Center for Precision Psychiatry
MGH Department of Psychiatry

TAPPING INTO COGNITION: CONNECTING BRAIN IMAGING AND DIGITAL BIOMARKERS FOR PRECISION PSYCHIATRY

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DISCLOSURES

Center for Precision Psychiatry
MGH Department of Psychiatry

I have the following relevant financial relationship with a commercial interest to disclose:

- KeyWise AI (cofounder)
- Embodied Labs (advisory board)
- Blueprint Health (advisory board)
- Otsuka (consultant)

AMERICAN

JOURNAL OF INSANITY.

APRIL, 1891.

THE MECHANISM OF INSANITY.*

BY EDWARD COWLES, M. D.,

Superintendent of the McLean Asylum, Somerville, Mass.

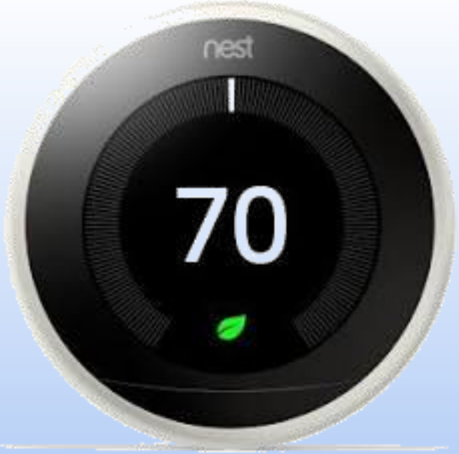
The "empirical valuation" of morbid manifestations of these mental phenomena [retention, reproduction, and association of ideas], that is commonly made by the alienist, has the greater value when, by careful study and comparison with the action of the normal mechanisms…by a like "tireless observation". Then knowing what to look for, as he who is expert with the microscope, he may report what he sees….with more completeness and precision"

THE LANCET.

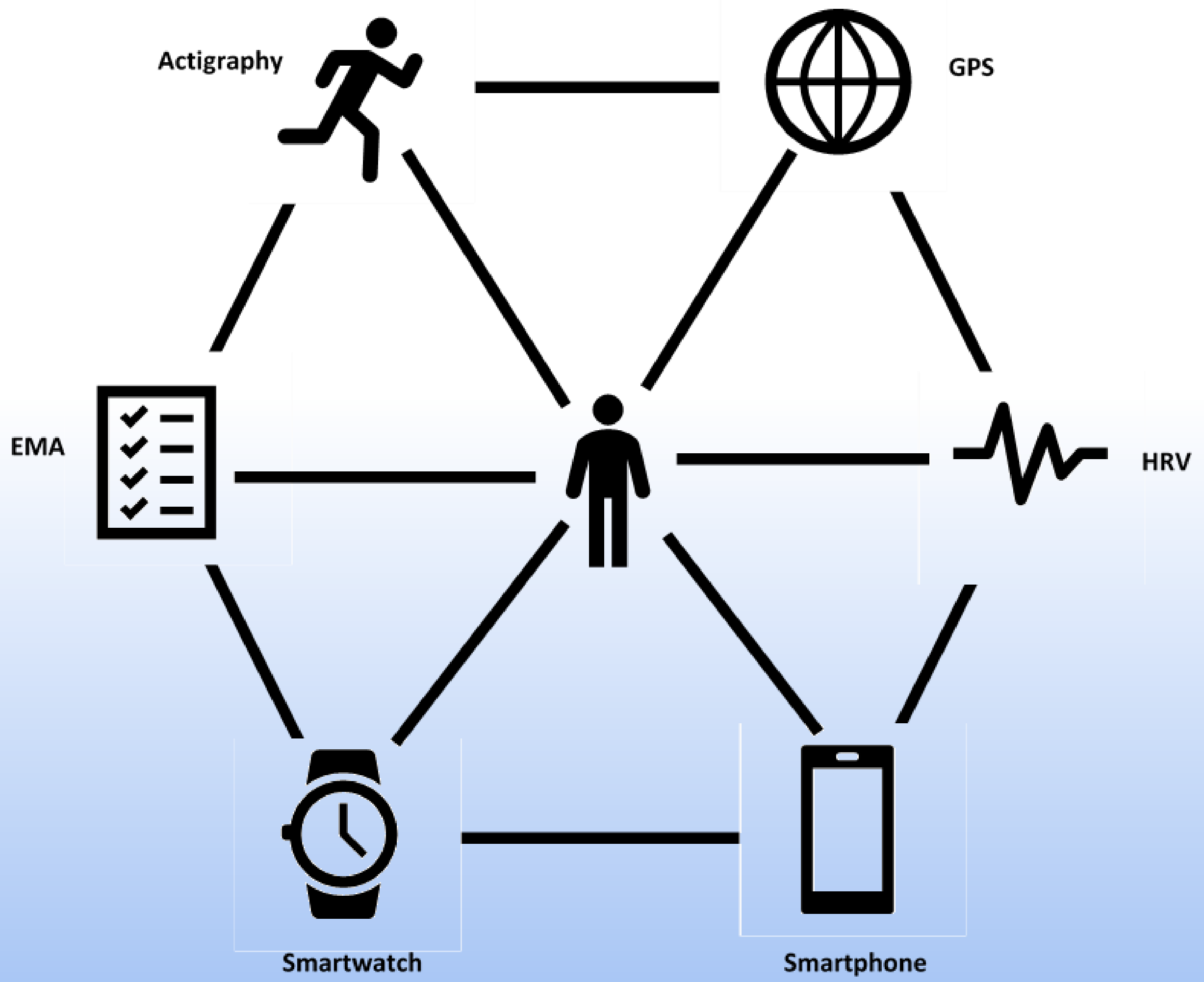
LONDON: SATURDAY, MAY 14, 1859.

When a lunatic is received into an asylum, he is removed by an interval of time, and of locality, from the origin of his disease; he is completely isolated from the sphere, and separated from all the surrounding conditions, in which he passed his life. The necessary clues to trace back the causes of his malady are broken by the reserve of friends, the want of knowledge of others, and by numerous difficulties which, in most cases, reduce the formal statement entered in the asylum case-book to a mere hypothesis, void of precision and of authority.

TOOLS OF "TIRELESS OBSERVATION" IN OUR "SURROUNDING CONDITIONS"



ECOLOGICAL MOMENTARY ASSESSMENT (EMA)/UBIQUITOUS SENSING

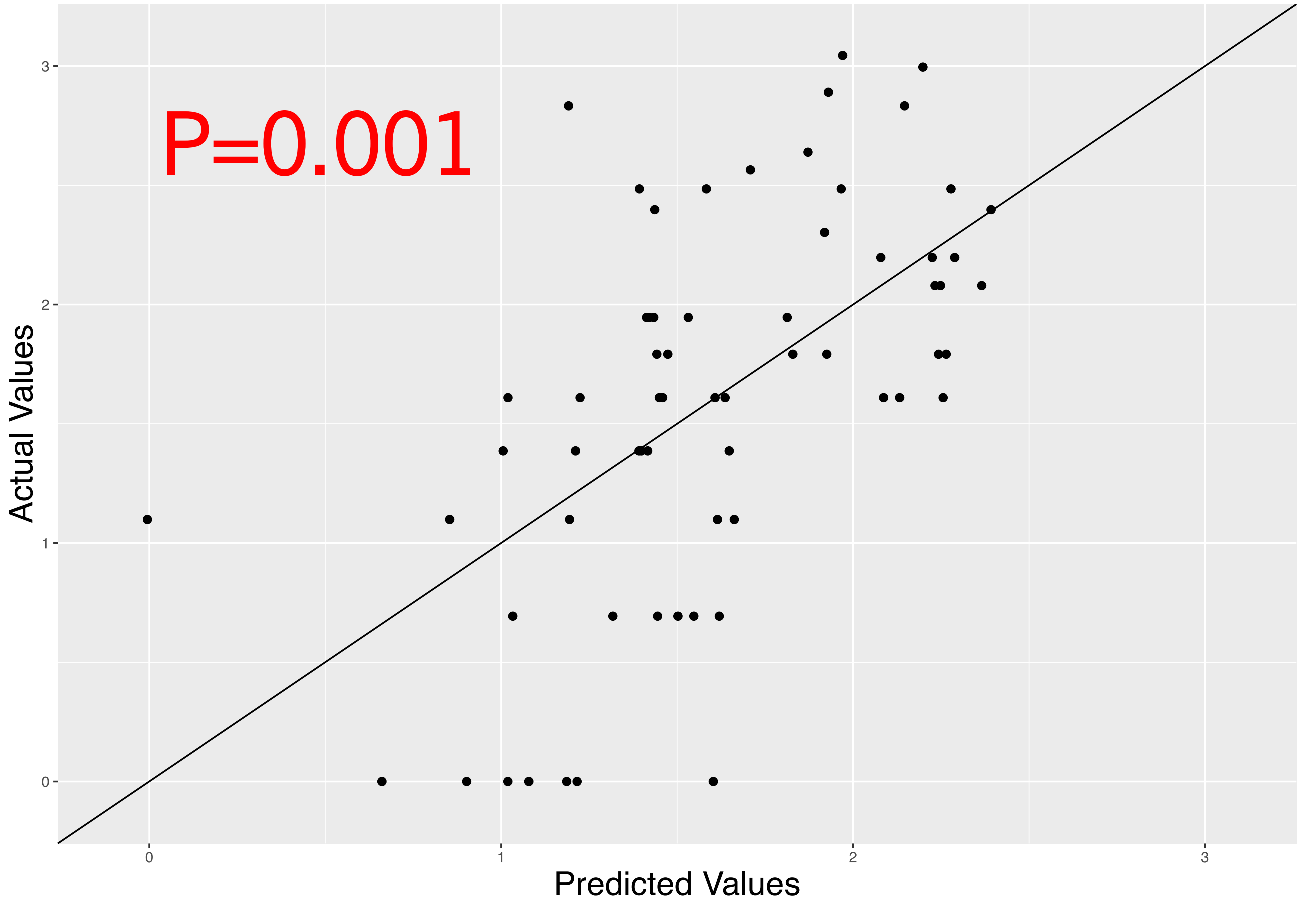


PASSIVE MONITORING OF MOOD AND COGNITION: DEEP EMBEDDED REAL-TIME DIGITAL SAMPLING

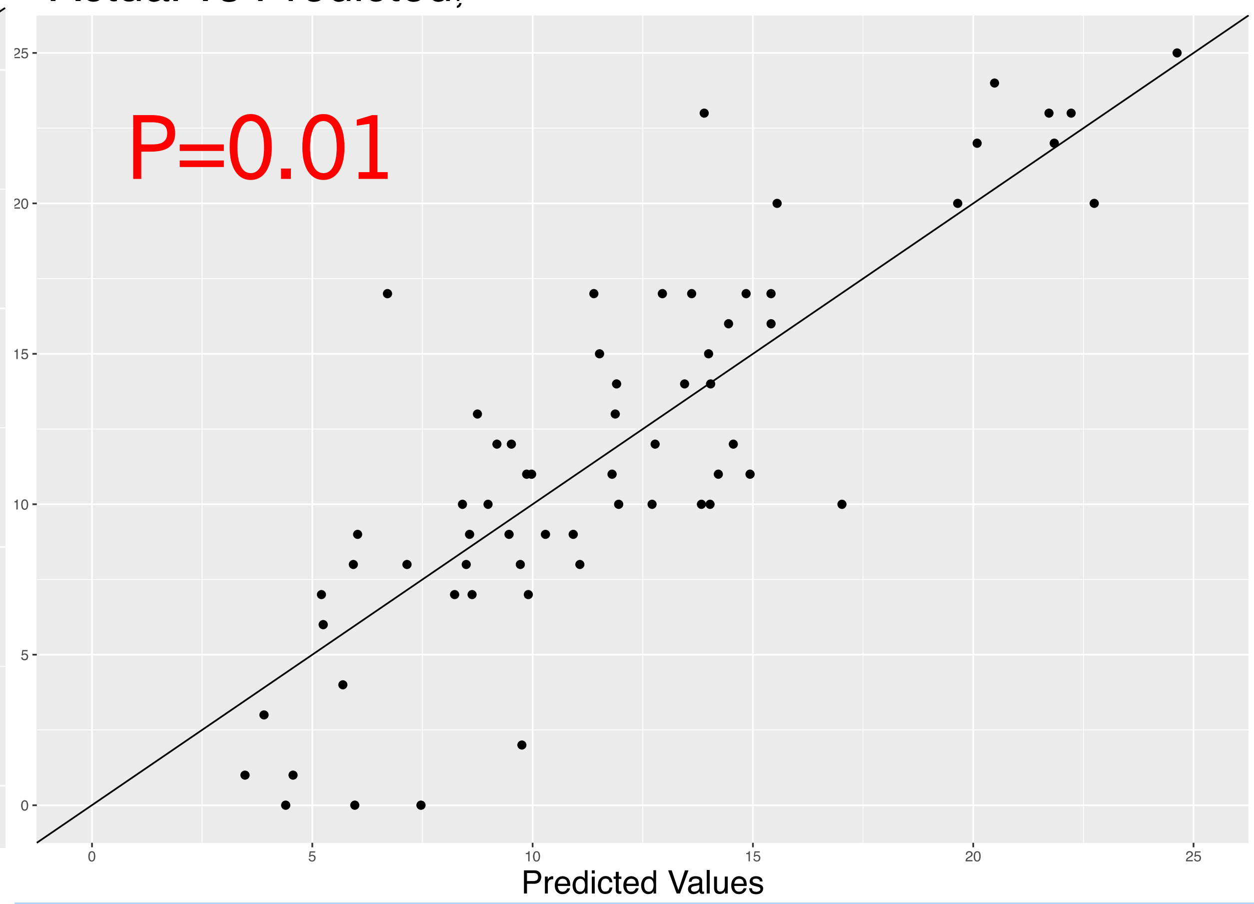
iOS BiAffect Keyboard

- The core is a custom keyboard that tracks **ALL keystroke metadata in the background**. E.g.,
  - Force of key presses measured by accelerometer
  - Residence time
  - Inter-key time
  - Character count
  - Backspace ratio
  - Auto-correction rate
- Using both keystroke dynamics and iPhone sensor data, BiAffect builds a mathematical model that performs **neuropsychological testing without actually testing**.

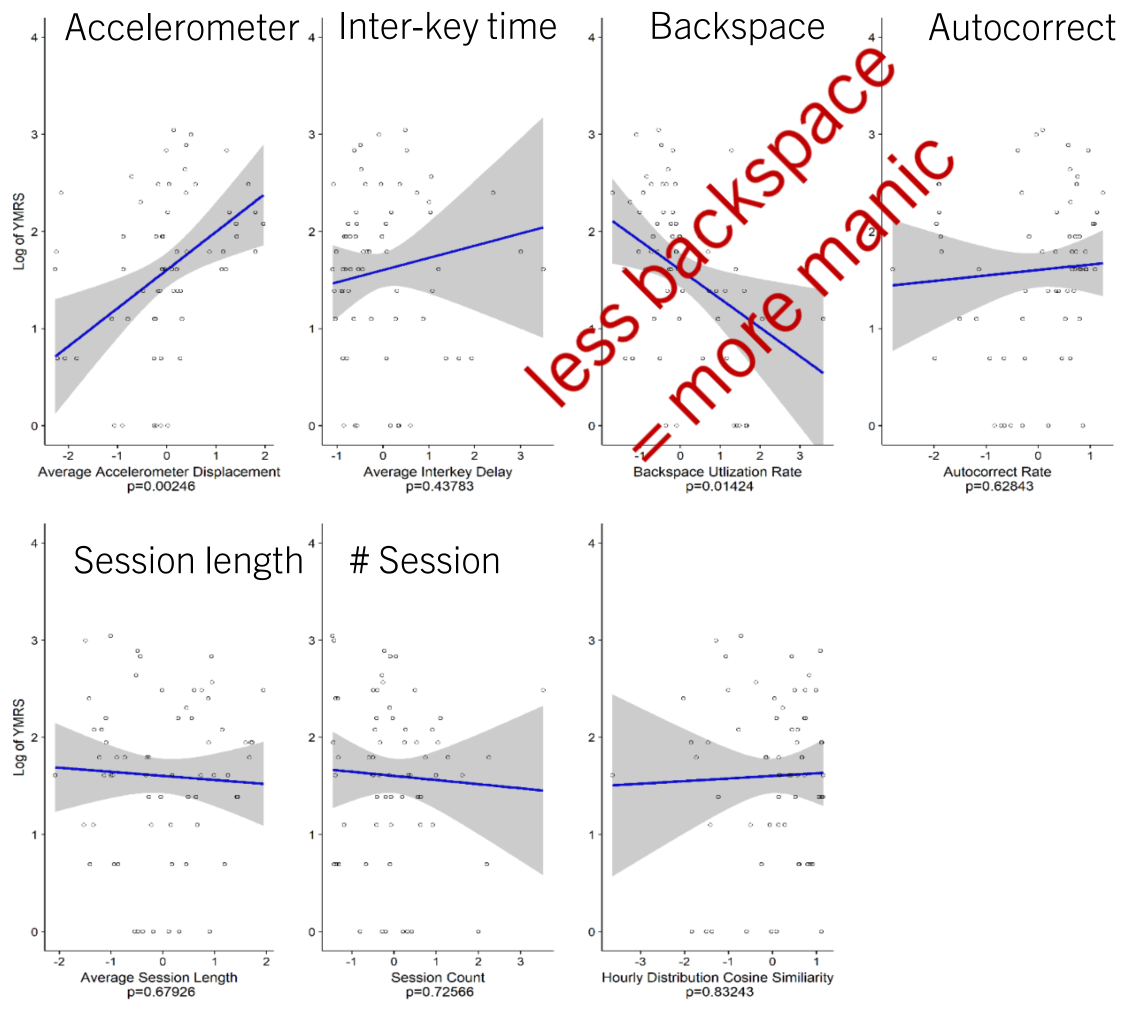
Young Mania Rating Scale Scores Actual vs Predicted,

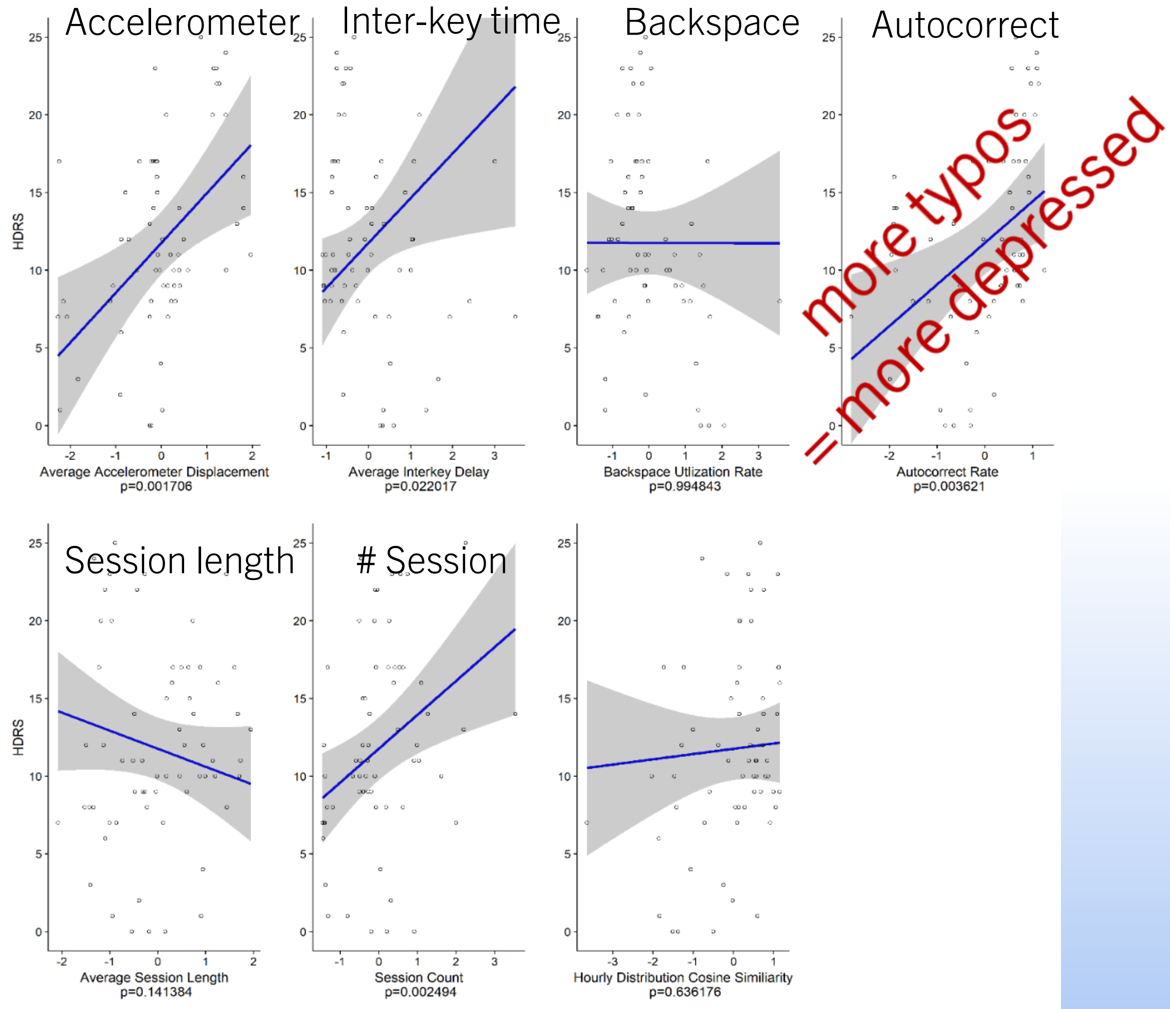


Hamilton Depression Rating Scale Scores Actual vs Predicted,

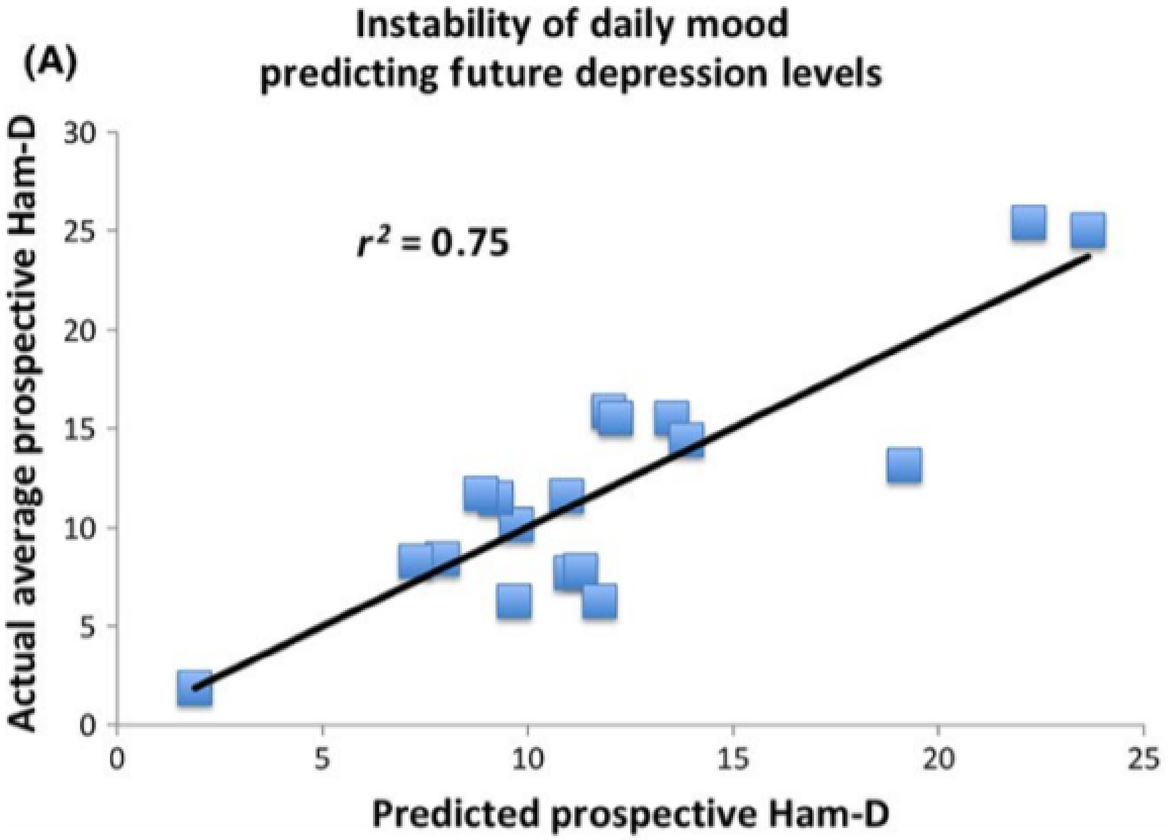


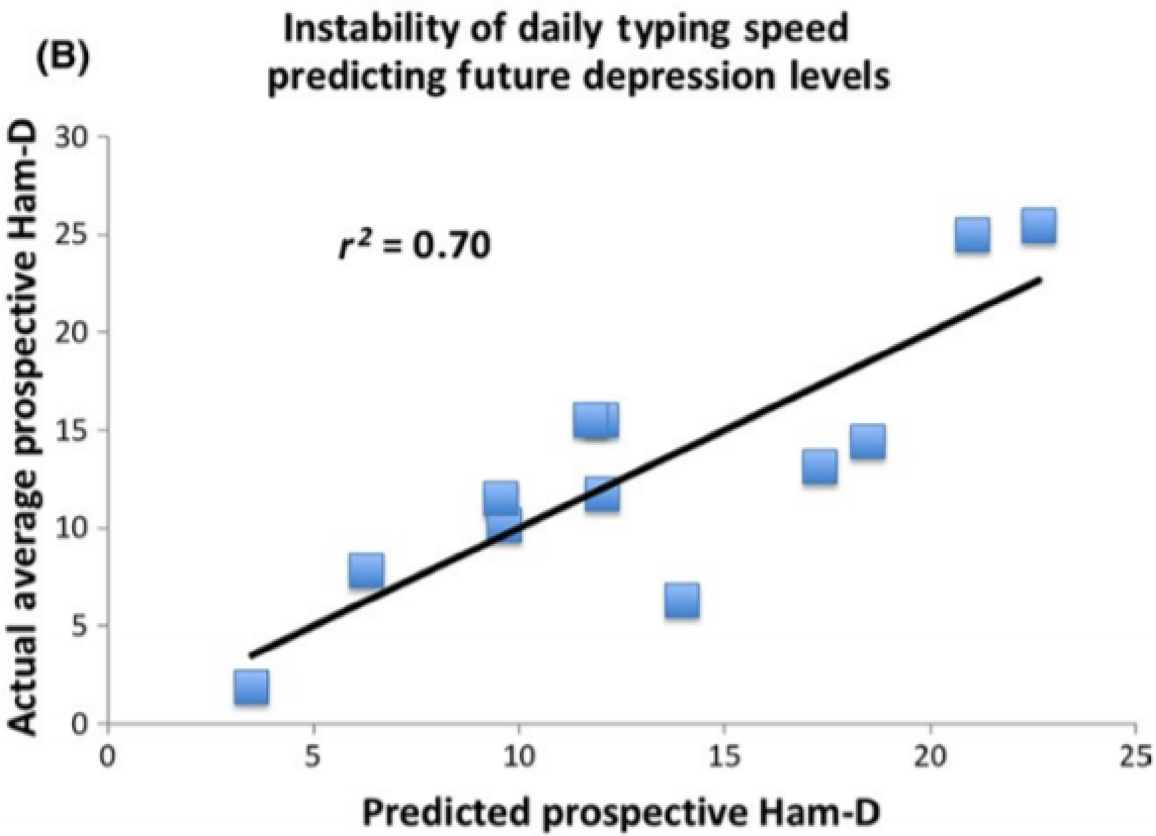
Zulueta et al, JMIR 2018



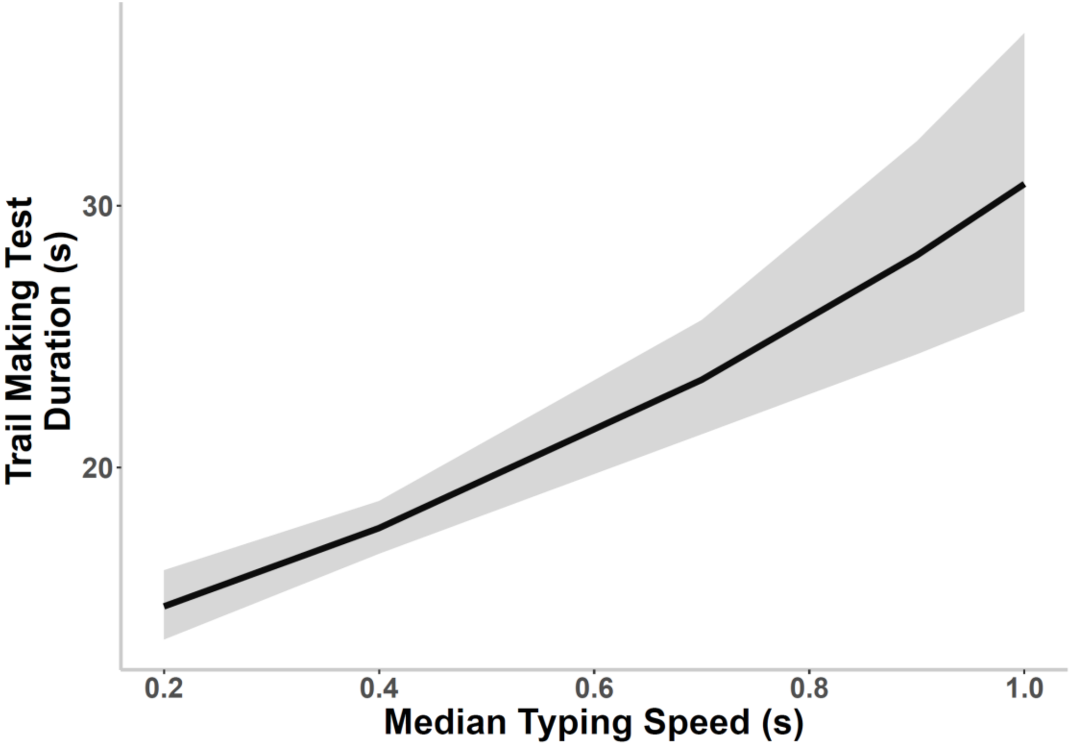


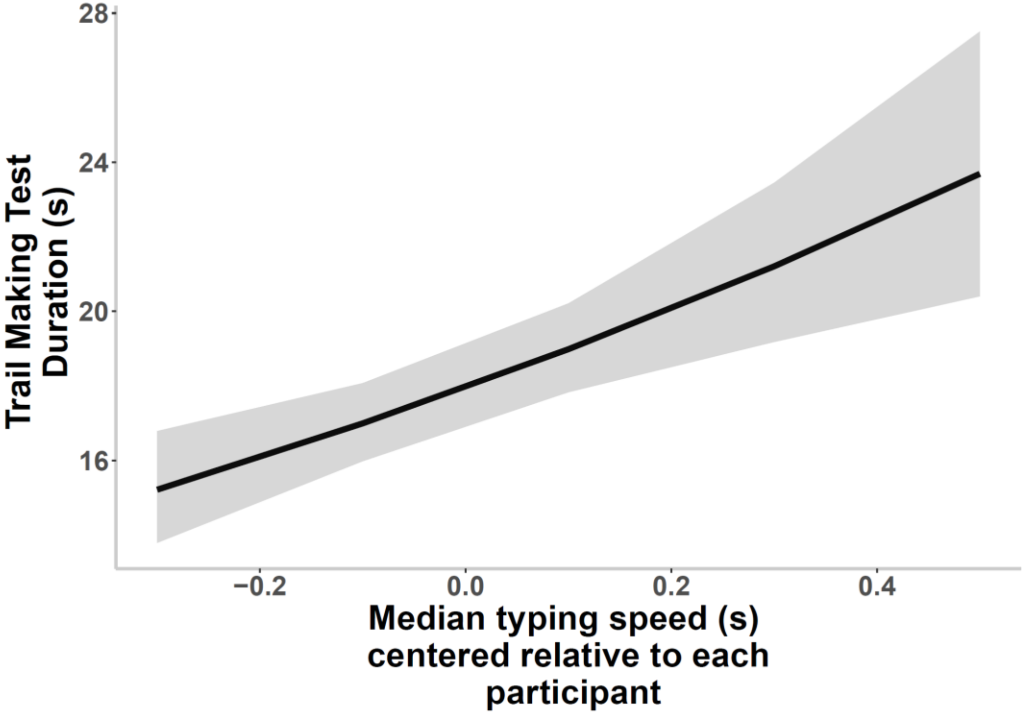
Zulueta et al, JMIR 2018





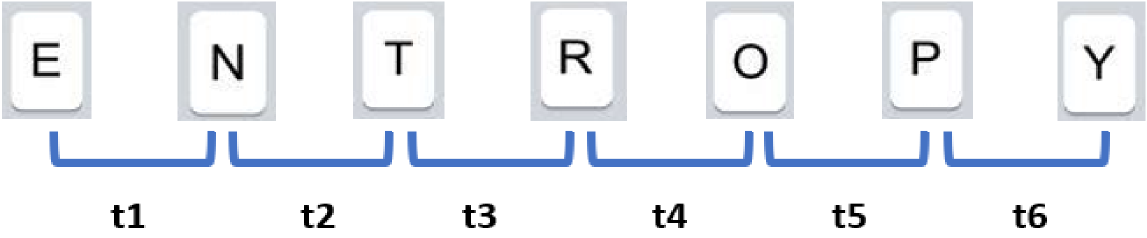
Stange et al, Bipolar Disorders 2018



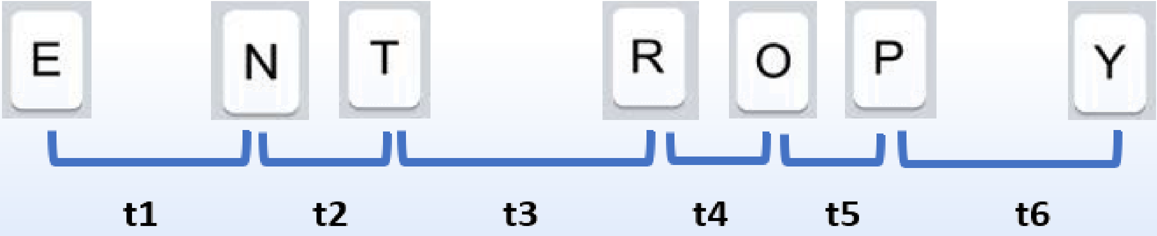


Ross et al, Brain and Behavior 2021

TIME-SERIES OF KEYPRESSES



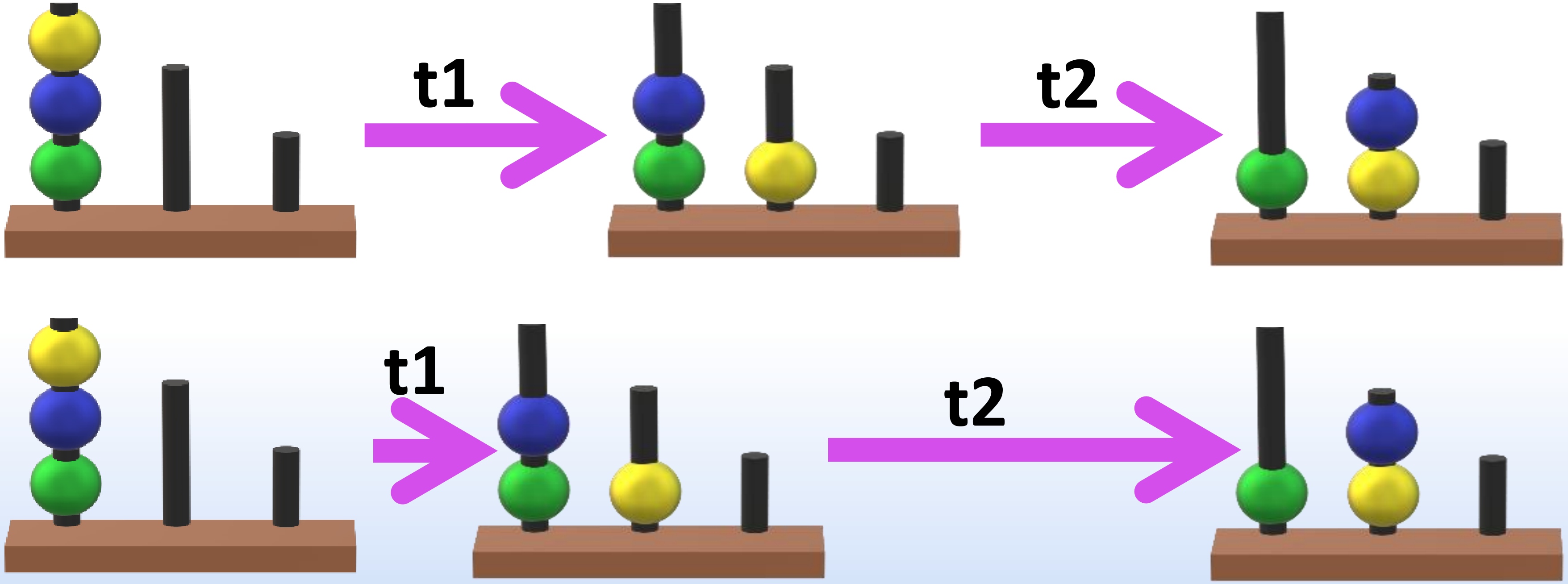
↓ entropy, ↑ regularity time-series



↑ entropy, ↓ regularity time-series

Ajilore et al, Frontiers in Psych 2025

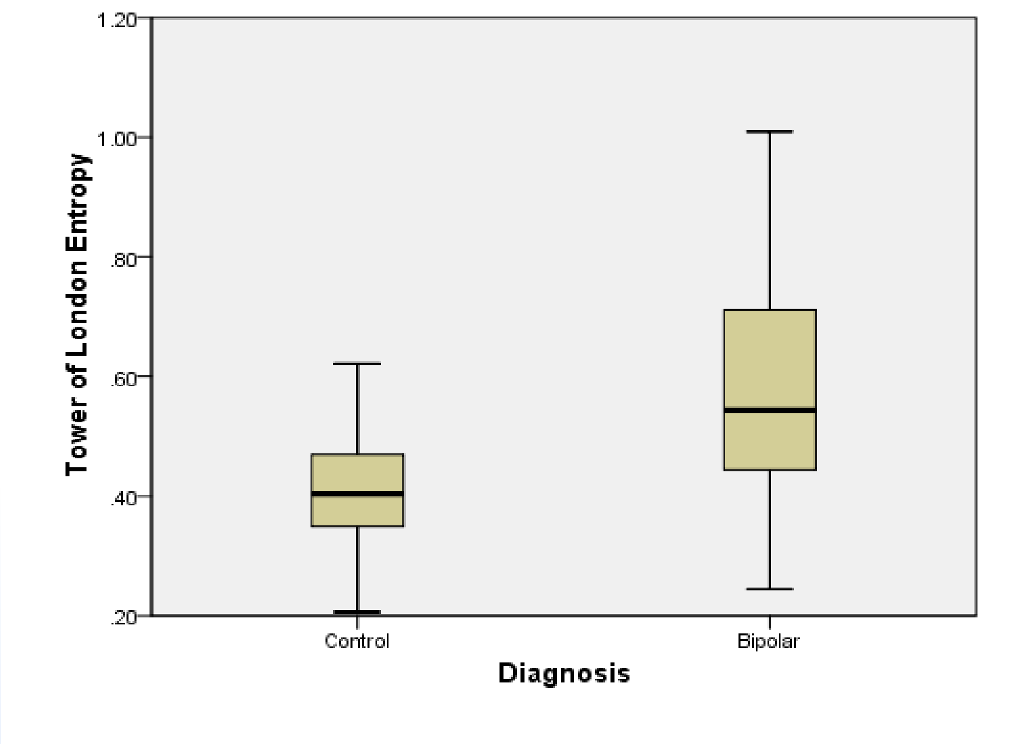
TIME-SERIES OF TOWER OF LONDON MOVES

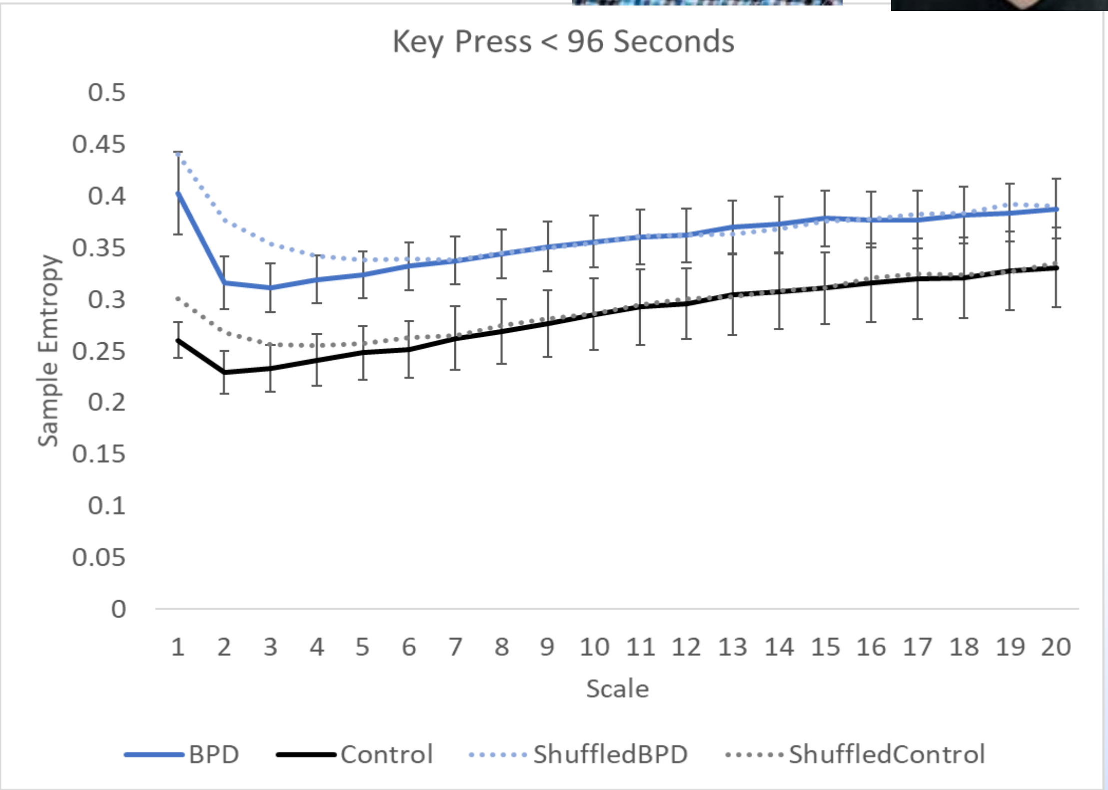


↓ entropy, ↑ regularity time-series

↑ entropy, ↓ regularity time-series

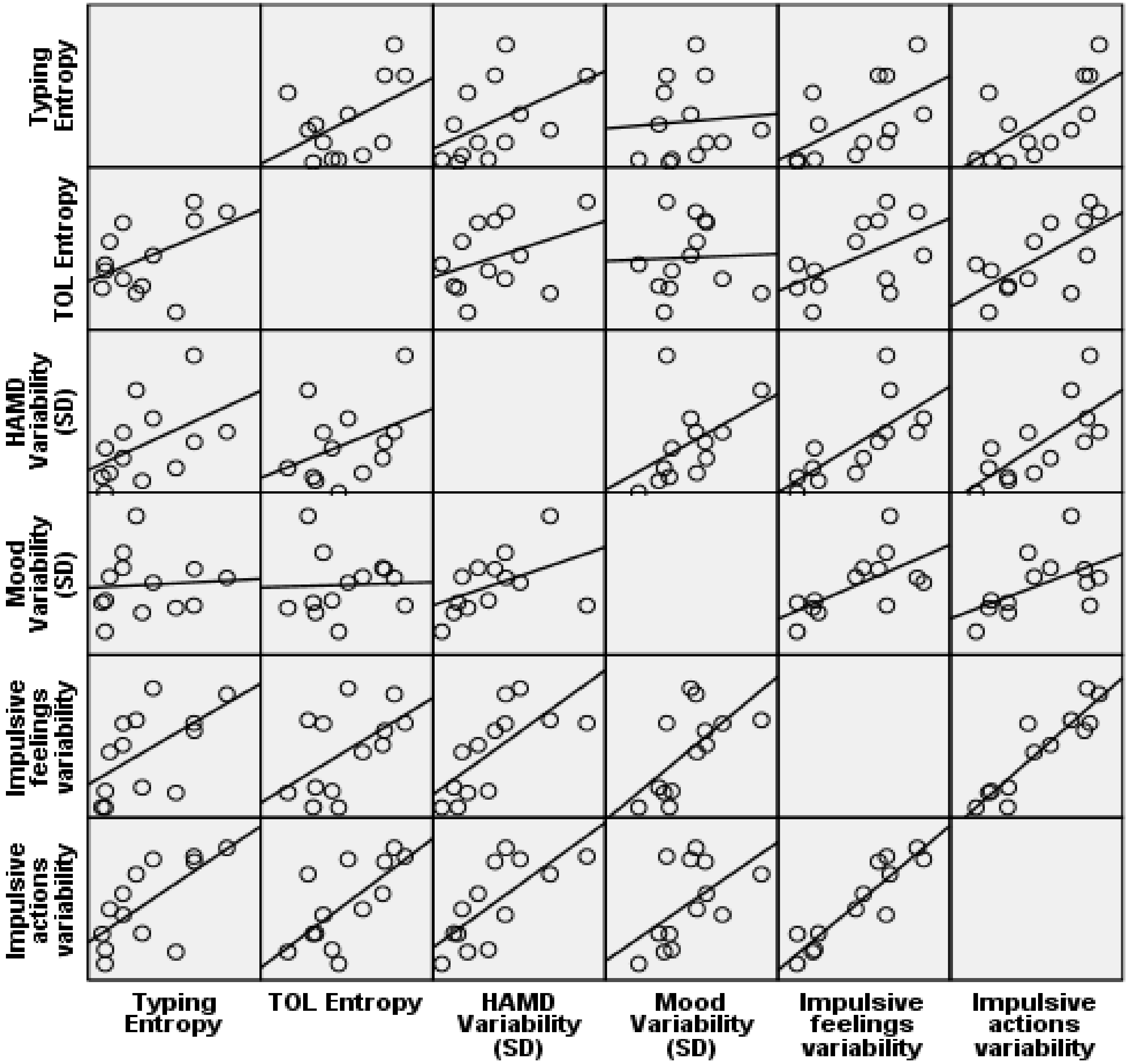
Ajilore et al, Frontiers in Psych 2025



Participants with bipolar disorder demonstrate significantly increased entropy/decreased regularity in move times for the Tower of London task and in typing ($p < .05$)

Ajilore et al, Frontiers in Psych 2025

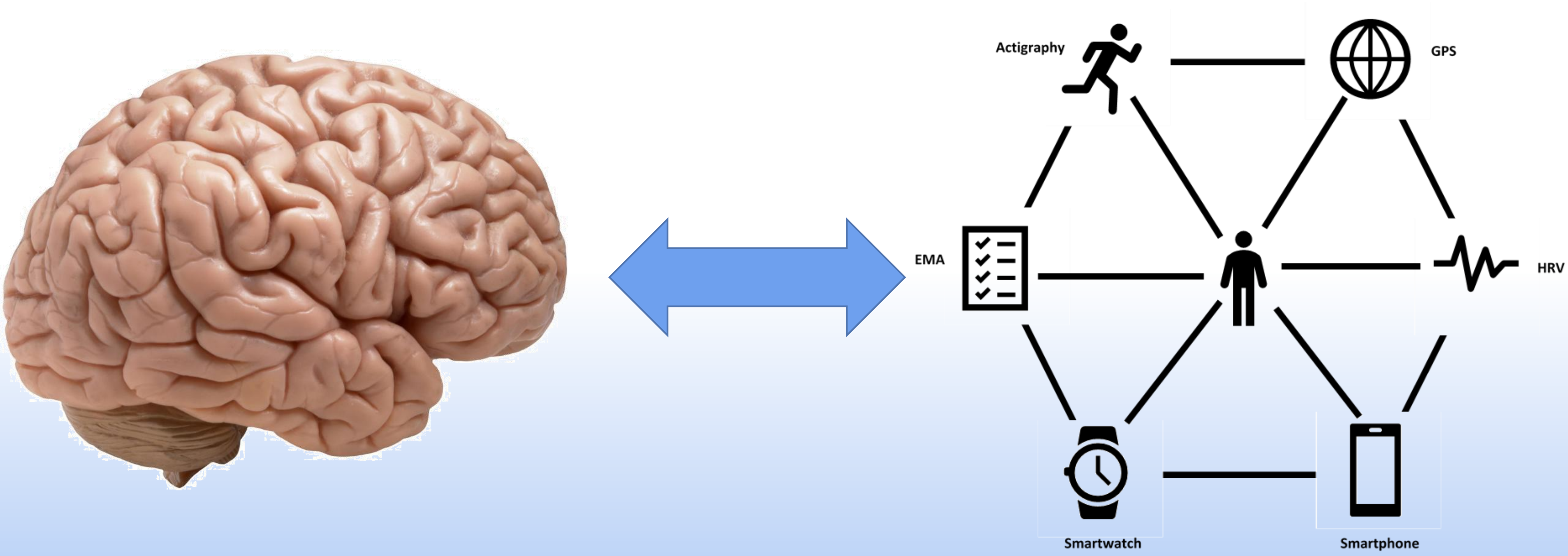


In participants with bipolar disorder, typing entropy was significantly correlated:

- TOL entropy (r=.53,p=.03)
- HAMD variability (r=.5, p=.03)
- Variability in impulsive actions (r=.55, p =.04)
- Variability in impulsive feelings (r=.63, p=.02).

Ajilore et al, Frontiers in Psych 2025

LINKING NEURAL AND DIGITAL SIGNATURES OF AFFECTIVE DISORDERS



UNOBTRUSIVE MONITORING OF AFFECTIVE SYMPTOMS AND COGNITION USING KEYBOARD DYNAMICS (UNMASCK)

UNMASCK - APPROACH

- Specific Aim 1. To evaluate whether keyboard dynamics prospectively predict brain network correlates of cognitive dysfunction in 132 participants (100 with mood disorders, 32 controls) using multimodal neuroimaging (diffusion imaging, task-based and resting functional imaging)

- Specific Aim 2. To evaluate whether keyboard dynamics prospectively predict changes in clinical mood symptoms in 132 participants (100 with mood disorders, 32 controls) (increased depressive and/or manic symptoms)

- Exploratory Aim. To examine whether the relationship between keyboard dynamics and clinical mood symptoms is mediated in a mechanistic way by alterations in brain network properties.

UNMASCK - APPROACH

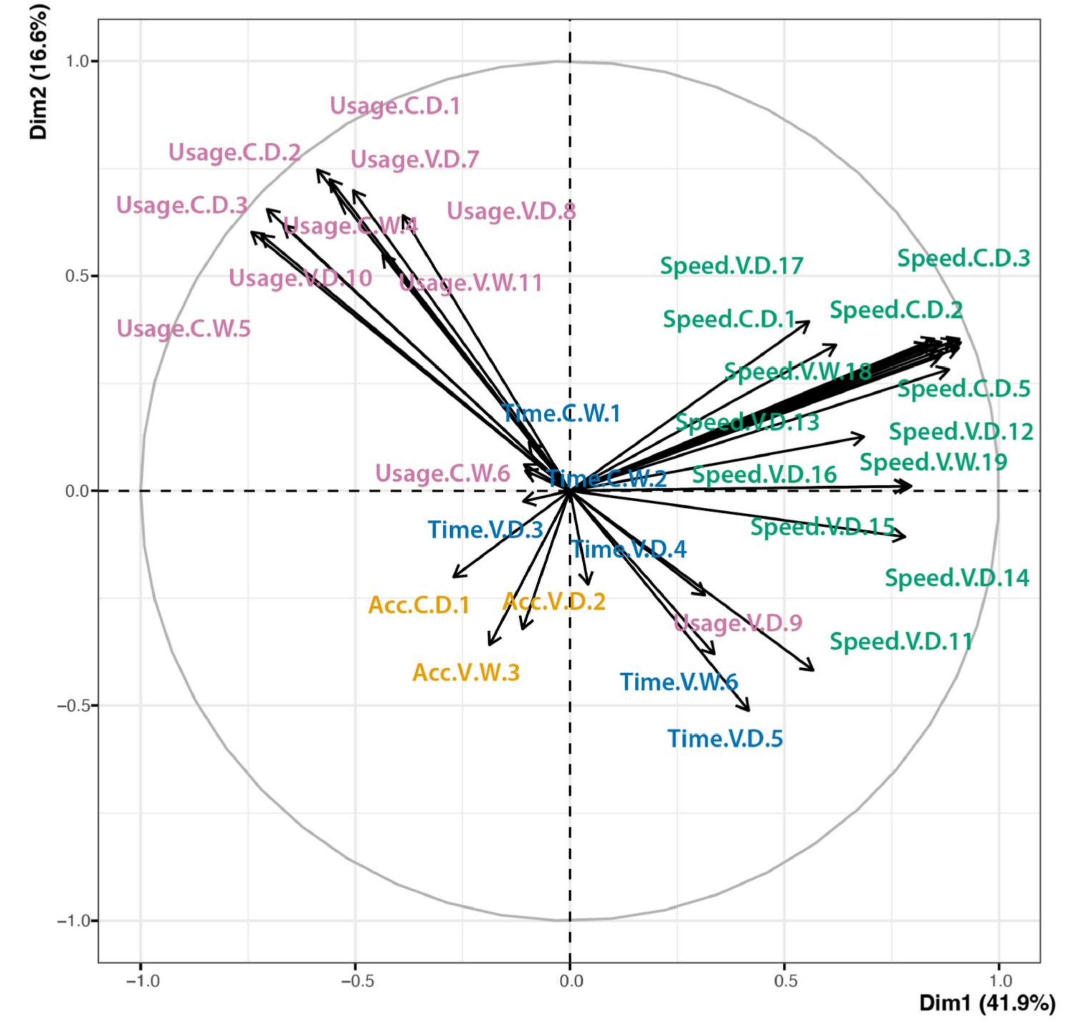
Baseline Assessment (T0)	2 weeks of BiAffect	1st Scan 2nd Assessment (T1)	2 weeks of BiAffect	2nd Scan 3rd Assessment (T2)

BIAFFECT METRIC	CONNECTOMIC CORRELATE	COGNITIVE DOMAIN/CONSTRUCT
Typing speed	Structural brain network Efficiency Interhemispheric Efficiency	Processing speed
Instability in typing speed	Reduced nodal efficiency in ventrolateral prefrontal cortex/altered modularity	Response inhibition
Backspace	Reduced nodal efficiency in anterior cingulate cortex	Performance monitoring
Autocorrect	Reduced nodal efficiency in salience networks	Attention

WHAT TYPING FEATURES MAP ONTO COGNITION?

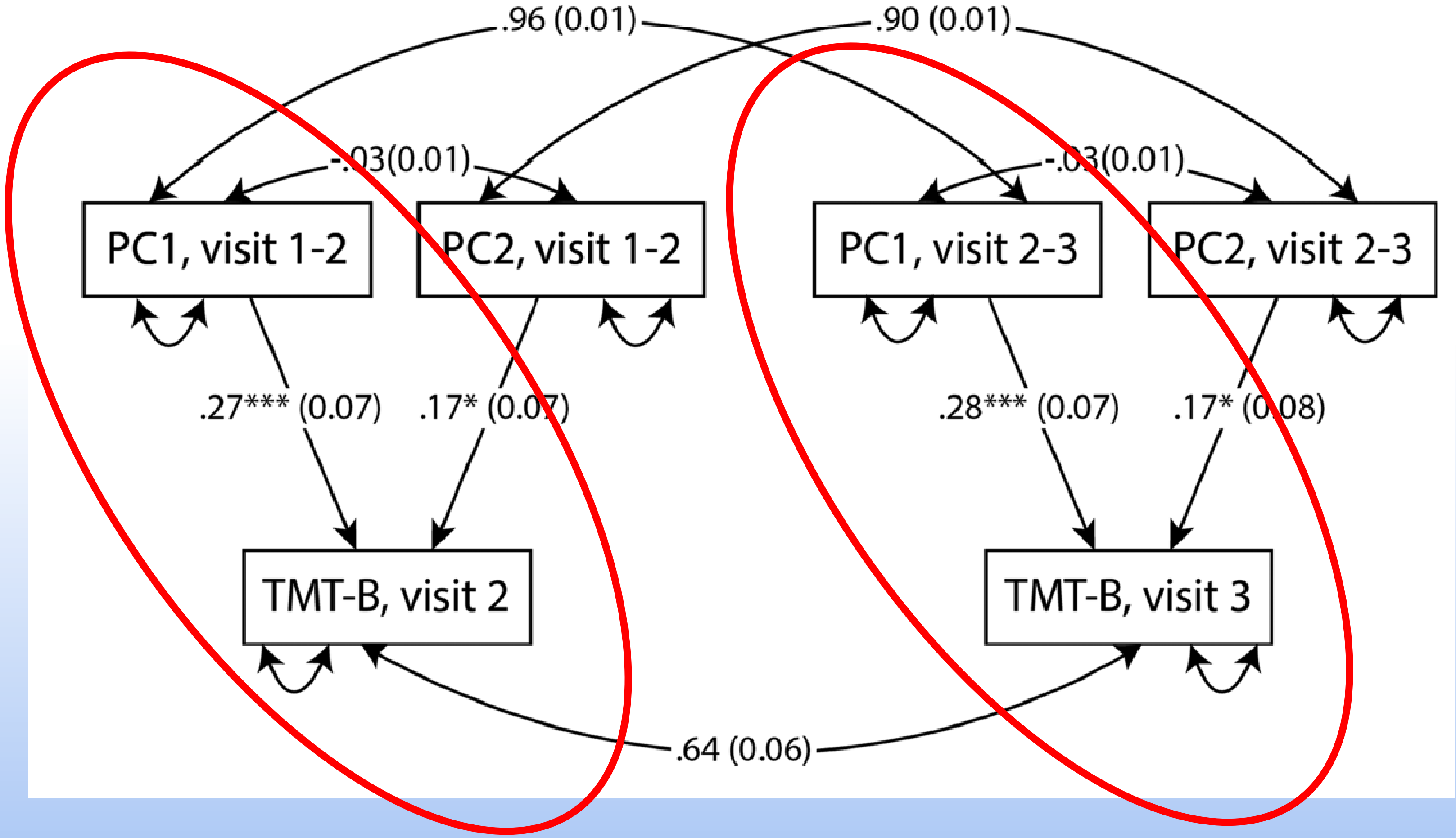
PRINCIPLE COMPONENT ANALYSIS OF TYPING FEATURES

- PC1 – Typing Speed
- PC2 – Typing Volume



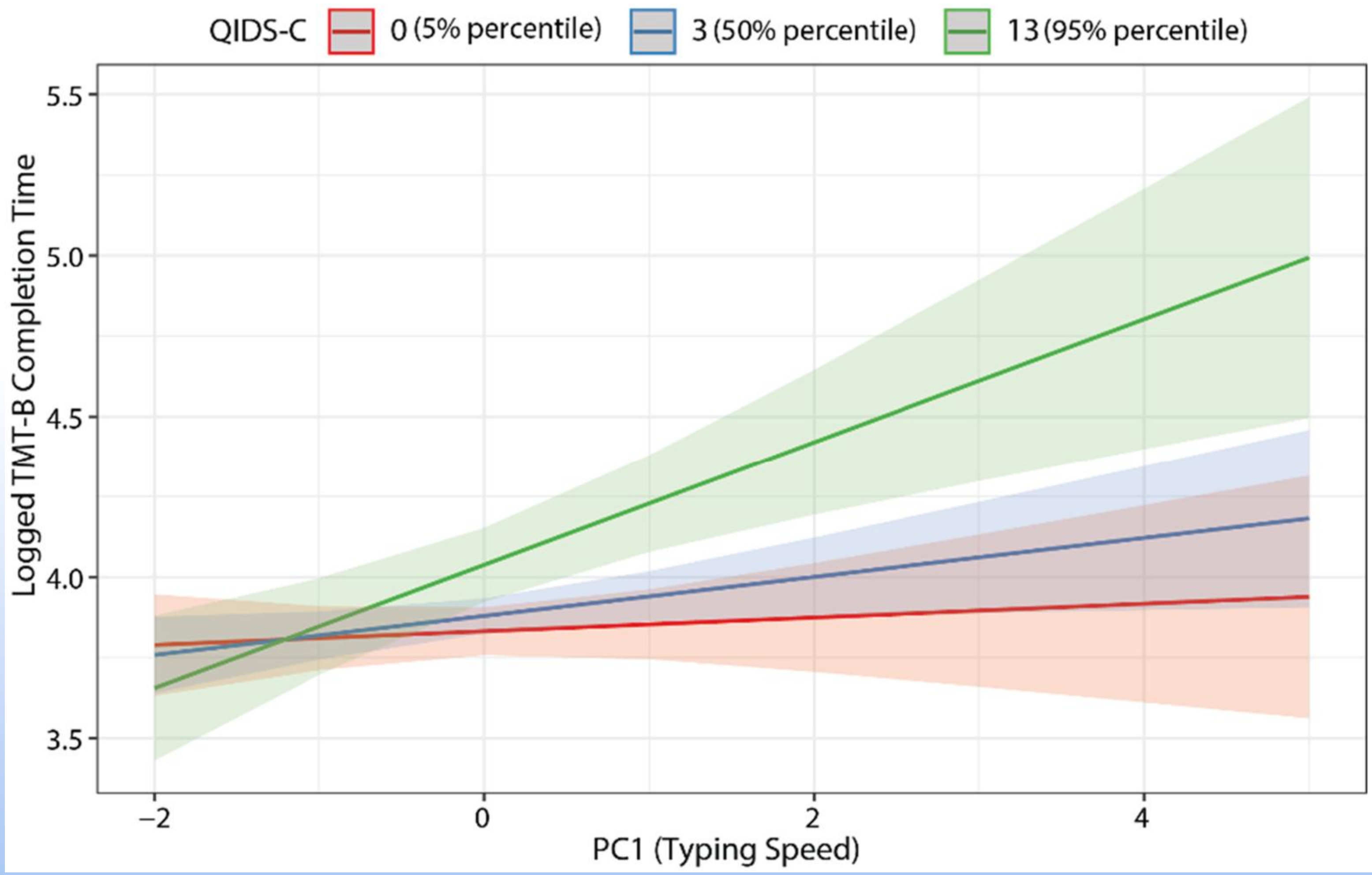
Ning et al, 2025

TYPING SPEED PREDICTS TMT-B PERFORMANCE



Ning et al, 2025

DEPRESSION MODERATES THE RELATIONSHIP BETWEEN TYPING SPEED AND PROCESSING SPEED



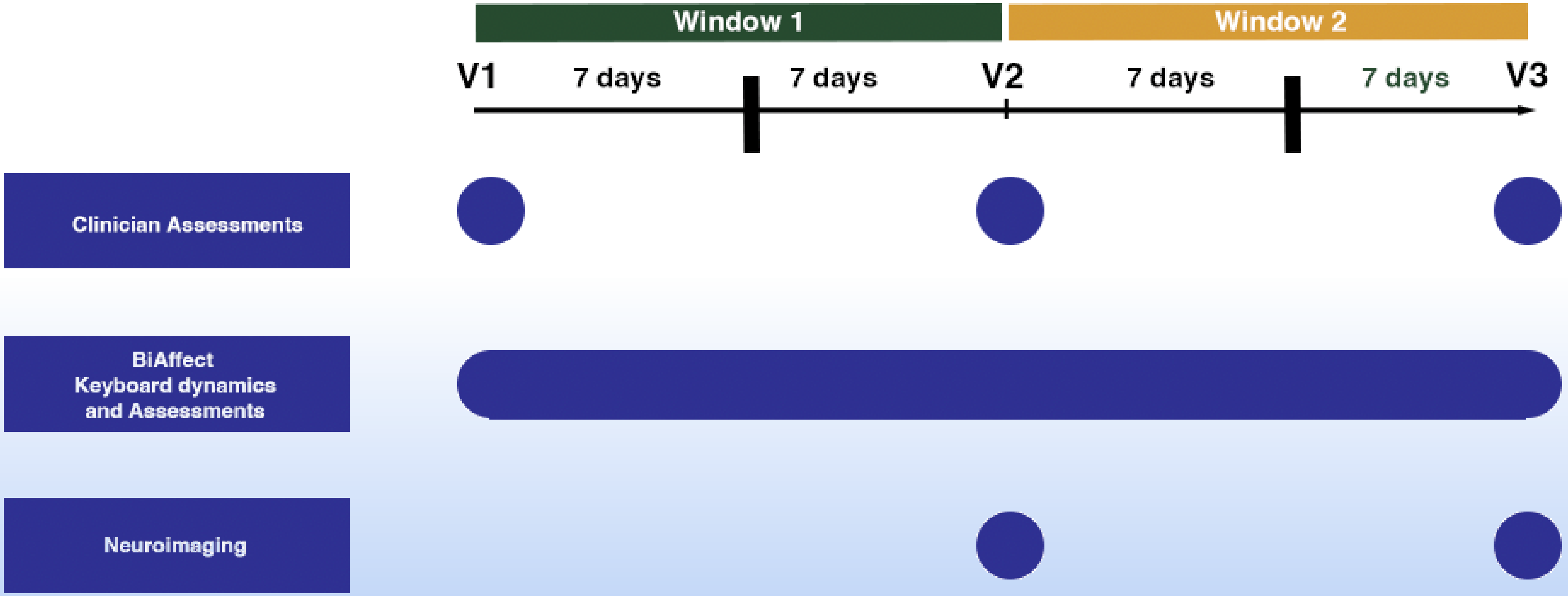
Ning et al, 2025

SUMMARY

- Typing features such as typing speed and typing volume predict processing speed

- The relationship between typing speed and processing speed is strongest for participants with more depressive symptoms

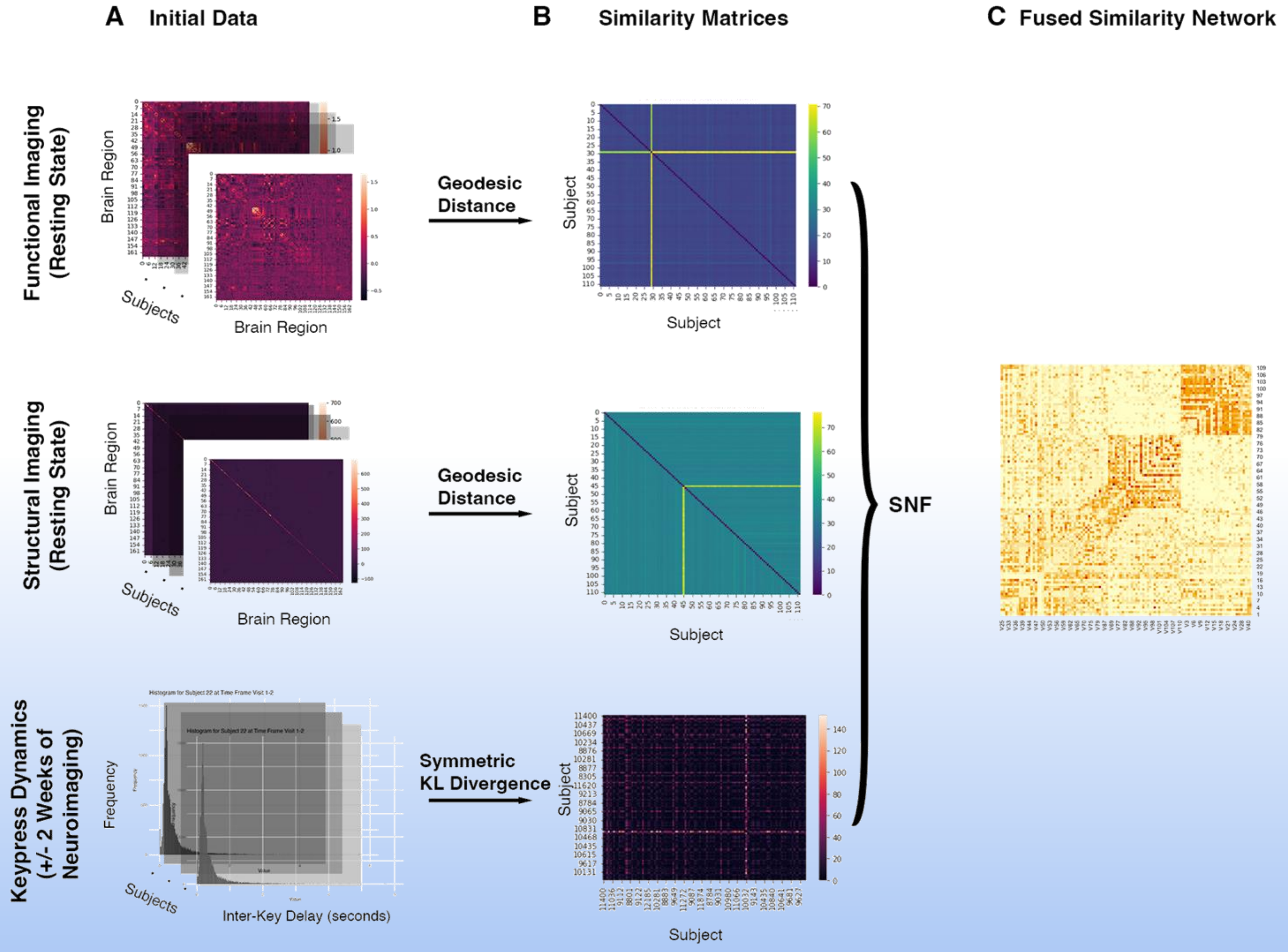
UNMASCK STUDY TIMELINE OVERVIEW:

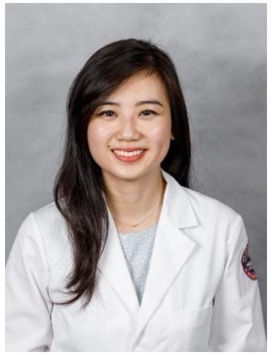


WHICH BRAIN NETWORKS ARE ASSOCIATED WITH TYPING FEATURES AND COGNITION?

Identify altered brain networks via digital phenotypes by extracting features from multimodal data sets (i.e., structural and functional neuroimaging and longitudinal keypress data) that can be associated with predicting differences in cognitive performance.

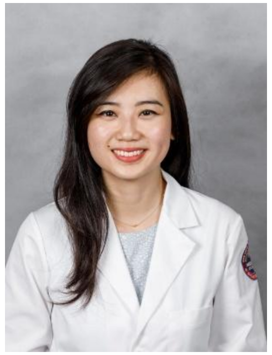
SIMILARITY NETWORK FUSION





Nguyen et al, in prep

CLUSTER ANALYSIS RESULTS



- Inputs:
  1) Functional Neuroimaging Data
  2) Structural Neuroimaging Data
  3) Smartphone Keyboard Typing Data

- SNF clustered participants by similarity from all three inputs
- SNF → 3 clusters
- Examined cluster differences to use in a data driven approach for regression models

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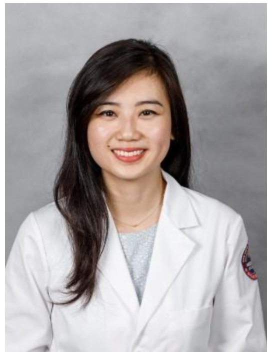
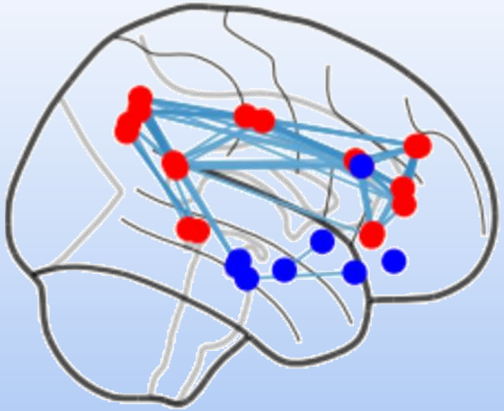
CLUSTER DIFFERENCES



- Age
- Gender
- Typing Speed
- Cognitive Function
- Between-network Functional Connectivity (centered on salience network)



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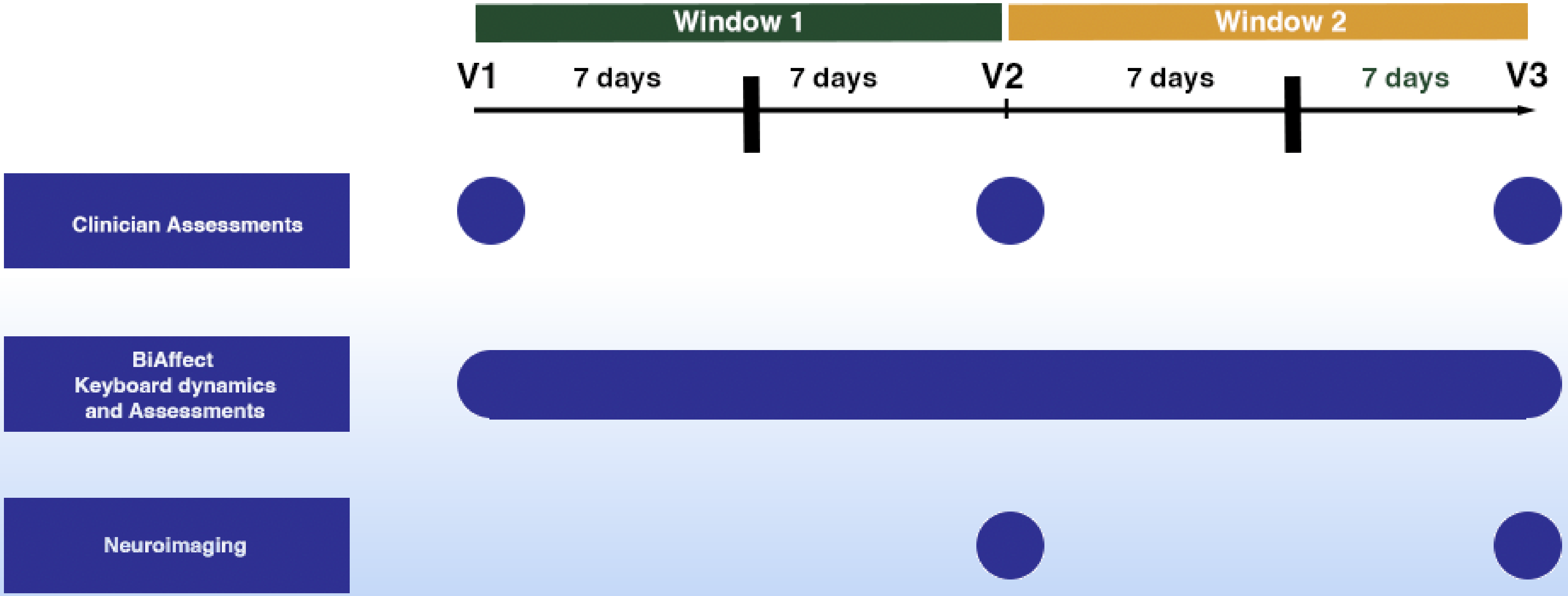
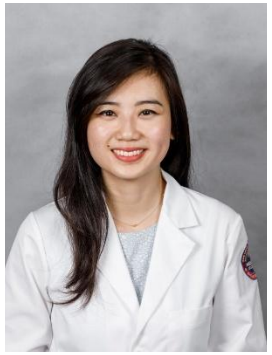
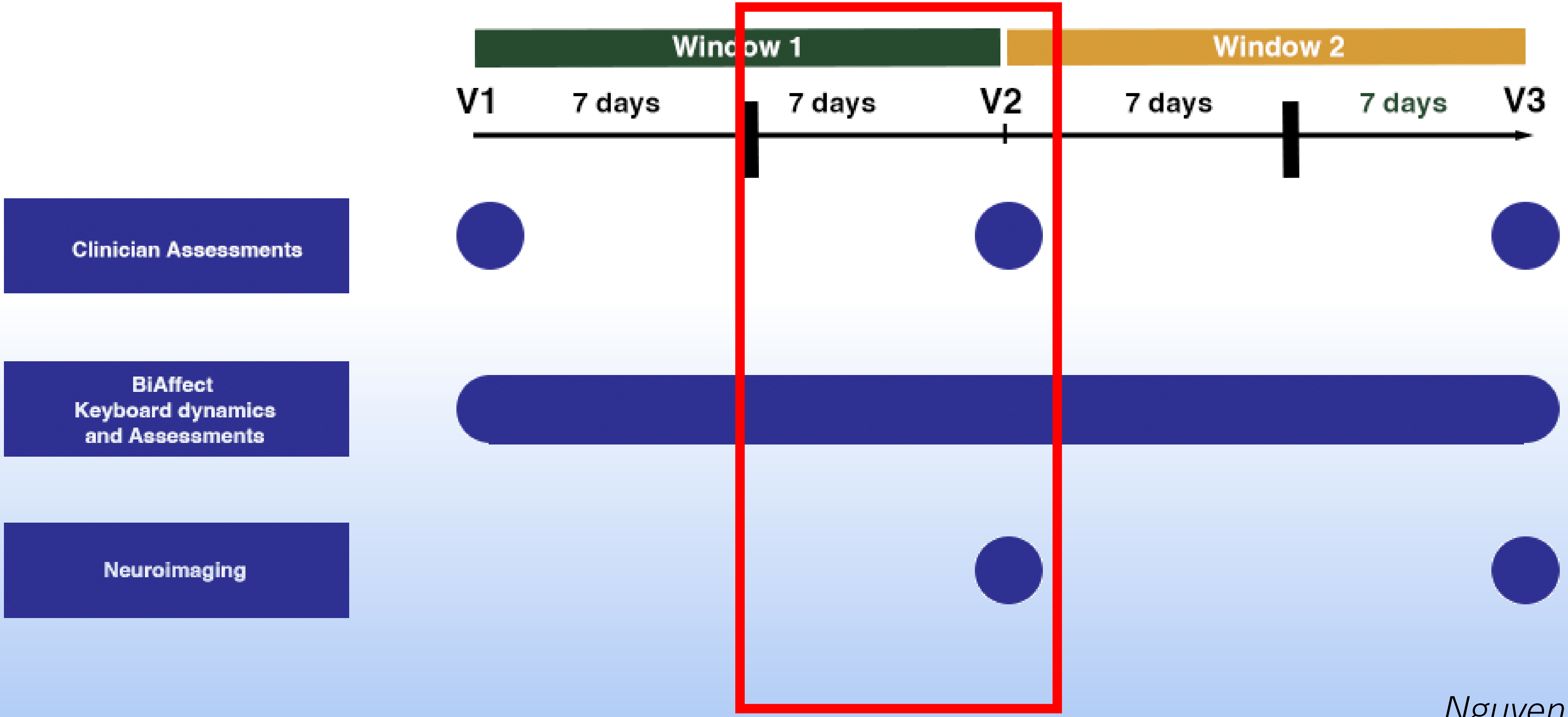
HOW DO THESE FEATURES RELATE TO EACH OTHER?

UNMASCK STUDY TIMELINE OVERVIEW:



TYPING SPEED PREDICTS BRAIN CONNECTIVITY





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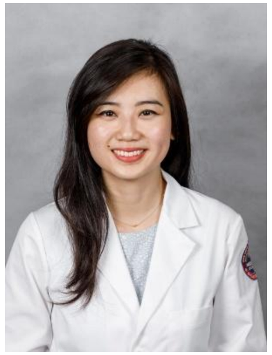
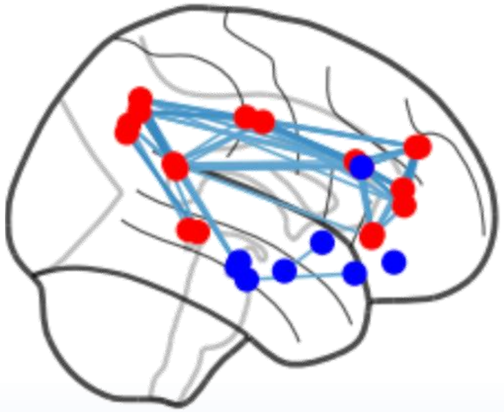
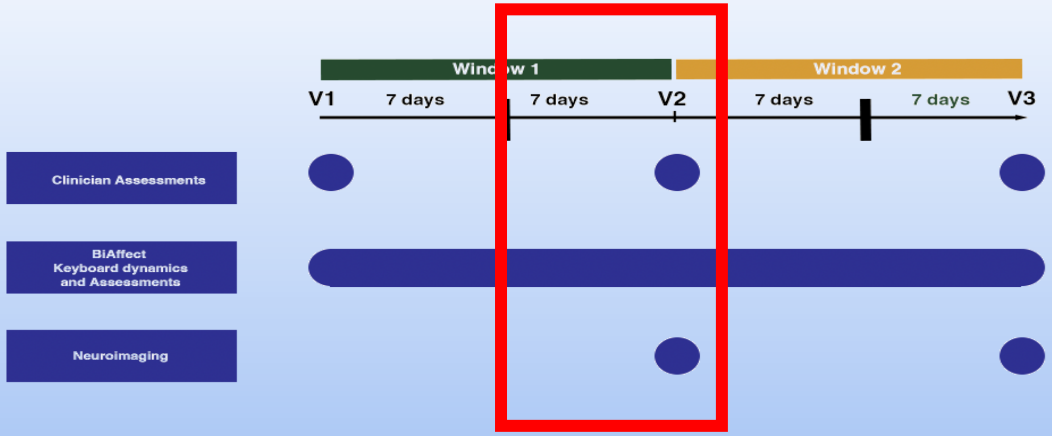


1 Week Before V2 median IKD

	log(IKD)				log(IKD)				log(IKD)			
Predictors	*Estimates*	*std. Beta*	*p*	*std. p*	*Estimates*	*std. Beta*	*p*	*std. p*	*Estimates*	*std. Beta*	*p*	*std. p*
(Intercept)	-1.52	0.81	**<0.001**	**<0.001**	-1.48	0.87	**<0.001**	**<0.001**	-1.47	0.88	**<0.001**	**<0.001**
SN to DMN	-0.06	-0.09	**0.009**	**0.008**	-0.05	-0.07	**0.025**	**0.023**	-0.06	-0.09	**0.026**	**0.025**
age					0.12	0.17	**<0.001**	**<0.001**	0.12	0.17	**<0.001**	**<0.001**
gender [Female]					-0.09	-0.13	**0.029**	**0.028**	-0.10	-0.14	**0.020**	**0.018**
age × SN to DMN									0.02	0.03	0.408	0.343
gender [Female] × SN to DMN									0.04	0.05	0.366	0.388





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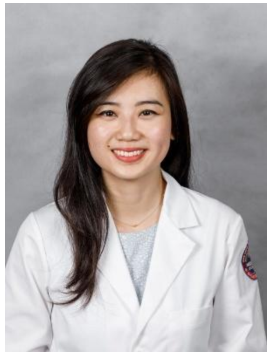
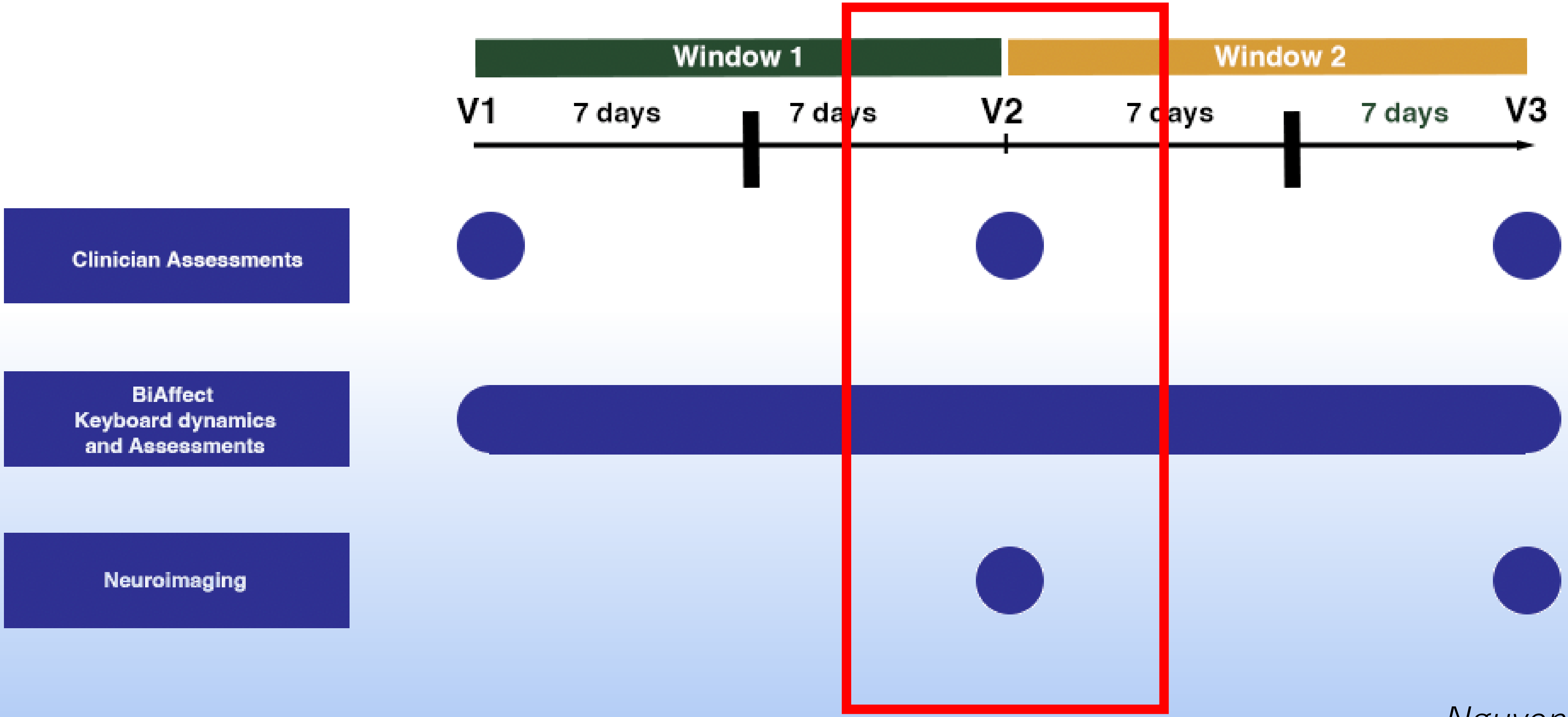
TYPING SPEED IS ASSOCIATED WITH BRAIN CONNECTIVITY





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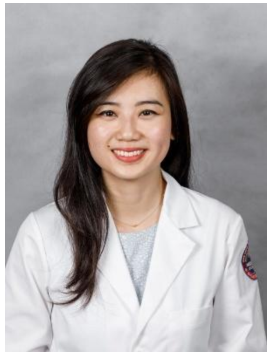
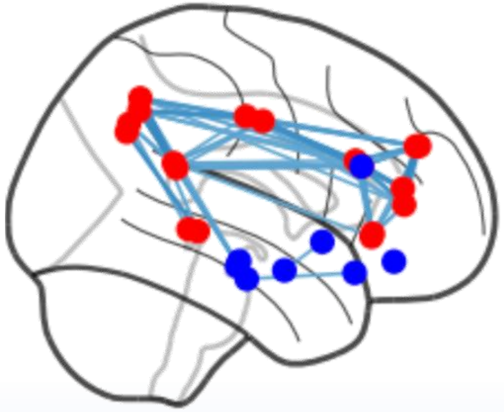
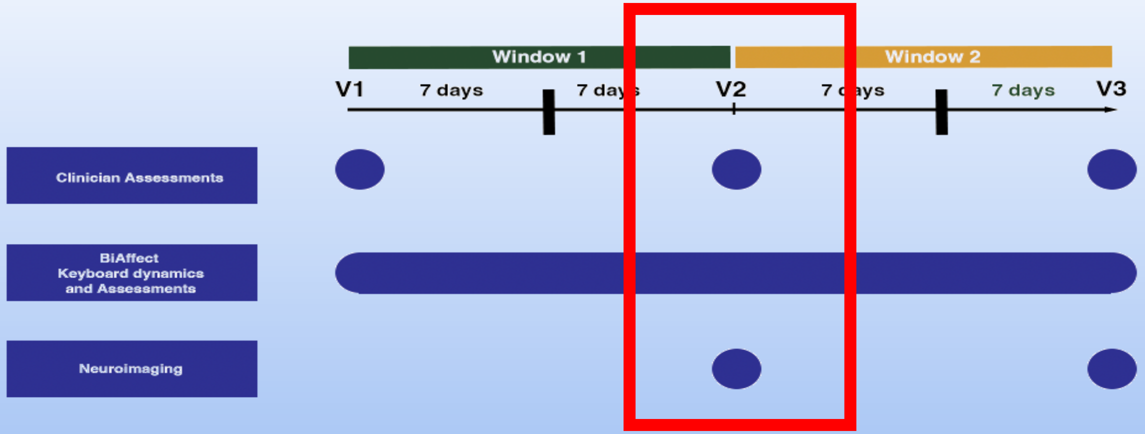


Week of V2 median IKD

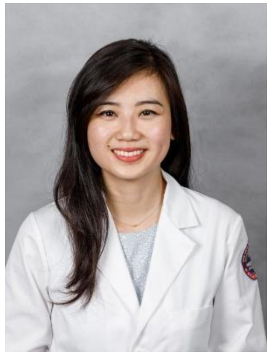
	log(IKD)				log(IKD)				log(IKD)			
Predictors	*Estimates*	*std. Beta*	*p*	*std. p*	*Estimates*	*std. Beta*	*p*	*std. p*	*Estimates*	*std. Beta*	*p*	*std. p*
(Intercept)	-1.52	0.78	**<0.001**	**<0.001**	-1.49	0.83	**<0.001**	**<0.001**	-1.48	0.84	**<0.001**	**<0.001**
SN to DMN	-0.06	-0.09	**0.012**	**0.010**	-0.05	-0.07	**0.035**	**0.029**	-0.06	-0.08	0.051	**0.045**
age					0.12	0.17	**<0.001**	**<0.001**	0.12	0.17	**<0.001**	**<0.001**
gender [Female]					-0.07	-0.10	0.095	0.090	-0.08	-0.11	0.076	0.068
age × SN to DMN									0.02	0.03	0.514	0.425
gender [Female] × SN to DMN									0.03	0.04	0.520	0.533

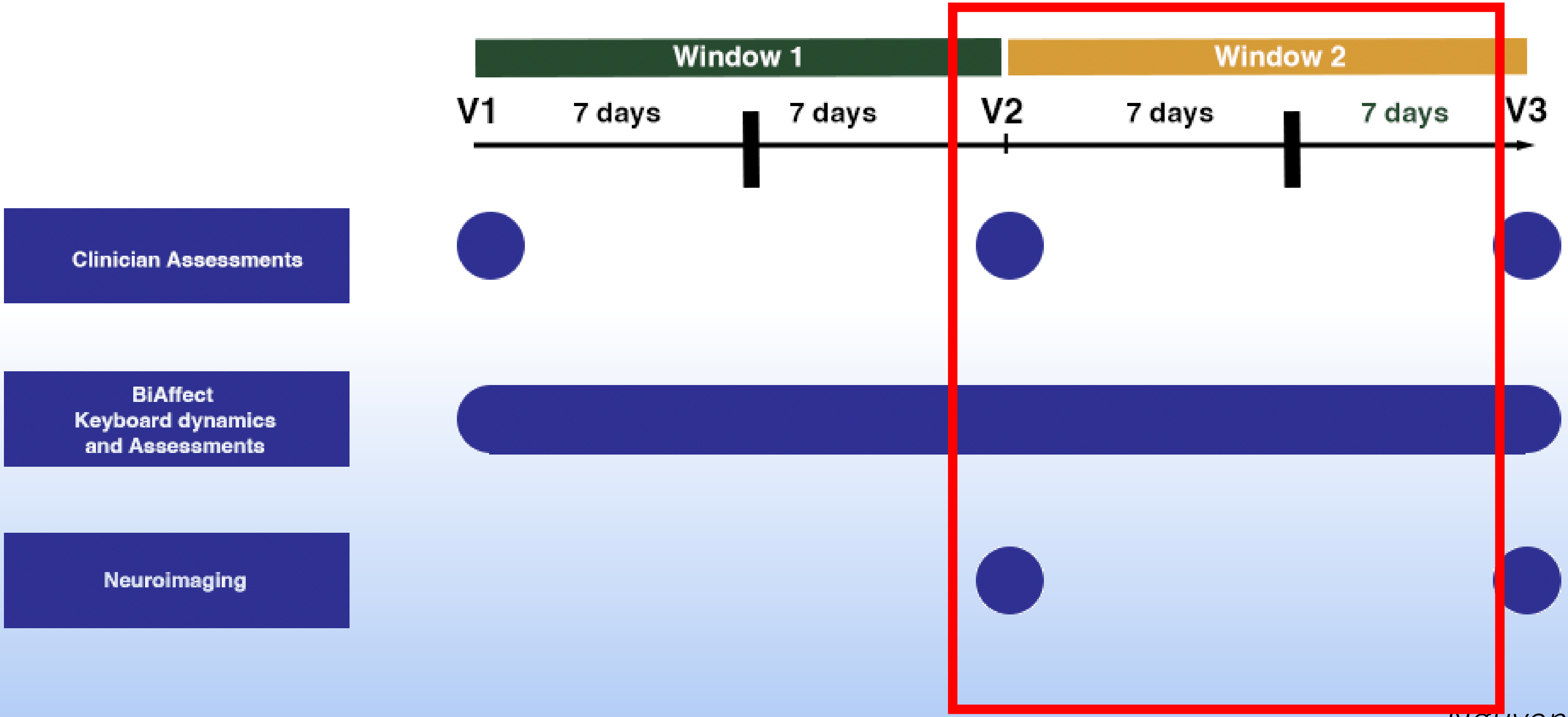




Nguyen et al, in prep

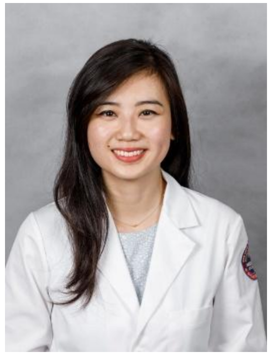
BRAIN CONNECTIVITY PREDICTS TYPING SPEED





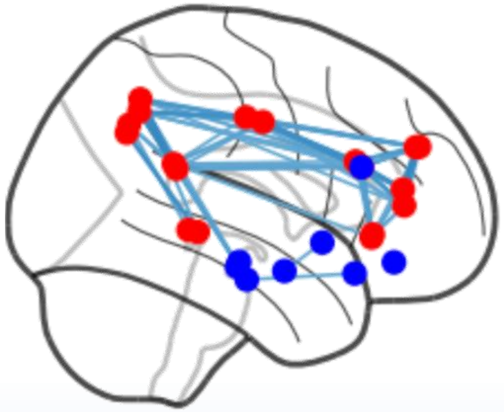
Nguyen et al, in prep

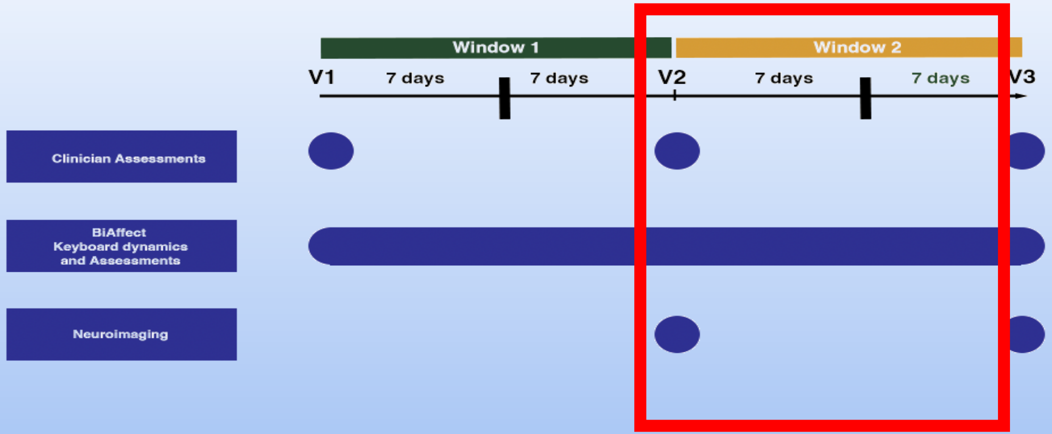
BRAIN CONNECTIVITY PREDICTS TYPING SPEED



2 weeks after V2 median IKD

	log(IKD)				log(IKD)				log(IKD)			
Predictors	*Estimates*	*std. Beta*	*p*	*std. p*	*Estimates*	*std. Beta*	*p*	*std. p*	*Estimates*	*std. Beta*	*p*	*std. p*
(Intercept)	-1.53	0.77	**<0.001**	**<0.001**	-1.50	0.82	**<0.001**	**<0.001**	-1.50	0.82	**<0.001**	**<0.001**
SN to DMN	-0.08	-0.11	**0.002**	**0.002**	-0.06	-0.09	**0.006**	**0.005**	-0.08	-0.11	**0.008**	**0.008**
age					0.13	0.19	**<0.001**	**<0.001**	0.13	0.19	**<0.001**	**<0.001**
gender [Female]					-0.07	-0.10	0.107	0.099	-0.07	-0.11	0.095	0.081
age × SN to DMN									0.01	0.02	0.782	0.619
gender [Female] × SN to DMN									0.04	0.06	0.326	0.348



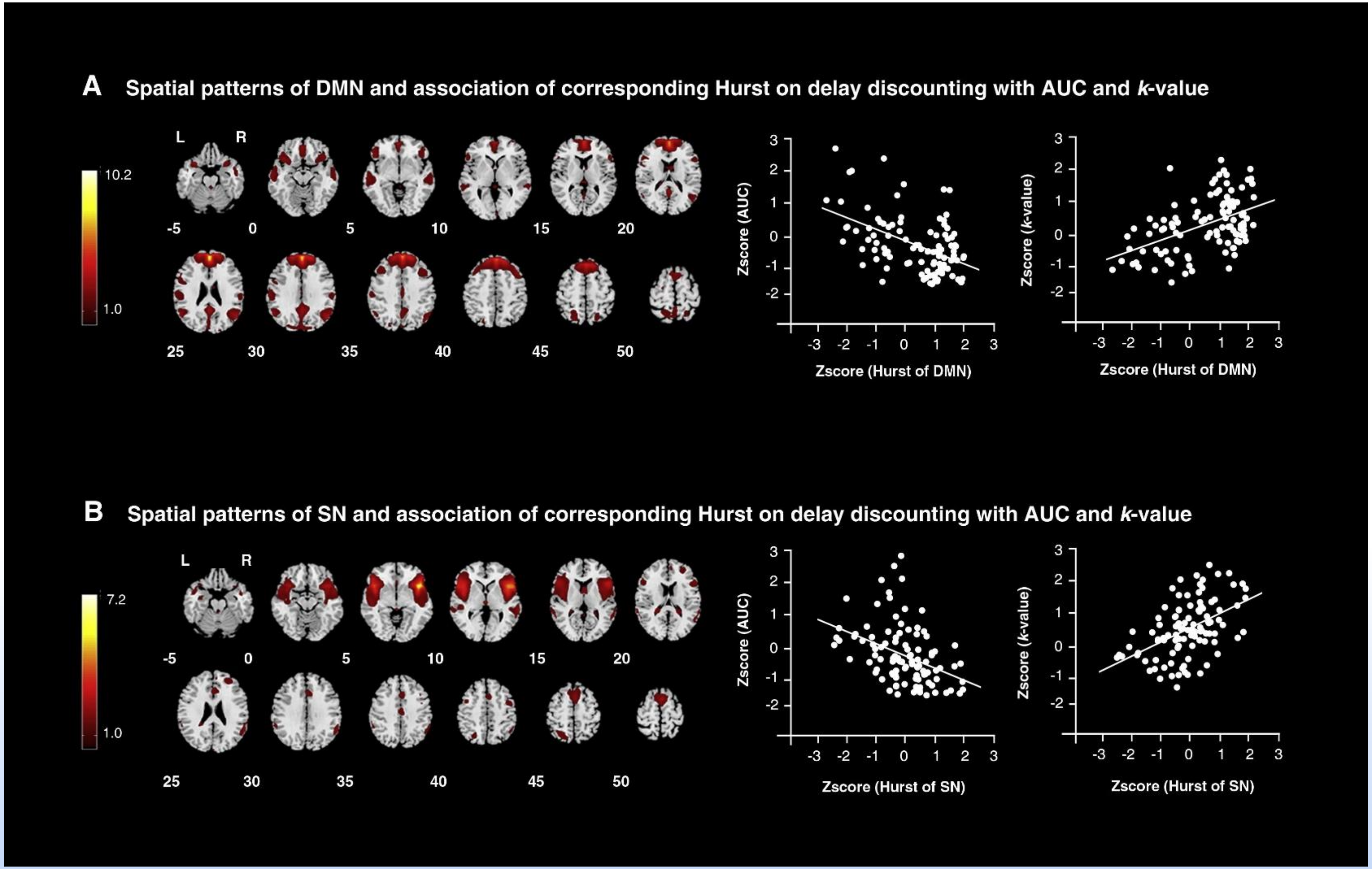


Nguyen et al, in prep

SUMMARY

- Similarity Network Fusion can be used to model joint properties of neuroimaging and digital biomarkers to inform relevant clusters of participants that can identify linked features.

- The salience network may play a key role in linking typing dynamics to cognitive dysfunction in the context of mood disorders



Network dynamics of SN and DMN associated with delayed discounting

(“Give me $5 now, instead of $50 in a week”)

Chen et al, Neuroscience 2017

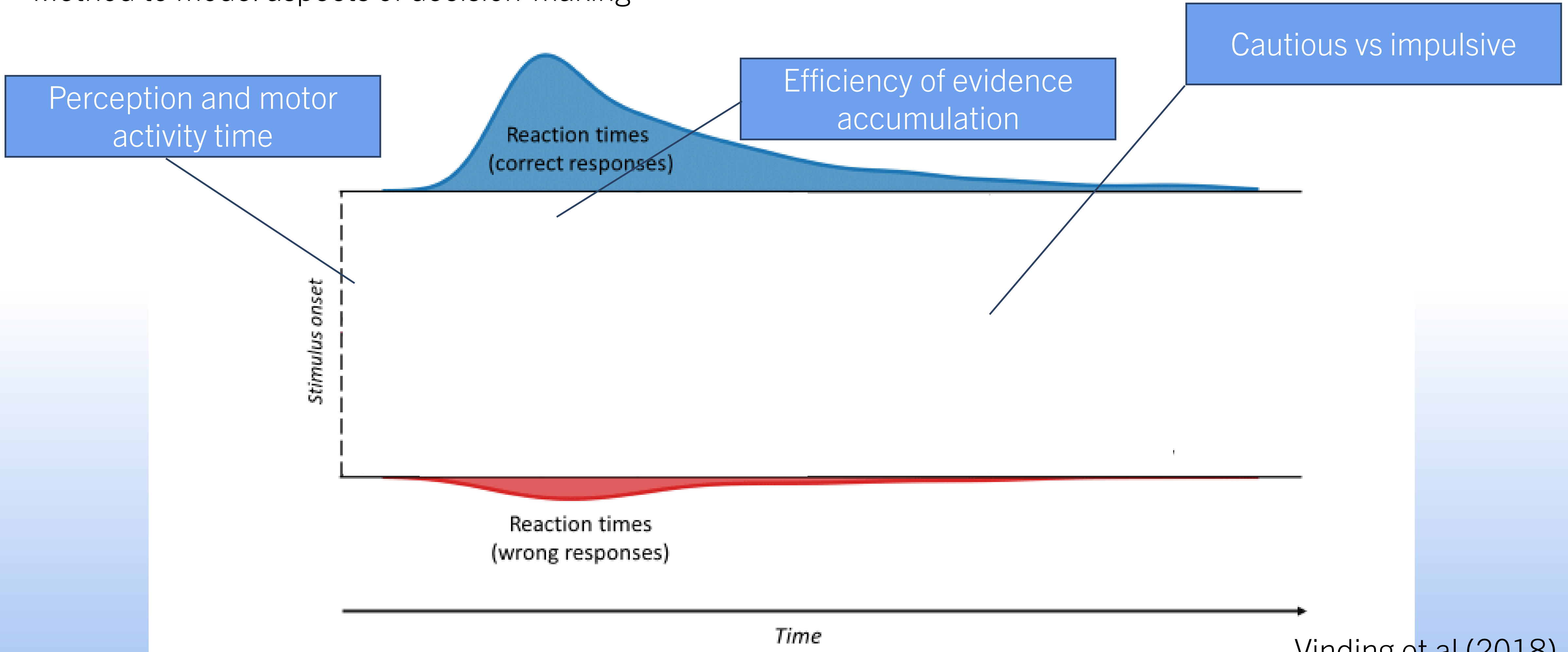
Major Depressive Disorder

Alcohol Use Disorder

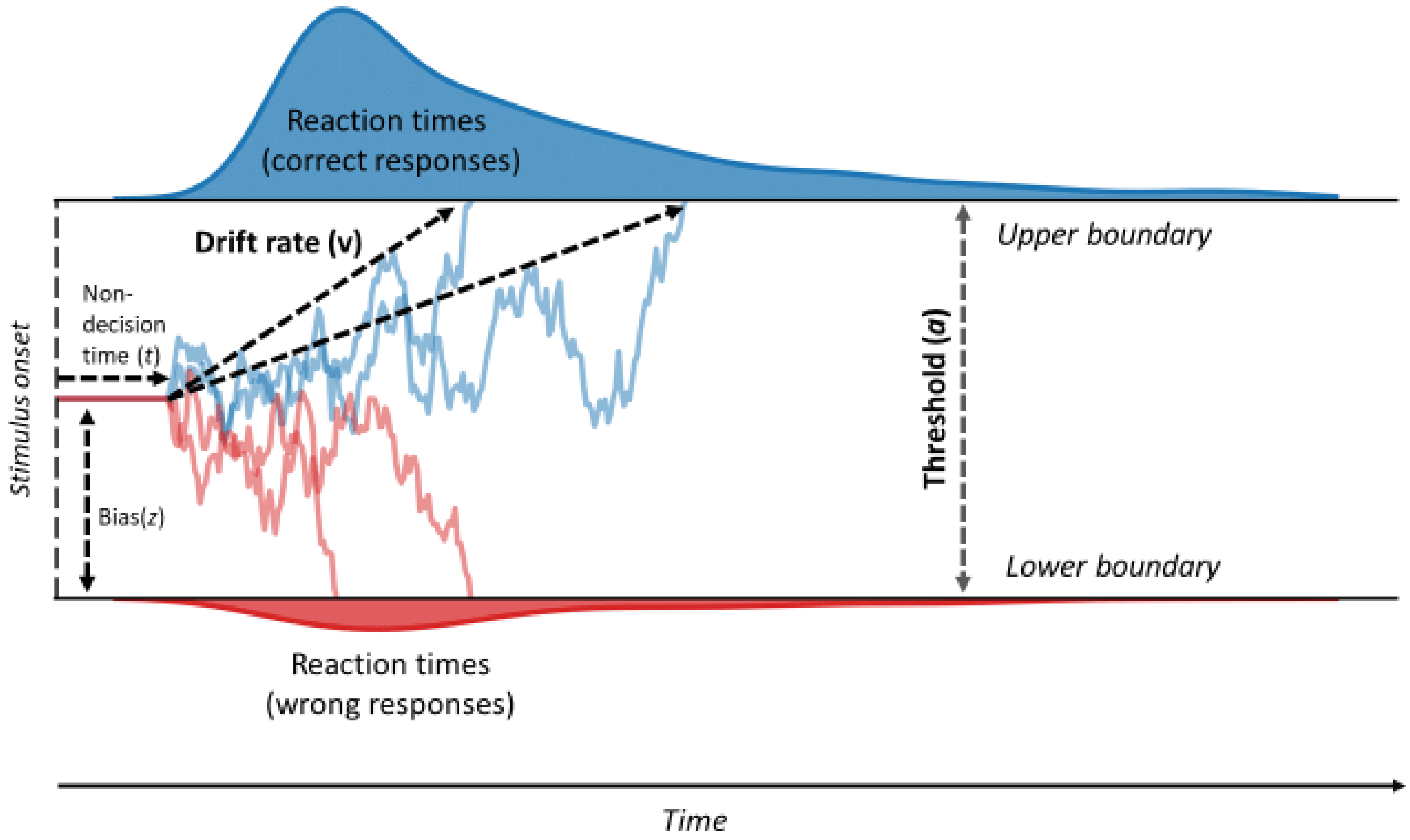
Bipolar Disorder

HIERARCHICAL DRIFT DIFFUSION MODEL (HDDM)

- Method to model aspects of decision-making

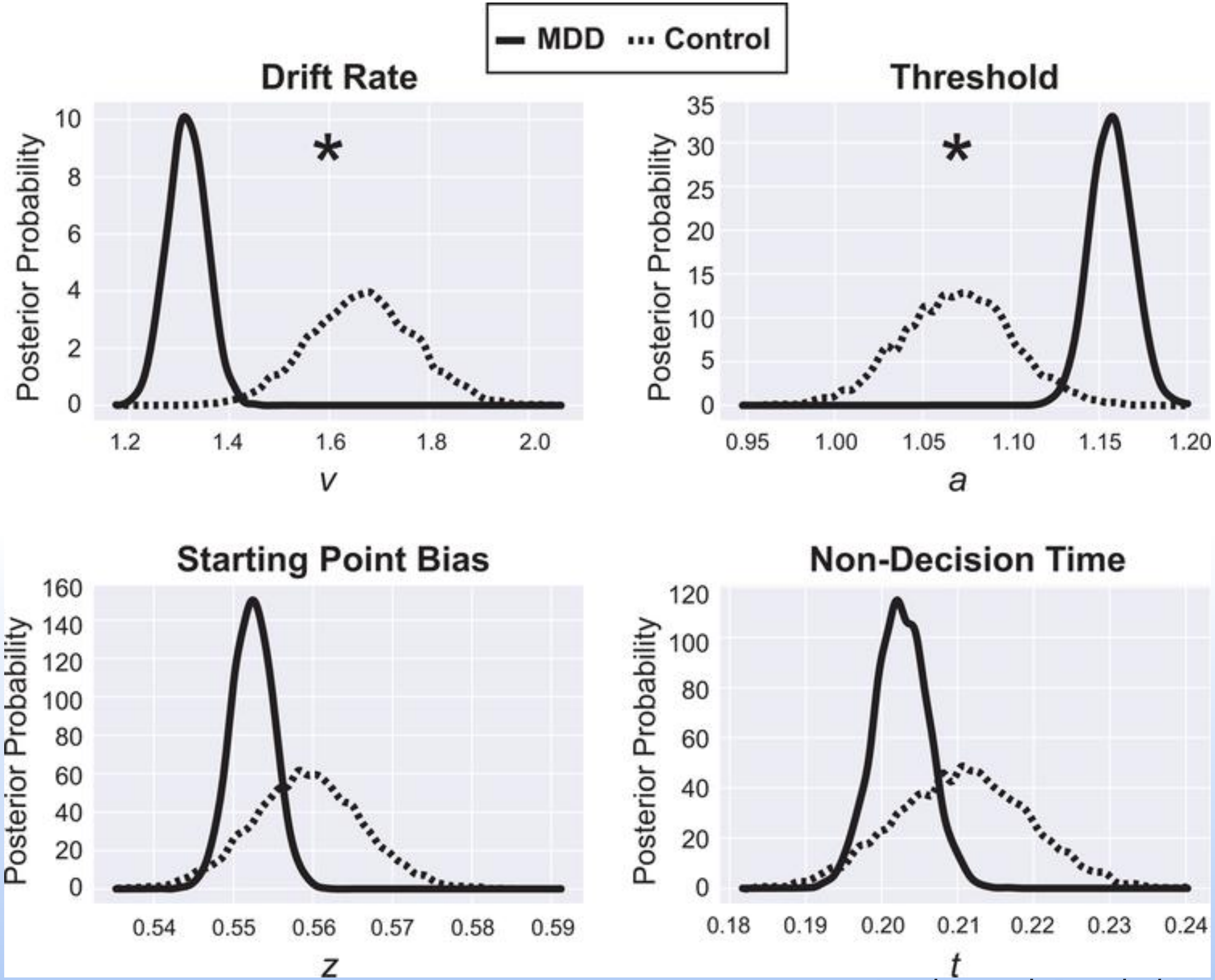


Vinding et al (2018)



Vinding et al (2018)

DISSECTING THE IMPACT OF DEPRESSION ON DECISION-MAKING

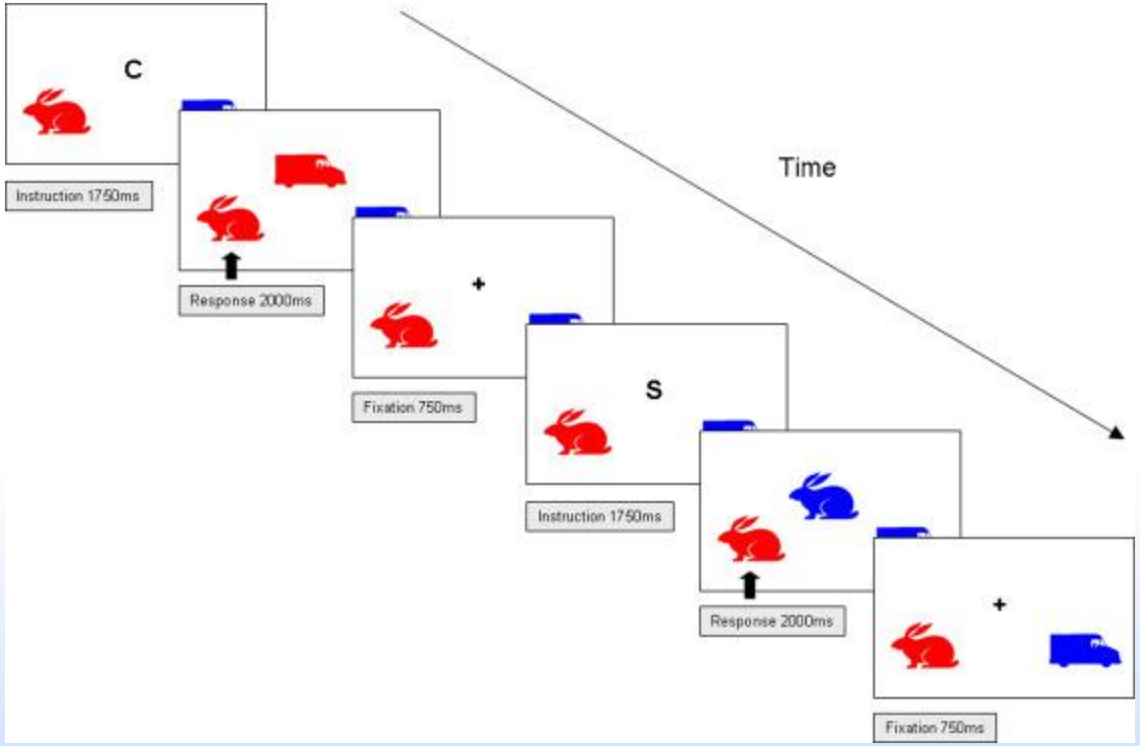


Lawlor et al, Psychol Med. 2020 Jul; 50(10): 1613–1622.

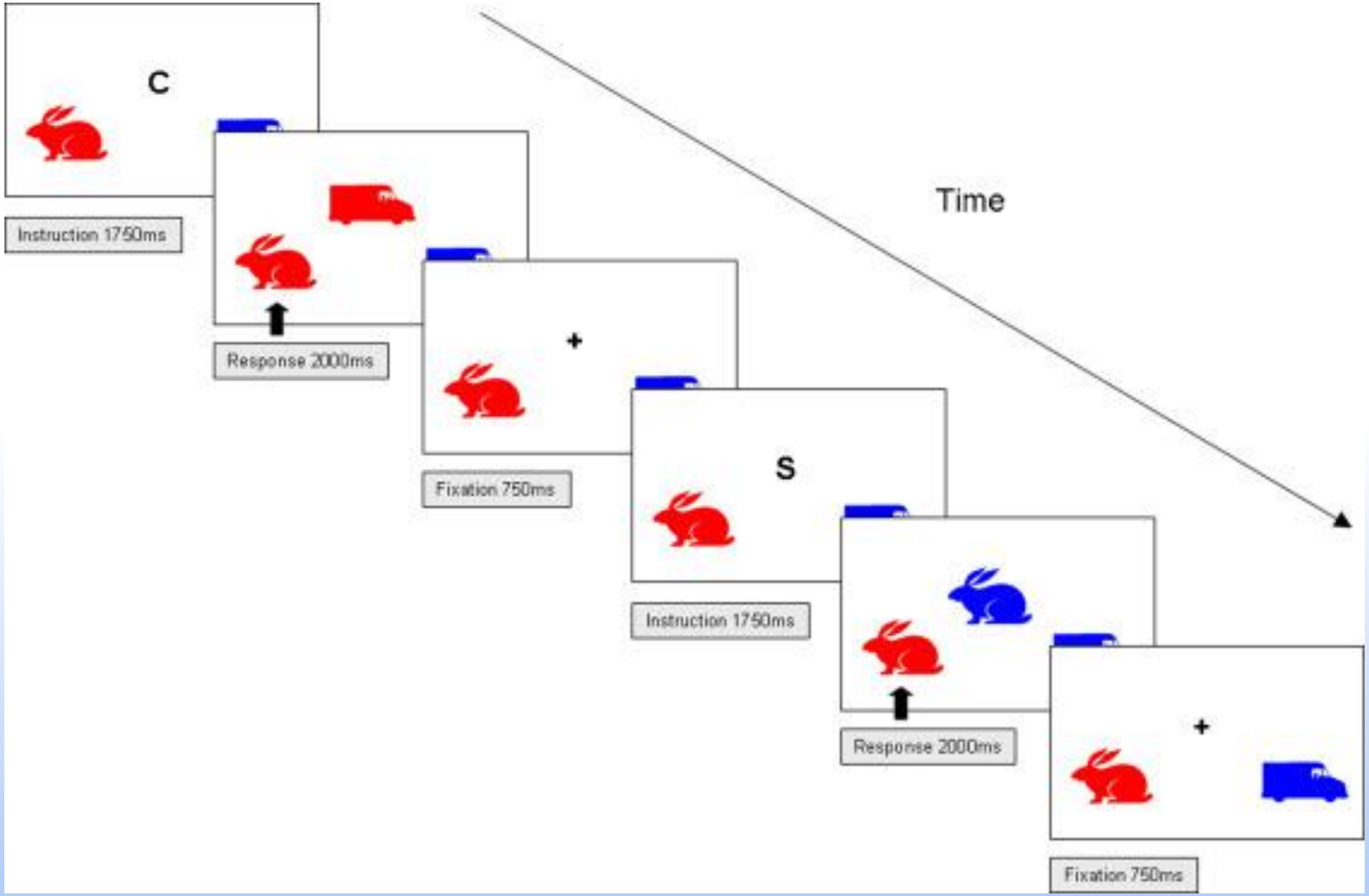
UNMASCK STUDY

- Neuropsychological assessment

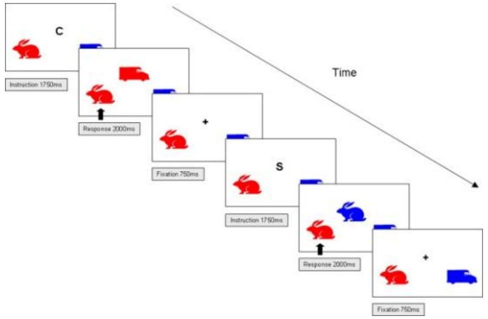
Dimensional Change Card Sort

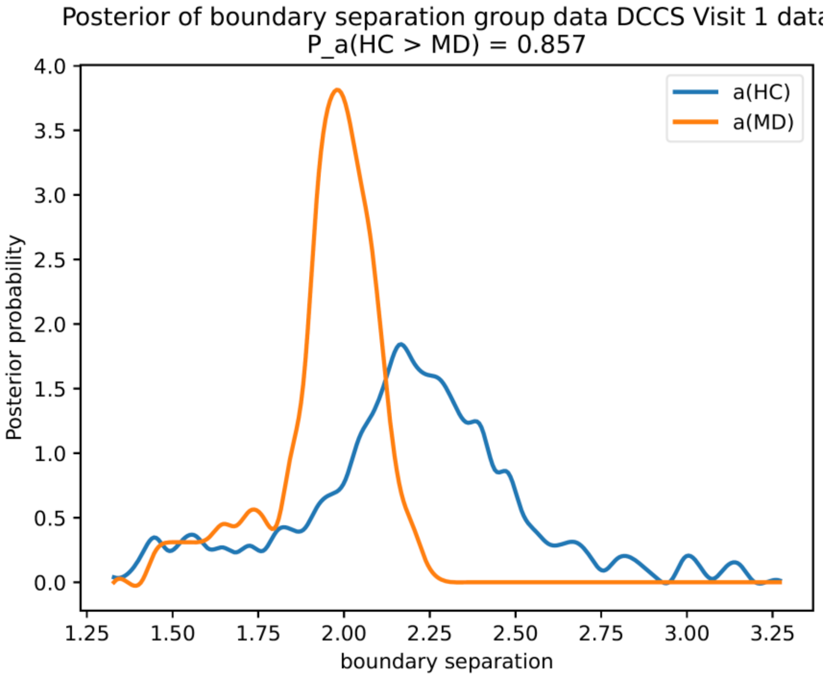


DIMENSIONAL CHANGE CARD SORT TASK (DCCS)

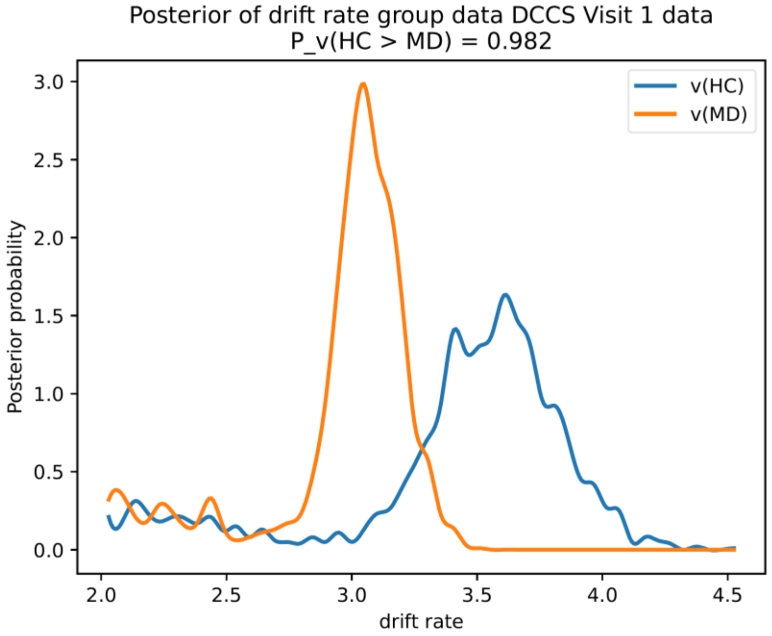


VISIT 1 RESULTS

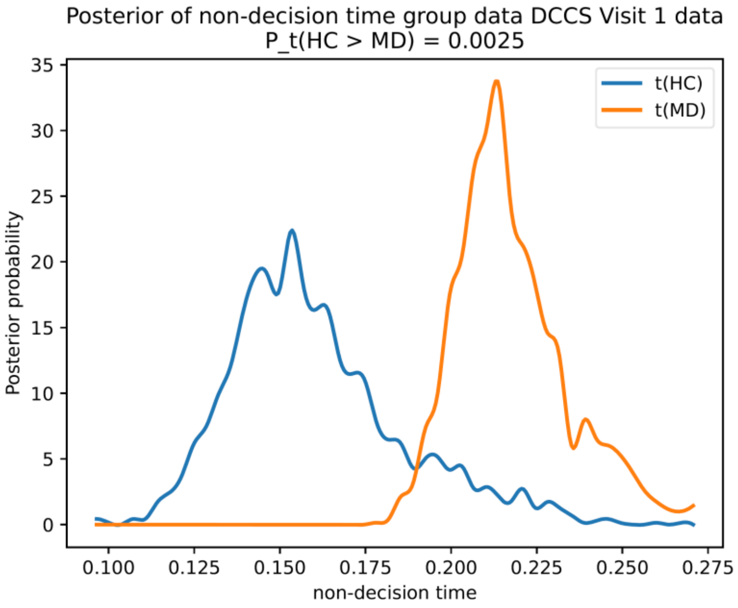




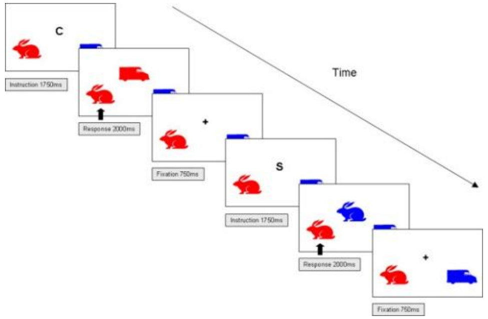
MD have smaller boundary separation compared to HC



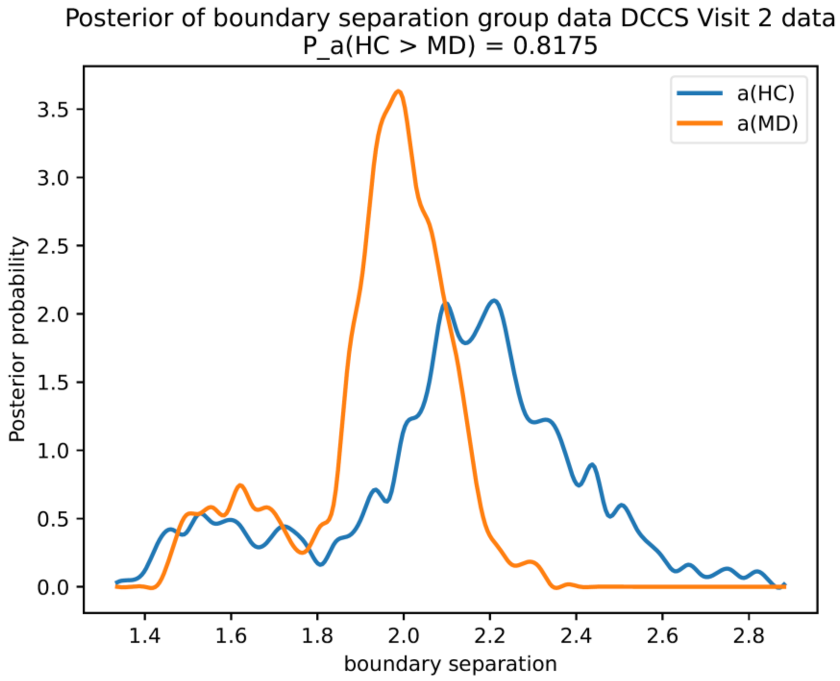
MD have slower drift rates compared to HC

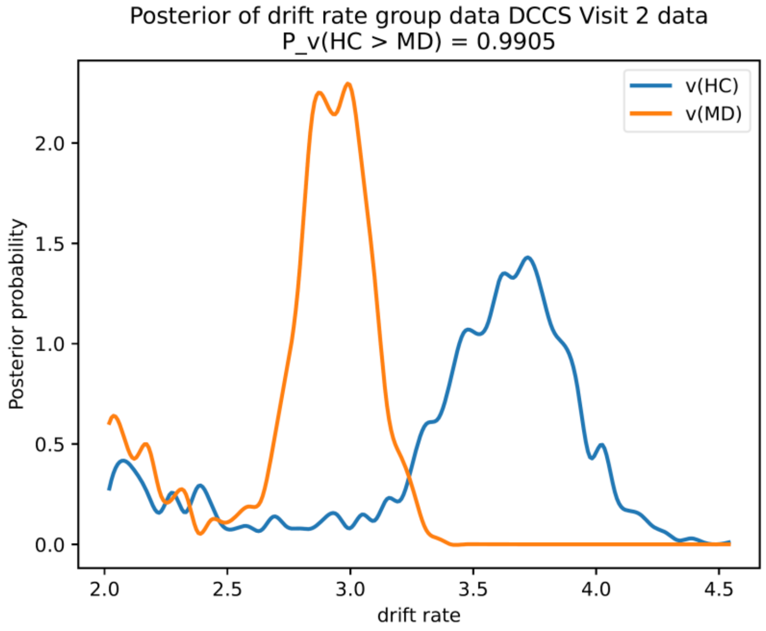


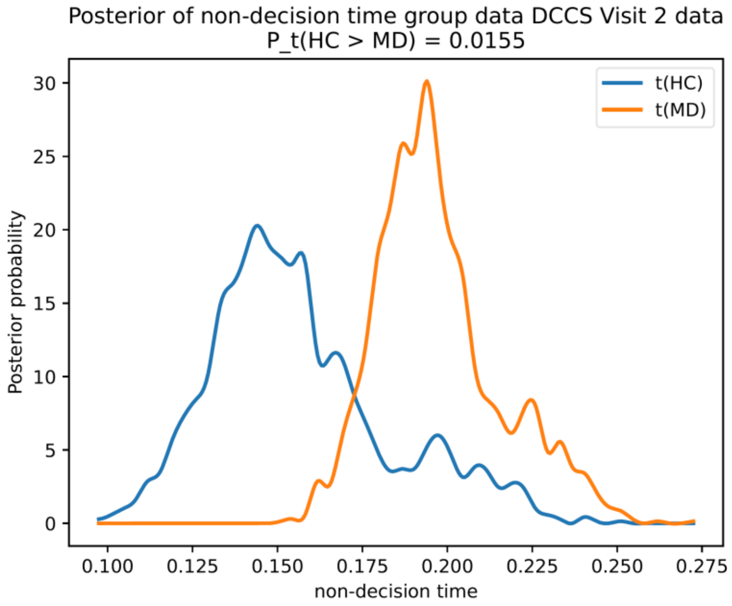
MD have slower non-decision times compared to HC



VISIT 2 RESULTS







MD have smaller boundary separation compared to HC

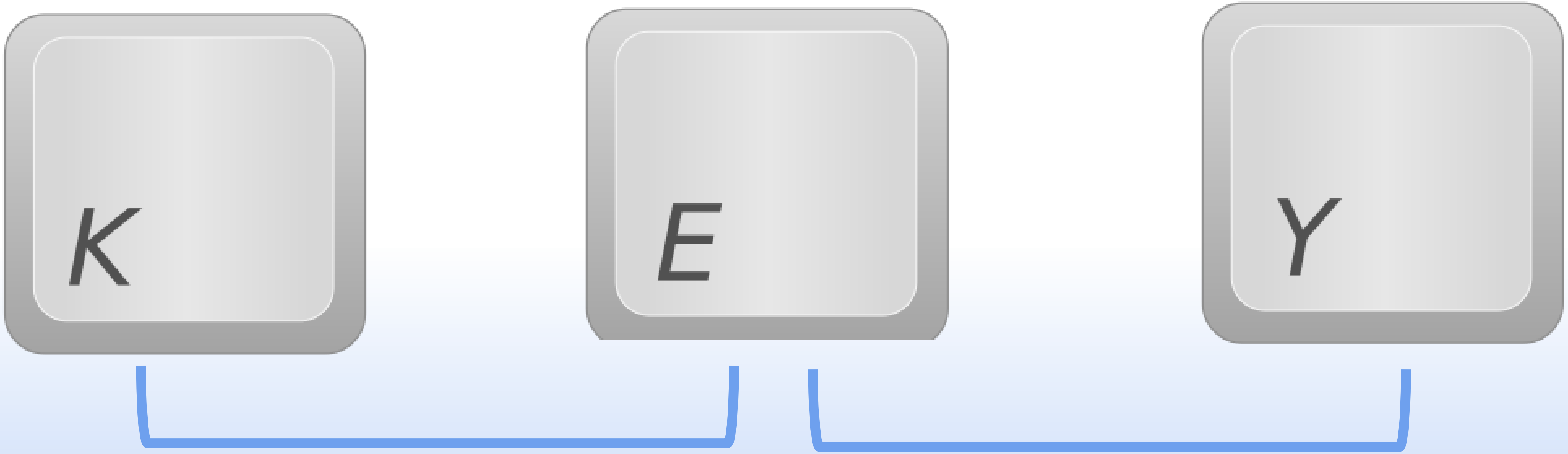
MD have slower drift rates compared to HC

MD have slower non-decision times compared to HC

BIAFFECT TYPING DATA

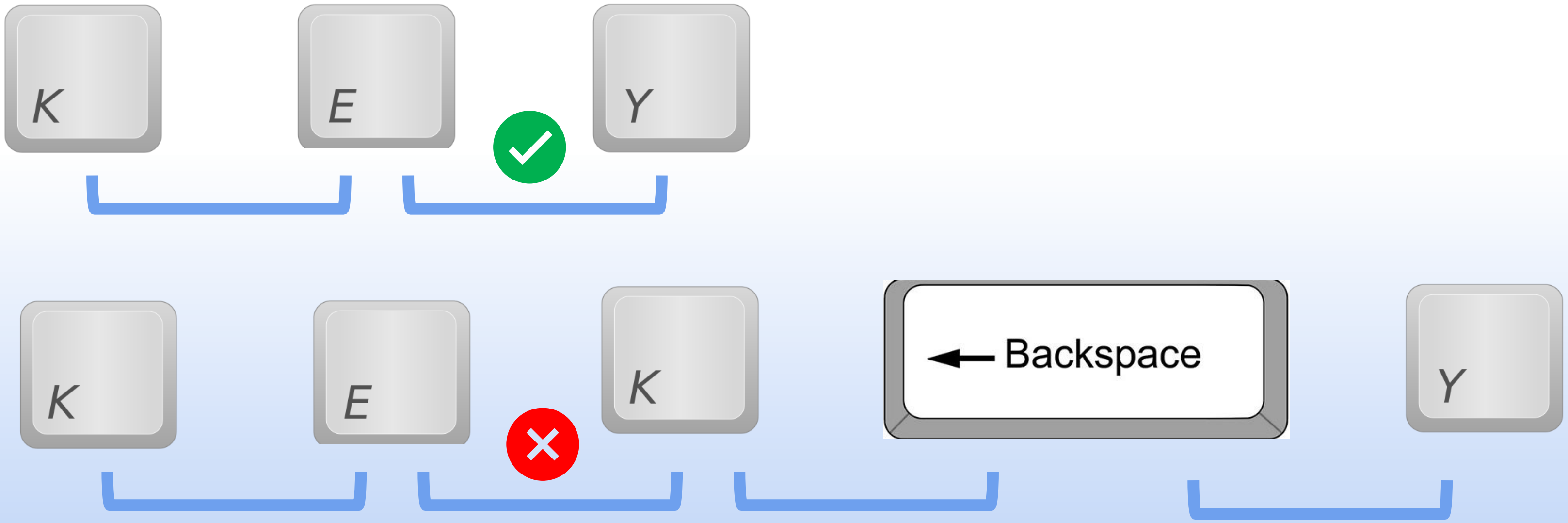
HOW CAN WE COMPARE THIS TO TYPING DATA?

- Typing speed measured by inter-key delay ~ reaction time

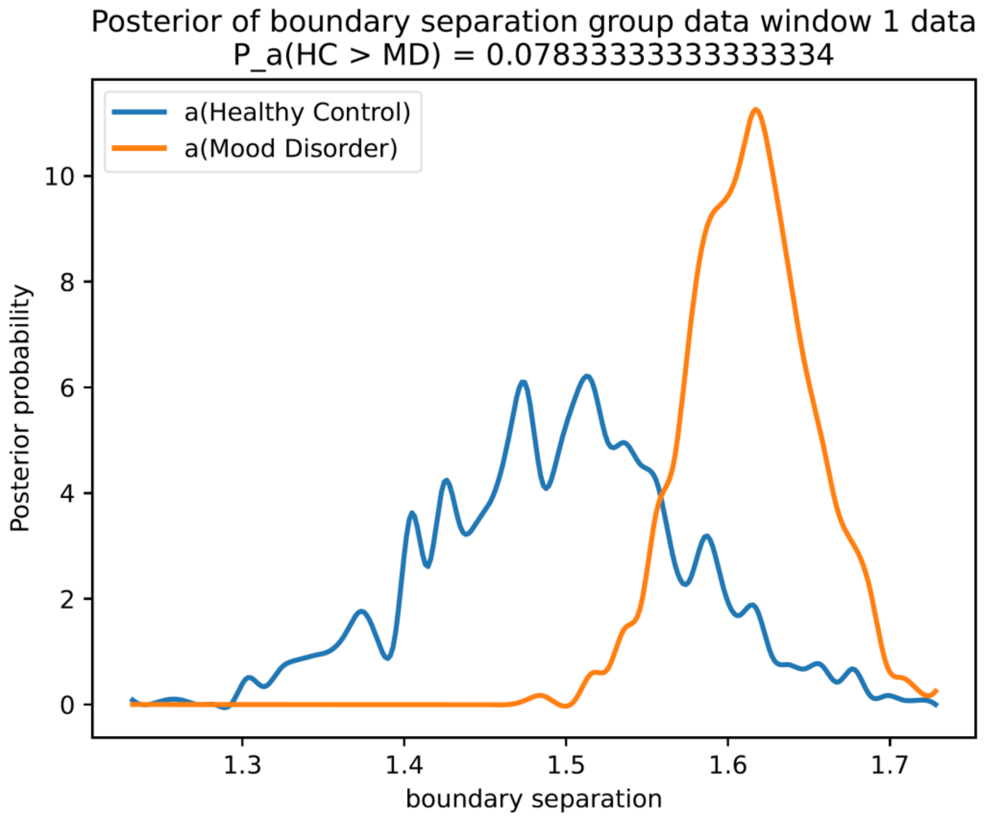


HOW CAN WE COMPARE THIS TO TYPING DATA?

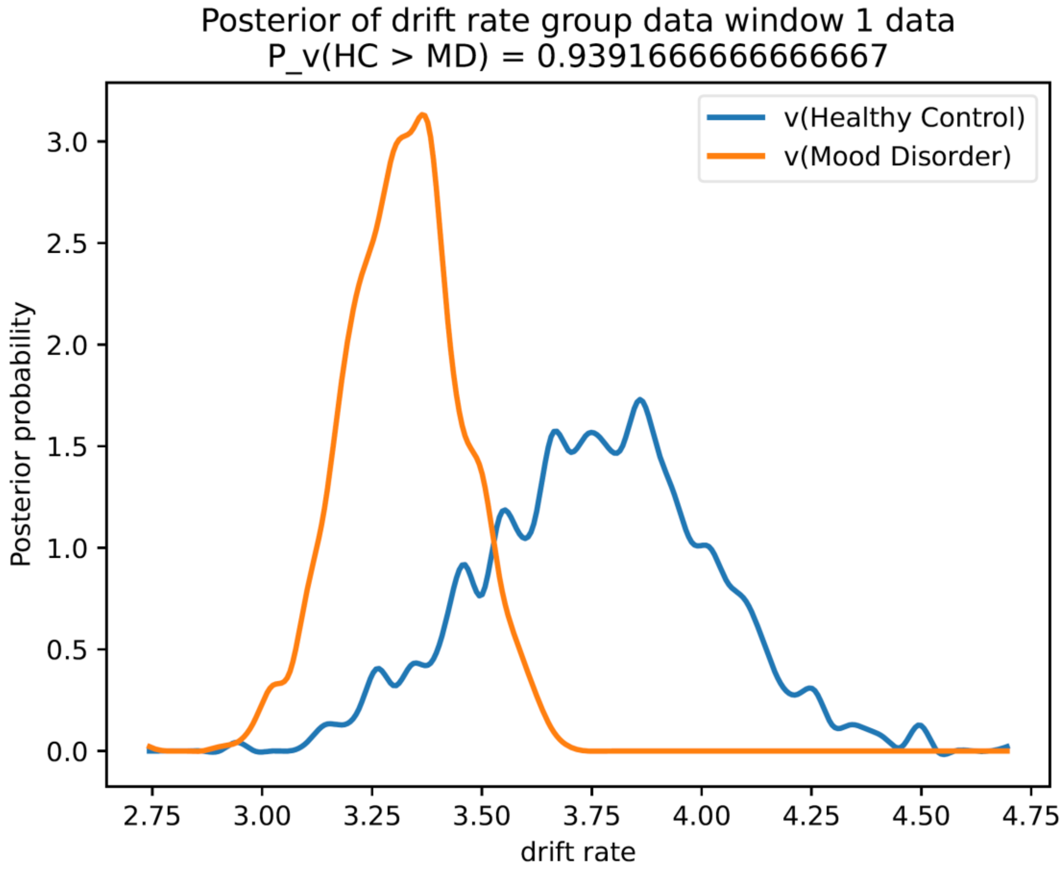
- Intended keypress – “correct RT”
- Typo - “incorrect RT”



WINDOW 1 RESULTS

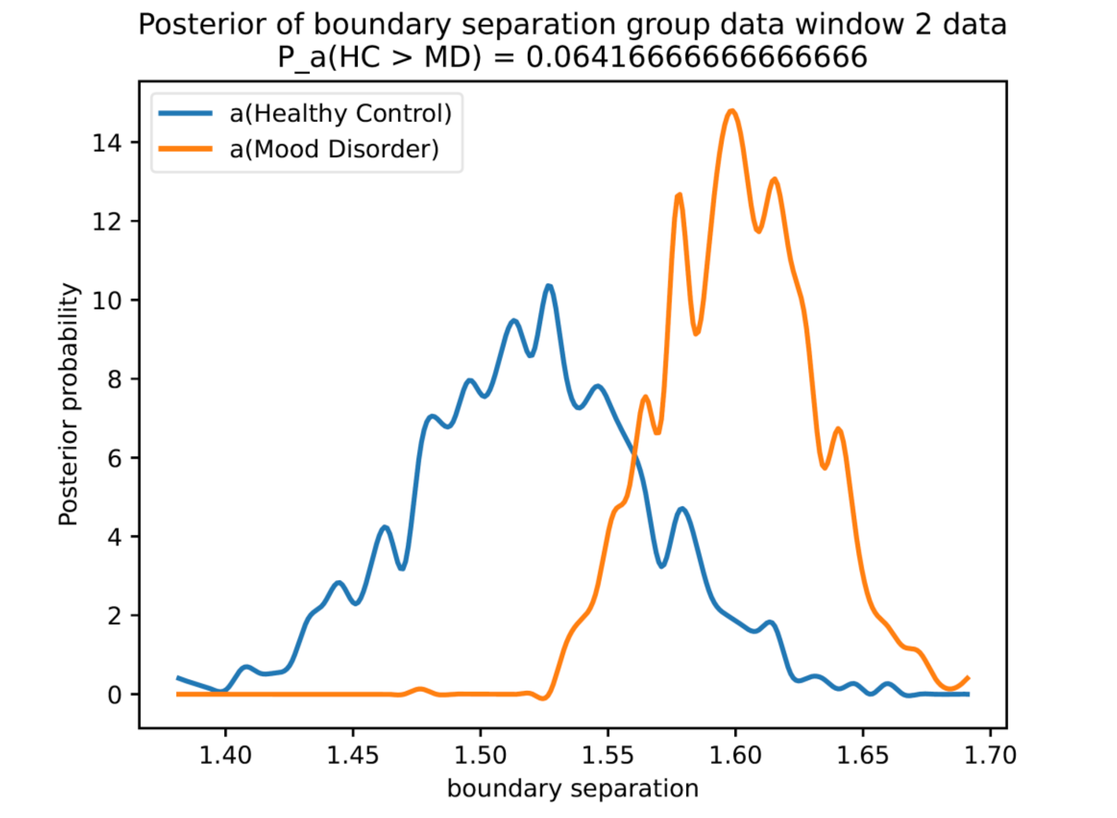


MD have wider boundary separations compared to HC

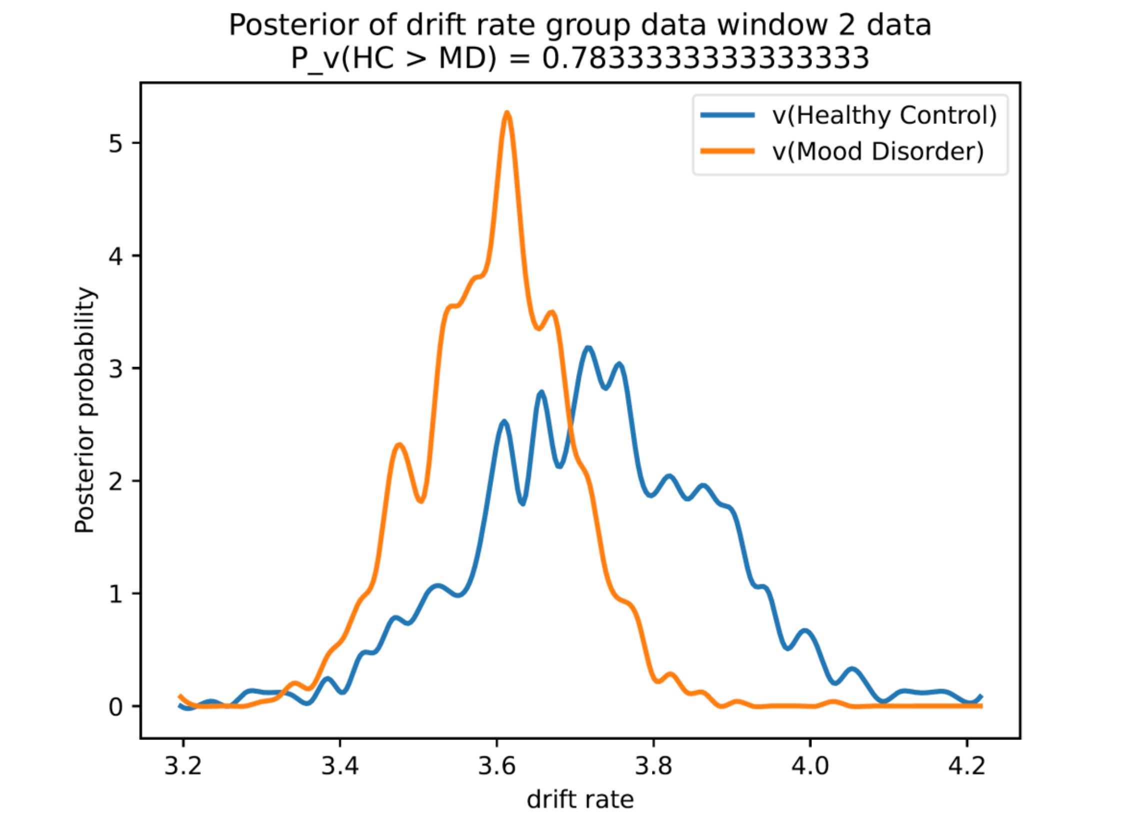


MD have slower drift rates compared to HC

WINDOW 2 RESULTS

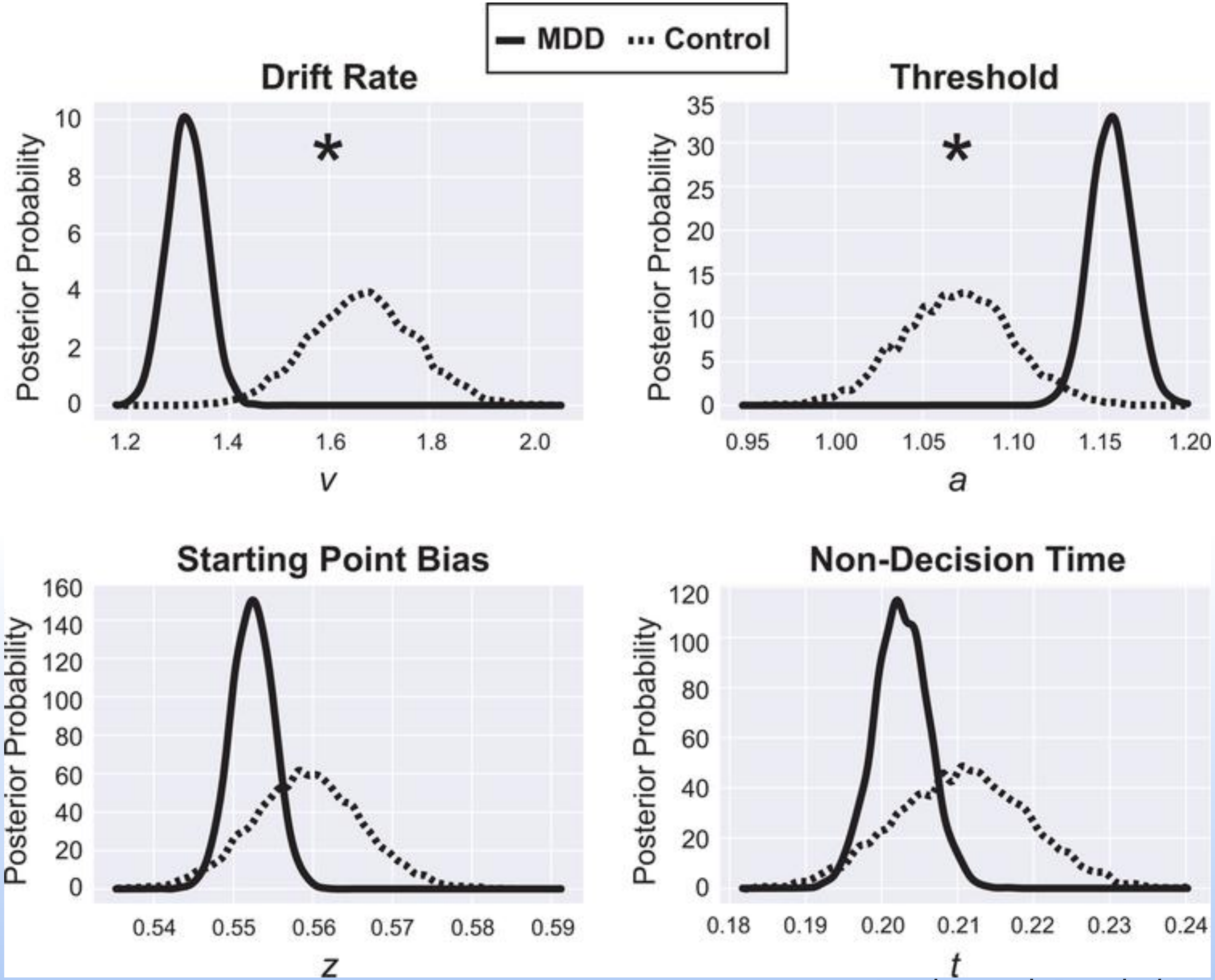


MD have wider boundary separations compared to HC



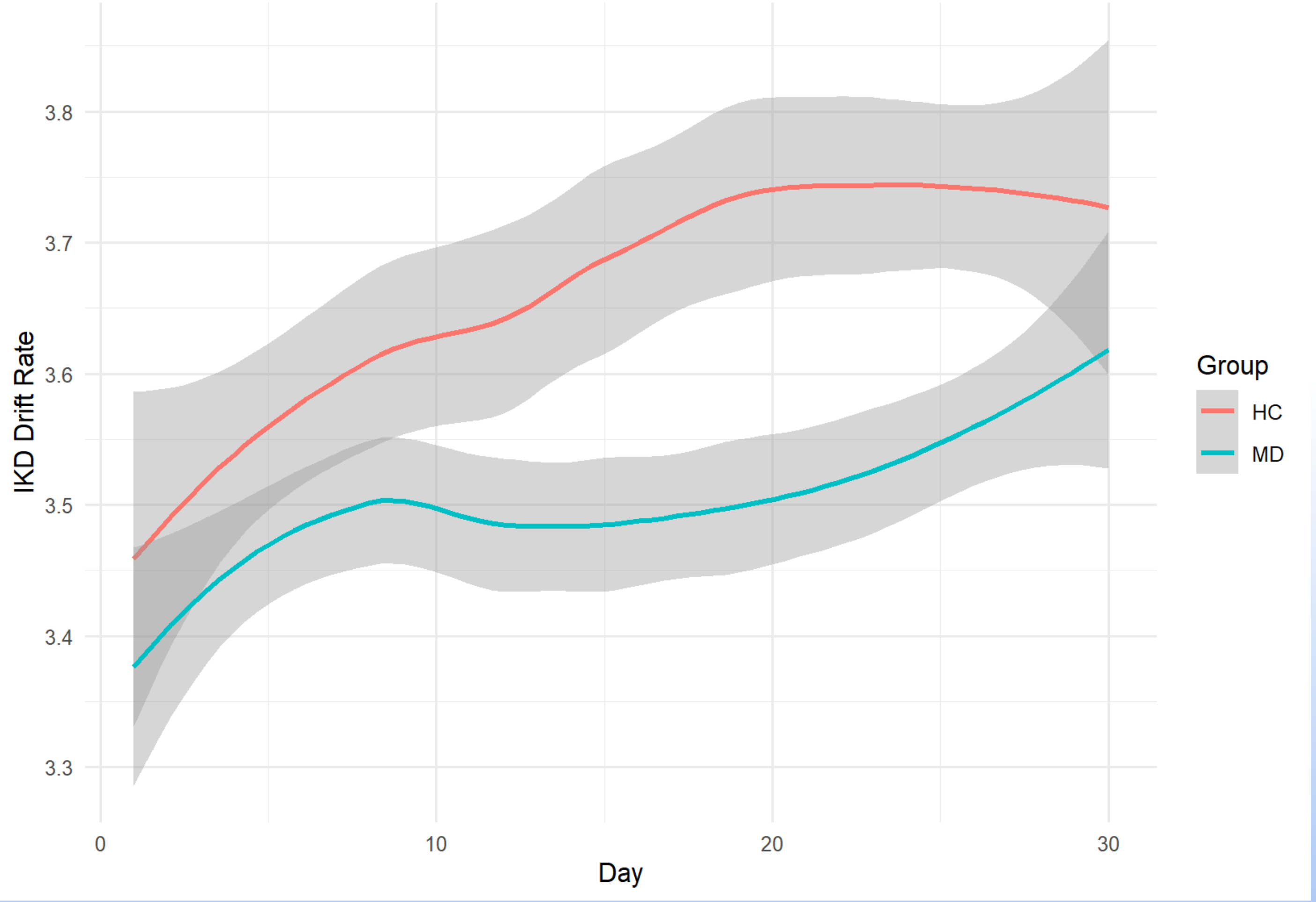
MD have slower drift rates compared to HC

DISSECTING THE IMPACT OF DEPRESSION ON DECISION-MAKING



Lawlor et al, Psychol Med. 2020 Jul; 50(10): 1613–1622.

DAILY DRIFT RATE



SUMMARY

- Aspects of decision-making derived from standard neuropsychological tests may be captured by passive, unobtrusively obtained naturalistic smartphone data

- Dense temporal sampling of keyboard data have the potential to be a daily measure of decision-making capacity

CONCLUSIONS

- Using passive sensing to track cognition has the potential to enhance precision is diagnosis and symptom tracking
- This may be particularly relevant for emerging subtypes of psychiatric disorders (i.e. cognitive biotypes of MDD)

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