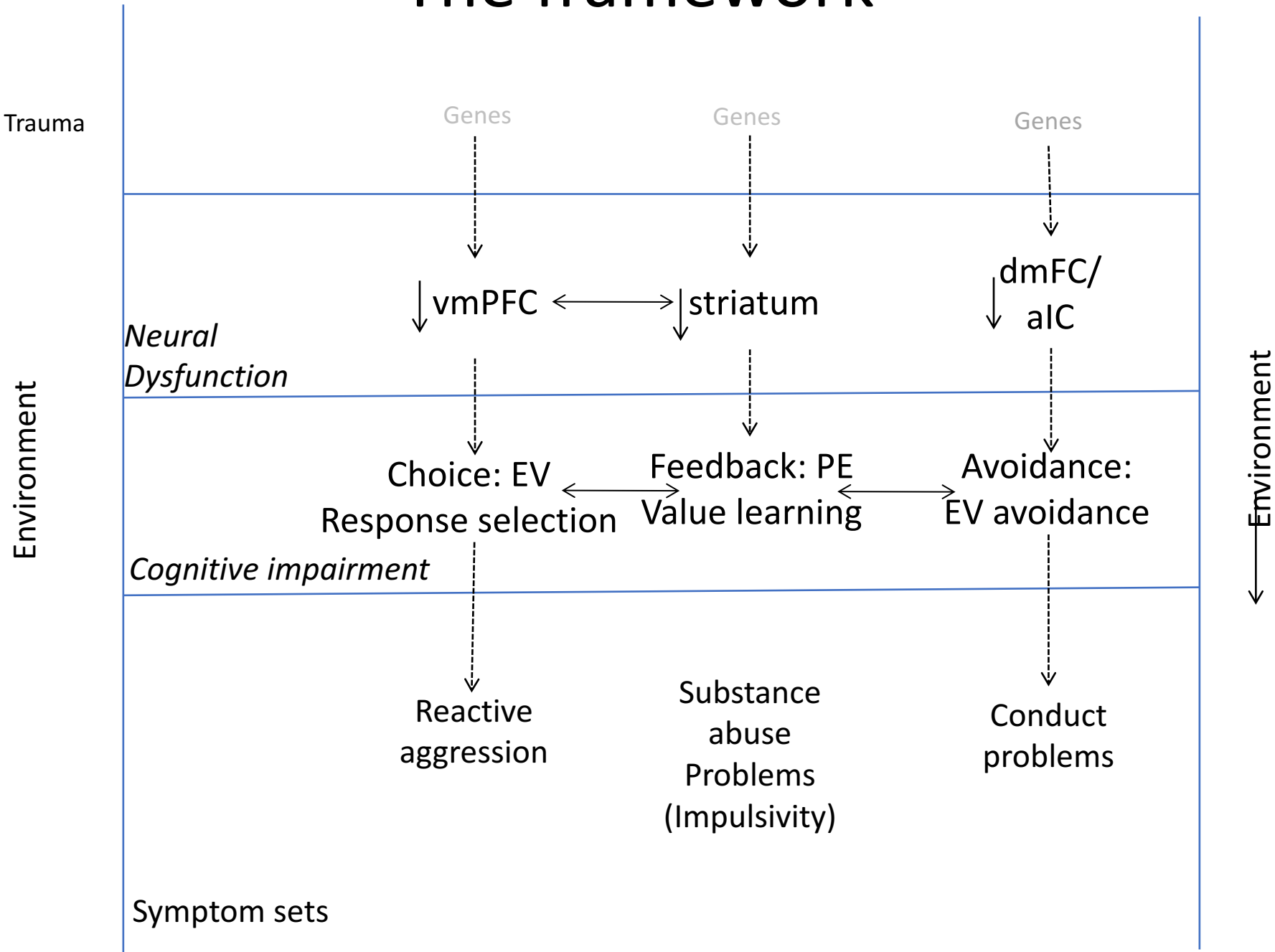
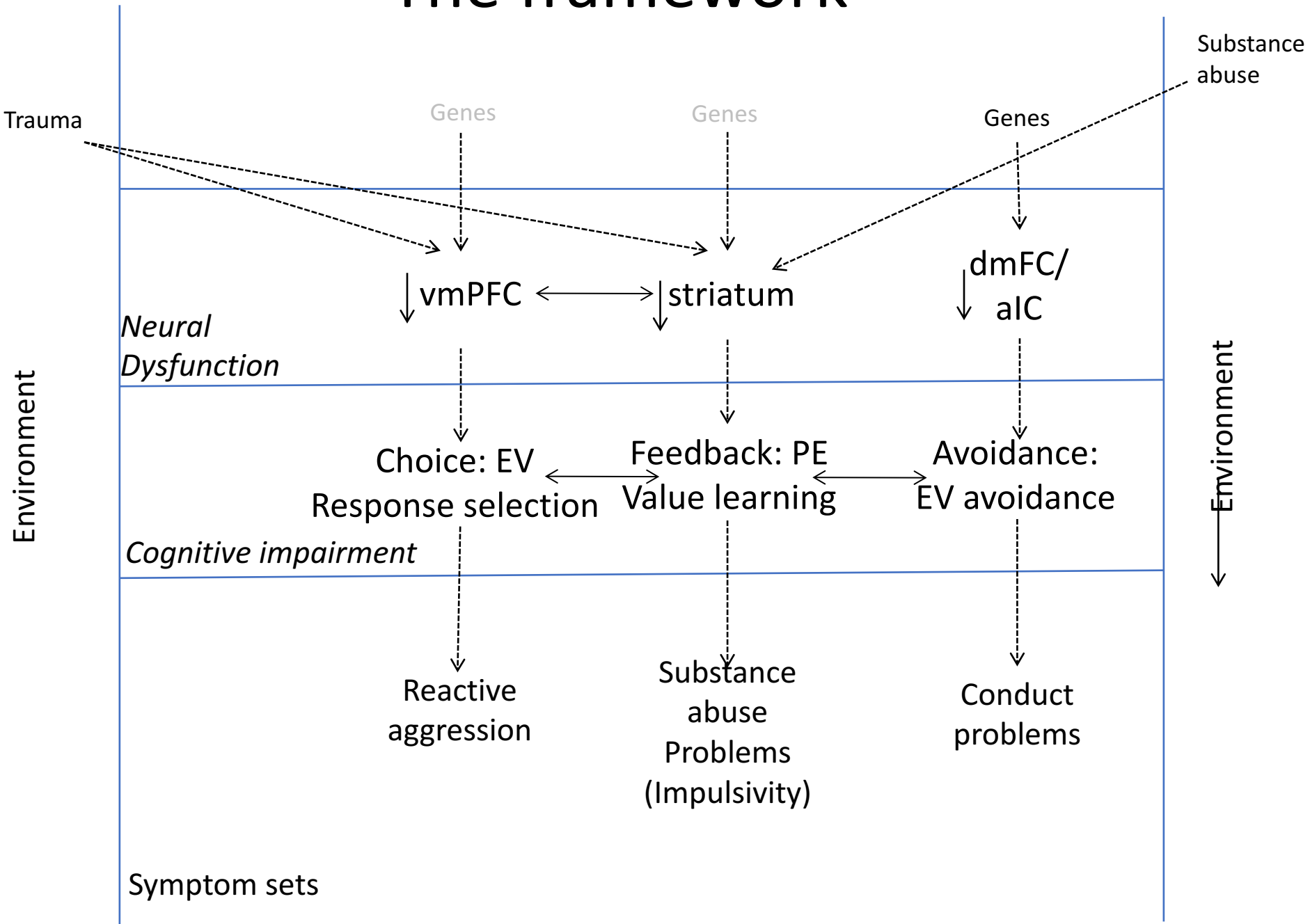


Figure 2. Peak activation in each ROI modulated by EV during avoidance responses. Error bars represent 95% CI. * = p<.05 FWE. Initial threshold p<.005 uncorrected.

The framework



The framework



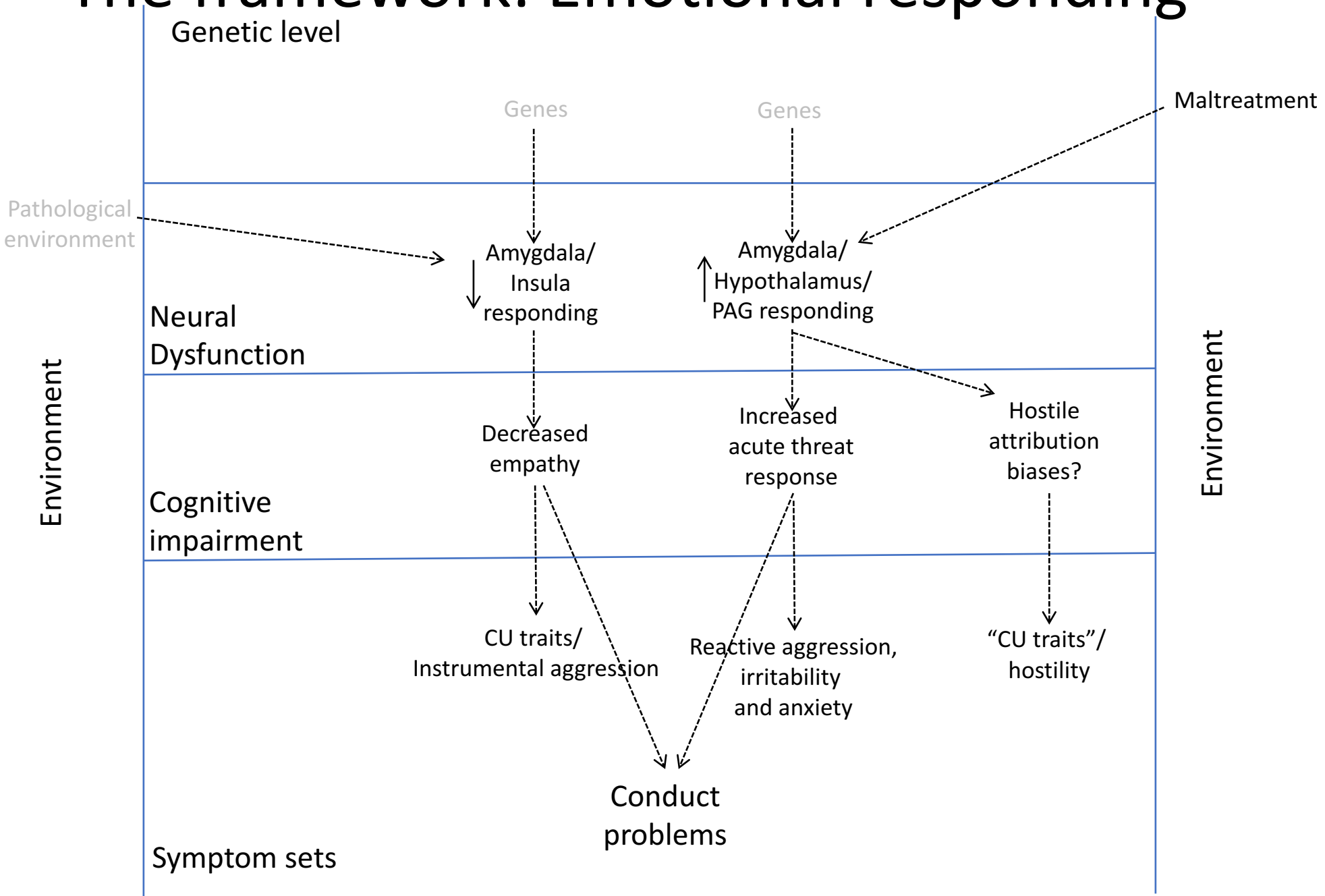
Conclusions

- **The extent to which vmPFC fails to represent the value of choices relates to level of reactive aggression.**
- **The individual fails to represent the potential reward loss of retaliation.**

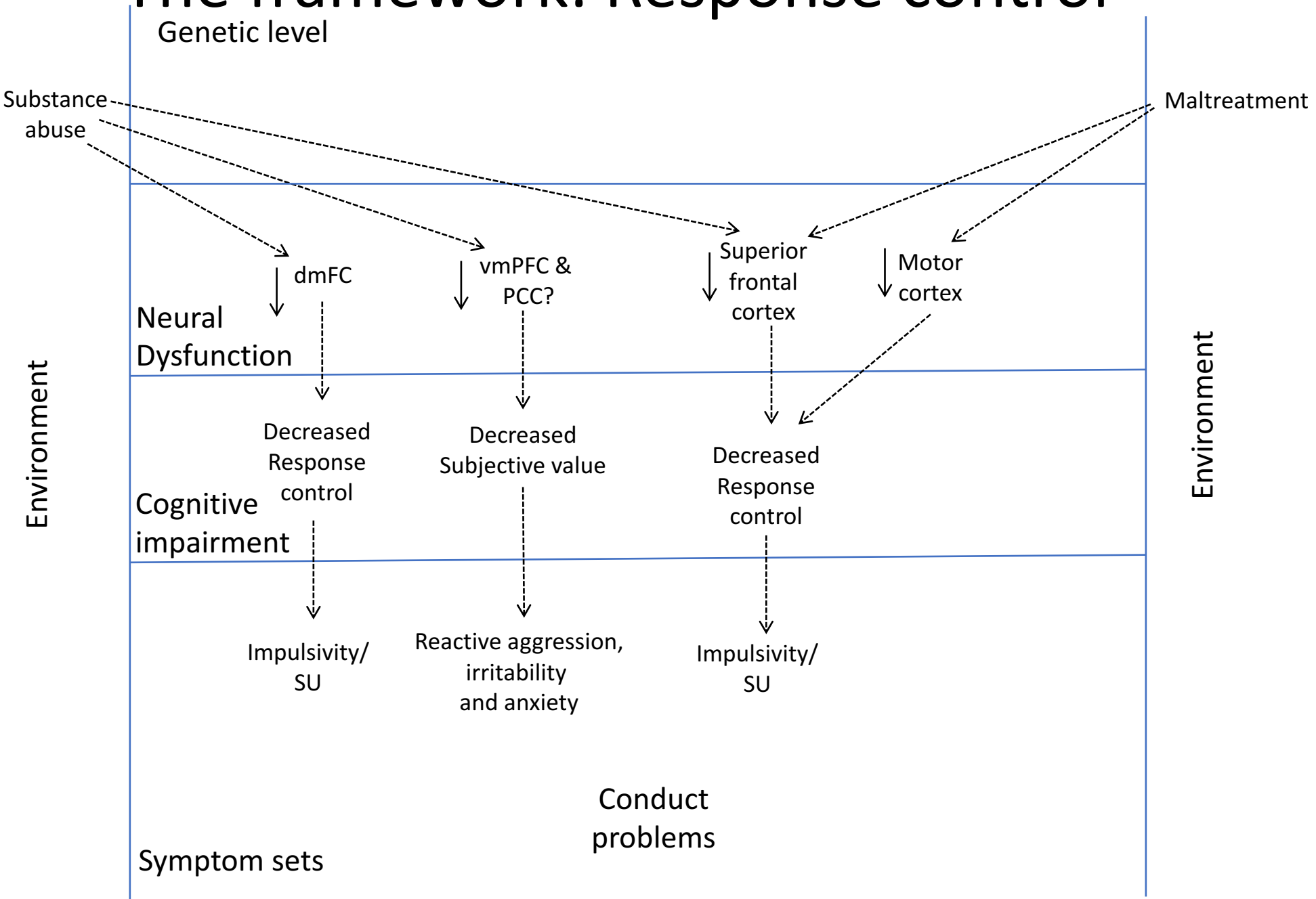
- **The extent to which aIC fails to represent the value of avoidances relates to level of conduct problems generally.**
- **The individual fails to avoid bad choices.**

- **A problem in PE signaling within striatum is also seen in youth with DBD but is not related to symptom severity.**
- **The individual is compromised in learning the value of actions.**
- **Failure in appropriate PE signaling is seen as a consequence of substance abuse and maltreatment.**

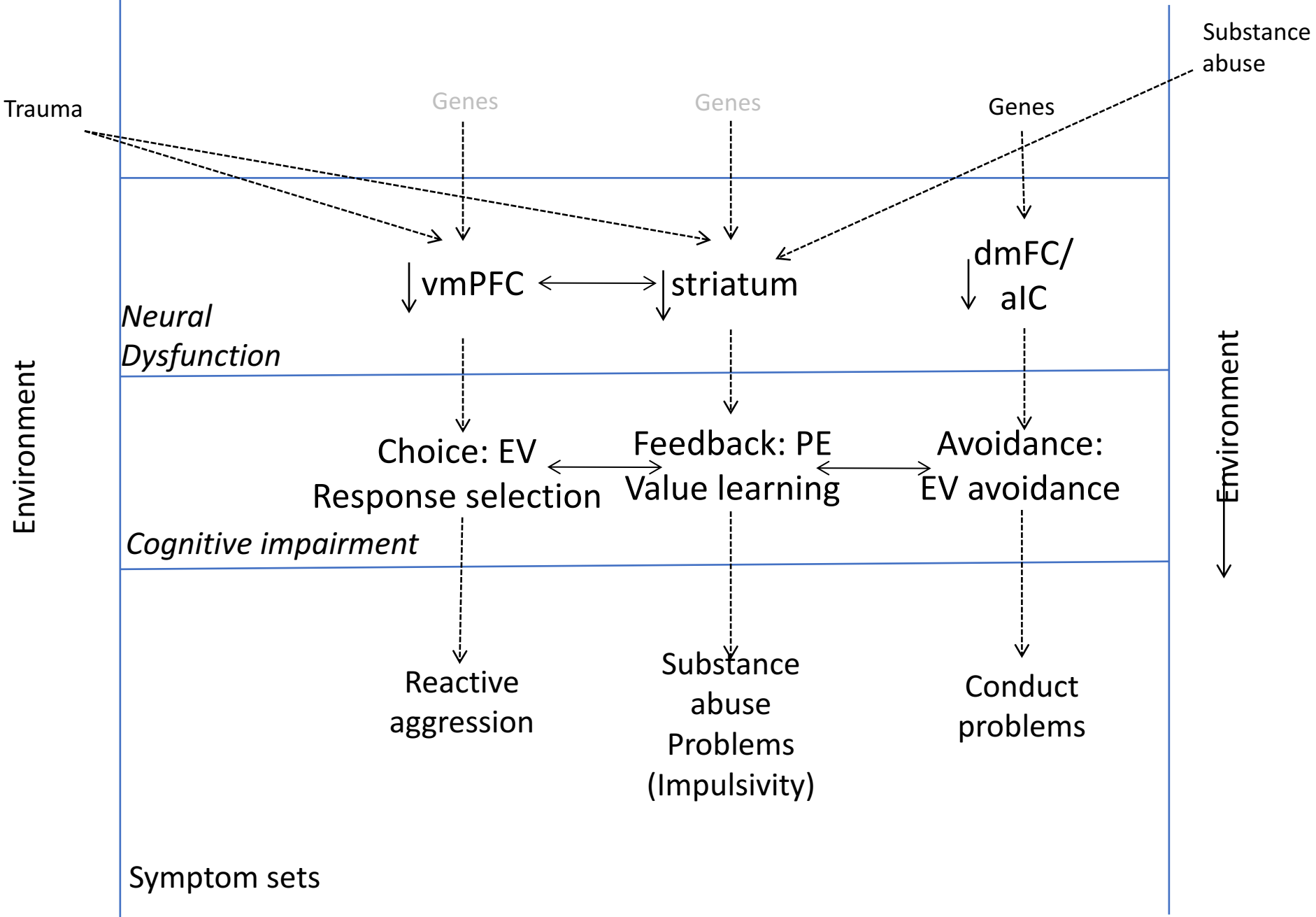
The framework: Emotional responding



The framework: Response control

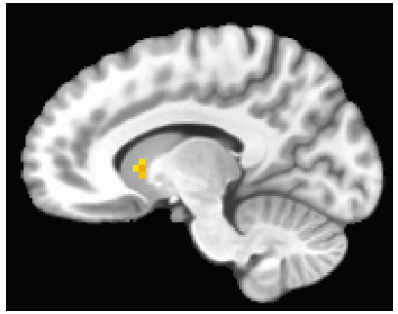


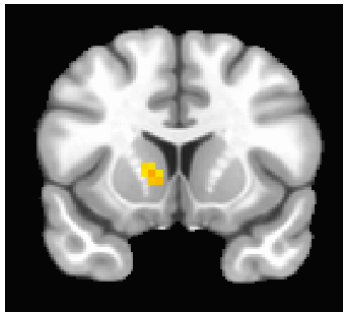
The framework: Reinforcement-based decision-making



PRELIMINARY data regarding the impact of the Boys Town program on adolescent brain development

BT program increases striatal responsiveness to reward





BT program increases emotional regulation (vmPFC) activity in response to threats