Resting-State Functional Connectivity for Prevention Researchers: What, Why, and How?

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Presentation Outline

Informational Content

- ❏ What is Resting-State Functional Connectivity (rsFC)?
- ❏ Why is rsFC relevant for prevention research?
- ❏ How is it measured?
- ❏ Common Functional Networks

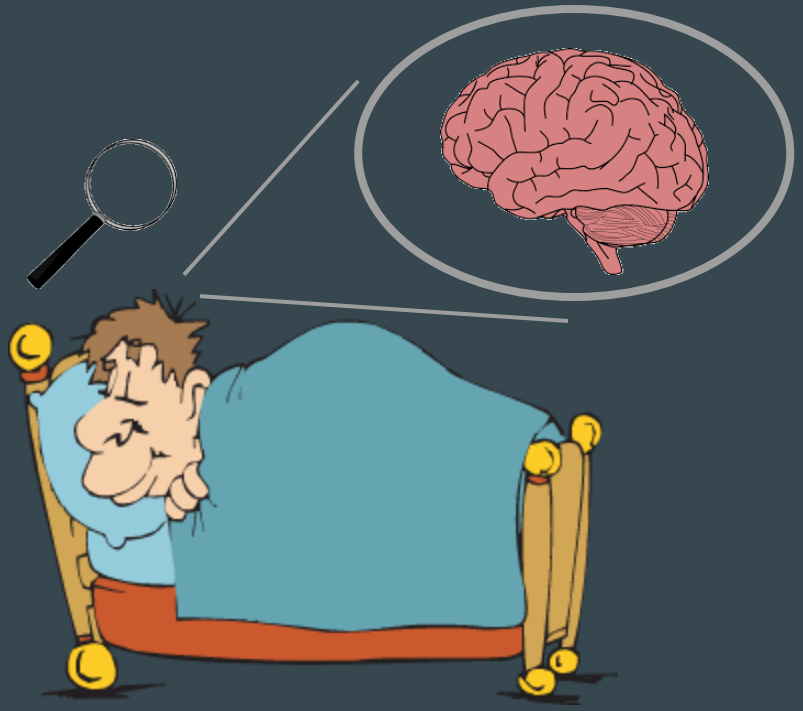
- ❏ Questions?

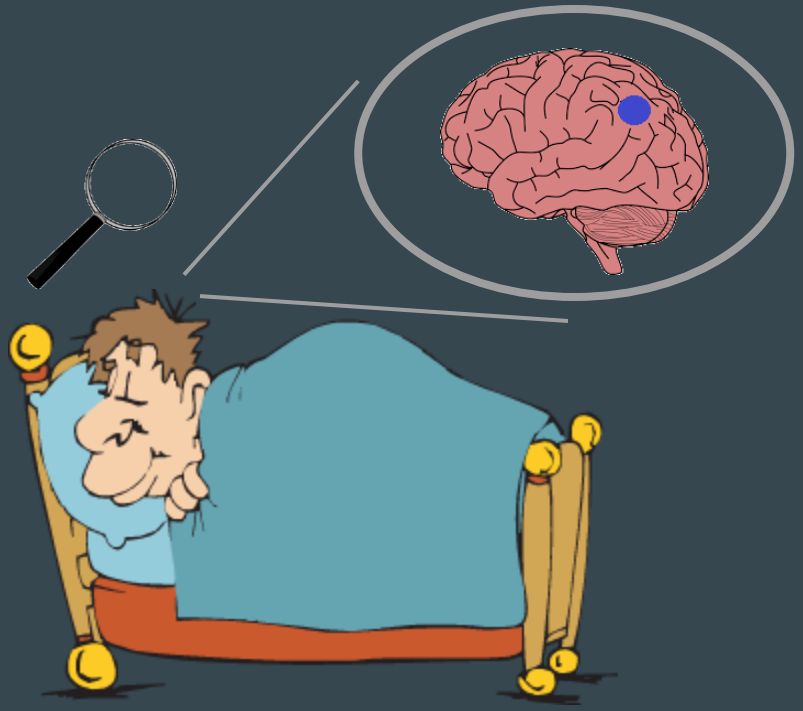
Hands-on Activity

- ❏ Quantifying the brain at rest: rsFC of the Executive-Control Network

What is Resting-State Functional Connectivity (rsFC)?

Correlation in neural activity between two or more brain regions, measured while participants are “at rest”.





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-18121.9
-38890.2
-13458.4
40374.2
53140.9
7176.48
-33219.7
-17254.5
21602.3
26660.1
4874.7
3125.57
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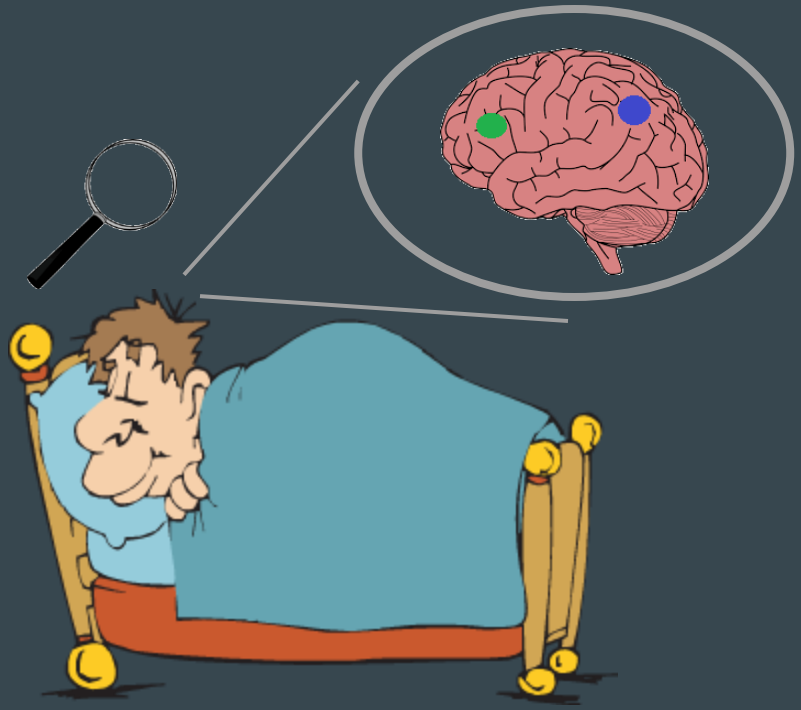

-18121.9	3125.57
-38890.2	26517.4
-13458.4	35373.4
40374.2	12301.5
53140.9	-19176.4
7176.48	-41626.4
-33219.7	-60912.8
-17254.5	-70316.9
21602.3	-45196.2
26660.1	9455.49
4874.7	47309.7
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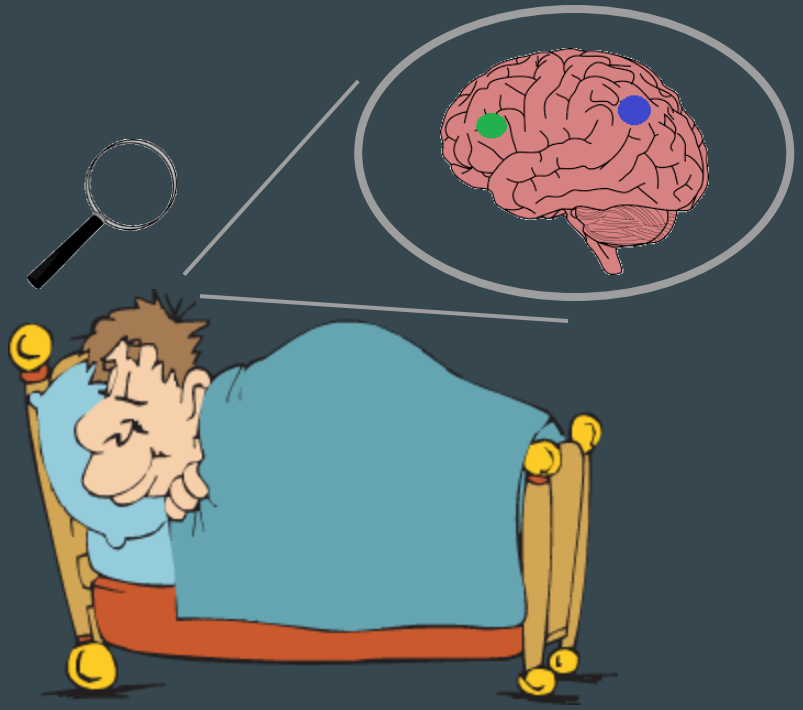

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3125.57	40451.2

$$r = \frac{\sum xy}{\sqrt{\sum x^2 \sum y^2}}$$

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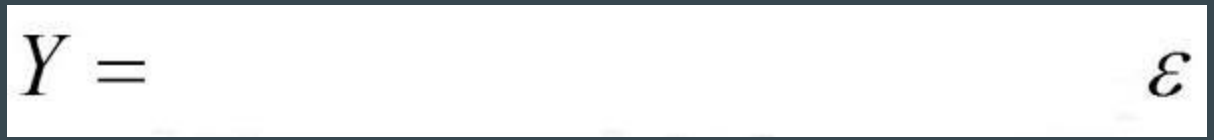
What is Resting-State Functional Connectivity (rsFC)?

Correlation in neural activity between two or more brain regions, measured while participants are “at rest”.

- Spontaneous activation. Random. Error term in regression model.

$$Y = \beta_0 + \beta_1 X_1 + \beta_2 X_2 + \beta_3 X_3 + \varepsilon$$


$Y =$
ε

What is Resting-State Functional Connectivity (rsFC)?

Correlation in neural activity between two or more brain regions, measured while participants are "at rest".

- Spontaneous activation. Random. Error term in regression model.
- If random, then correlation = 0.
- Correlation thought to reflect extent of interconnected functioning.

Seminal Contribution: Rather than operate independently, brain regions form a series of neural networks that interact to achieve advance human cognition.

- Fundamental organization of the human brain.
- Neural underpinnings of complex behavior (i.e. self-regulation, decision making).

Why is rsFC important in general?

- Allows brain to be observed without anyone looking/task interference.
- Reveals “true” extent of network based activity.
- Are brain regions primarily independent or part of a team (i.e. network)?
- What networks exist/how function?
- Investigate development/cortical maturity (density/homogeneity/heterogeneity).
- Understand how the brain actually achieves higher order behaviors.
- Indiv Connections or aggregates across network?
- Do group or individual differences in rsFC predict behavior?
- Prediction of group assignment.

Why is rsFC relevant for prevention research?

- Improve model fit
  - Important brain-behavior relationships missing from earlier research.
  - Outcome measures or predictors of outcomes.
  - Mediation of established predictor-outcome relationships. (ex: Parenting on Risk-taking)

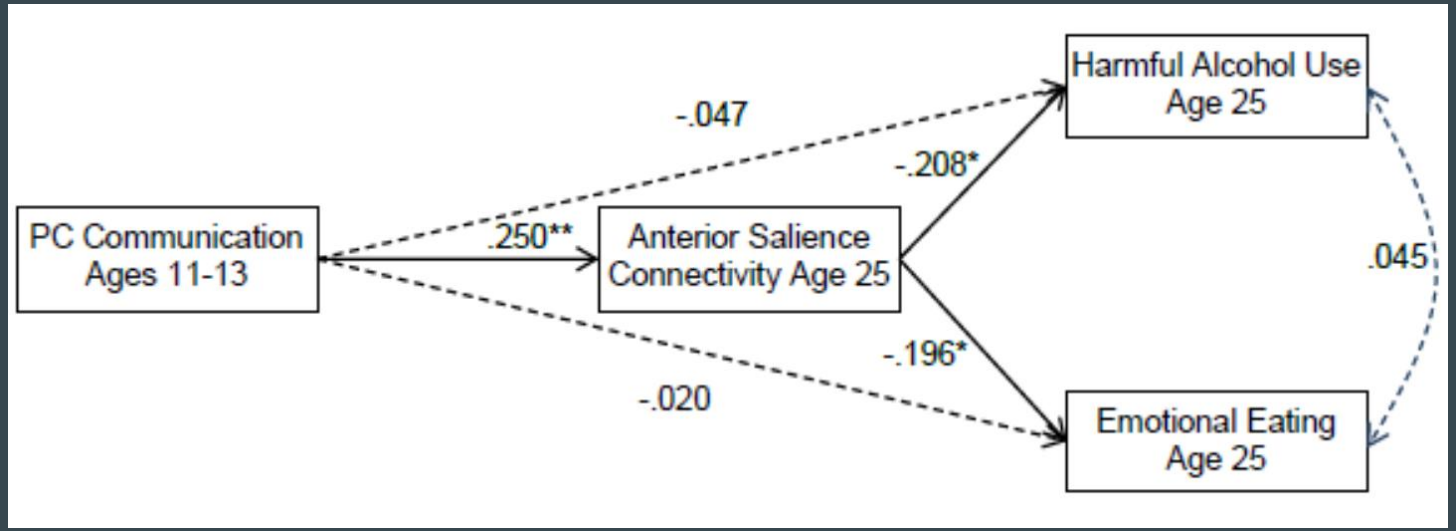
- Deeper understanding of how:
  - Risk and/or Protective factors affect the brain (cortical maturity, premature aging)
  - Prevention efforts affect the brain.
  - Prevention efforts ameliorate behavior by altering the brain.

Holmes et al. (in press)

- Strong African American Families Healthy Adult Project
  - Longitudinal, multimethod; Ages 11-adulthood.
- N=91 (52% female; N=119 before motion and technical exlclusions).
- All aged 25 at time of rsFC scan.

- Influence of parenting (ages 11-13) on rsFC of the Anterior Salience Network (ASN) at age 25.
- Influence of ASN rsFC on Harmful Alcohol Use and Emotional Eating at age 25.
  - Alcohol Use Disorders Identification Test (Saunders et al., 1993).
  - Emotional Eating Scale (Arnow et al., 1995)

Holmes et al. (in press)



- Parent-child communication at ages 11-13 predicted rsFC of the Anterior Salience Network at age 25.
- ASN connectivity at age 25 predicted two maladaptive behaviors independently.

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How is rsFC measured?

“rest in 3..2..1..”

- Length of scan varies; need min four minutes usable data. (get more!)
- “Timeseries” for each voxel (series of data points reflecting activation across time; one data point per TR).

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How is rsFC measured?

```
3017.41
-18121.9
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-41626.4
-60912.8
-70316.9
-45196.2
9455.49
47309.7
40451.2
17058.1
13545
20182.1
6450.8
-24755.9
```

How is rsFC measured?

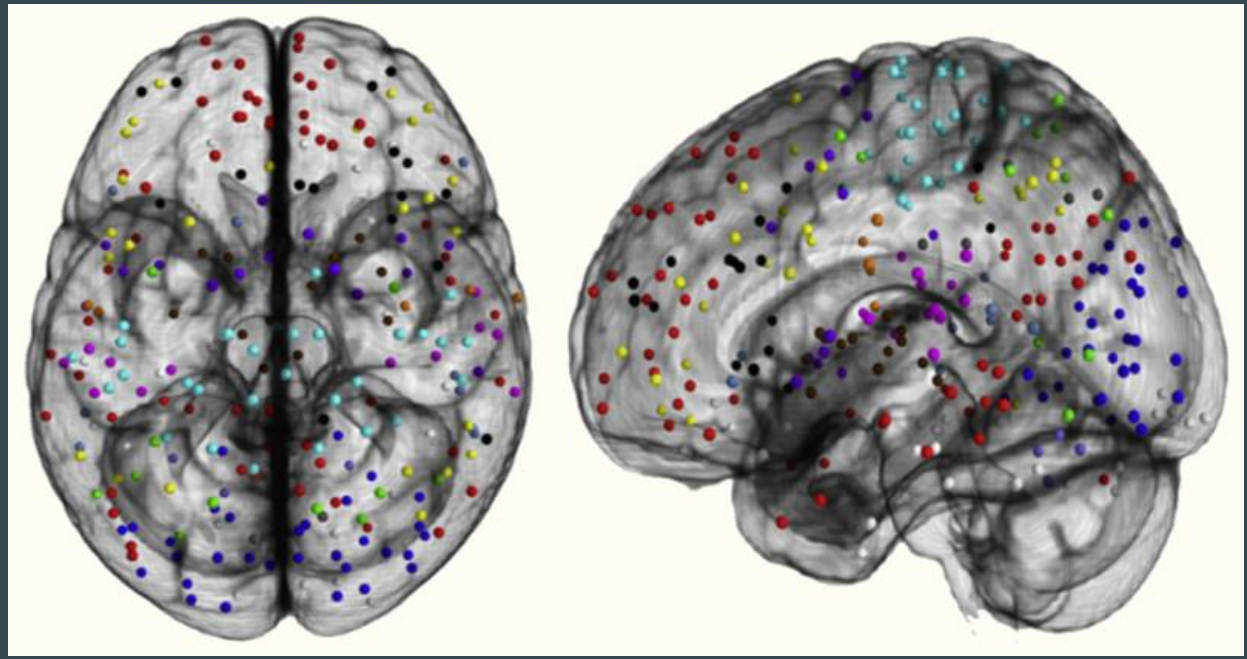
- Creates a 2D matrix for each subject: Voxel X Time.
- Issue!: Raw values from scanner are arbitrary
  - Percent signal change calculated first, then correlations
    - $p = ((a - m_a)/m_a)100$
- Then z-scores (using Fischer's r to z transform)
    - $z = \log((1+r)/(1-r))/2$
    - Analyses conducted on z-score dataset.

How is rsFC measured?

- Independent Components Analysis sometimes used to identify networks.
  - Data-driven approach. Makes little/no a-priori assumptions.
- Seed-based: one Region of Interest (ROI) and rest of brain.
  - Often based on significant activation during task performance.
- ROI-ROI
  - Hypothesis testing based on previous literature.
  - Single or multiple (i.e. network) connections.
  - Allows "graph theory" approach.

Common Functional Networks

- Somatomotor/Hand
- Somatomotor/Mouth
- Cingulo-Opercular Control
- Auditory
- Default Mode
- Memory Retrieval
- Visual
- Fronto-parietal Control
- Salience
- Subcortical
- Ventral Attention
- Dorsal Attention
- Cerebellar



(Satterthwaite et al., 2013)

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Common Functional Networks

- Default Mode Network (DMN): PCC, mPFC, IPL
  - Active when task not present.
  - Associated with disengagement and internal/subjective thought processes.
- Executive-Control Network (EC): IPL(IPS), dlPFC
  - Active when completing a task.
  - Associated with task engagement, external thought processes, and cognitive control.
- Salience Network (SN): dACC and aI
  - Activates as stimuli are more salient.
  - Involved in switching activation between the EC and DMN.
- Ventral Valuation & Dorsal Control Networks (VS/DS): Striatum based
  - Active when processing option value (VS) or controlling for appropriate responses (DS)

Questions?

Activity: Quantifying Network Level rsFC (one way)

- Four easy steps:

    1. Determine which networks you want to study (theory; research question).
    2. Determine how you want to define your networks (previous lit; current findings; both).
    3. Correlate neural activity between all possible connections for each subject.
        3.1 Convert correlations to Z-scores using Fisher's r to z transform.
        3.2 "Vectorize" results.
        3.3 Add row to dataset containing all participants.
    4. Calculate average of all connections within each network (and between).

- Conduct t-test to compare mean values against 0, correcting as needed.

Activity: Quantifying Network Level rsFC (one way)

- Fair (2009):

Regions of Interest (ROI)	ROI Abbreviations	Coordinates			Functional Network
		x	*y*	*z*	
dorsolateral prefrontal cortex	dlPFC	−43	22	34	Fronto_Parietal
dorsolateral prefrontal cortex	dlPFC	43	22	34	Fronto_Parietal
Frontal	frontal	−41	3	36	Fronto_Parietal
Frontal	frontal	41	3	36	Fronto_Parietal
mid cingulate cortex	mCC	0	−29	30	Fronto_Parietal
inferior parietal lobule	IPL	−51	−51	36	Fronto_Parietal
inferior parietal lobule	IPL	51	−47	42	Fronto_Parietal
intraparietal sulcus	IPS	−31	−59	42	Fronto_Parietal
intraparietal sulcus	IPS	30	−61	39	Fronto_Parietal
Precuneus	Precun	−9	−72	37	Fronto_Parietal
Precuneus	Precun	10	−69	39	Fronto_Parietal
anterior Prefrontal Cortex	aPFC	−28	51	15	Cingulo_Opercular
anterior Prefrontal Cortex	aPFC	27	50	23	Cingulo_Opercular
anterior insula/frontal operculum	al/fO	−35	14	5	Cingulo_Opercular
anterior insula/frontal operculum	al/fO	36	16	4	Cingulo_Opercular
dorsal anterior cingulate/medial superior frontal cortex	dACC/msFC	−1	10	46	Cingulo_Opercular
superior frontal cortex	ant thal	−12	−15	7	Cingulo_Opercular
anterior thalamus	ant thal	10	−15	8	Cingulo_Opercular
anterior thalamus	amPFC	1	54	21	Default
ventromedial prefrontal cortex	vmPFC	−3	39	−2	Default
superior frontal cortex	sup frontal	−14	38	52	Default
superior frontal cortex	sup frontal	17	37	52	Default
inferior temporal	inf templ	−61	−33	−15	Default
inferior temporal	inf templ	65	−17	−15	Default
parahippocampal	parahippo	−22	−26	−16	Default
parahippocampal	parahippo	25	−26	−14	Default
posterior cingulate cortex	pCC	−2	−36	37	Default
lateral parietal	latP	−47	−67	36	Default
lateral parietal	latP	53	−67	36	Default
retro splenial	retro splen	3	−51	8	Default

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Activity: Quantifying Network Level rsFC (one way)

- Anderson (2011):

Default mode network		*Attention control network*	
Hub	*MNI coordinates*	*Hub*	*MNI coordinates*
Left posterior cingulate	−4−52 32	Left intraparietal sulcus	−43−38 46
Right posterior cingulate	4−53 35	Right intraparietal sulcus	40−39 51
Left medial prefrontal	−2 55−13	left frontal eye field	−21−4 59
Right medial prefrontal	2 55−13	Right frontal eye field	27−6 54
Left temporoparietal junction	−49−62 34	Left anterior insula	−38 14 8
Right temporoparietal junction	50−57 36	Right anterior insula	40 15 8

Activity: Quantifying Network Level rsFC (one way)

- Fair (2009):

-43	22	34	dlPFC-432234
43	22	34	dlPFC432234
-41	03	36	Front-410336
41	03	36	Front410336
00	-29	30	mCC00-2930
-51	-51	36	IPL-51-5136
51	-47	42	IPL51-4742
-31	-59	42	IPS-31-5942
30	-61	39	IPS30-6139
-09	-72	37	PREC-09-7237
10	-69	39	PREC10-6939
01	54	21	amPFC015421
-03	39	-02	vmPFC-0339-02
-14	38	52	SupFr-143852
17	37	52	SupFr173752
-61	-33	-15	InfTemp-61-33-15
65	-17	-15	InfTemp65-17-15
-22	-26	-16	ParaHipp-22-26-16
25	-26	-14	ParaHipp25-26-14
-02	-36	37	PCC-02-3637
-47	-67	36	LatPar-47-6736
53	-67	36	LatPar53-6736
03	-51	08	RetSplin03-5108

Activity: Quantifying Network Level rsFC (one way)

- Anderson (2011):

-04	-52	32	PCC-04-5232
04	-53	35	PCC04-5335
-02	55	-13	vmPFC-0255-13
02	55	-13	vmPFC0255-13
-49	-62	34	TPJ-49-6234
50	-57	36	TPJ50-5736
-43	-38	46	IPS-43-3846
40	-39	51	IPS40-3951
-21	-04	59	EYE-21-0459
27	-06	54	EYE27-0654
-38	14	08	aINS-381408
40	15	08	aINS401508