

Target Engagement and Programming in Psychiatric DBS

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Disclosures

- Financial Conflicts:
 - Device donations, Medtronic + Boston Scientific
 - Consulting, Abbott
 - Issued/pending patents related to topics discussed today
- Off-Label/Investigational Device Use:
 - Deep brain stimulation for depression

The views throughout this talk are my own, not those of the sponsors/manufacturers.

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- **MnDRIVE Brain Conditions**
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Collaborators

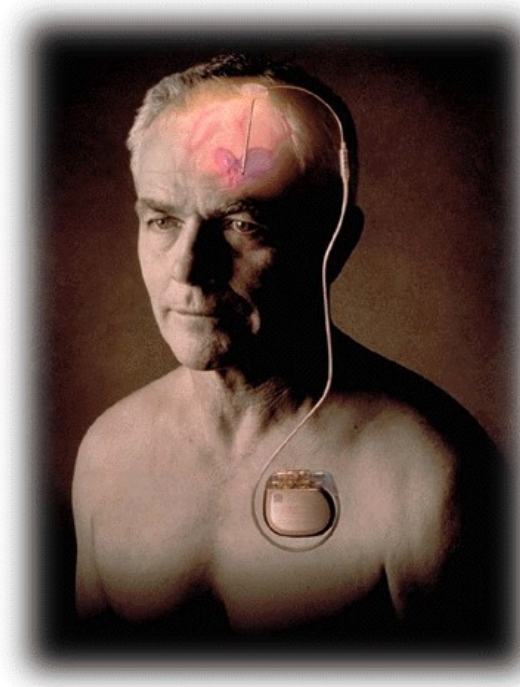
- **MGH: Syd Cash, Darin Dougherty**
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- EPFL: Mahsa Shoaran
- MIT: **Earl Miller**
- NWU: Joel Voss
- UMN: **Tay Netoff**

TLDR/Bottom Line Up Front

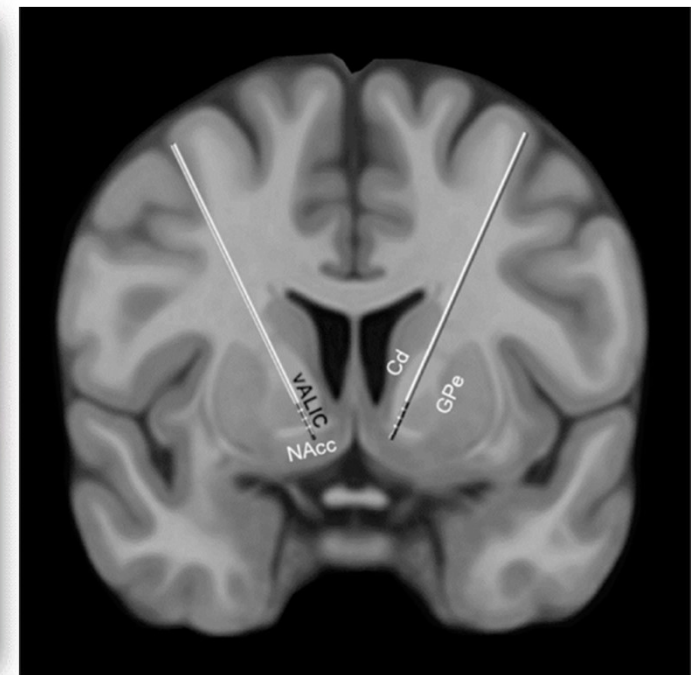
- Successful psychiatric DBS requires good target engagement
- Programming MUCH harder than in PD/ET bc current readouts too noisy / too long timescale
 - Fundamental barrier to widespread use
- One possible answer: objective biomarkers of engagement
- Today: worked example in VCVS DBS, cognitive control
- Future: same idea but in physiology, peripheral signals?

Model: Ventral Capsule/Ventral Striatum (VC/VS) DBS

- FDA (HDE) approval in OCD, also trials in depression, addiction, eating disorders

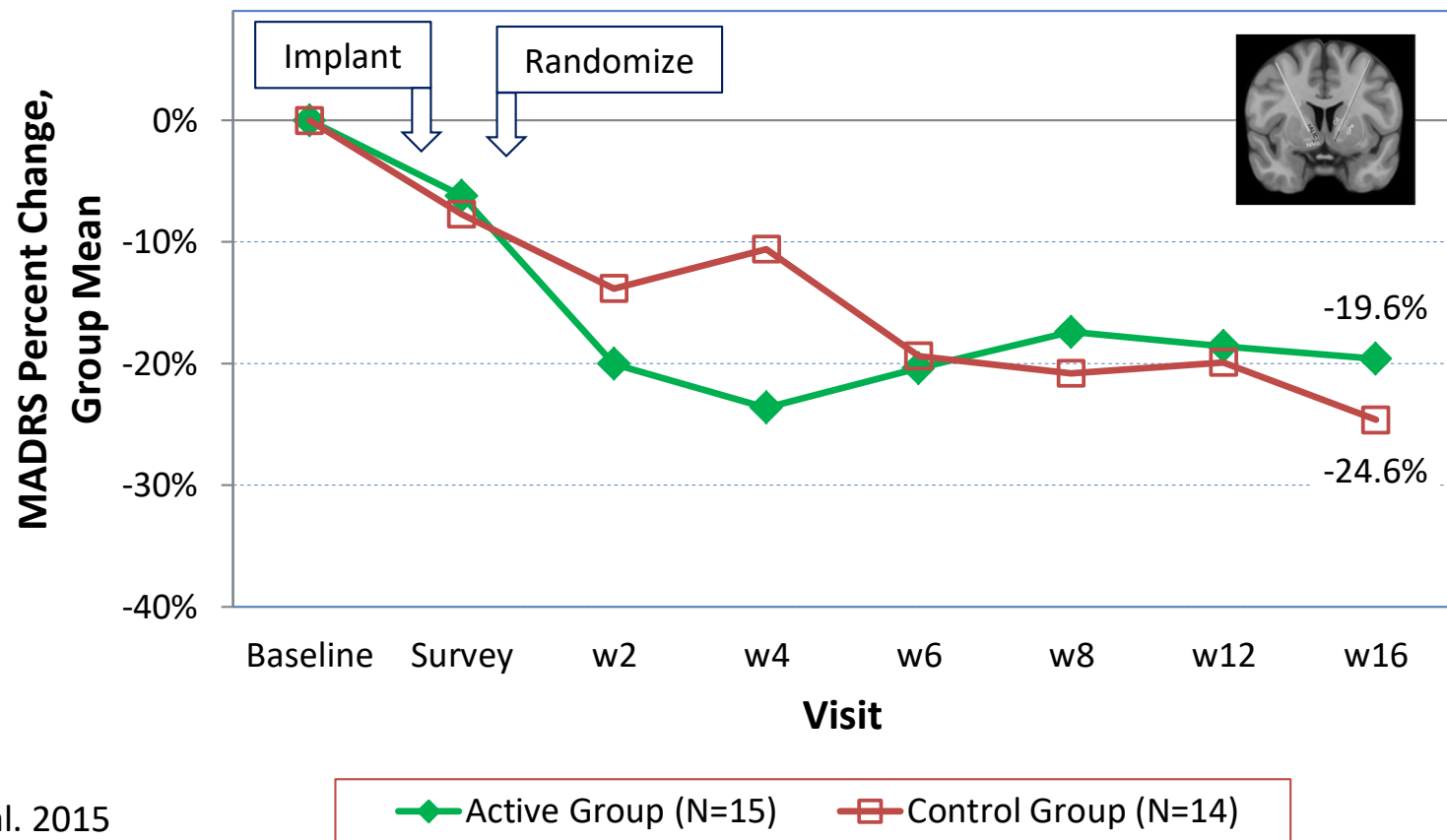


Medtronic



Denys et al. 2020

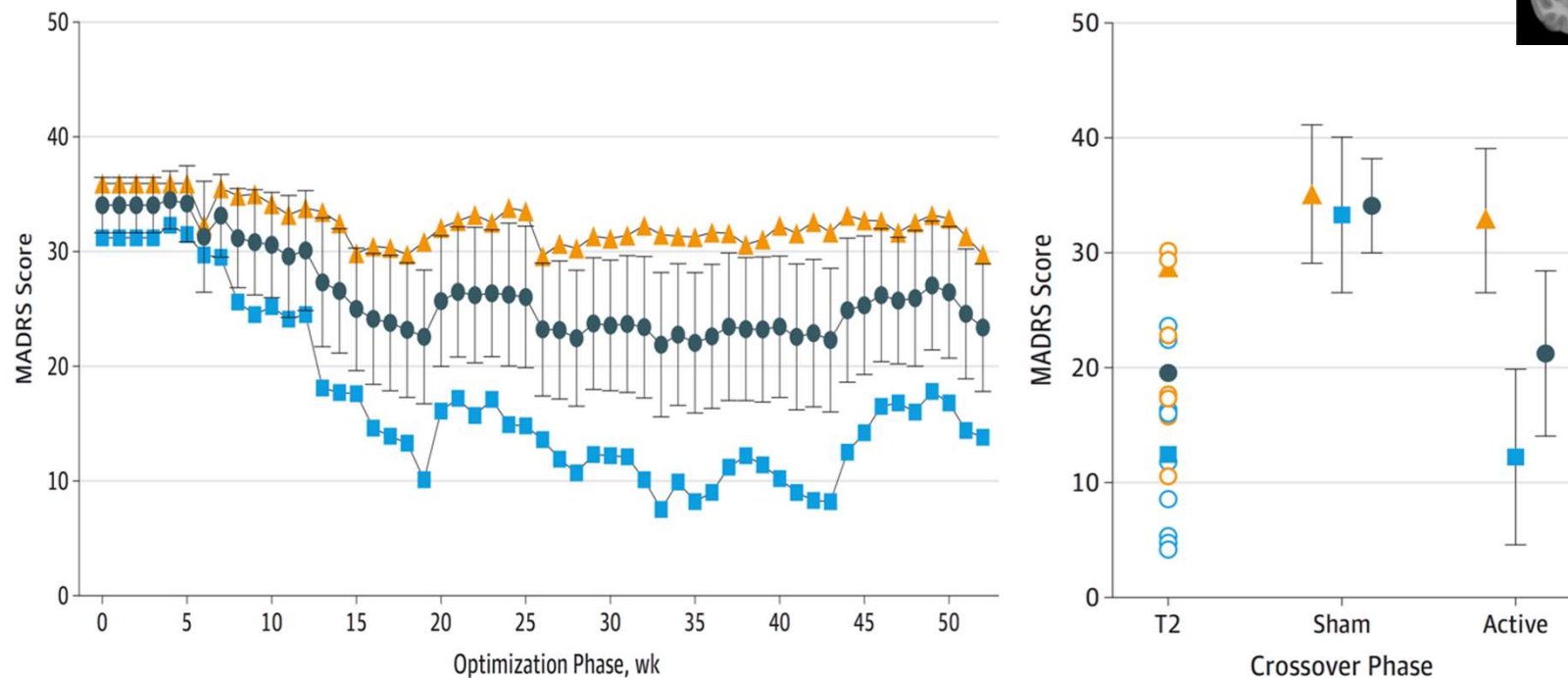
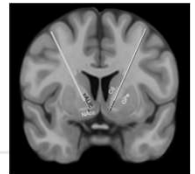
Multi-Site MDD RCT: No Discernable Effect???



Dougherty et al. 2015

Adequate Time to Program: Successful MDD RCT

- 52-week open-label then sham crossover



Bergfeld et al. 2016

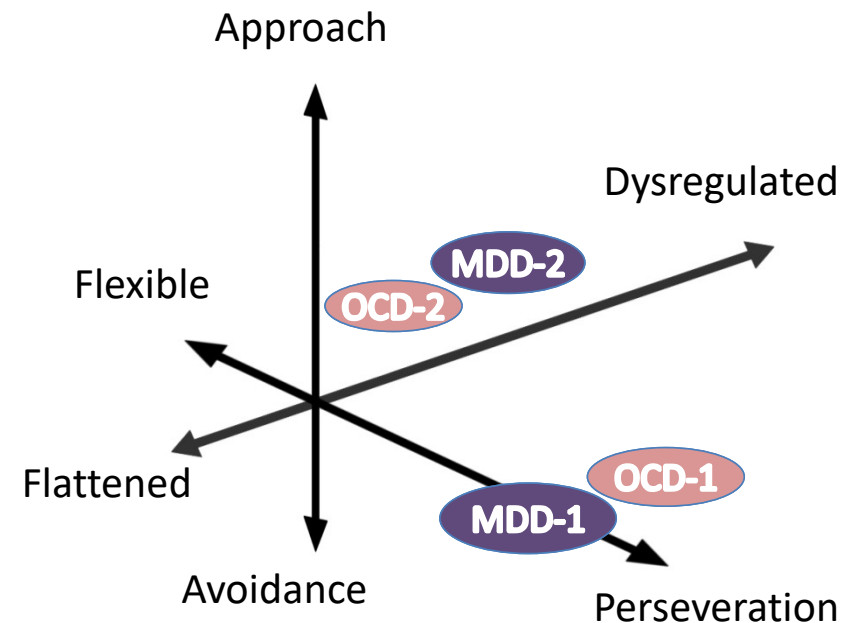
Why Is Psychiatric Programming Hard?

- No readout of target engagement!
- In PD/ET, tremor stops in seconds. In MDD/OCD, symptoms stop in weeks
 - Hemi smiles etc not reliable enough for acute titration, field modeling not ready
- **Need: something that changes in seconds to minutes, but predicts response!**



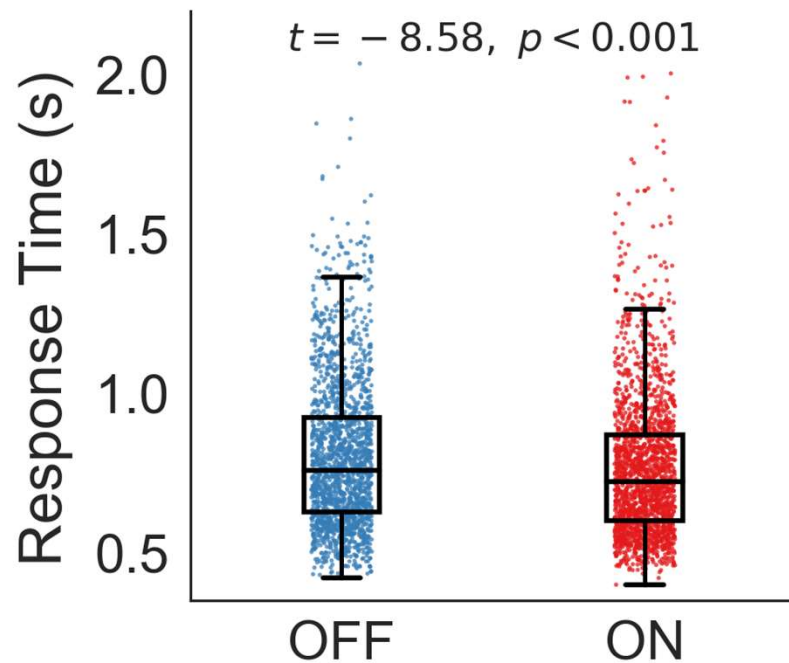
Thesis: Cognitive Readout (Cognitive Control)

- Shared efficacy in MDD, OCD
- Shared dysfunctions?
 - **Rigid, inflexible thinking (lack of cognitive control)**
 - Strong, overwhelming emotions
 - Risk-driven decision-making
- Could cognition (task-based measurement) be the marker for rapid programming?



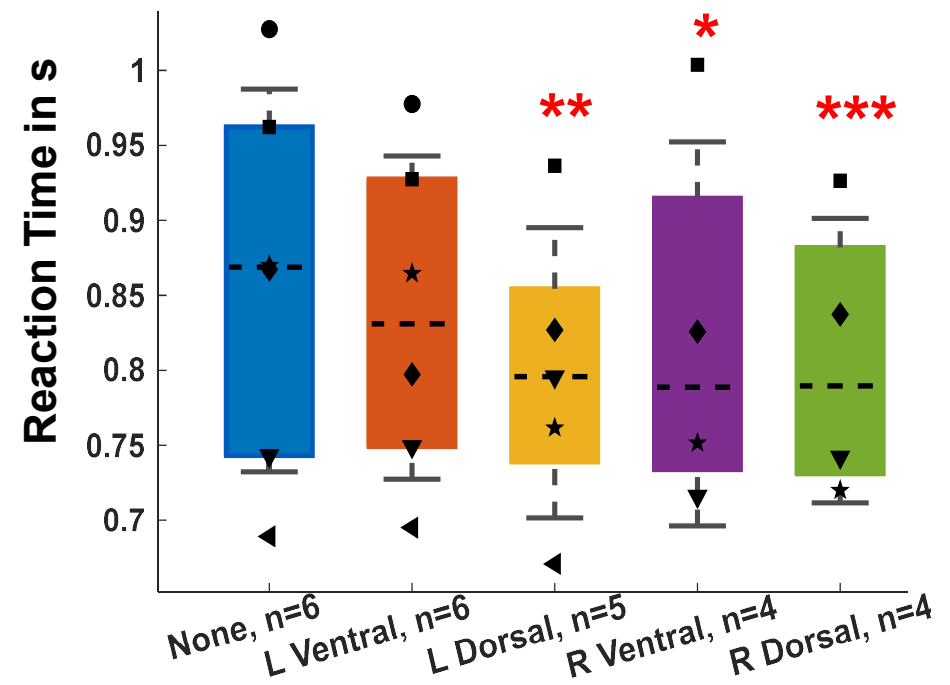
VCVS DBS Improves Cognitive Control

Retrospective Discovery



Widge, Zorowitz, et al. *Nature Comms* 2019

Prospective Replication



Basu et al., *Nature BME* 2023

Effect Can Support Better Programming!

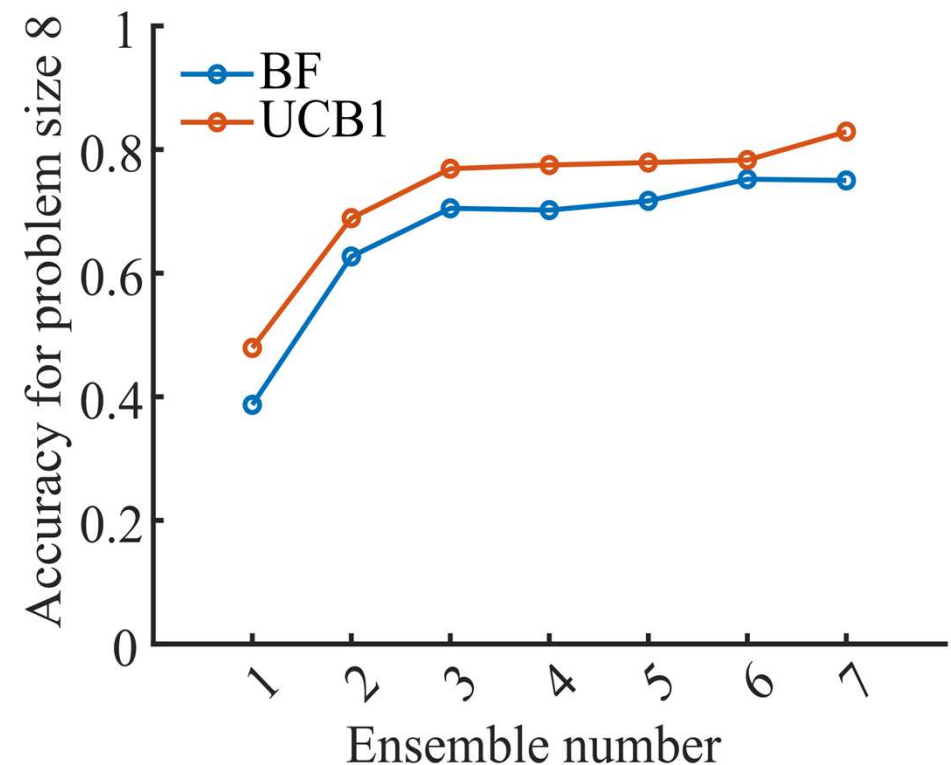
- Automatic, Bayesian search monitors behavior (task RT)
- Bayesian search finds best contact to improve it
- Now in front of FDA for feedback, trial planning



Theoden "Tay" Netoff



Sumedh Nagrale



Nagrale et al., *J Neural Eng* 2023

Bigger Picture: Psychiatric DBS as Rehabilitative

- Patients feel more able to ignore (but still have!) symptoms
- **Mechanism of benefit?**
- Very different from classic ideas of changing mood or eliminating thoughts!
- Needs new way of thinking/describing goals of treatment to patients

