Multimodal neuroimaging approach to studying alcohol addiction:

Pathways, prevention, and recovery

Jorge Martins, Ph.D.

William James Center for Research
ISPA–Instituto Universitário

My background and journey…

2010 – B.A., M.A., Psychology
University of Coimbra

2016 – M.A., Psychology
University of Missouri-Columbia

2020 – Ph.D, Psychology
Minor in Psychological Statistics
University of Missouri-Columbia

2020 – Postdoctoral Associate
Yale University

2022 – Postdoctoral Researcher

William James Center for Research
ISPA–Instituto Universitário

1 2 9 0 FACULDADE DE PSICOLOGIA E DE CIÊNCIAS DA EDUCAÇÃO UNIVERSIDADE D COIMBRA

1 2 9 0 UNIVERSIDADE D COIMBRA

My background and journey…

2010 – B.A., M.A., Psychology
University of Coimbra

2016 – M.A., Psychology
University of Missouri-Columbia

2020 – Ph.D, Psychology
Minor in Psychological Statistics
University of Missouri-Columbia

2020 – Postdoctoral Associate
Yale University

2022 – Postdoctoral Researcher

William James Center for Research
ISPA–Instituto Universitário

Mizzou
University of Missouri

My background and journey…

2010 – B.A., M.A., Psychology
University of Coimbra

2016 – M.A., Psychology
University of Missouri-Columbia

2020 – Ph.D, Psychology
Minor in Psychological Statistics
University of Missouri-Columbia

2020 – Postdoctoral Associate
Yale University

2022 – Postdoctoral Researcher

William James Center for Research
ISPA–Instituto Universitário

Yale University
School of Medicine

My background and journey…

2010 – B.A., M.A., Psychology
University of Coimbra

2016 – M.A., Psychology
University of Missouri-Columbia

2020 – Ph.D, Psychology
Minor in Psychological Statistics
University of Missouri-Columbia

2020 – Postdoctoral Associate
Yale University

2022 – Postdoctoral Researcher

William James Center for Research
ISPA–Instituto Universitário

Ispa Instituto Universitário

WJCR WILLIAM JAMES CENTER FOR RESEARCH

Disclosures

- I declare no conflicts of interest in relation to this presentation.
- Funding for this research was provided by the following grants:
  - **Fundação para a Ciência e a Tecnologia (FCT)**
    - CEECINST/0089/2021
    - SFRH/BD/9261/2013
  - **National Institute of Health (NIH)**
    - R01-AA026844 (PI: Dongju Seo, Ph.D)
    - R01-AA013892 (PI: Rajita Sinha, Ph.D)
    - R01-AA025451 (PI: Bruce Bartholow, Ph.D)

Program of research…

Why do some people become addicted to drugs and alcohol?

- Reward motivation and cognitive control deficits in addiction
- Differential reward valuation as an endophenotype for alcohol addiction
- Heterogeneity of problematic alcohol involvement

- **What are the effects of alcohol and drugs in the brain-body?**
  - Sex differences in neural responses among risky drinkers
  - Genetic and environmental effects on neural responses to alcohol cues

- **Why is it so difficult to stop or change and recover from addiction?**
  - Clinical prognostic indicators of AUD treatment and recovery
  - Neural correlates of AUD and treatment-based recovery

Why study alcohol?

- Alcohol abuse is a **major public health problem** worldwide.
- Alcohol use has the **highest economic cost to society**.
- Alcohol has **highest level of harm** compared to other risky behaviors.
- Alcohol consumption as **prototypic exemplar of a broad class of addictive behaviors**.

Experience of alcohol dependence …

"***I never chose to be an alcoholic, alcoholism, for some reason, chose me***. *It has no respect for age, gender, personal or financial circumstances - alcoholism is just a life sucking leech, which* ***once it has taken hold is extremely powerful and very difficult to detach****, but not impossible! It is very easy to say it takes courage, focus, determination and willpower to beat this illness but when I was drinking, I was a complete mess and (…)* ***all I wanted to do was drink and drink some more****. I was totally oblivious to the damage and hurt I was causing to myself, my husband, my children and my extended family. I was very rapidly killing myself (…) I will never know* ***how I crossed that boundary from being a fun social drinker into a chronic alcoholic****, but cross I did and initially from having one too many drinks at a party I descended into being a secretive dependent alcoholic at home. (...) I made promises time and time again to stop, and in my heart of hearts I meant it, I know what I was doing was wrong but by then* ***I was completely powerless over alcohol - I was soon to become another fatal statistic****. (...)*"

–Anonymous

Outline

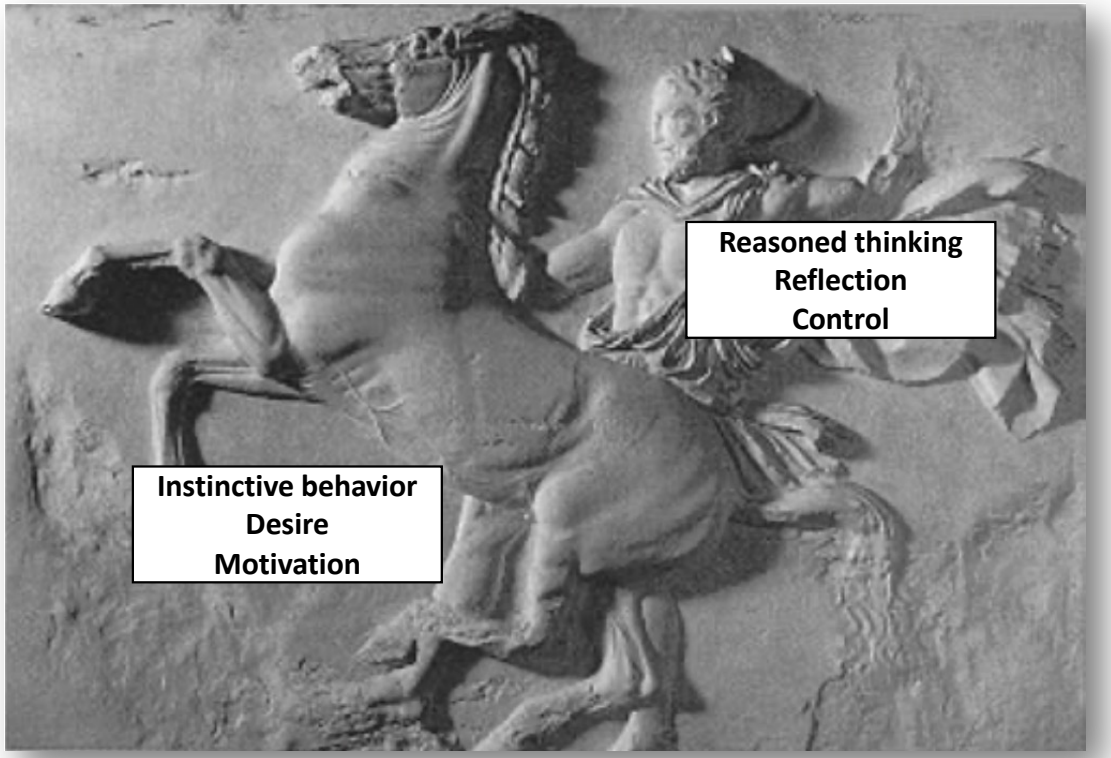
Why do some people become addicted to drugs and alcohol?

- Reward motivation and cognitive control deficits in addiction
- Differential reward valuation as an endophenotype for alcohol addiction
- Heterogeneity of problematic alcohol involvement

- **Why is it so difficult to stop or change and recover from addiction?**
  - Clinical prognostic indicators of AUD treatment and recovery
  - Neural correlates of AUD and treatment-based recovery

Reward motivation and cognitive control deficits in addiction

A metaphor for self-control…



"Even those who have the weakest souls could acquire absolute mastery over all their passions if we employed sufficient ingenuity in training and guiding them."

–René Descartes

Dual-process models of addiction

- **Traditional dual-process models of addiction** (Wiers et al., 2007; Wiers & Stacy, 2006; Hofmann et al., 2008) propose that **motivational** and **cognitive processes** interact in predicting problematic behaviors.
  - **Assumption**: desire or motivational factors compel addictive behaviors while cognitive control regulate those behaviors.
- These perspectives also hold that **strong motivation to use drugs**, **coupled with weak or compromised cognitive control**, is a **disastrous combination** setting the stage for entering the cycle of addiction.

Wiers & Stacy (2006) *CDPS*
Hofmann et al. (2008) *HP*
Wiers et al. (2007) *PBP*

Motivation and cognitive control

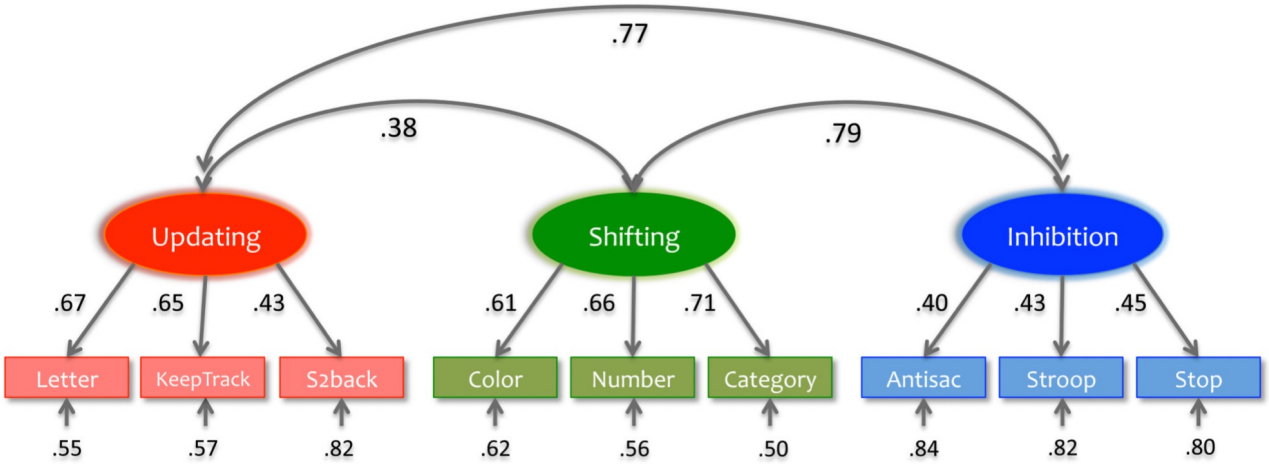
- *N* = 729 nondependent young adults (ages 18-60; 49.2% women) completed measures of drinking motives and EF lab-based tasks.
  - **Drinking motives:** Drinking Motives Questionnaire-Revised (Cooper, 1994)

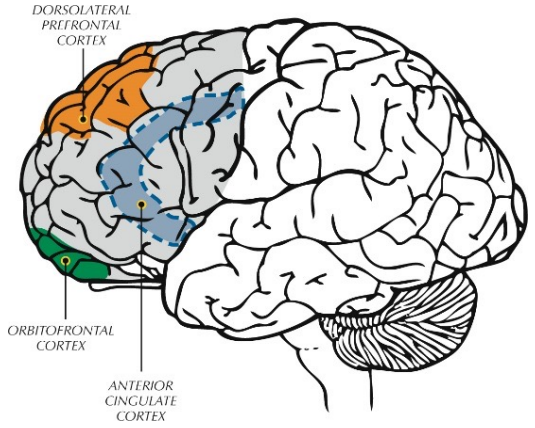
Enhancement motives: to enhance positive internal (emotional) experiences (approach motivational process or positive reinforcement motivation)

Coping motives: to alleviate aversive and undesired internal (emotional) states (avoidance motivational process or negative reinforcement motivation)

Motivation and cognitive control

- *N* = 729 nondependent young adults (ages 18-60; 49.2% women) completed measures of drinking motives and EF lab-based tasks.
  - **Executive functions (EFs):** higher-level cognitive control processes such as control and execution of motor responses; action planning; inhibition.

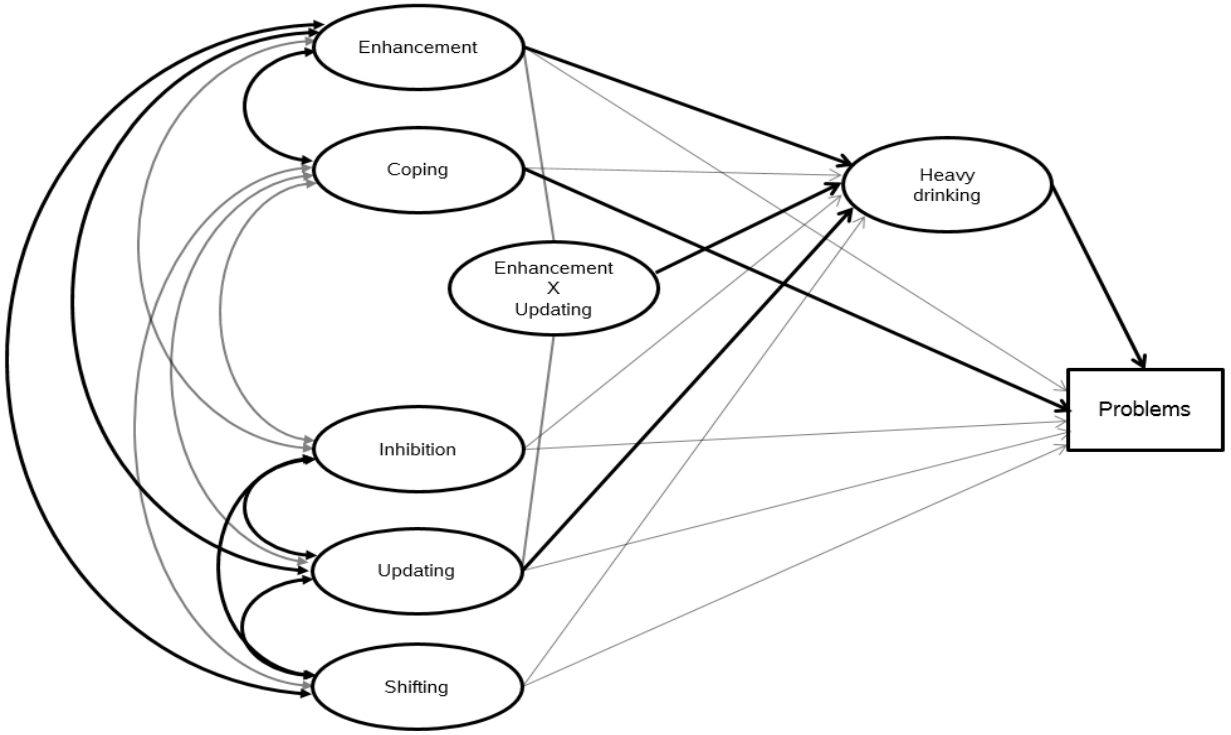




Miyake & Friedman (2012) *CDPS*

Predicting problematic drinking

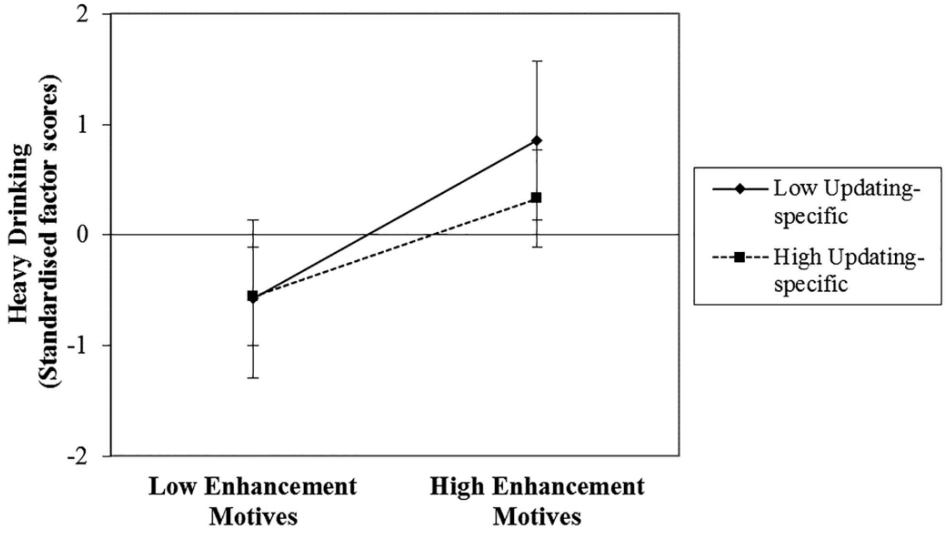
- 12 interactions between drinking motives (enhancement and coping) and executive functions (inhibition, shifting, updating).

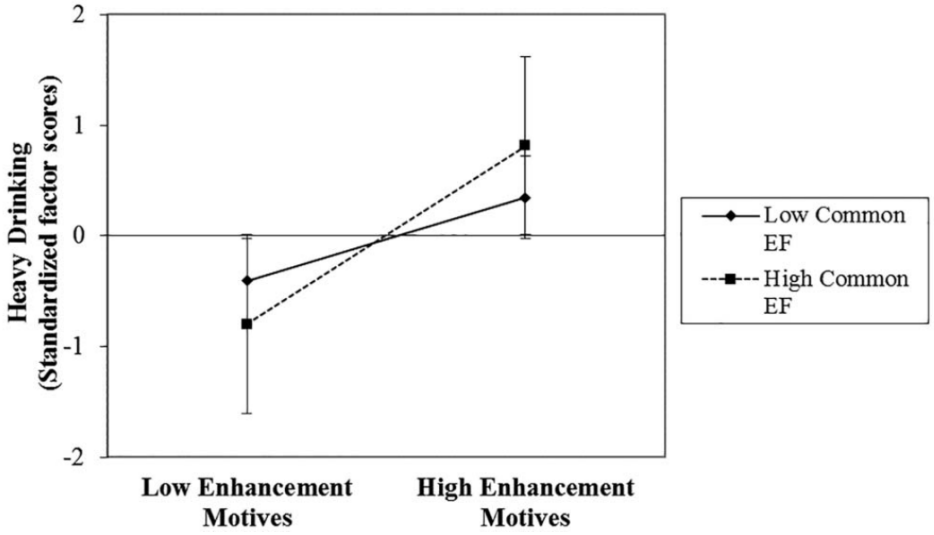


Martins et al. (2018) *PAB*

Drinking motives × Executive functions

- Findings related to these interaction effects were generally weak in magnitude (i.e., small effect sizes) and inconsistent.
  - 2 statistically significant interaction effects out 12 interactions tested.





Martins et al. (2018) *PAB*

Take Home Message

(1) The **interaction effects** between **motivational** and **cognitive systems** do **not always borne out** in empirical work.

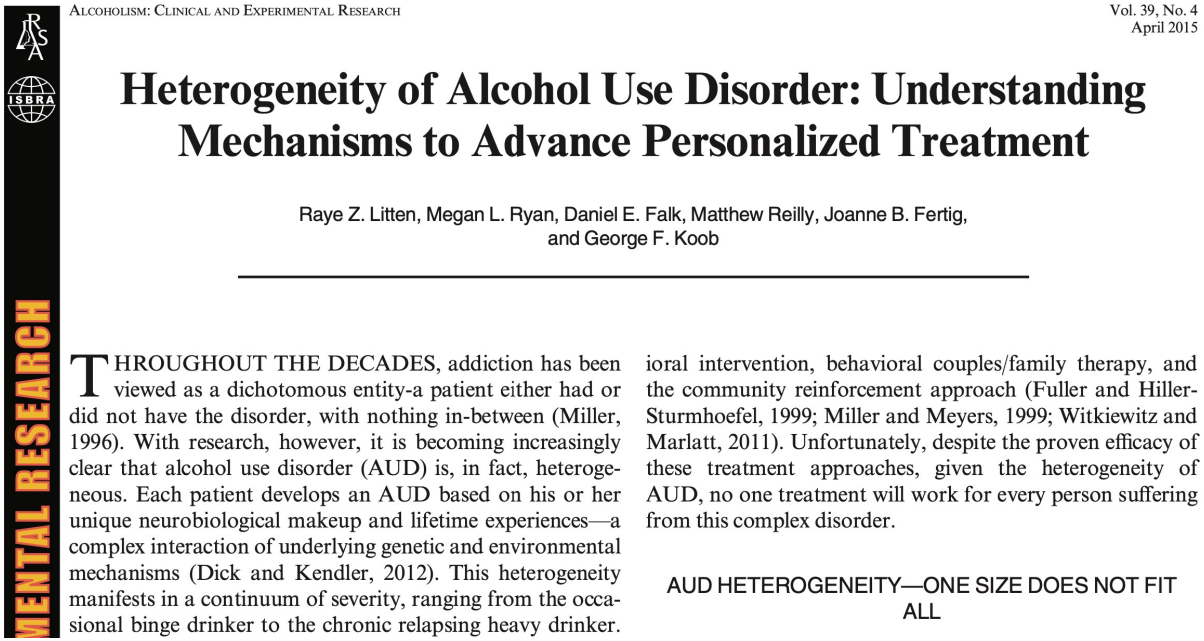
(2) Potential **theoretical and methodological reasons**:

- **Motivation to control drinking** is critical and essential factor
- **The horse rider "fallacy":** no single horse is the same

Heterogeneity of problematic alcohol involvement

Heterogeneity of problematic drinking

- Problematic alcohol involvement is highly heterogeneous.
  - Current prevention and treatment interventions are still largely *ineffective*.
  - More and better research aimed at understanding this heterogeneity for prevention.



ALCOHOLISM: CLINICAL AND EXPERIMENTAL RESEARCH

Vol. 39, No. 4
April 2015

Heterogeneity of Alcohol Use Disorder: Understanding Mechanisms to Advance Personalized Treatment

Raye Z. Litten, Megan L. Ryan, Daniel E. Falk, Matthew Reilly, Joanne B. Fertig, and George F. Koob

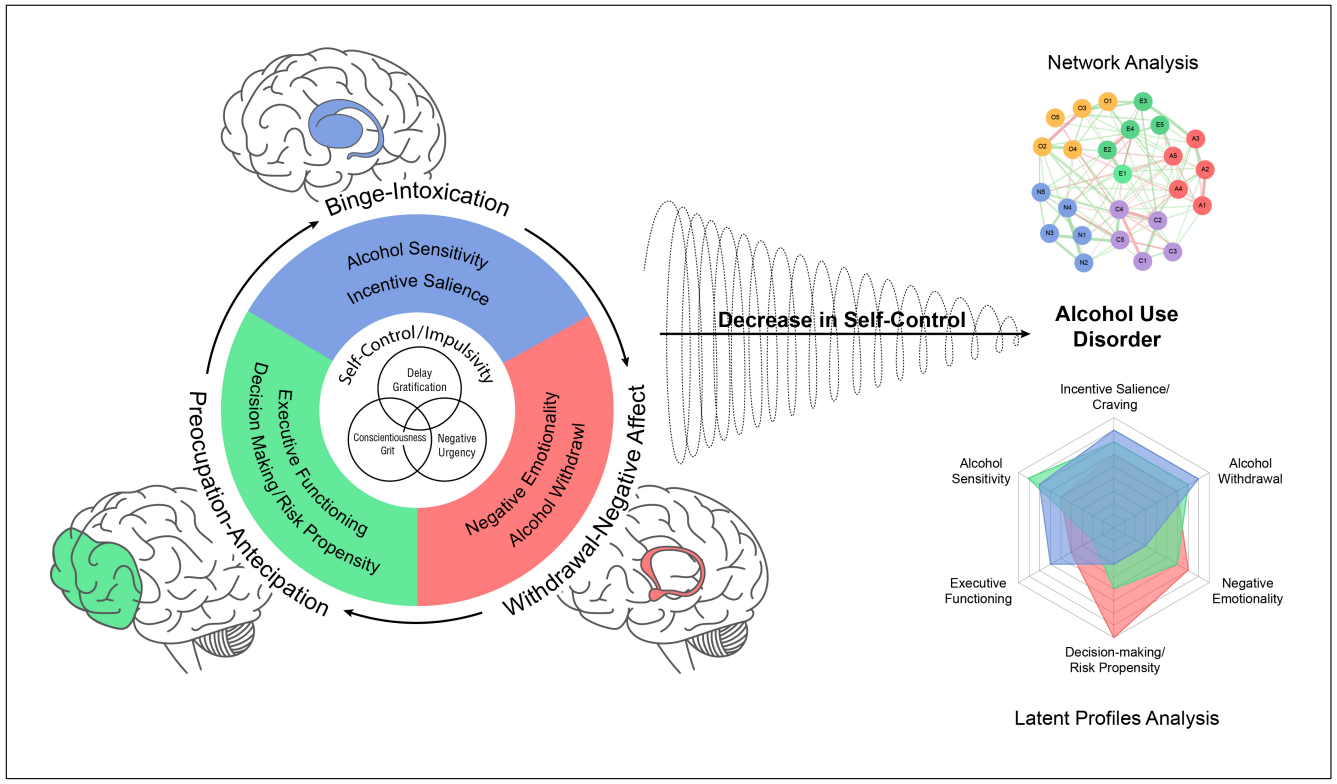
THROUGHOUT THE DECADES, addiction has been viewed as a dichotomous entity-a patient either had or did not have the disorder, with nothing in-between (Miller, 1996). With research, however, it is becoming increasingly clear that alcohol use disorder (AUD) is, in fact, heterogeneous. Each patient develops an AUD based on his or her unique neurobiological makeup and lifetime experiences—a complex interaction of underlying genetic and environmental mechanisms (Dick and Kendler, 2012). This heterogeneity manifests in a continuum of severity, ranging from the occasional binge drinker to the chronic relapsing heavy drinker. ioral intervention, behavioral couples/family therapy, and the community reinforcement approach (Fuller and Hiller-Sturmhoefel, 1999; Miller and Meyers, 1999; Witkiewitz and Marlatt, 2011). Unfortunately, despite the proven efficacy of these treatment approaches, given the heterogeneity of AUD, no one treatment will work for every person suffering from this complex disorder.

AUD HETEROGENEITY—ONE SIZE DOES NOT FIT ALL

Litten et al. (2015) *ACER*

Neuroscience-based functional domains

- *N* = 552 nondependent young adults (ages 18-30; 61% women) completed a battery of lab-based tasks and self-report measures.

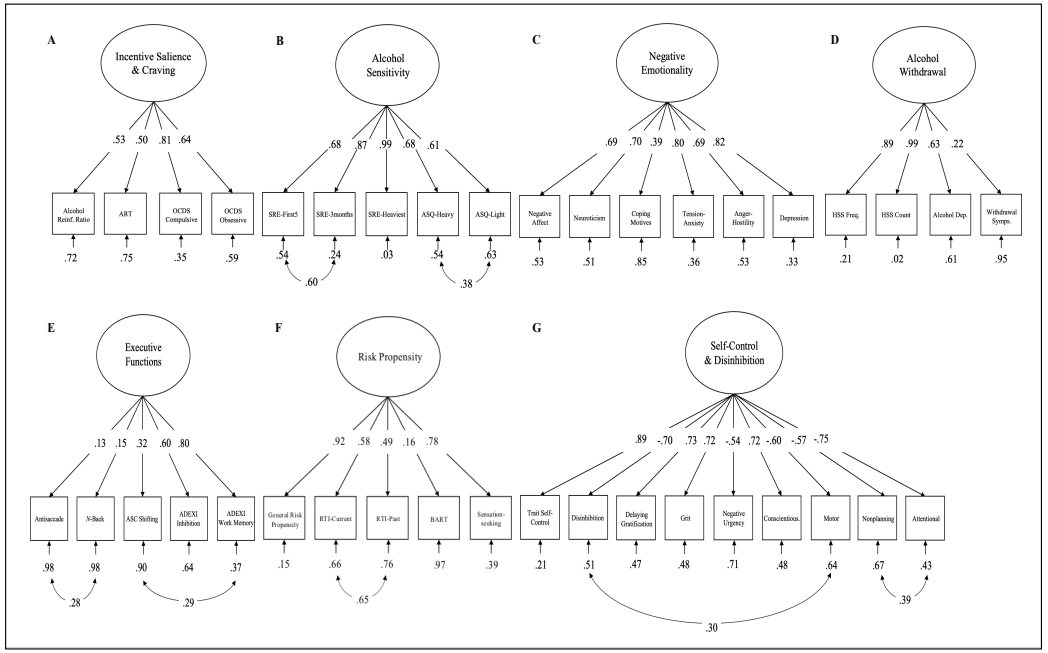


Functional domains:

- Alcohol sensitivity
- Incentive salience/craving
- Negative emotionality
- Alcohol withdrawal
- Executive functions
- Risk propensity
- Self-control/disinhibition

Deep neurobehavioral phenotyping

- Neuroscience-informed alcohol-related neurofunctional domains: Confirmatory factor analysis (CFA) measurement models.



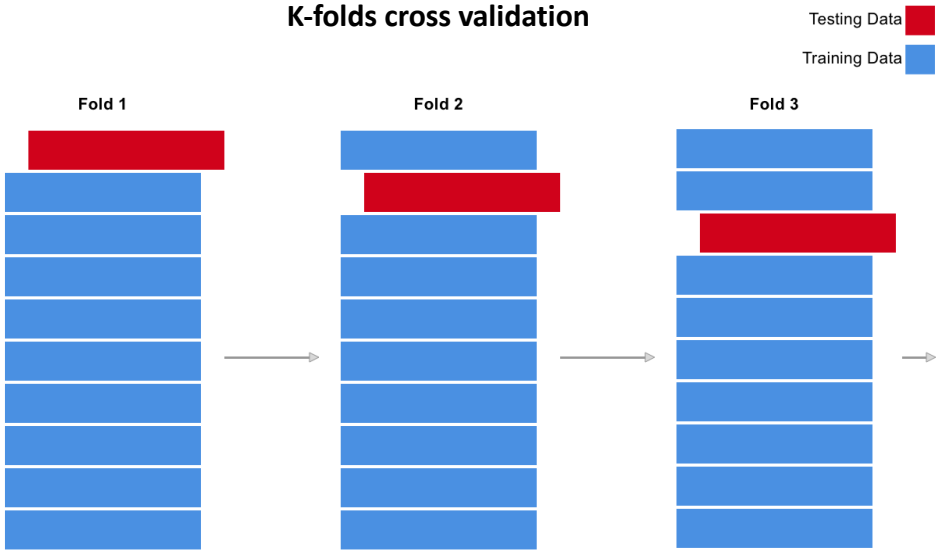
	Model Fit						
Functional Domain	χ^2	*df*	SRMR	RMSEA [90% CI]	CFI	TLI	FD
Executive Functions	2.18	3	.011	.000 [.000-.064]	1.00	1.00	.84
Risk Propensity	0.47	4	.003	.000 [.000-.000]	1.00	1.00	.94
Negative Emotionality	39.14***	9	.026	.078 [.054-.104]	.97	.95	.93
Alcohol Withdrawal	10.86**	2	.028	.090 [.043-.145]	.99	.96	.99
Incentive Salience/Craving	2.94	2	.014	.029 [.000-.094]	1.00	.99	.88
Alcohol Sensitivity	6.97**	3	.015	.049 [.000-.099]	.99	.98	.99
Self-Control/Disinhibition	141.89***	25	.043	.092 [.078-.107]	.95	.92	.95

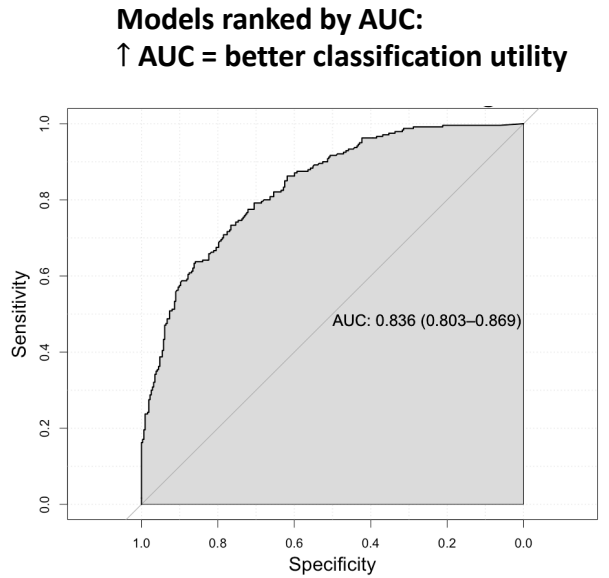
Note. *df* = degrees of freedom; SRMR = standardized root-mean residual; RMSEA = root-mean-square error approx CI = confidence interval; CFI = comparative fit index; TLI = Tucker-Lewis index; FD = factor scores determinacy; $^{*}p \leq .05$

Martins et al. (2023) *in prep*

Classification and predictive utility

- Classification utility of varying combinations of functional domains in discriminating risk for problematic drinking?
  - 7 functional domains = 128 models (2^7 = 128 possible combinations)





Martins et al. (2023) *in prep*

Classification and predictive utility

- Incentive salience, alcohol withdrawal, and alcohol sensitivity showed the optimal combination with the best classification utility.

Total Sample ($N = 541$)[a]

Models[b]	Out-of-Sample Model Evaluation Metrics										Variable Importance[c]						
	AUC	Accuracy	Sensitivity	Specificity	Precision	Recall	F1 Score	Kappa	Concordance	Somers *D*	IS	AS	NE	AW	EF	DM	SC
AS+AW+IS+NE+SC	.867	.758	.802	.708	.774	.802	.786	.510	.866	.734	7.036	4.342	2.698	3.546	–	–	2.762
AS+AW+DM+IS+NE+SC	.865	.758	.800	.712	.776	.800	.786	.510	.866	.730	7.052	4.352	2.756	3.574	–	0.626	2.834
AS+AW+IS+SC	.864	.750	.802	.688	.764	.802	.780	.492	.862	.730	7.09	4.608	–	3.194	–	–	1.754
AS+AW+EF+IS+NE+SC	.862	.756	.796	.712	.774	.796	.784	.506	.864	.724	7.058	4.362	2.566	3.53	0.85	–	2.682
AS+AW+DM+EF+IS+NE+SC	.862	.764	.802	.720	.780	.802	.790	.520	.862	.724	7.056	4.592	–	3.204	–	0.326	1.774
AS+AW+DM+IS+SC	.862	.756	.806	.696	.770	.806	.784	.502	.860	.726	7.072	4.374	2.624	3.554	0.824	0.596	2.742
AS+AW+IS+NE	.862	.746	.800	.680	.754	.800	.776	.480	.864	.724	8.012	4.322	1.676	3.652	–	–	–
AS+AW+EF+IS+SC	.861	.754	.798	.698	.768	.798	.782	.494	.860	.722	7.128	4.612	–	3.192	1.08	–	2.052
AS+AW+IS	.860	.754	.802	.700	.770	.802	.782	.500	.858	.720	7.932	4.524	–	3.414	–	–	–
AS+AW+DM+IS	.859	.758	.804	.704	.772	.804	.786	.508	.858	.720	7.764	4.49	–	3.404	–	0.436	–
AS+AW+DM+IS+NE	.859	.746	.802	.676	.754	.802	.778	.480	.858	.718	7.862	4.298	1.676	3.644	–	0.43	–
AS+AW+DM+EF+IS+SC	.859	.752	.798	.694	.764	.798	.780	.490	.858	.720	7.094	4.596	–	3.198	1.076	0.308	2.068
AS+AW+EF+IS	.858	.756	.802	.706	.772	.802	.786	.506	.858	.718	7.69	4.538	–	3.388	0.576	–	–
AS+AW+DM+EF+IS	.857	.756	.804	.702	.768	.804	.786	.506	.856	.716	7.58	4.5	–	3.382	0.54	0.348	–
AS+AW+EF+IS+NE	.857	.748	.794	.694	.762	.794	.774	.486	.860	.712	7.714	4.342	1.904	3.644	1.024	–	–
AS+IS+NE+SC	.856	.784	.838	.712	.786	.838	.812	.560	.856	.714	8.22	4.516	2.192	–	–	–	2.904
AS+AW+DM+EF+IS+NE	.856	.746	.788	.694	.764	.788	.772	.482	.856	.712	7.632	4.326	1.908	3.642	0.968	0.3	–
AS+DM+IS+NE+SC	.855	.782	.836	.716	.788	.836	.812	.560	.854	.710	8.196	4.52	2.232	–	–	0.466	2.93
AS+IS+SC	.854	.766	.814	.704	.774	.814	.794	.520	.852	.706	8.184	4.712	–	–	–	–	2.148
AS+DM+IS+SC	.853	.766	.814	.700	.772	.814	.792	.516	.850	.704	8.124	4.702	–	–	–	0.344	2.136
AW+IS+NE+SC	.852	.760	.816	.692	.768	.816	.790	.508	.852	.706	7.468	–	3.19	3.85	–	–	2.746
AS+IS	.852	.772	.830	.698	.776	.830	.802	.532	.850	.704	9.28	4.62	–	–	–	–	–
AS+DM+IS	.851	.768	.828	.694	.774	.828	.800	.528	.852	.704	9.03	4.59	–	–	–	0.484	–
AS+IS+NE	.851	.772	.832	.704	.776	.832	.802	.538	.850	.700	9.274	4.5	0.986	–	–	–	–
AS+EF+IS+NE+SC	.851	.788	.834	.728	.794	.834	.814	.568	.850	.702	8.234	4.532	2.056	–	0.92	–	2.834
AS+EF+IS+SC	.850	.766	.812	.708	.776	.812	.792	.520	.852	.702	8.212	4.716	–	–	1.054	–	2.348
AS+DM+EF+IS+SC	.850	.764	.812	.704	.774	.812	.790	.516	.848	.700	8.152	4.702	–	–	1.05	0.336	2.344
AW+DM+IS+NE+SC	.849	.762	.820	.692	.768	.820	.794	.512	.850	.698	7.424	–	3.178	3.86	–	0.398	2.72
AS+DM+EF+IS+NE+SC	.849	.786	.838	.720	.790	.838	.814	.562	.848	.698	8.208	4.536	2.094	–	0.906	0.44	2.862
AS+DM+IS+NE	.849	.768	.834	.692	.772	.834	.800	.530	.848	.698	9.042	4.474	0.986	–	–	0.484	–
AS+EF+IS	.849	.766	.826	.698	.776	.826	.800	.526	.848	.698	8.918	4.636	–	–	0.718	–	–

Martins et al. (2023) *in prep*

Classification and predictive utility

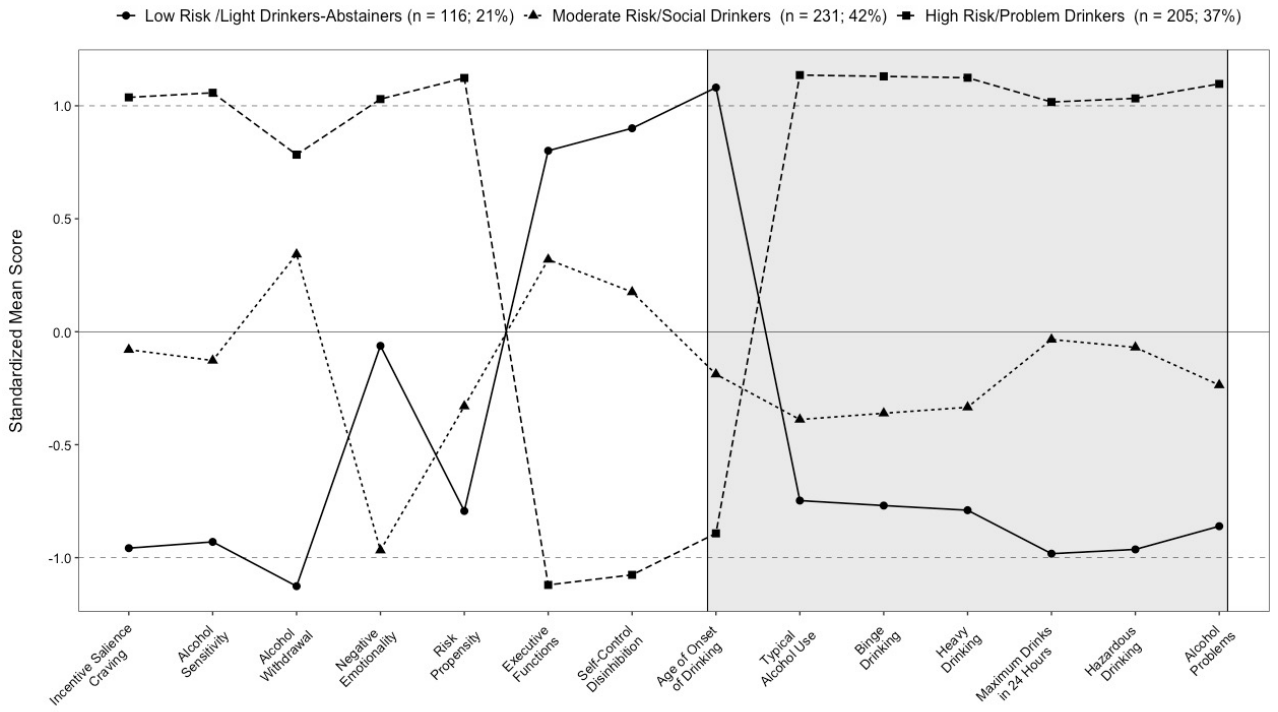
- Incentive salience & craving function domain demonstrated by far the strongest performance, predictive utility, and diagnostic value.

AW+DM+IS	.841	.750	.810	.676	.758	.810	.782	.488	.842	.682	7.988	–	–	3.61	–	0.672	–
AW+DM+EF+IS+NE	.841	.748	.800	.688	.762	.800	.778	.490	.840	.684	7.95	–	2.342	3.93	0.832	0.466	–
AW+EF+IS	.840	.758	.810	.698	.768	.810	.790	.508	.842	.680	8.054	–	–	3.616	0.56	–	–
AW+DM+EF+IS+SC	.840	.756	.812	.690	.764	.812	.784	.504	.840	.676	7.456	–	–	3.448	1.232	0.556	1.84
AW+EF+IS+SC	.840	.756	.810	.690	.764	.810	.786	.502	.840	.678	7.564	–	–	3.442	1.206	–	1.892
AW+DM+EF+IS	.838	.752	.810	.684	.762	.810	.784	.496	.84	.678	7.886	–	–	3.612	0.54	0.622	–
IS+NE+SC	.837	.758	.810	.692	.768	.810	.788	.506	.836	.674	8.822	–	2.662	–	–	–	2.882
DM+IS+NE+SC	.835	.752	.806	.684	.760	.806	.782	.494	.834	.672	8.744	–	2.644	–	–	0.352	2.816
EF+IS+NE+SC	.832	.748	.802	.680	.756	.802	.778	.484	.832	.662	8.834	–	2.518	–	0.874	–	2.856
DM+EF+IS+NE+SC	.831	.748	.802	.680	.758	.802	.778	.484	.832	.664	8.748	–	2.49	–	0.878	0.356	2.814
IS+NE	.831	.750	.814	.666	.754	.814	.786	.488	.832	.662	9.81	–	1.532	–	–	–	–
DM+IS+NE	.830	.746	.812	.662	.750	.812	.782	.480	.832	.658	9.52	–	1.514	–	–	0.692	–
IS+SC	.830	.750	.824	.658	.748	.824	.784	.488	.830	.662	8.806	–	–	–	–	–	1.868
IS	.829	.742	.816	.652	.744	.816	.778	.472	.830	.658	9.768	–	–	–	–	–	–
DM+IS+SC	.829	.752	.826	.662	.750	.826	.784	.492	.830	.658	8.684	–	–	–	–	0.51	1.772
DM+IS	.828	.740	.810	.652	.746	.810	.776	.468	.828	.654	9.466	–	–	–	–	0.712	–
EF+IS+NE	.828	.748	.814	.666	.752	.814	.782	.484	.828	.656	9.552	–	1.76	–	0.942	–	–
EF+IS+SC	.828	.752	.814	.672	.754	.814	.784	.490	.828	.656	8.824	–	–	–	1.188	–	2.21
DM+EF+IS+NE	.827	.742	.810	.658	.746	.810	.778	.472	.828	.654	9.352	–	1.698	–	0.822	0.532	–
DM+EF+IS+SC	.826	.748	.818	.662	.748	.818	.780	.486	.826	.654	8.696	–	–	–	1.214	0.532	2.146
EF+IS	.825	.74	.808	.656	.746	.808	.774	.468	.824	.65	9.486	–	–	–	0.55	–	–
DM+EF+IS	.824	.742	.810	.656	.748	.810	.778	.472	.824	.650	9.278	–	–	–	0.514	0.676	–
AS+AW+NE+SC	.820	.734	.782	.676	.752	.782	.766	.460	.818	.642	–	5.004	2.942	6.284	–	–	5.424
AS+AW+DM+NE+SC	.818	.748	.796	.690	.762	.796	.776	.484	.818	.638	–	4.91	2.844	6.218	–	0.676	5.062
AS+AW+EF+NE+SC	.815	.738	.784	.684	.756	.784	.770	.466	.816	.628	–	5.01	2.874	6.272	0.614	–	4.706
AS+AW+DM+EF+NE+SC	.814	.752	.798	.698	.770	.798	.780	.492	.816	.628	–	4.918	2.766	6.206	0.632	0.696	4.478
AS+AW+DM+SC	.807	.726	.770	.676	.748	.77	.758	.444	.806	.614	–	5.116	–	5.938	–	1.05	4.348
AS+AW+SC	.807	.724	.774	.668	.744	.774	.758	.440	.808	.612	–	5.258	–	6.02	–	–	4.75
AS+AW+DM+EF+SC	.805	.722	.766	.672	.746	.766	.754	.436	.802	.612	–	5.094	–	5.928	0.768	1.076	3.924
AS+AW+EF+SC	.804	.724	.772	.668	.744	.772	.758	.440	.804	.608	–	5.246	–	6.012	0.728	–	4.176
AS+AW+DM+EF+NE	.794	.704	.750	.656	.730	.750	.738	.406	.796	.586	–	4.896	1.598	6.716	2.512	1.724	–
AS+AW+DM+EF	.791	.714	.768	.656	.736	.768	.748	.422	.792	.582	–	5.008	–	6.598	2.07	1.866	–
AS+AW+EF+NE	.791	.708	.752	.656	.732	.752	.740	.410	.790	.580	–	5.05	1.752	6.912	2.936	–	–
AS+AW+DM	.788	.702	.766	.630	.724	.766	.742	.398	.790	.576	–	4.904	–	6.894	–	2.312	–
AS+AW+DM+NE	.788	.708	.768	.638	.728	.768	.746	.410	.788	.576	–	4.832	0.688	6.82	–	2.304	–
AS+AW+EF	.786	.700	.746	.652	.730	.746	.736	.398	.784	.570	–	5.202	–	6.782	2.484	–	–
AW+DM+NE+SC	.785	.728	.774	.672	.750	.774	.760	.446	.786	.570	–	–	3.272	6.85	–	1.256	4.942
AS+AW	.784	.696	.746	.642	.724	.746	.734	.388	.784	.568	–	5.094	–	7.18	–	–	–
AW+NE+SC	.784	.722	.770	.668	.746	.770	.752	.436	.782	.568	–	–	3.466	6.954	–	–	5.424
AS+AW+NE	.783	.704	.756	.646	.728	.756	.740	.404	.784	.566	–	5.018	0.708	7.096	–	–	–
AW+DM+EF+NE+SC	.783	.716	.764	.664	.742	.764	.748	.428	.782	.564	–	–	3.152	6.828	0.622	1.286	4.468

Martins et al. (2023) *in prep*

‘Subtypes” or latent classes

- 3 “subtypes”: low-risk/light drinkers (n=116), moderate-risk/social drinkers (n=231), high-risk/problem drinkers (=205).



Martins et al. (2023) *in prep*

‘Networks” and centrality analysis

- Self-control/Disinhibition as the most interconnected domain

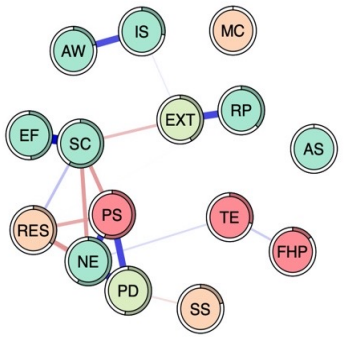
Functional Domains
- AW: Alcohol withdrawal
- AS: Alcohol sensitivity
- RP: Risk propensity
- EF: Executive functions
- IS: Incentive salience/craving
- NE: Negative emotionality
- SC: Self–control/disinhbition

Externalizing and Internalizing
- EXT: Externalizing deviancy
- PD: Psycological distress

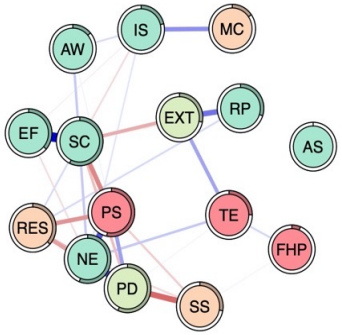
Intra & Interpersonal Protective Factor_
- RES: Resilience
- MC: Motivation to control drinking
- SS: Social support

Family History & Situational Risk Factors
- PS: Perceived stress
- FHP: Family positive history
- TE: Trauma experiences

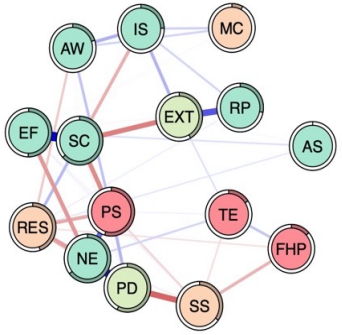
Low-risk, light drinkers

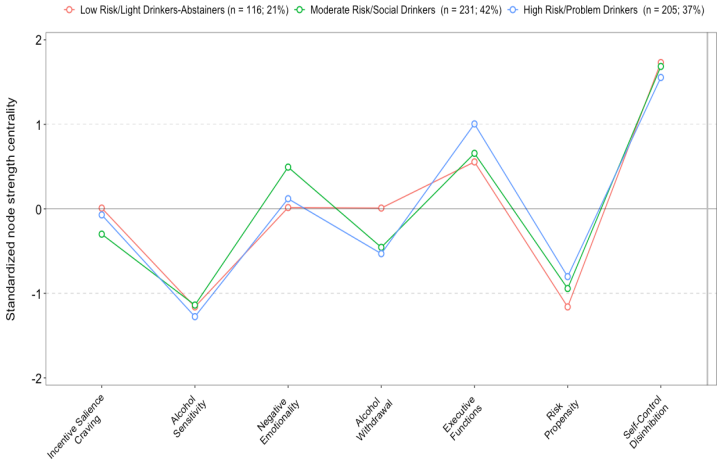


Moderate-risk, social drinkers



High-risk, problem drinkers





Martins et al. (2023) *in prep*

Take Home Message

(1) **Incentive Salience/craving**, **alcohol sensitivity**, and **alcohol withdrawal** produced **the most optimal combination** with the best classification utility.

– **Incentive Salience/craving** domain demonstrated by far the strongest predictive utility and diagnostic value.

(2) **Self-Control/disinhibition** was consistently identified as **the most interconnected** and **highly central domain** in all networks.

– Self-Control/disinhibition could prove to be an **important** and **useful target** for promoting efficacy of prevention efforts.

Outline

Why do some people become addicted to drugs and alcohol?

- Reward motivation and cognitive control deficits in addiction
- Differential reward valuation as an endophenotype for alcohol addiction
- Heterogeneity of problematic alcohol involvement

- **Why is it so difficult to stop or change and recover from addiction?**
  - Clinical prognostic indicators of AUD treatment and recovery
  - Neural correlates of AUD and treatment-based recovery

Clinical prognostic indicators of AUD treatment response

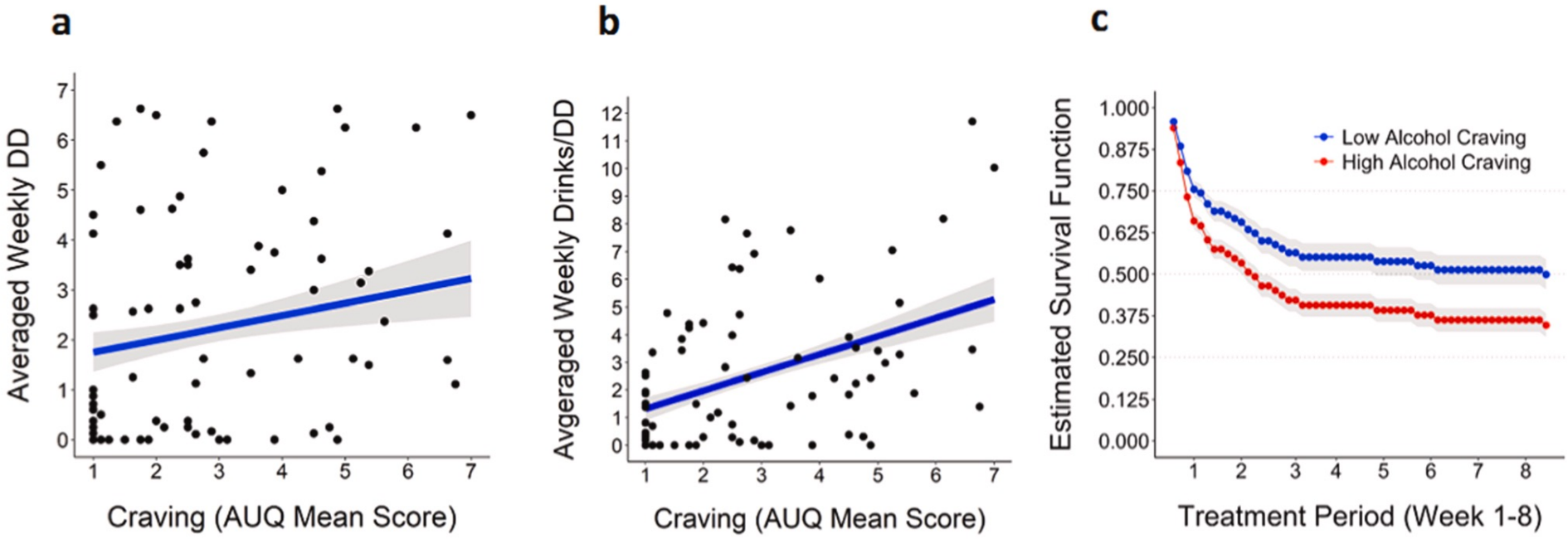
Prognostic indicators of AUD treatment

- *N* = 80 treatment-seeking adults with AUD completed an 8-week treatment and were daily assessed using a smartphone app.

Sinha et al. (2021) *AmJP*
Martins et al. (2022) *DAD*

Prognostic indicators of AUD treatment

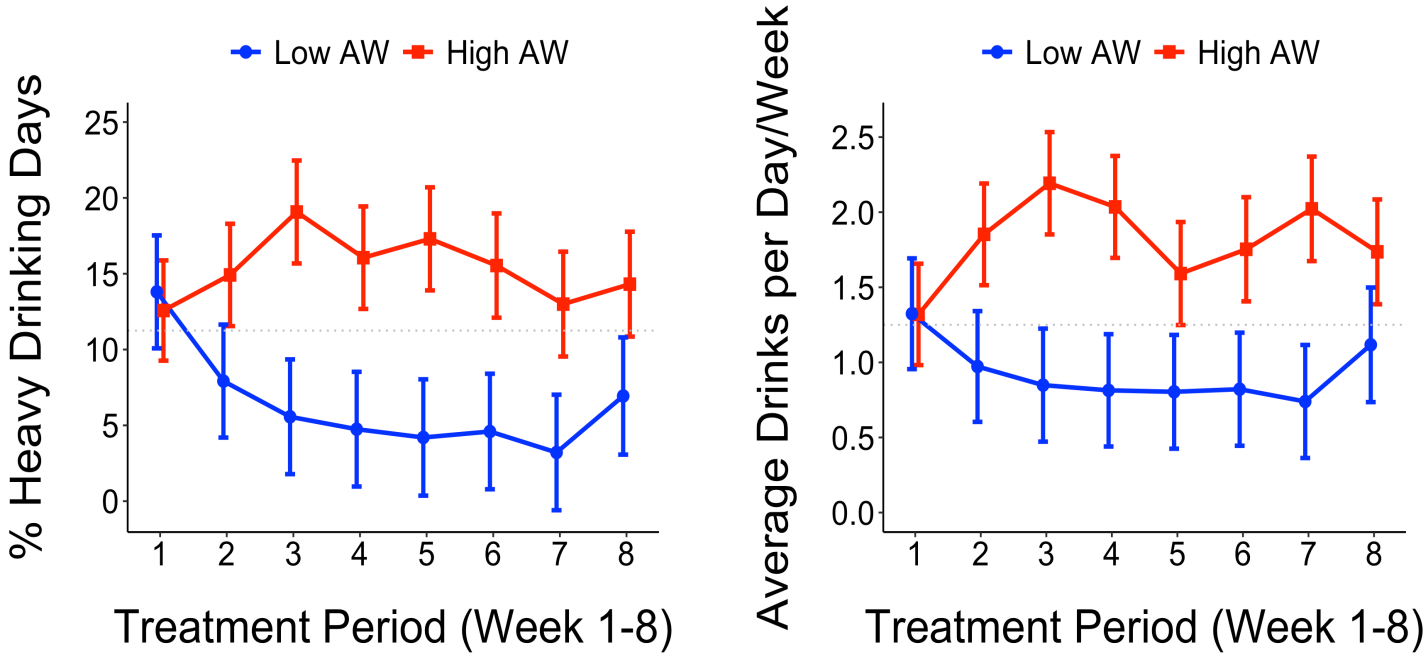
- Pretreatment alcohol craving predicted subsequent alcohol use outcomes and risk of relapse to heavy drinking during treatment.



Martins et al. (2022) *DAD*

Prognostic indicators of AUD treatment

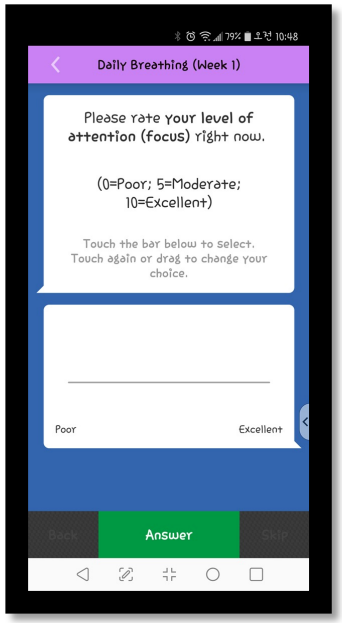
- Pretreatment alcohol withdrawal predicted subsequent alcohol use outcomes including heavy drinking days and drinks per day.



Martins et al. (2022) *DAD*

Self-guided breathing in AUD recovery

- *N* = 23 treatment-seeking adults with AUD completed an 8-week treatment with standard treatment + daily breathing exercises.



METRICwire Breakthrough Research

Ratings – BEFORE and AFTER breathing exercise

Attention: Please rate your level of attention right now. (0=Poor to 10=Excellent)

Mood: Please rate your mood now. (1=Negative to 10=Positive)

Arousal: Please rate your level of arousal now. (1=Calm/Relaxed to 10=Excited)

Stress: How stressed do you feel right now? (0=Not at all to 10=Extremely)

Anxiety: How anxious do you feel right now? (0=Not at all to 10=Very much)

Craving: How much do you want to drink alcohol? (0=Not at all to 10=Very much)

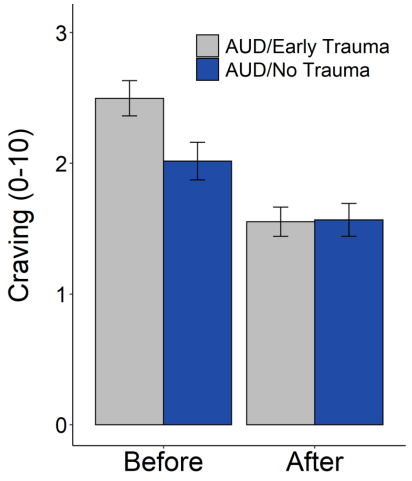
Pain: Please rate your level of physical pain right now. (0=No pain to 10=Severe pain)

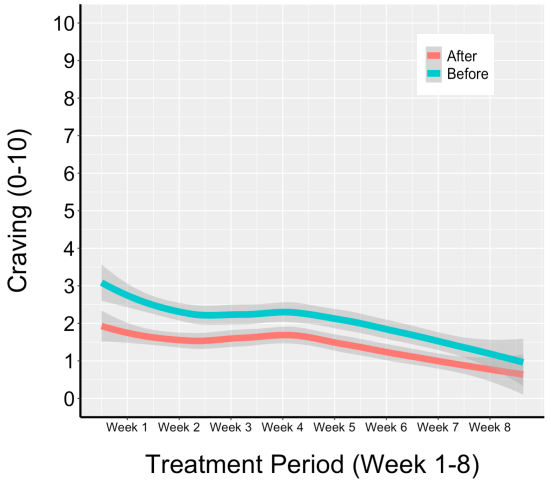
Fatigue: Please rate your level of fatigue. (0=Very low to 10=Very high)

Self-guided breathing in AUD recovery

- AUD patients showed reductions in craving and stress; reductions in craving and stress are accompanied by declines in baseline levels.

Alcohol Craving

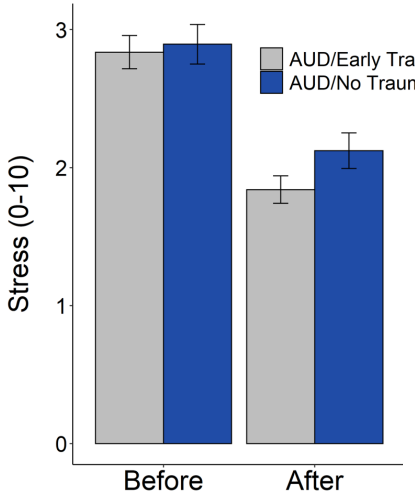


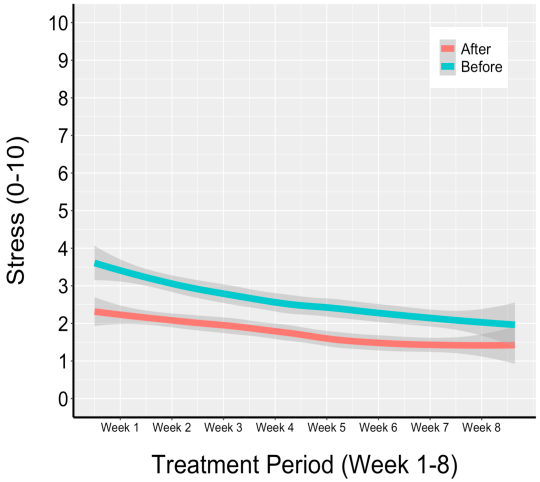


Breathing: $F(1,1908) = 6.75$, $p = 0.010$

Breathing × Time: $F(1,2900.15) = 5.17$, $p = 0.023$

Stress





Breathing: $F(1,2897.03) = 96.30$, $p < 0.001$

Breathing × Time: $F(1,2897.03) = 8.13$, $p = 0.004$

Dauginikas, Martins, et al. (2022) *ABCT*

Take Home Message

(1) **Pretreatment AW** and **alcohol craving** may serve as **clinical prognostic indicators** of alcohol use outcomes and **AUD treatment response**.

– Evidence suggesting that manifestations of **AUD-related disruptions** reflect manifestations of **stress pathophysiology**.

– Critical for understanding the wide **heterogeneity of AUD treatment responses** to improve AUD treatment outcomes.

(2) **Daily breathing** significantly **reduced** levels of **stress** and **alcohol craving** throughout the treatment period.

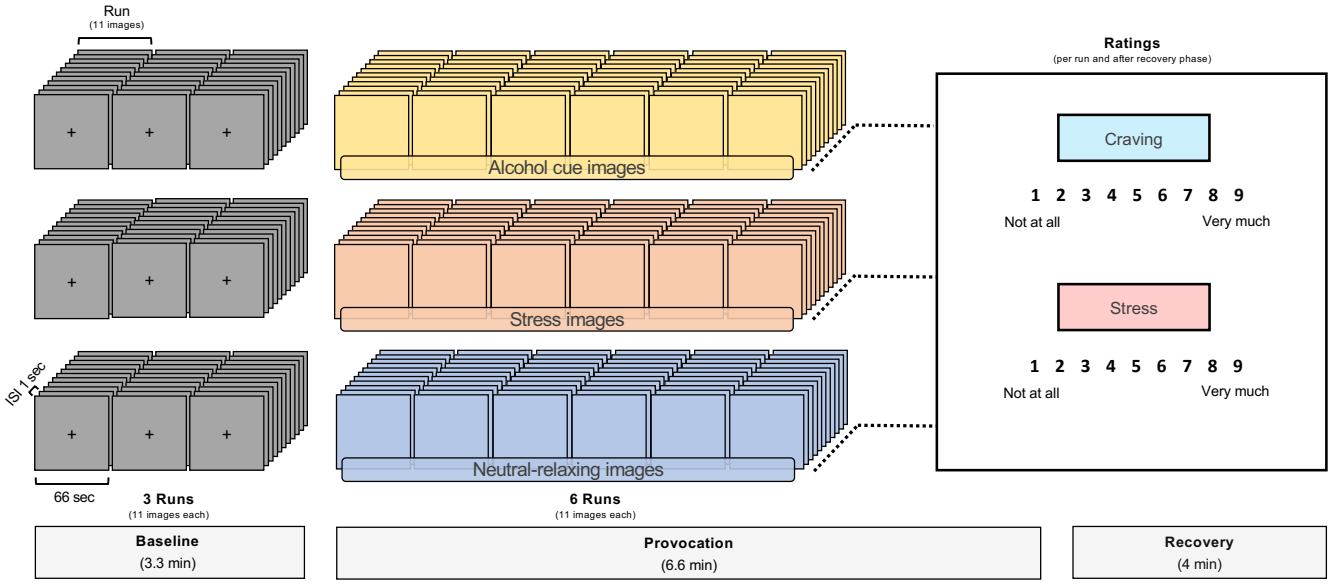
– **Self-guided breathing exercises** via a smartphone app is a **cost-effective** and **readily available** treatment tool for **normalizing** and **stabilizing** AUD disruptions.

Neural correlates of AUD and treatment-related recovery

Neural AUD treatment-related recovery

- N=30 demographically and clinically matched AUD treatment-seeking community adults (AUD) and 55 moderate drinkers (MD)

fMRI paradigm



3T Prisma MRI scanner

Sinha et al. (2016) *PNAS*

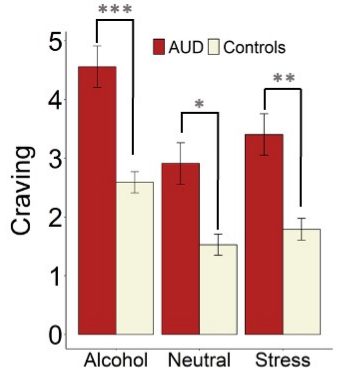
Neural AUD treatment-related recovery

- AUD treatment-seeking patients completed an 8-week treatment and were daily assessed using a smartphone app.

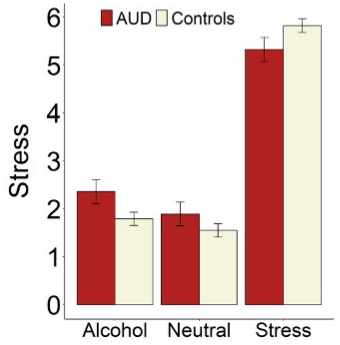
Sinha et al. (2021) *AmJP*
Martins et al. (2022) *DAD*

Altered stress & alcohol cue responses

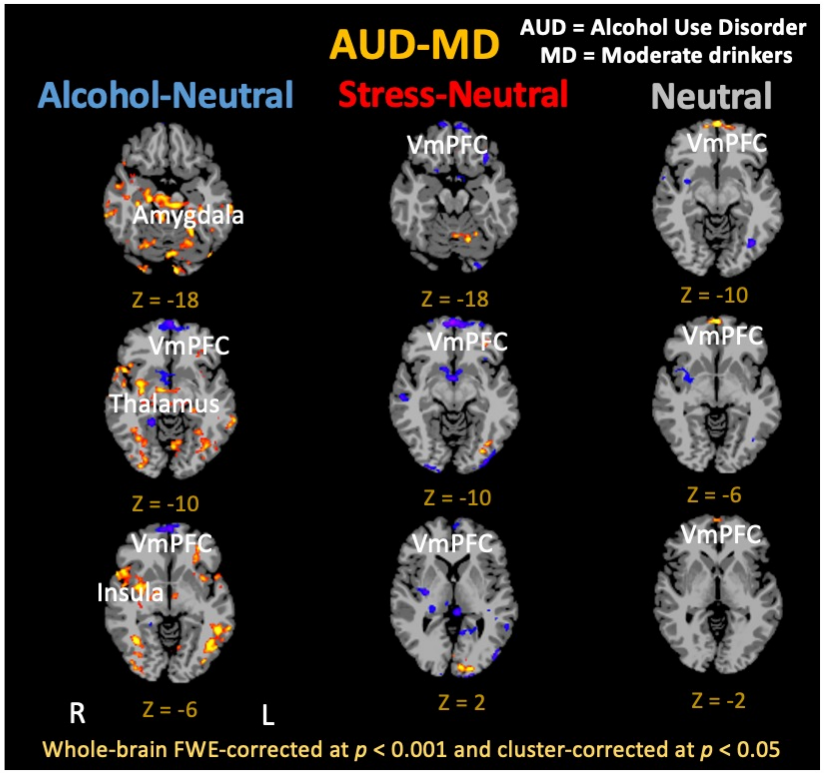
- AUD showed greater craving and hypoactive VmPFC but hyperactive limbic responses to alcohol cues and hypoactive VmPFC to stress cues.



Group: $\chi^2(1) = 17.95, p < 0.001$

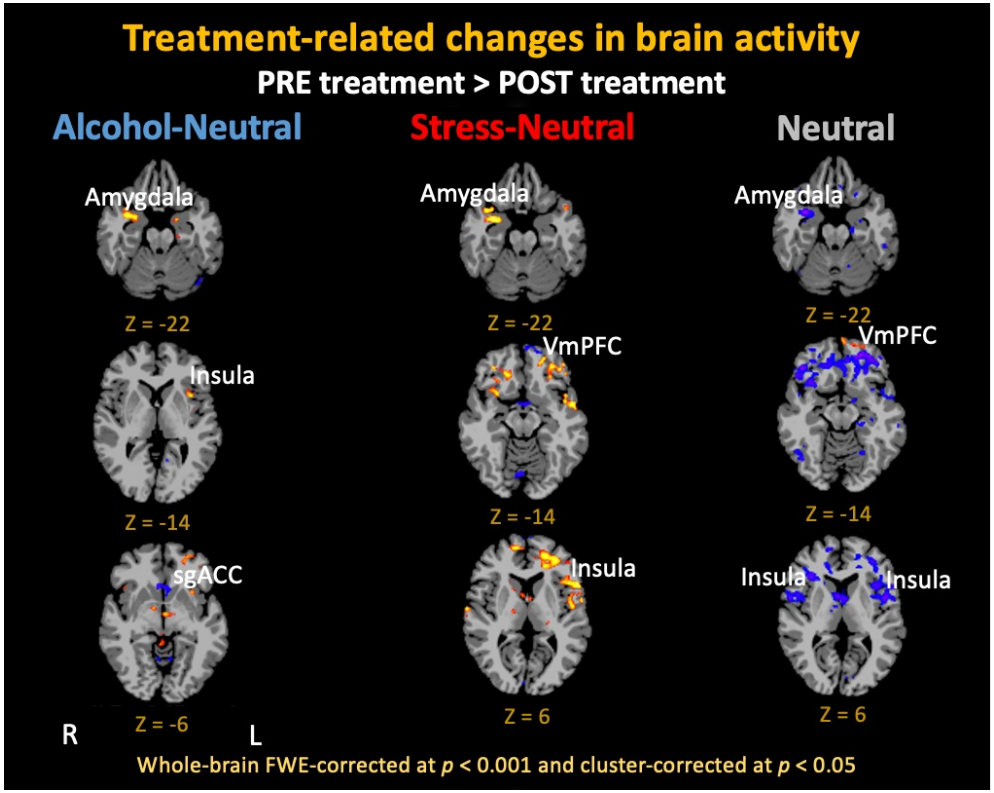


Group × Task: $\chi^2(2) = 9.87, p = 0.007$



Neural correlated of AUD recovery

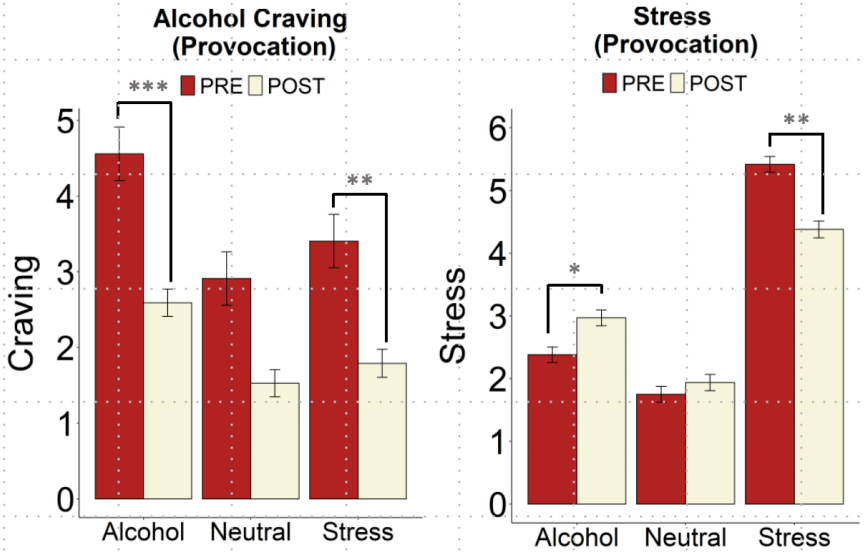
- When comparing pre- vs. post-treatment fMRIs : amygdala and insula responses were reduced; VmPFC and sgACC activity was increased.



AUD treatment-related recovery

- Stress and craving ratings were reduced after treatment.
- Daily craving reduced but stress coping improved with treatment.

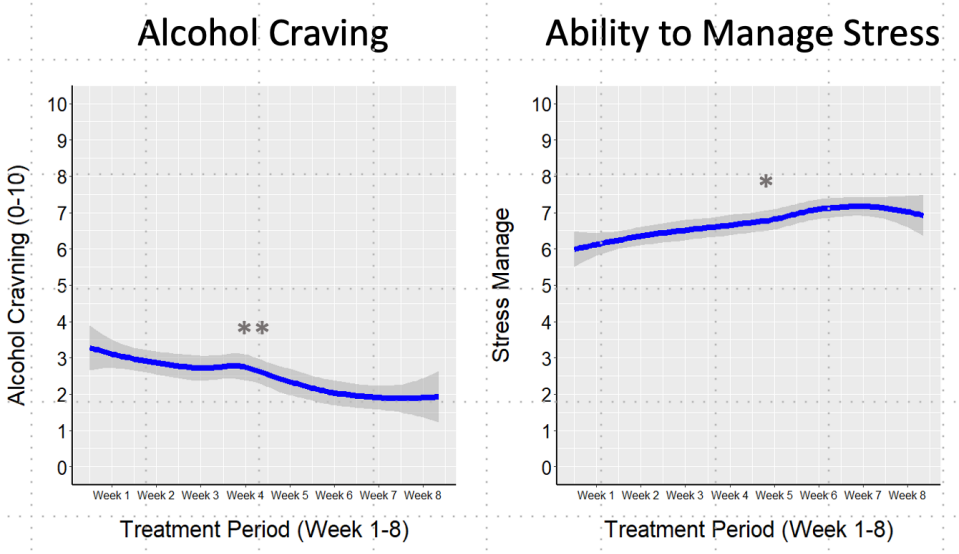
Initial vs. Post-Treatment Craving and Stress Ratings



Task × Session: $\chi^2(2) = 10.49$, $p = 0.005$

Task × Session: $\chi^2(2) = 24.40$, $p < 0.001$

Treatment-Related Changes over the Treatment Period (Weeks 1-8)



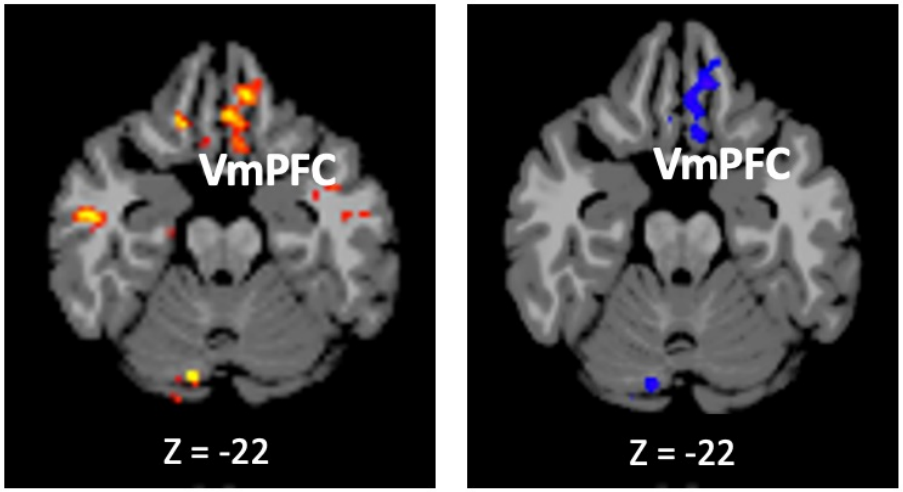
Time (day): $F(1,20.55) = 8.32$
$b = -0.033$, $p = 0.009$

Time (day): $F(1,23.33) = 5.43$
$b = 0.015$, $p = 0.029$

Ability to manage stress and VmPFC

- VmPFC recovery during stress was associated with greater improvements in stress management ability during treatment.

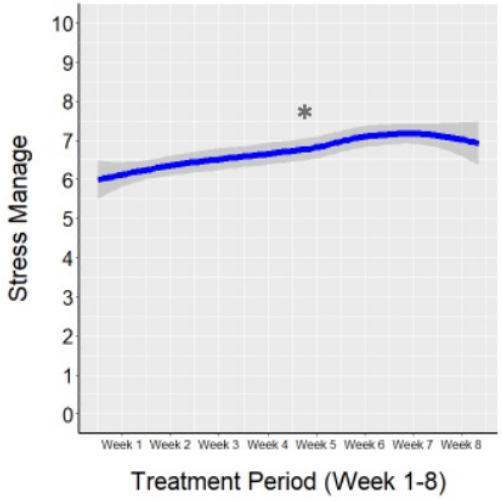
Stress Manage × Task (PRE-POST)



Whole-brain FWE-corrected at $p < 0.001$ and cluster-corrected at $p < 0.05$

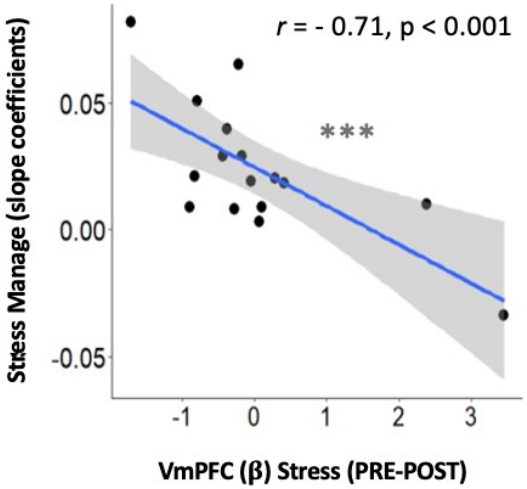
Stress Manage on Stress (PRE-POST)

Treatment-Related Changes in Stress Manage



Time (day): $F(1,23.33) = 5.43$
$b = 0.015$, $p = 0.029$

Stress Manage and VmPFC (Stress) Recovery



Take Home Message

(1) **disrupted neural responses** to **stress** and **alcohol cues** in **AUD patients** in **prefrontal and limbic regions**:

– altered neural circuits of **stress and emotion regulation**, marked by **decreased VmPFC**, and **sgACC** but **increased limbic responses** in the **amygdala**, **hippocampus**, and **thalamus**.

(2) **this neural pattern** that appears to **improve after treatment**:

– **reduction** of **amygdala** and **insula** responses

– **recovery** of **VmPFC** and **sgACC** activity

(3) **recovered VmPFC** responses were associated with **greater improvements in stress regulation**.

Acknowledgements

Jorge Martins, Ph.D.

Postdoctoral Researcher

jorgesmartins@ispa.pt

@jorgescmartins

www.jorgesmartins.com

Dongju Seo, Ph.D.
Yale University

Rajita Sinha, Ph.D.
Yale University

Keanan Joyner, Ph.D.
UC Berkeley

Bruce Bartholow, Ph.D.
University of Missouri-Columbia

Andrey Anokhin, Ph.D.
Washington University in St. Louis

Roberto Cofresi, Ph.D.
University of Missouri-Columbia

Ispa Instituto Universitário de Ciências Psicológicas, Sociais e da Vida

POPH QUALIFICAR É CRESCER.

QREN QUADRO DE REFERÊNCIA ESTRATÉGICO NACIONAL PORTUGAL 2007.2013

GOVERNO DA REPÚBLICA PORTUGUESA

UNIÃO EUROPEIA Fundo Social Europeu

FCT Fundação para a Ciência e a Tecnologia

REPÚBLICA PORTUGUESA | CIÊNCIA, TECNOLOGIA E ENSINO SUPERIOR

NIH National Institute on Alcohol Abuse and Alcoholism


Q
&
A


THANK YOU