National Academy of Sciences: Exploring the Bidirectional Relationship Between AI and Neuroscience
Session 2: R&D Considerations for Neuroscience & AI

Harnessing Rapidly Advancing AI in Pharmaceutical Development to Enhance Patients' Lives Today

Gayle Wittenberg
VP, Neuroscience Data Science & Digital Health
Johnson & Johnson Innovative Medicines, R&D

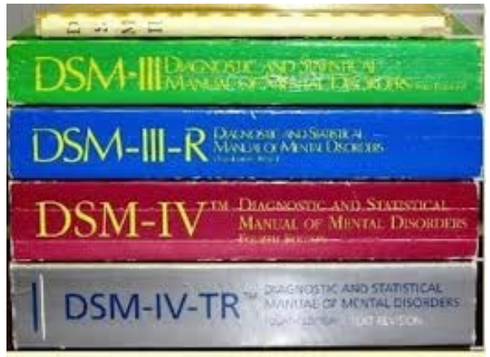
Disclosure & Disclaimers

Dr. Wittenberg is a full -time employee of J&J Innovative Medicines, and a J&J stockholder

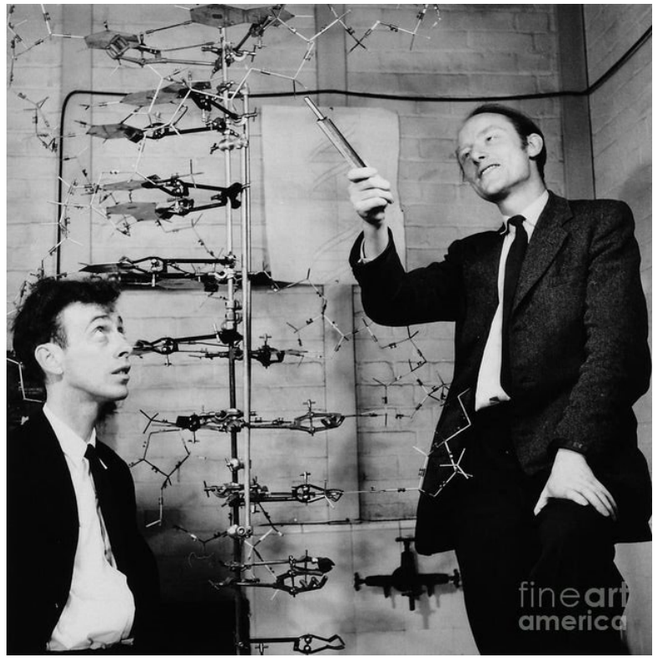
The views expressed in this presentation are those of Dr. Wittenberg, and do not reflect the views of J&J Innovative Medicine

Precision Neuroscience

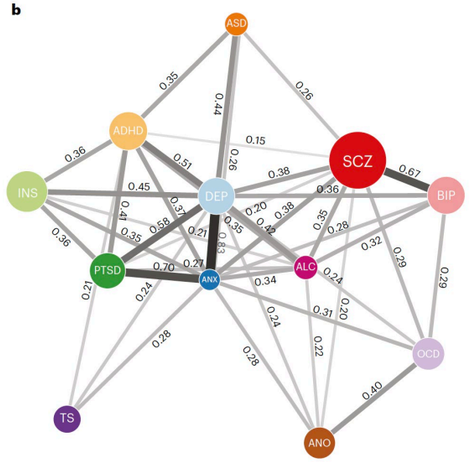
Clinical Diagnoses Based on Symptoms



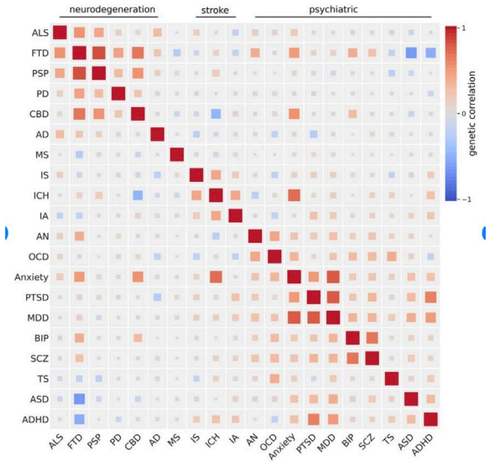
Diseases Defined Before Modern Biology



High Genetic Correlation Among Diseases

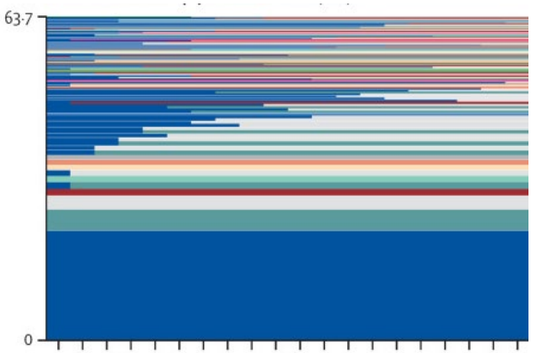


Romero et al., Nature Genetics 2022



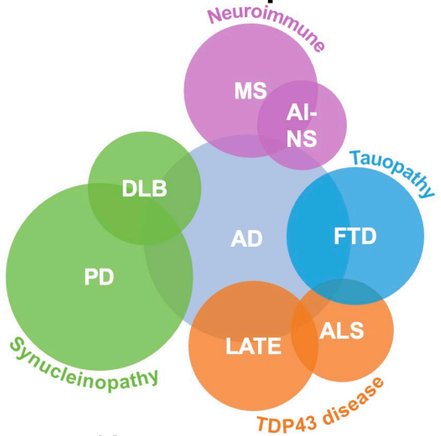
Van Rheenen et al., Nature Genetics 2021

Diagnoses Change Over Time



Jørgensen et al., Lancet Psych 2023

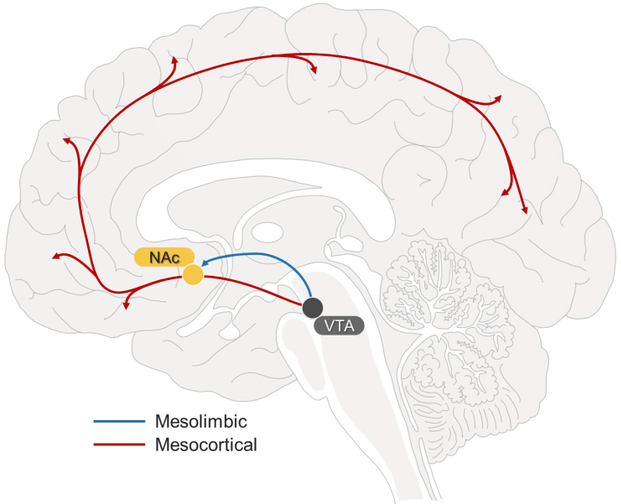
Biological Pathology Overlaps

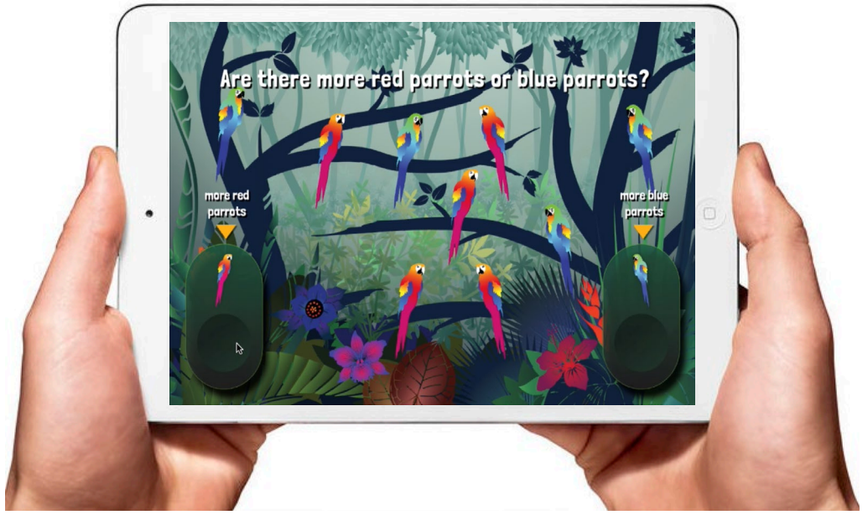


Courtesy of Simon Lovestone

Precision Measures

Digital Measures Access Neural Computations





Reinforcement learning is based on algorithms that learn by maximizing future rewards.

- Early ML modeled after dopaminergic reward signaling

Reward learning is humans is quantifiable: we can measure how subjects perform during reward learning tasks fitting parameters to game play.

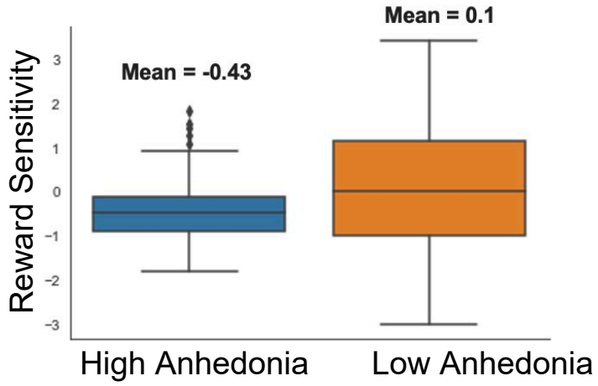
$$Q_{t+1} = Q_t + \varepsilon(\rho\, r_t - Q_t)$$

Reward sensitivity

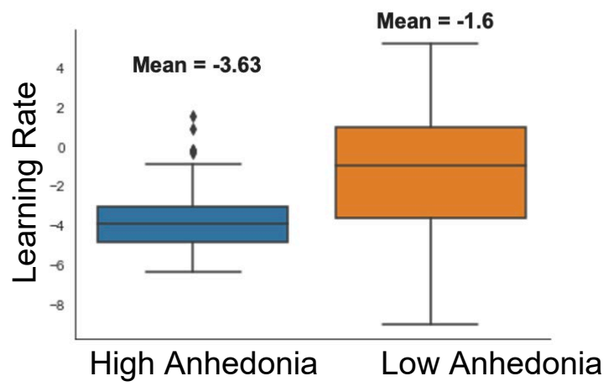
Learning rate

Reward Sensitivity ~determines how good your performance gets
Learning rate ~determines how fast you get there

Lower Reward Sensitivity
(p=0.014)



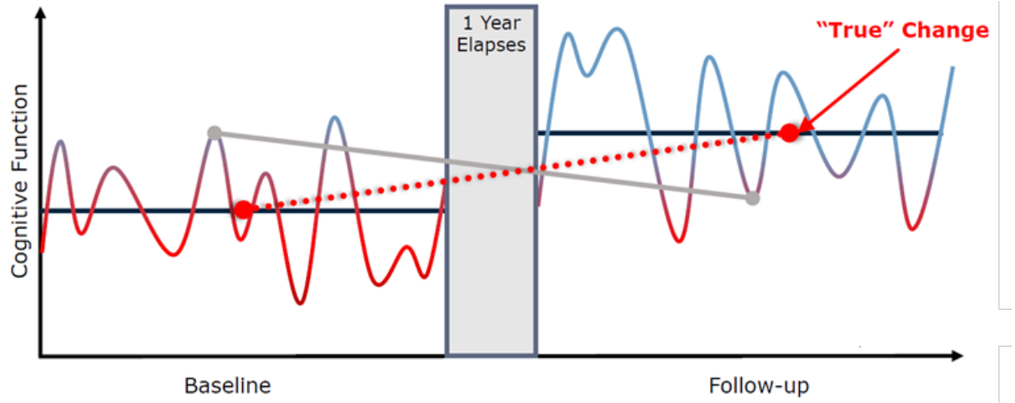
Lower Learning Rate
(p=1.5e-07)



Meenakshi Chatterjee, Qingqin Li
Johnson & Johnson Innovative Medicines

Digital Measures Unveil Hidden Symptoms

The Hubble View of Cognition and Function

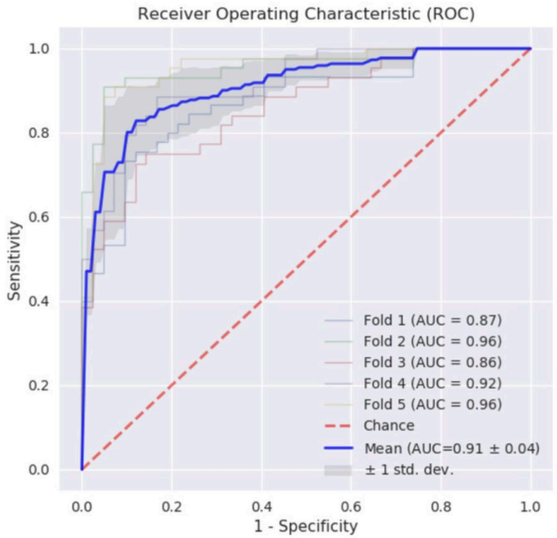


Altoida: Multi-Modal AR app

- 10 minute in-home task
- Integration of hundreds of measures extracted from sensor data
- Multi-modal, inclusive of task performance and sensor data

Courtesy of Altoida

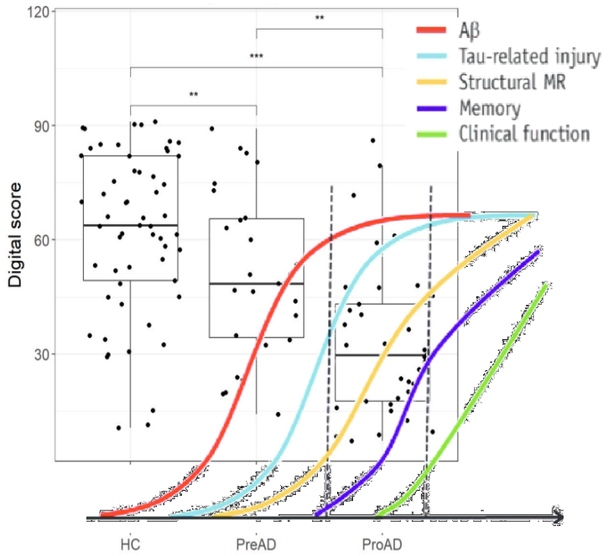
Development of Digital Neuro Signature (DNS)



- 100 MCI-AD Converters
- 113 Non-Converters
- XGBoost model trained to predict from baseline data 3-year conversion to MCI.

Buegler et al., Alzheimer's & Dementia: Diagnosis, Assessment & Disease Monitoring 2020

Evaluation of DNS in IMI RADAR-AD



RADAR-AD

- Digital measures can detect preclinical AD
- Previously defined as patients with measurable amyloid and tau pathology with *no cognitive symptoms.*

Muurling et al., NPJ Digital Medicine 2023

The Increasing Power of Prediction

Tau PET is currently the best biomarker predictor of cognitive decline

www.nature.com/mp

Molecular Psychiatry

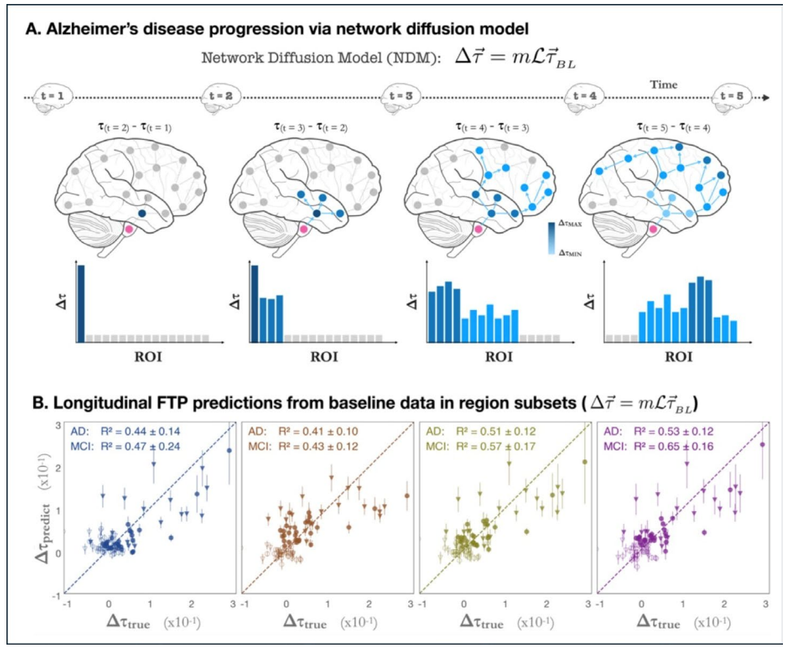
ARTICLE OPEN

Check for updates

Alzheimer's disease profiled by fluid and imaging markers: tau PET best predicts cognitive decline

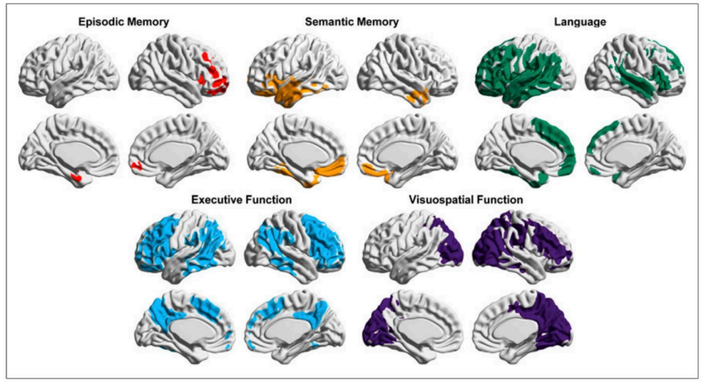
Marco Bucci[1], Konstantinos Chiotis[1,2] and Agneta Nordberg[1,3]✉ for the Alzheimer's Disease Neuroimaging Initiative

Tau PET spread is predictable along the connectome



Damasceno et al., *Alzheimer's & Dementia 2020*

Tau PET deposition pattern predicts cognitive deficit



Tanner and Rabinovici, J. Nuclear Med 2021

Towards Digital Twins

- Parameterize patient-specific model from measurements
- Model / simulate impact of treatment or intervention options on future state
- Inform decision-making

Adjusting for Covariates in Randomized Clinical Trials for Drugs and Biological Products

Guidance for Industry

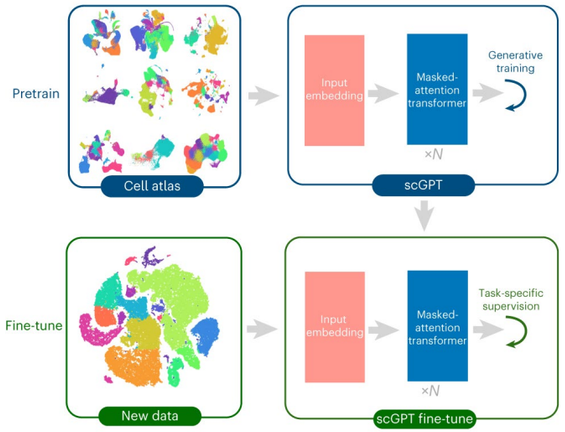
U.S. Department of Health and Human Services
Food and Drug Administration
Center for Drug Evaluation and Research (CDER)
Center for Biologics Evaluation and Research (CBER)
Oncology Center of Excellence (OCE)

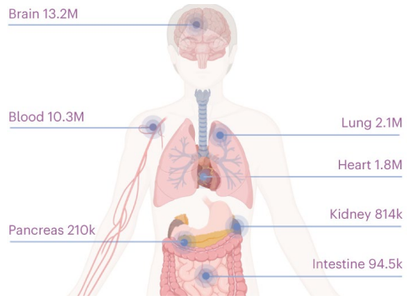
May 2023
Biostatistics

A Foundational Perspective on Scale

Where, today, is data being aggregated at a large enough scale for foundational models to be near -term transformational?

Cells



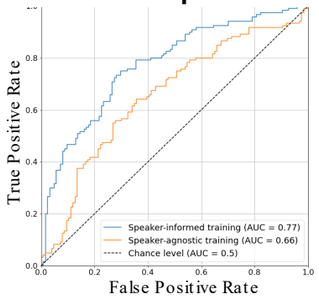


scGPT: >30 Million human cells

Cui et al, Nature Methods 2024

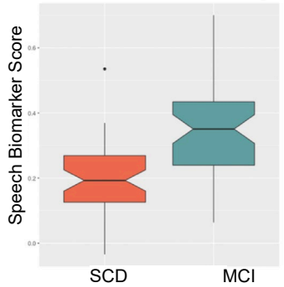
Speech

Predict Depression

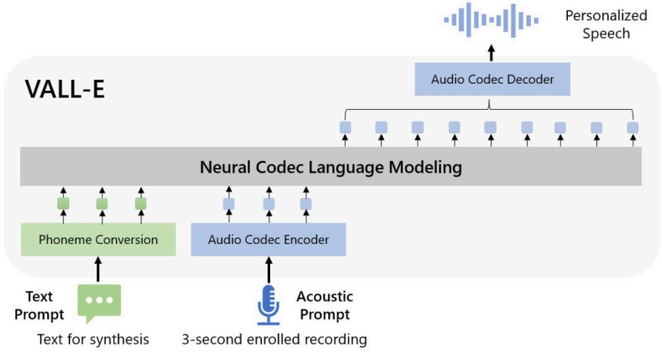


Parisi et al., in review Interspeech 2024

Predict Alz Stage



Linz et al., *Alz&Dem 2022*

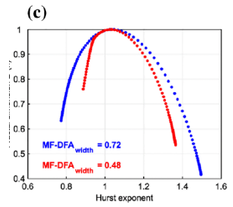


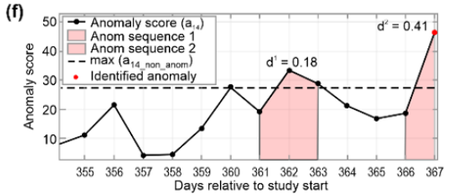
VALL-E: 60h speech , 7k speakers

Wang et al, arXiv 2023

100M Amazon Echo sold/yr

Activity



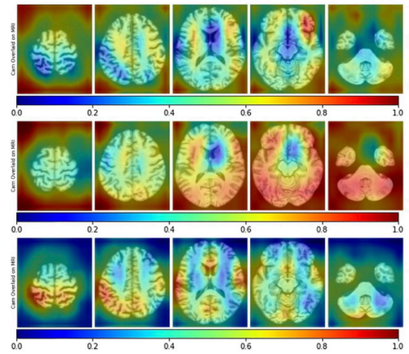


N-of-1 anomaly detection model predicts relapse 2 weeks prior to clinical visit

Vairavan et al., Sci Rep 2023

>60 M Activity-measuring devices sold/yr (Apple, Fitbit, ..)

MRI



Deep learning models fit to MRI to predict positive in amyloid, tau, neurodegeneration.

N=500-3000

Lew et al., Radiology 2023

~10M Brain MRI per year in US Healthcare Setting

A Foundational Perspective on the Healthcare System

“All that exists is the seed of what will emerge from it” – Marcus Aurelius

Thank You