

camh



Psychiatry  
UNIVERSITY OF TORONTO

# Neurostimulation for Cognition in Alzheimer's Dementia and High Risk Populations

**TAREK K. RAJJI**

Stein Institute (Virtual) Symposium:  
“Healthy Aging in the Era of Pandemics”  
October 22, 2021

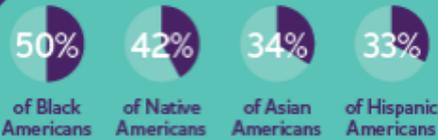
# Faculty/Presenter Disclosure

- Received for an investigator-initiated study in-kind equipment support from Newronika, and in-kind research online accounts from Scientific Brain Training Pro.
- Participated in an advisory board for Biogen Canada Inc.

# 2021 ALZHEIMER'S DISEASE FACTS AND FIGURES

## DISCRIMINATION

is a barrier to Alzheimer's and dementia care. These populations reported discrimination when seeking health care:



**1 IN 3**

seniors dies with Alzheimer's or another dementia



It kills more than

**BREAST CANCER**

+

**PROSTATE CANCER**

**COMBINED**

**MORE THAN 6 MILLION**

Americans are living with Alzheimer's

Between 2000 and 2019, deaths from heart disease have

**DECREASED 7.3%**

while deaths from Alzheimer's disease have

**INCREASED 145%**



Alzheimer's and dementia deaths have increased

**16%**

during the COVID-19 pandemic



In 2021, Alzheimer's and other dementias will cost the nation **\$355 BILLION**



By 2050, these costs could rise to more than

**\$1.1 TRILLION**

**OVER 11 MILLION**

Americans provide unpaid care for people with Alzheimer's or other dementias

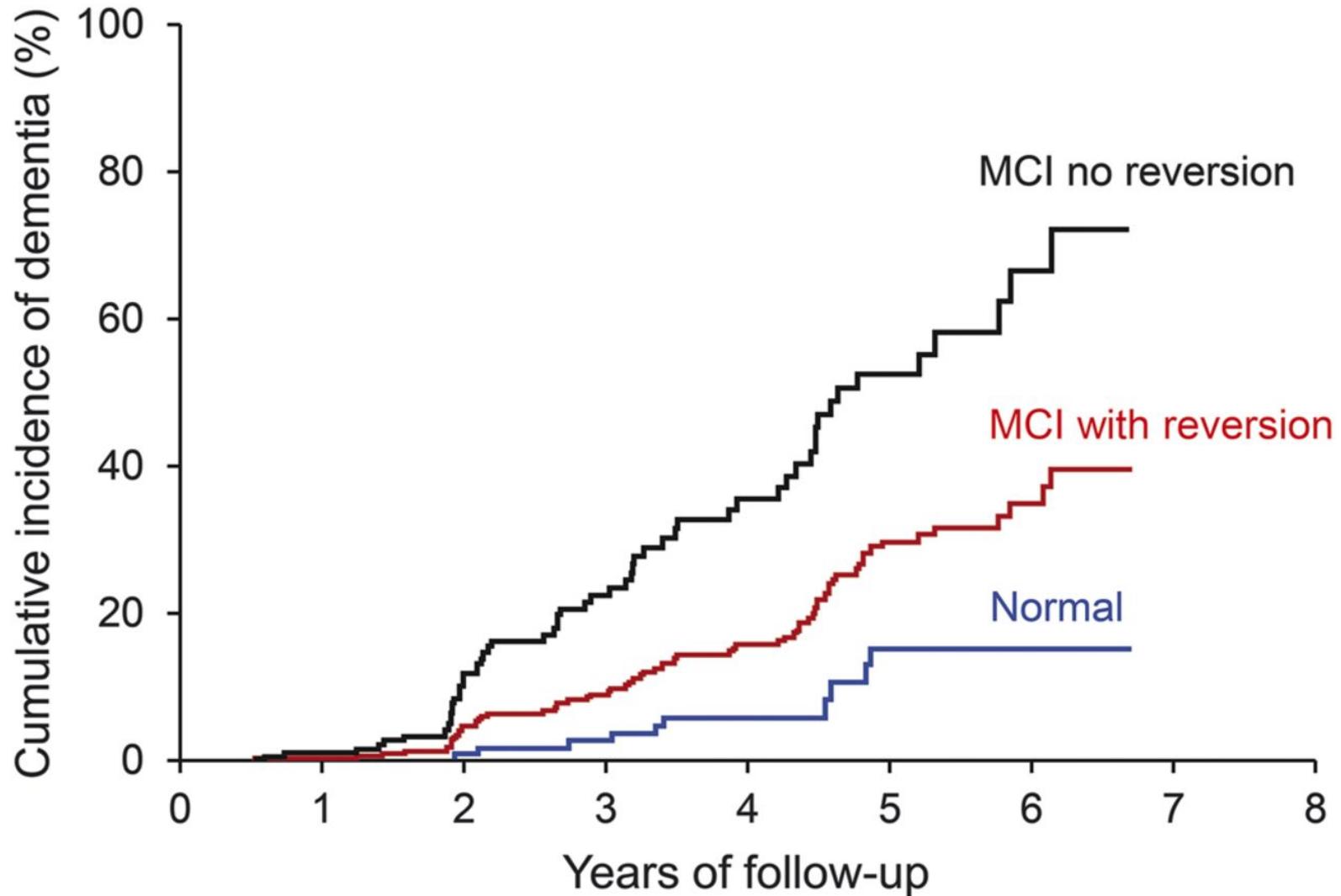


These caregivers provided an estimated 15.3 billion hours valued at nearly

**\$257 BILLION**



# Mild Cognitive Impairment

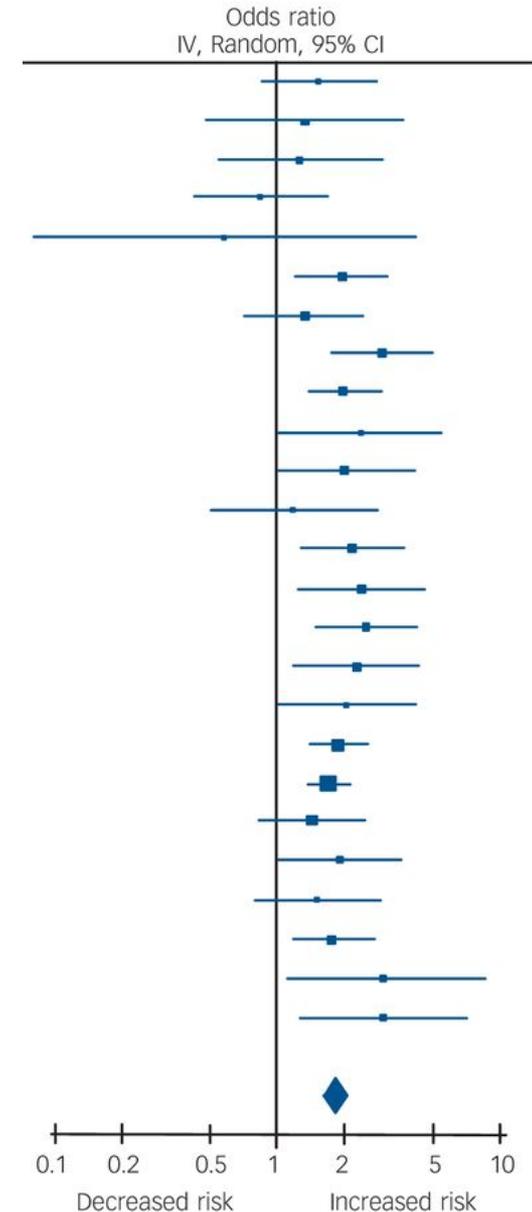


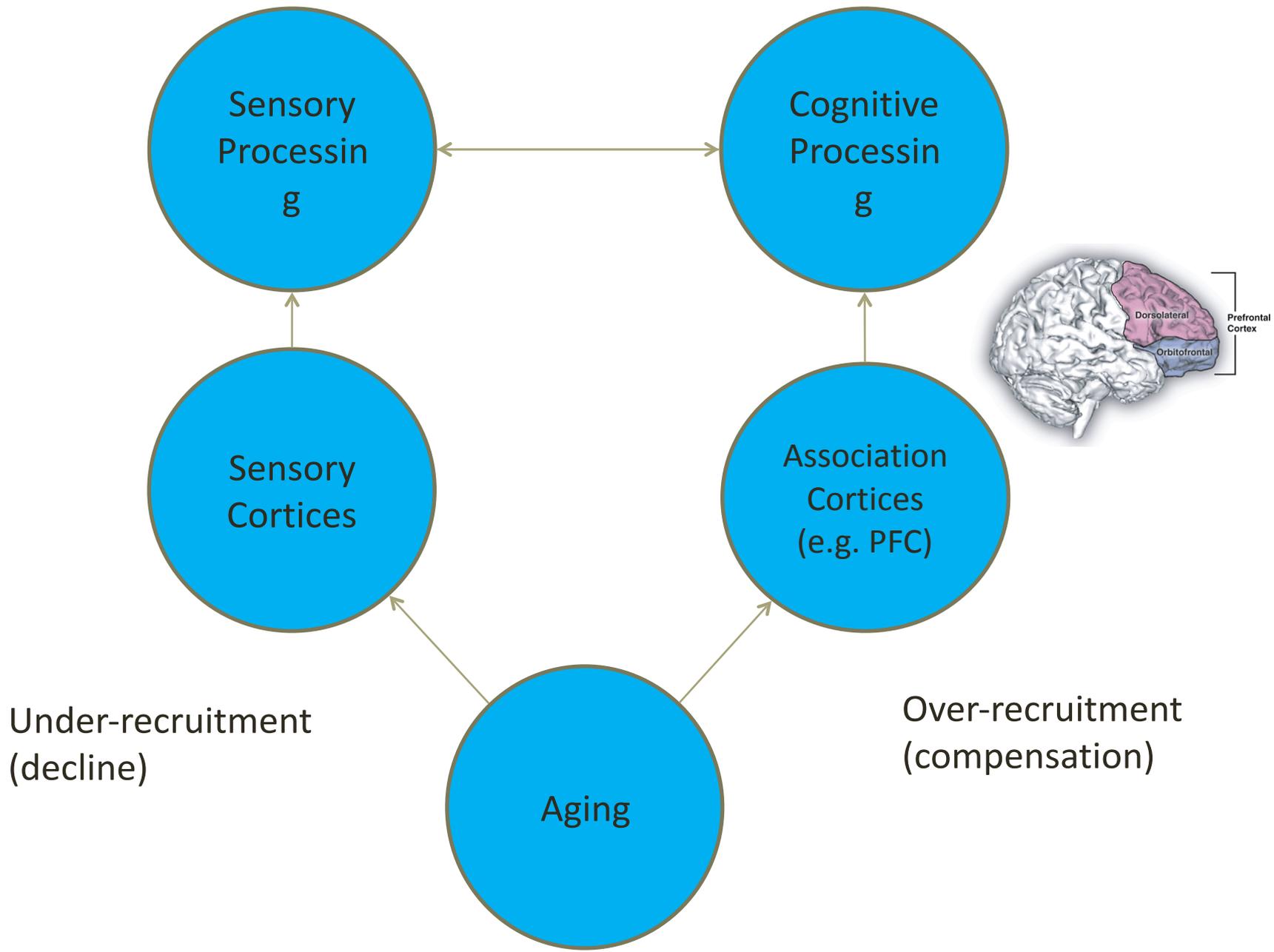
# Late-Life Depression & Risk of Dementia

## 23 Prospective Studies

Bassuk, 1998  
Becker, 2009  
Chen, 1999  
Chen, 2008 (UK)  
Chen, 2008 (Chinese)  
Dal Forno, 2005 (Males)  
Dal Forno, 2005 (Females)  
Devanand, 1996  
Fuhrer, 2003  
Gatz, 2005  
Geerlings, 2000  
Geerling, 2008  
Goveas, 2011  
Hébert, 2000  
Irie, 2008  
Kim, 2010  
Köhler, 2011  
Lenoir, 2011  
Li, 2001  
Lindsay, 2002  
Palmer, 2007  
Palsson, 1999  
Saczynski, 2010  
Spira, 2012  
Yaffe, 1999

**Summary: 1.85 (1.67-2.04)**





# PACT-MD

**P**reventing  
**A**lzheimer's dementia with  
**C**ognitive remediation plus  
**t**DCS in  
**M**CI and  
**D**epression



Brain Canada  
Foundation

# Transcranial Direct Current Stimulation (tDCS)



HDCKit

# Electrical Stimulation

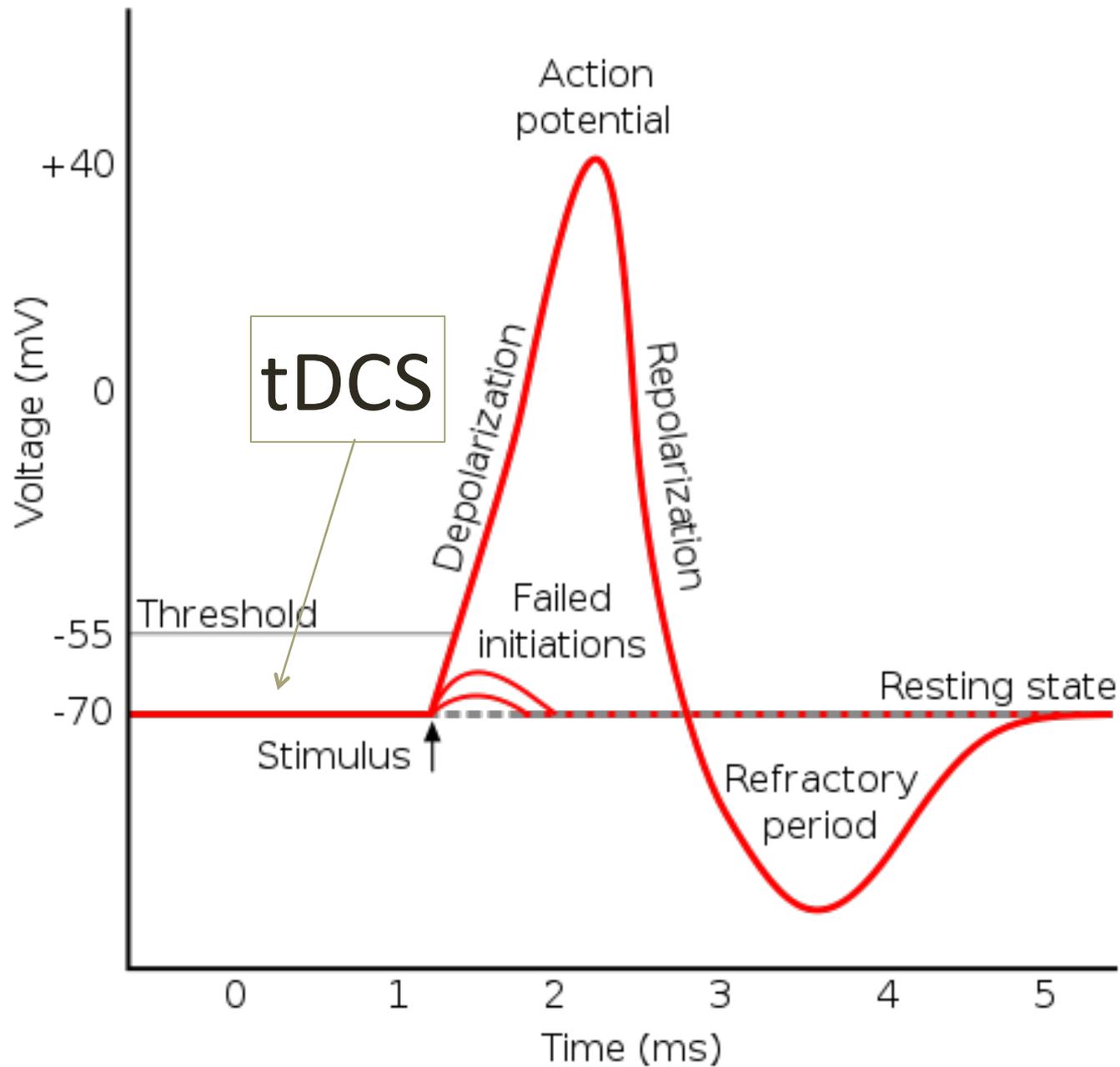


Egyptian Nile Catfish -  
**Malapterurus electricus**  
-2,500 BC → Arthritis

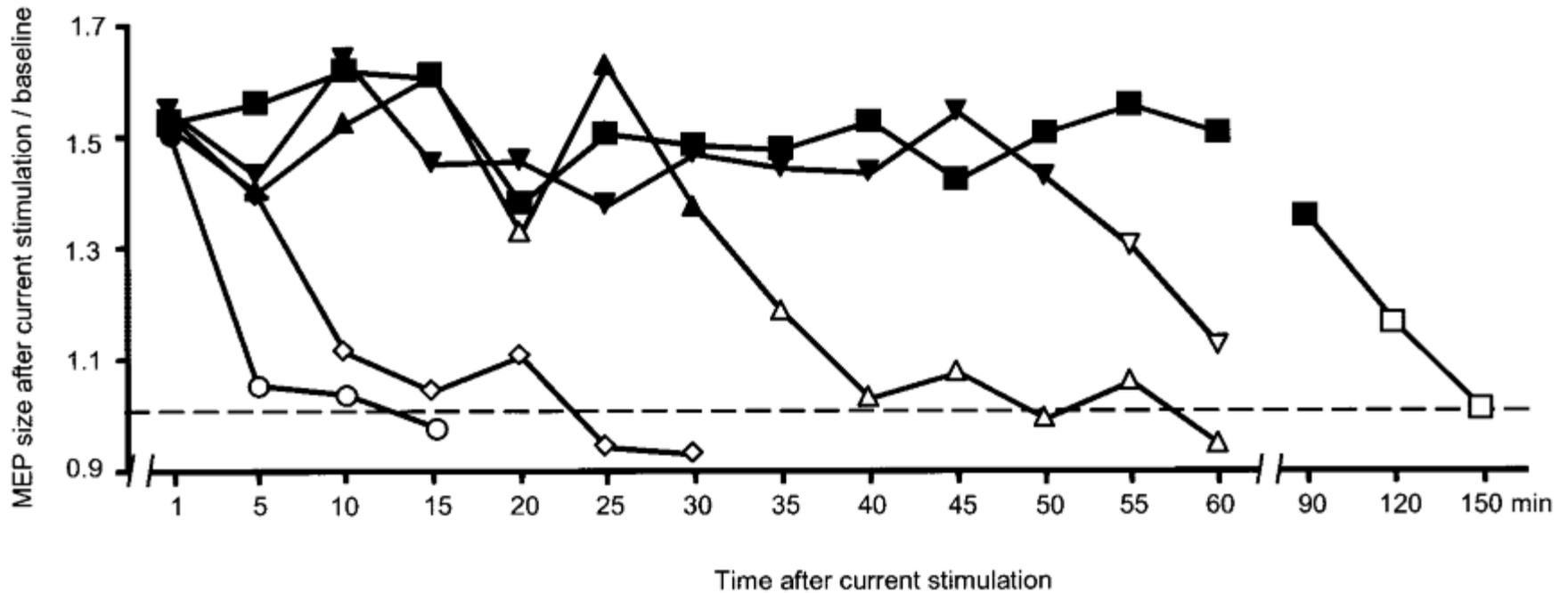
Scribonius Largus used a live torpedo fish to treat a patient with gout and wrote in 46 AD that headaches and gout ... other pains could be cured by standing in shallow water near these electric fish



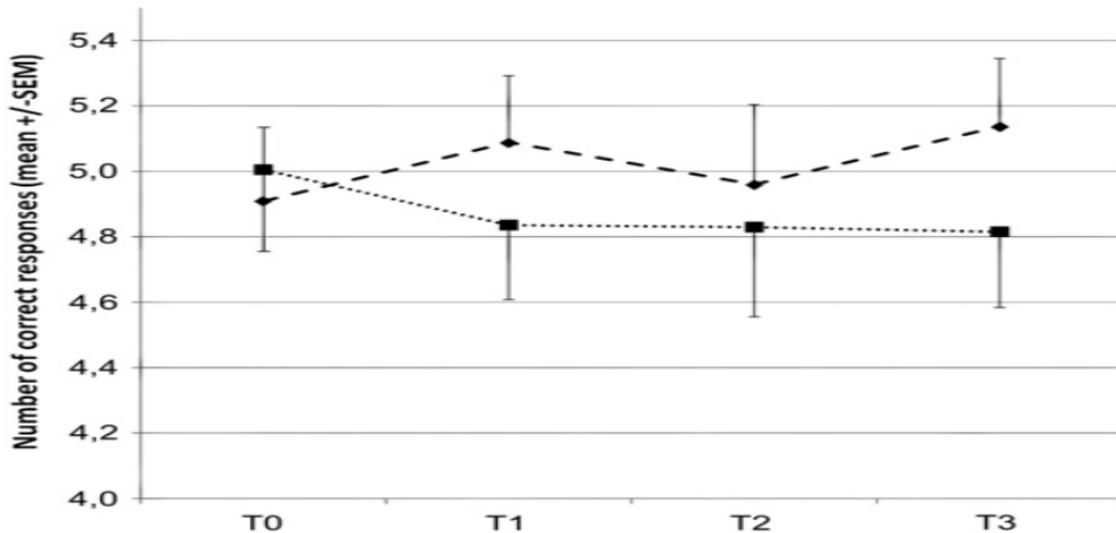
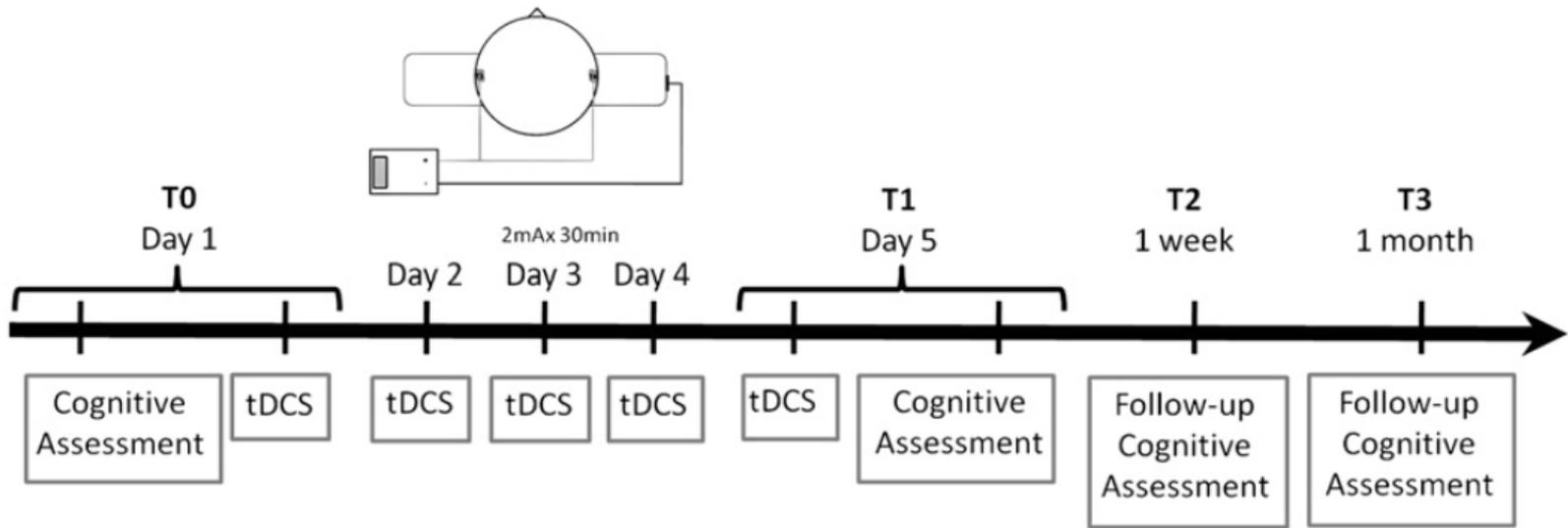
The Arabians emphasized the virtues of the sleep, which followed the jolting contact with fish. Haly Abbas referred to the latter as the Pisces dormitans. Avicenna and Averhoes thought it was efficacious when placed on the brow of persons afflicted with migraine, melancholy, or epilepsy



# tDCS to the Motor Cortex



# tDCS in Alzheimer Dementia

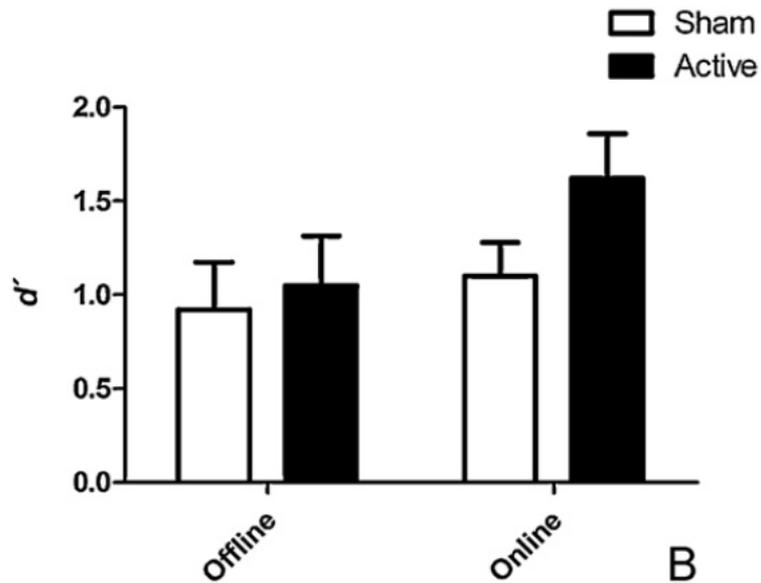
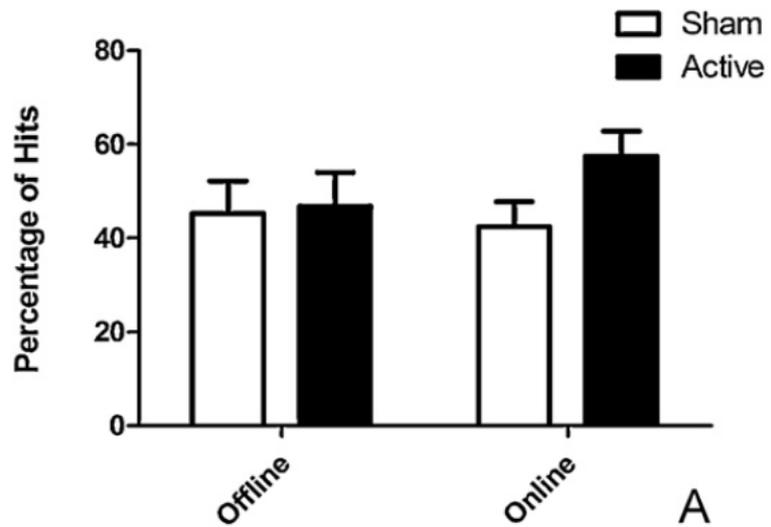


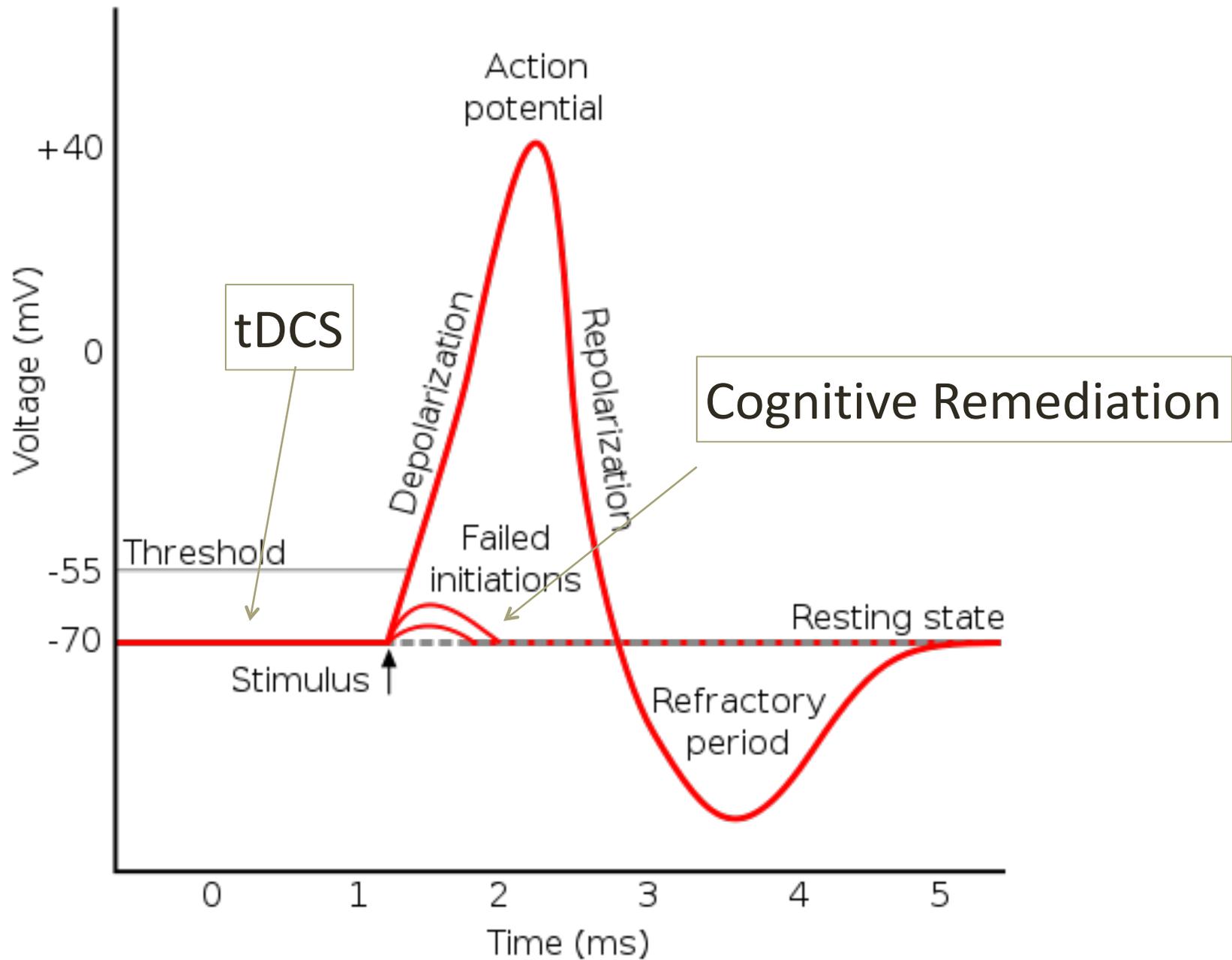
—◆— Anodal tDCS  
 -●- Sham tDCS

N = 15  
 Mean Age ~ 79  
 Number of sessions = 5

Bitemporal Anodal tDCS  
 (cathode right deltoid)  
 2 mA

# tDCS in Major Depression - Cognition





# Principles of Cognitive Remediation

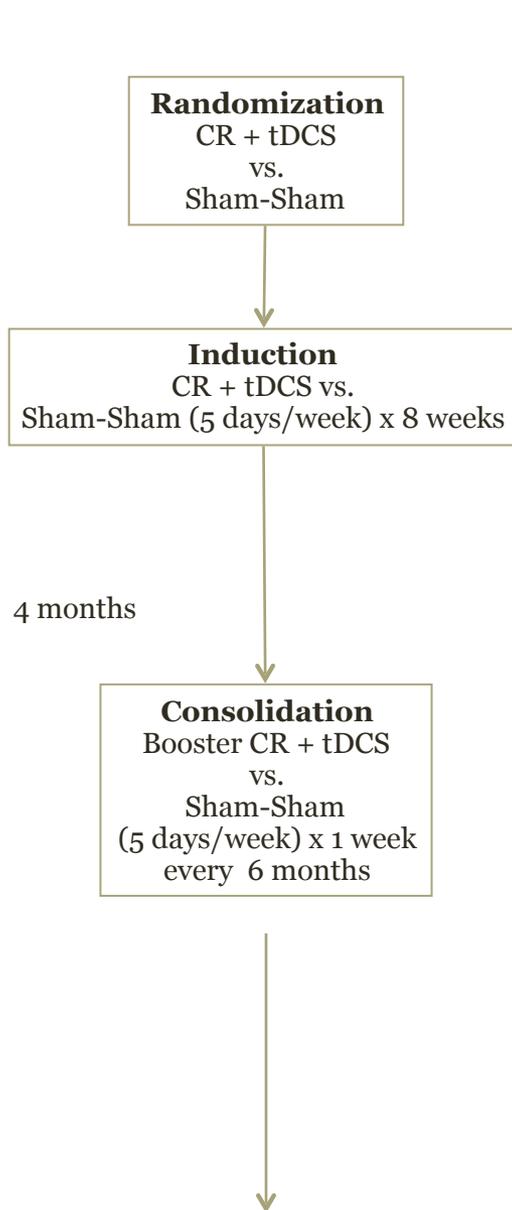
Principle	Description
Strategic	The development of mental strategies to optimize cognitive performance and task completion
Drill and Practice	The repetition of cognitive exercises over many sessions until performance has improved
Hierarchical	The progression of targeted cognitive abilities from the basic to more complex
Cueing	The use of external aids (usually auditory or visual) to support cognitive performance
Fading	The gradual removal of cues and external aids in cognitive exercises to increase difficulty
Adaptive	The adjustment of the difficulty of cognitive exercises so they remain challenging and engaging
Anchoring	The linking of cognitive exercises to "real world" behaviors and areas functioning domains they support
Integration with Other Treatments	The use of additional schizophrenia treatments and supports to maximize the benefits of cognitive remediation

Eligibility criteria for PACT-MD participants with mild cognitive impairment (MCI) or major depressive disorder (MDD)

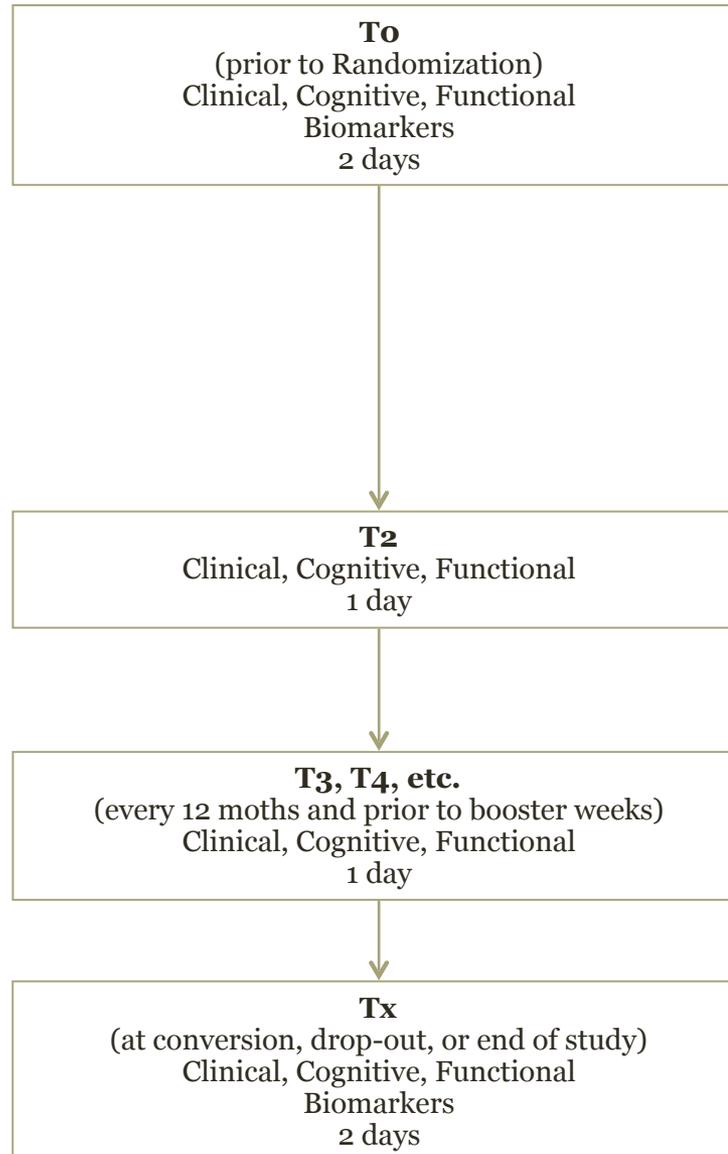
	MCI group	MDD group with or without MCI
Inclusion criteria	<ul style="list-style-type: none"> <li>*Age &gt; 60</li> <li>*Meets DSM-5 criteria for Mild Neurocognitive Disorder</li> </ul>	<ul style="list-style-type: none"> <li>*Age <math>\geq</math> 65</li> <li>*Meets DSM-5 criteria for one or more major depressive episode with an offset between 2 months and 5 years or an offset of 5 years or longer if at least one episode was during the participant's adult life and it received medical attention (e.g., hospitalization; saw a psychiatrist or primary care physician; or treatment with an antidepressant)</li> </ul>

\*MADRS score of 10 or below

## Randomized Blind Interventions



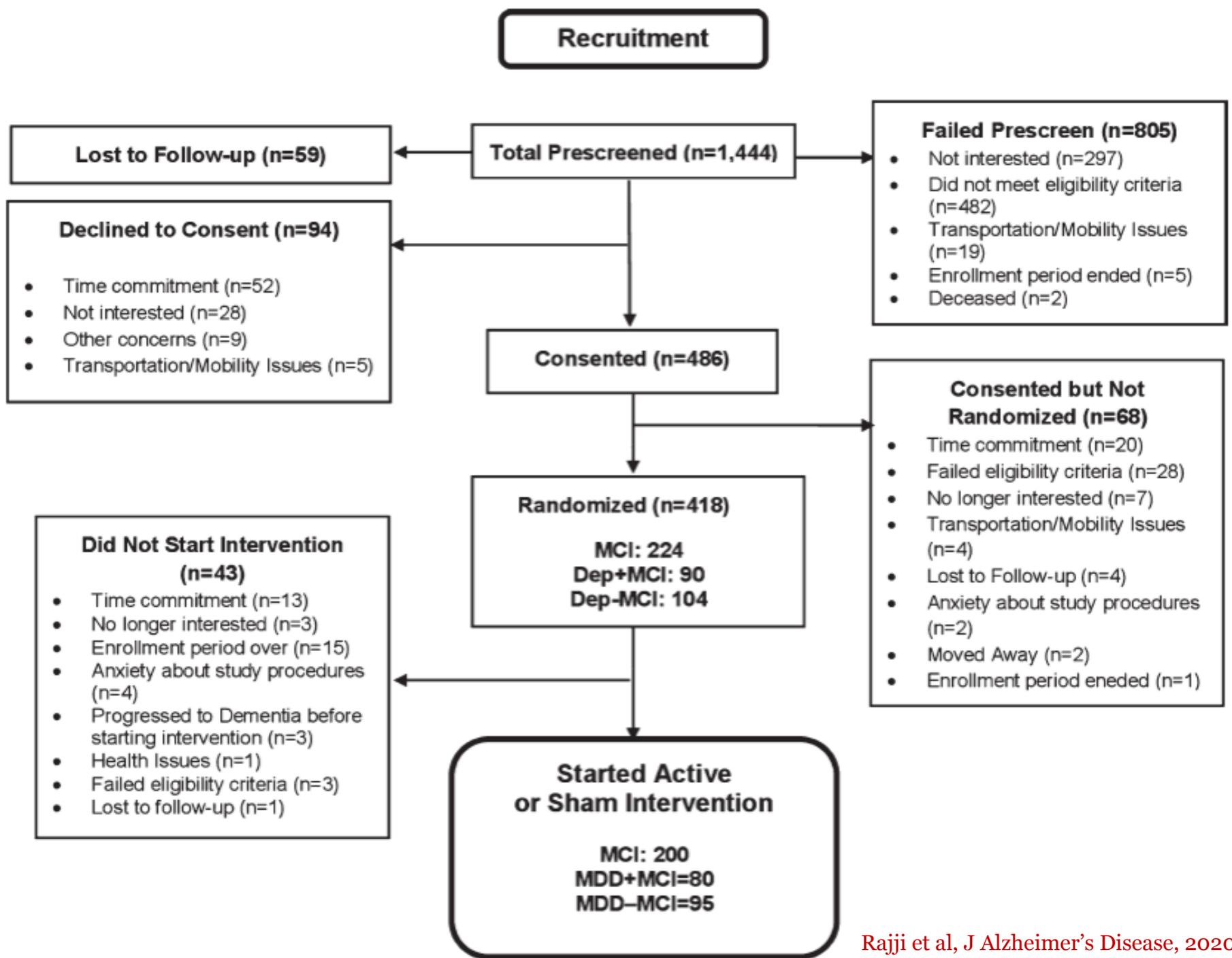
## Assessments and Biomarkers



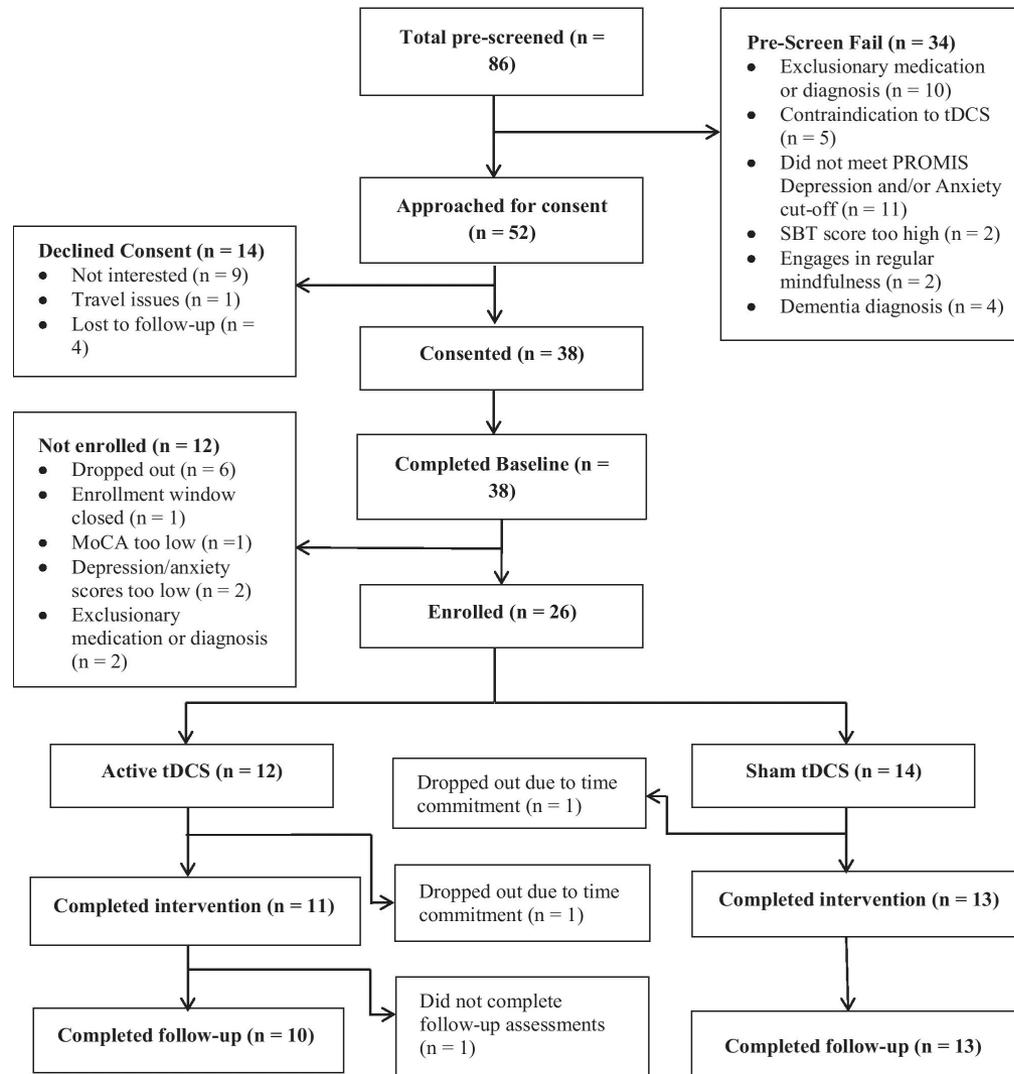
# Hypotheses

Compared to sham + sham, CR + tDCS will:

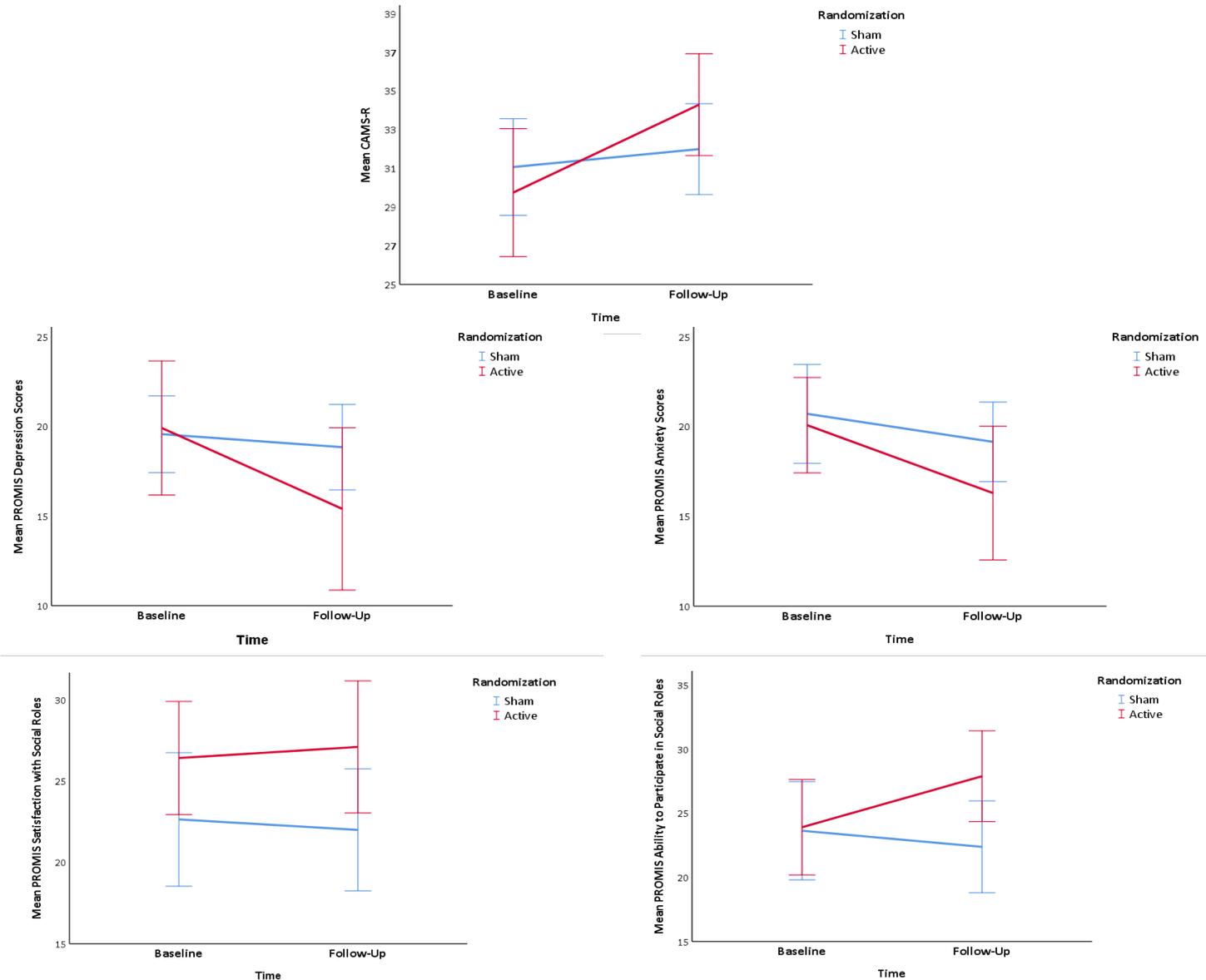
- (1) slow down cognitive decline;
- (2) reduce the progression to MCI or dementia;
- (3) improve cognition acutely.



# Mindfulness-Based Stress Reduction (MBSR) + tDCS



# Mindfulness-Based Stress Reduction (MBSR) + tDCS



# Acknowledgments

## PACT-MD

Benoit Mulsant  
Nathan Herrmann  
Bruce Pollock  
Tarek Rajji

Marom Bikson  
Christopher Bowie  
Daniel Blumberger  
Meryl Butters  
Zafiris J. Daskalakis  
Corrine Fischer  
Alastair Flint  
Sanjeev Kumar  
Krista Lanctôt  
Eric Lenze  
Benoit Mulsant  
Bruce Pollock  
Kevin Thorpe  
Reza Zomorodi

