Dynamic resting connectivity of the mesolimbic system is associated with individual differences in reward sensitivity

Sarah Kark, Joren Adams, Liv McMillan, Michael Yassa

[1]Department of Neurobiology and Behavior, [2]Center for the Neurobiology of Learning and Memory, University of California, Irvine

YASSALAB
Translational Neurobiology Laboratory

CNS 2020
#A16

BACKGROUND

- Reward sensitivity largely relies on functioning of the meso-cortico-limbic system
- Prior work has linked subjective reward sensitivity with **traditional** measures of resting striatal connectivity (Angelides, Gupta, and Vickery, 2017)
  - **Assumes connectivity is static across time**
- Mood disorders have been linked with changes in **time-varying** resting connectivity (Kaiser et al., 2016)

We test links between trait reward sensitivity and variability in meso-cortico-limbic resting connectivity.

METHODS

Resting state fMRI scan sample:

- **61 adults**
  - ages 18-37 (M=23.0 , SD=5.0)
  - 45 females
- **≥ 5 minutes** useable resting state data

Self-Report Surveys:

- *Reward sensitivity* (Carver and White, 1994)

Behavioral Approach System Scale (BAS)

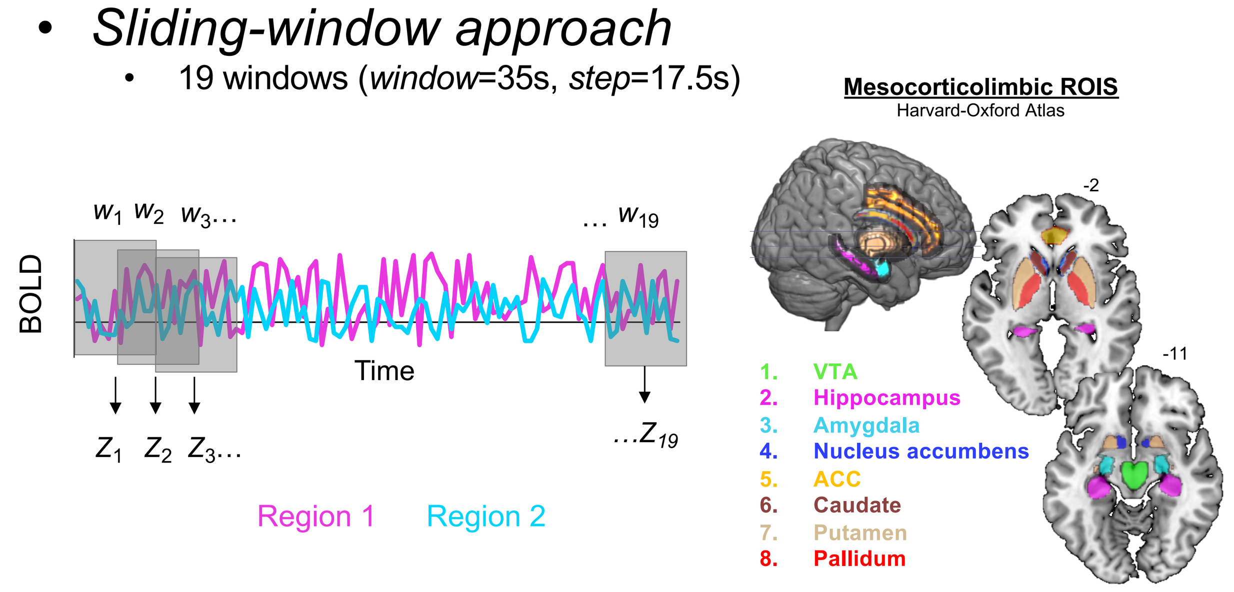
Responsiveness	Fun-seeking	Drive
Consummatory, anticipatory reactivity	Seek for potential rewards	Pursuit of desired goals

- *Depressive symptoms* (Beck Depression Inventory [BDI-II]; M=25.0, SD=15.25, Range: 0-58)
- **ROI-to-ROI resting state analysis**
  - Partial Spearman correlations between resting state and BAS scores (**controlling for age, sex, BDI, mean MRI motion**)

Static connectivity: r-to-Z connectivity values (whole timeseries)
Dynamic connectivity: SD of windowed r-to-Z connectivity values

Dynamic resting state connectivity analysis:

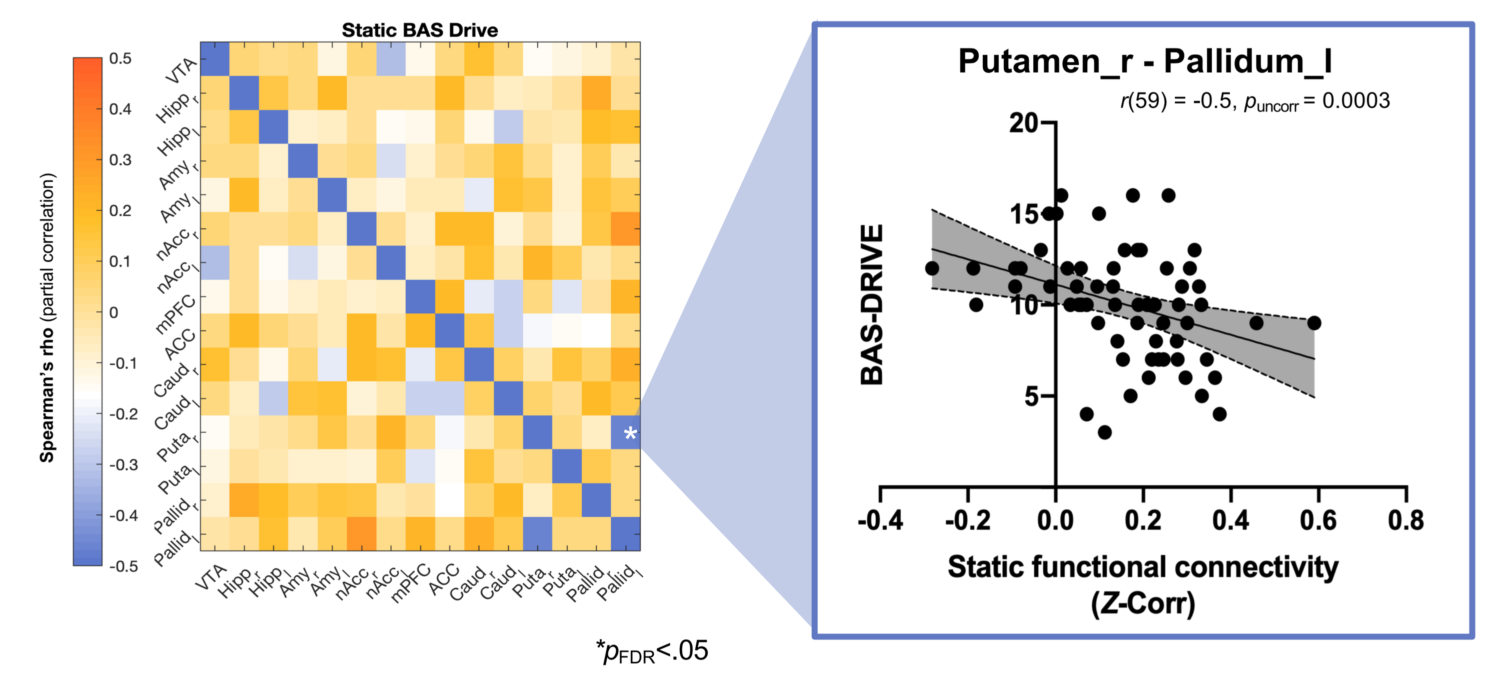
- *Sliding-window approach*
  - 19 windows ($window$=35s, $step$=17.5s)



CENTRAL HYPOTHESIS

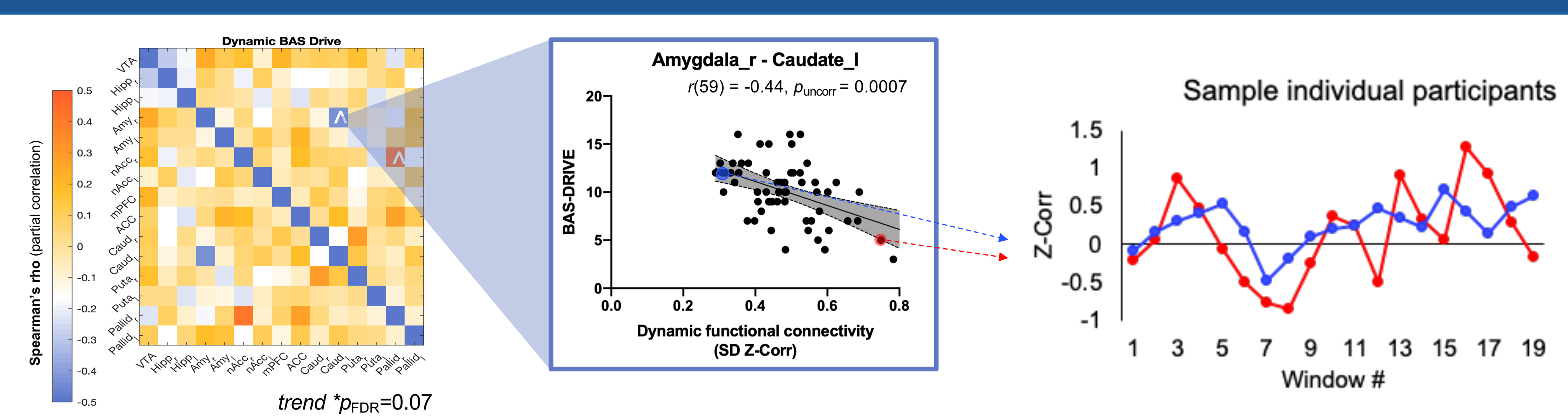
Irregular functional connectivity along the reward pathway is associated with diminished reward sensitivity

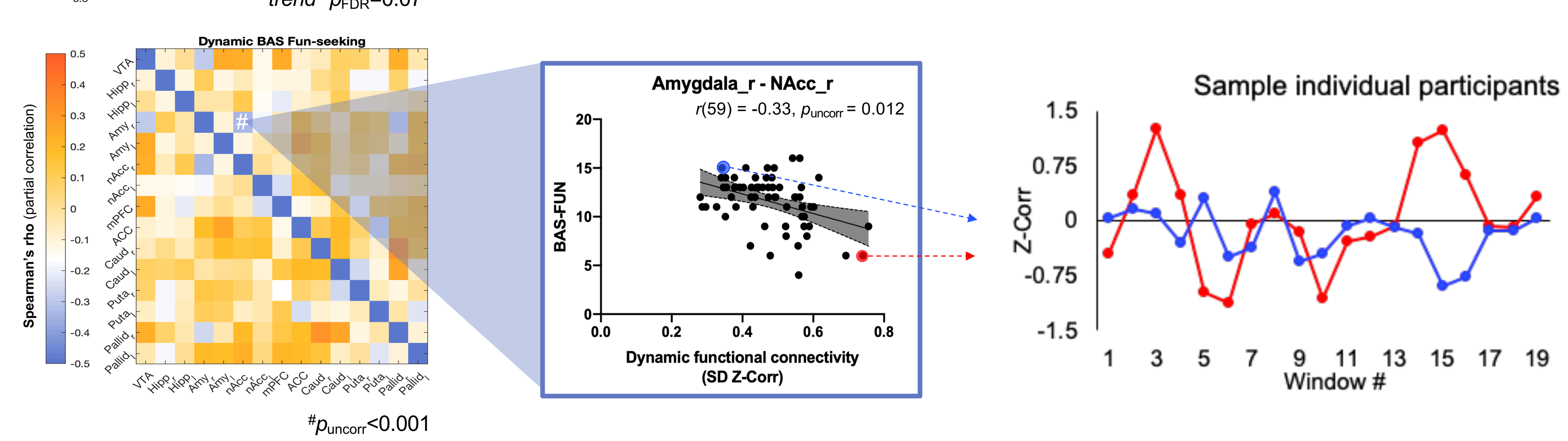
STATIC RESTING CONNECTIVITY
HEIGHTENED STRIATAL FC AND REDUCED DRIVE



- Link with **drive** is broadly consistent with basal ganglia contributions to **habitual control over motivated and goal-directed actions** (Reeve, 2008)
- Low drive might be related to perturbation of the **default inhibitory relationship** between putamen and globus pallidus (GABAergic)

DYNAMIC RESTING CONNECTIVITY
AMYGDALA FC AND REDUCED DRIVE





- Low drive and fun-seeking were linked with more **alternations between periods of high and low amygdala connectivity with caudate and nucleus accumbens, respectively.**
- High drive was linked with **greater dynamic nAcc-pallidum functional connectivity.**

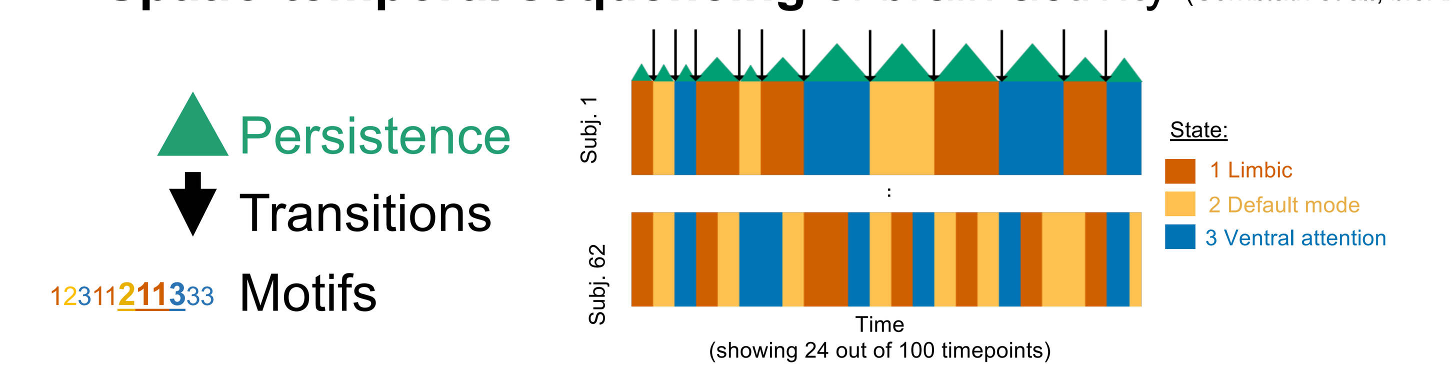
TAKE HOME MESSAGES

Present findings:

- **Time-varying functional connectivity** indices are sensitive to subjective reward-related behaviors
  - Implicate different parts of the reward circuit
- **Striatal resting functional connectivity** are linked to individual differences in ***drive***
- **Meso-limbic** dynamic functional connectivity is linked with reduced ***fun-seeking***

Future Directions:

- **Frontal control** (e.g., dorsolateral prefrontal cortex control over striatum)
- **Sub-areas** (e.g., external globus pallidus and baso-lateral amygdala)
- **Spatio-temporal sequencing** of brain activity (Cornblath et al., *bioRxiv*)



- Preliminary evidence links **reward responsiveness** with **state transition probabilities**

REFERENCES

- **Angelides,** N. H., Gupta, J., & Vickery, T. J. (2017). Associating resting-state connectivity with trait impulsivity. Soc Cogn Affect Neurosci, 12(6), 1001-1008.
- **Carver**, C. S., & White, T. L. (1994). Behavioral inhibition, behavioral activation, and affective responses to impending reward and punishment: The BIS/BAS scales. Journal of Personality and Social Psychology, 67, 319-333.
- **Cornblath** EJ, *et al.* (2019). Temporal sequences of brain activity at rest are constrained by white matter structure and modulated by cognitive demands. *arXiv preprint arXiv:1809.02849, 2019.*
- **Beck**, A.T., Steer, R.A., & Brown, G.K. (1996). Manual for the Beck Depression Inventory-II. San Antonio, TX: Psychological Corporation.
- **Kaiser**, R. H., Whitfield-Gabrieli, S., Dillon, D. G., Goer, F., Beltzer, M., Minkel, J., . . . Pizzagalli, D. A. (2016). Dynamic Resting-State Functional Connectivity in Major Depression. Neuropsychopharmacology, 41(7), 1822-1830. doi:10.1038/npp.2015.352
- **Reeve, J. (2008).** Understanding Motivation and Emotion, 5th Edition: Wiley Global Education.

Acknowledgements

This research was supported by NIH-NIMH grant 5R01MH102392-05. We would like to thank Ruth Benca, Ivy Chen, Mithra Sathishkumar, Jessica Noche, Jody Rawles, Liz Murray, and Amanda Chun for their work on this project. We thank the participants for their time and effort in participating.

https://bit.ly/2T7akHU

University of California, Irvine

smkark@uci.edu | joren.adams@uci.edu | liv@uci.edu | myassa@uci.edu | www.yassalab.org