



Multi-Modal Therapies for Brain Disorders

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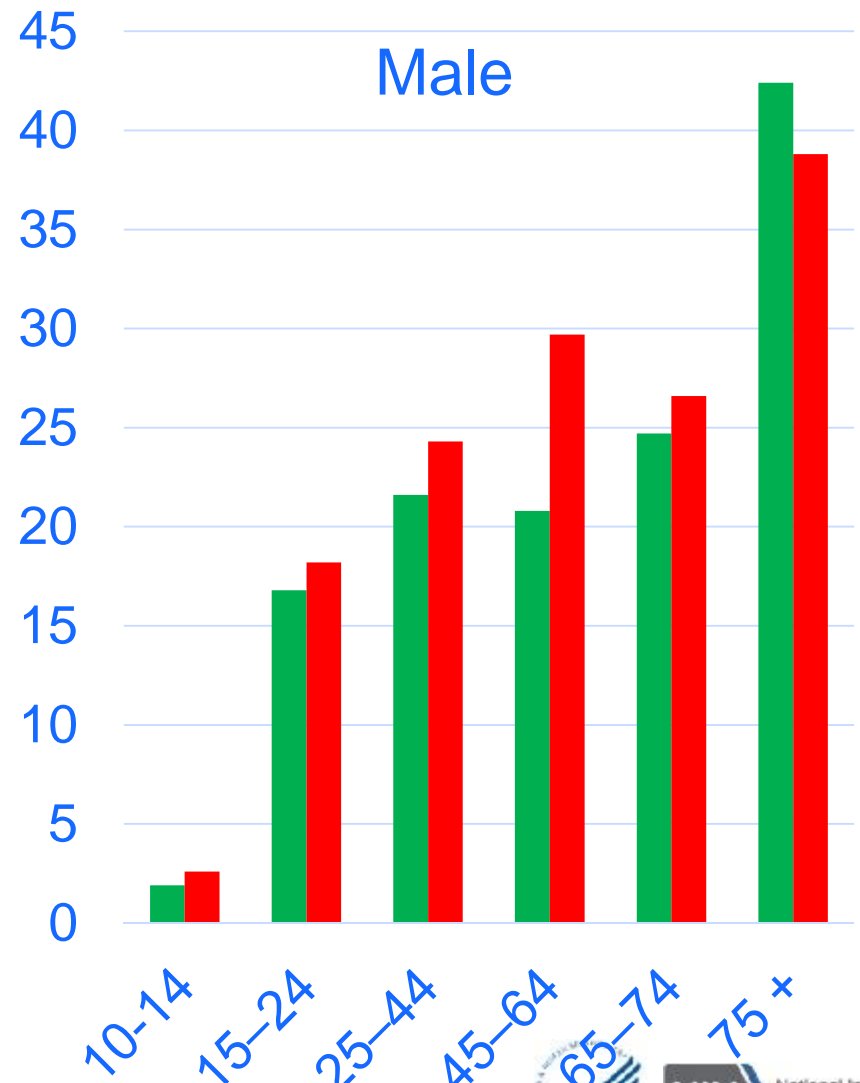
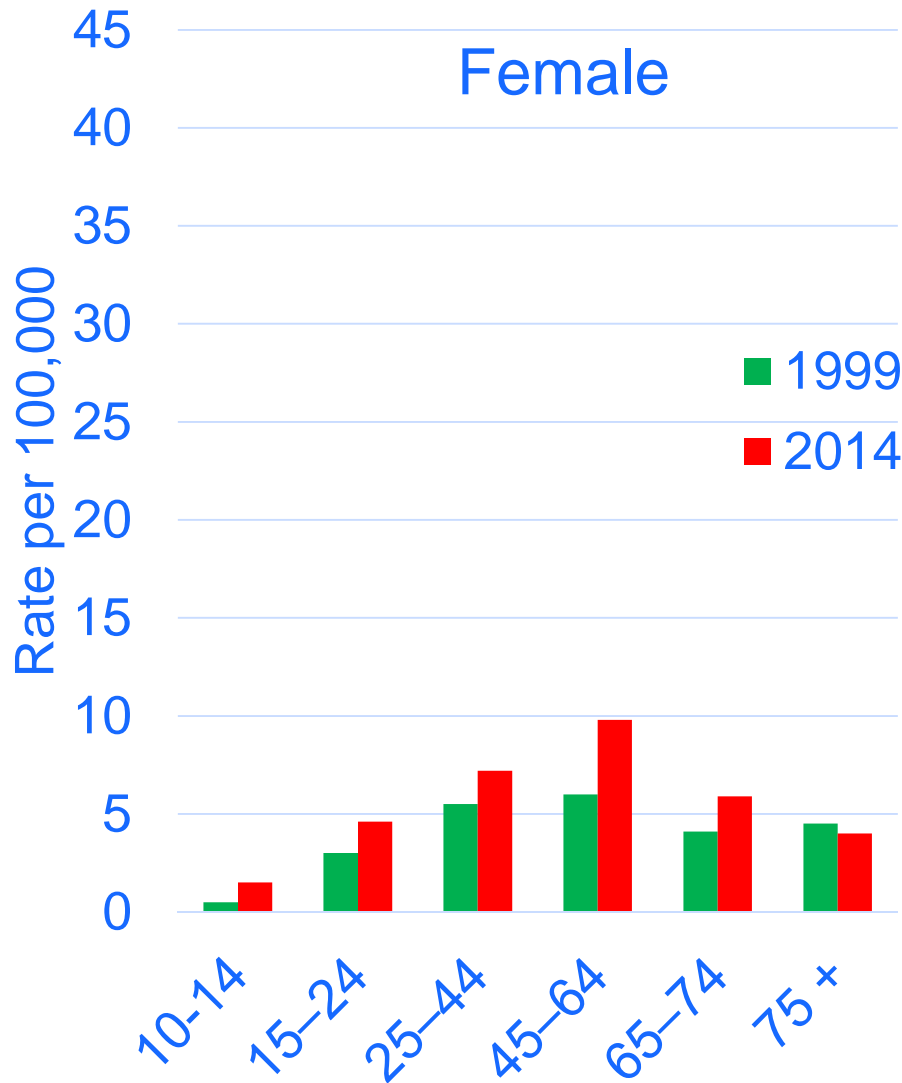
NIMH

6/14/2016



National Institute
of Mental Health

Suicide Rates Climbing: CDC Report



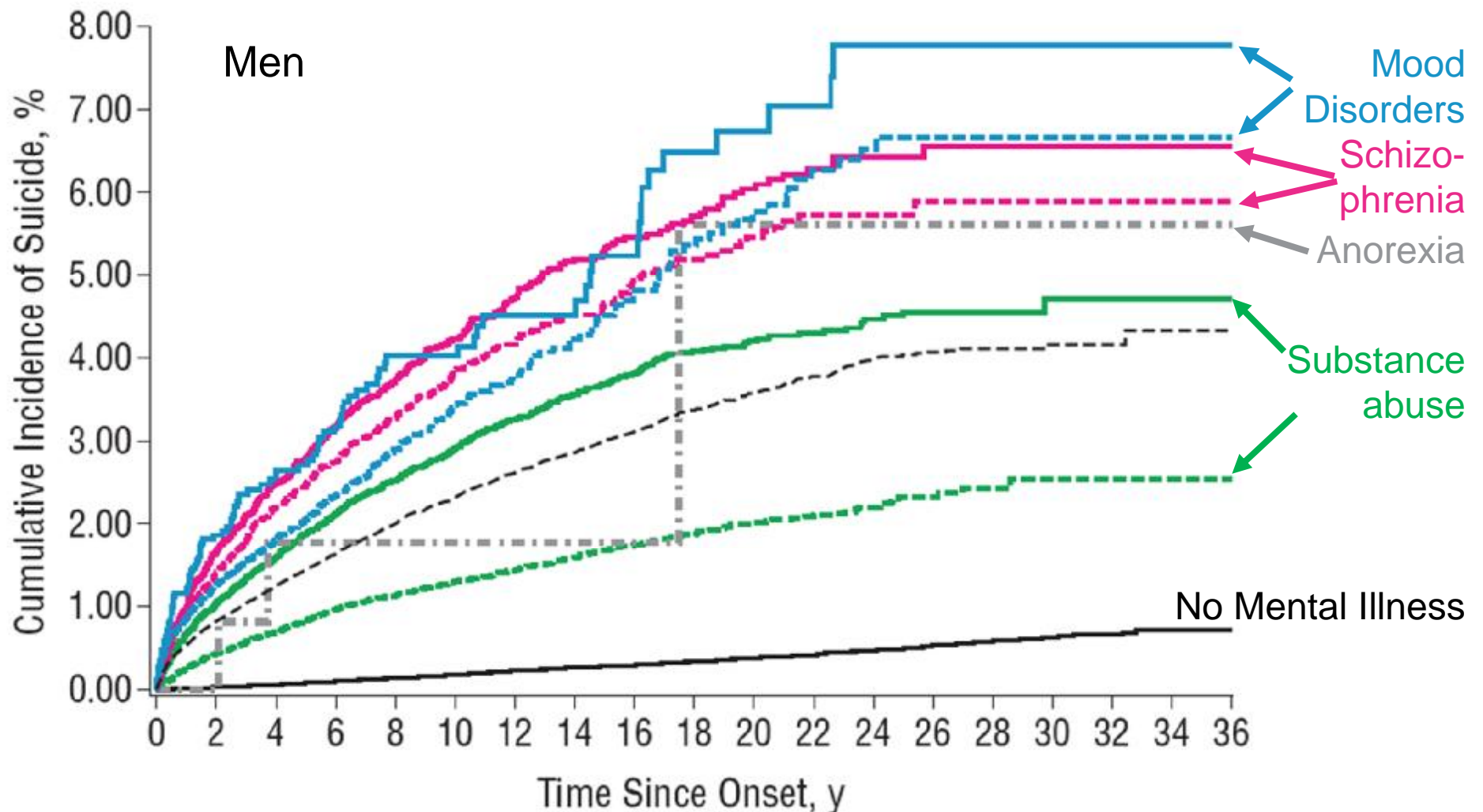
All differences significant



CDC National Center for Health Statistics April 2016

Risk for Suicide: Mental Illness

Nordentoft et al JAMA Psychiatry 2011



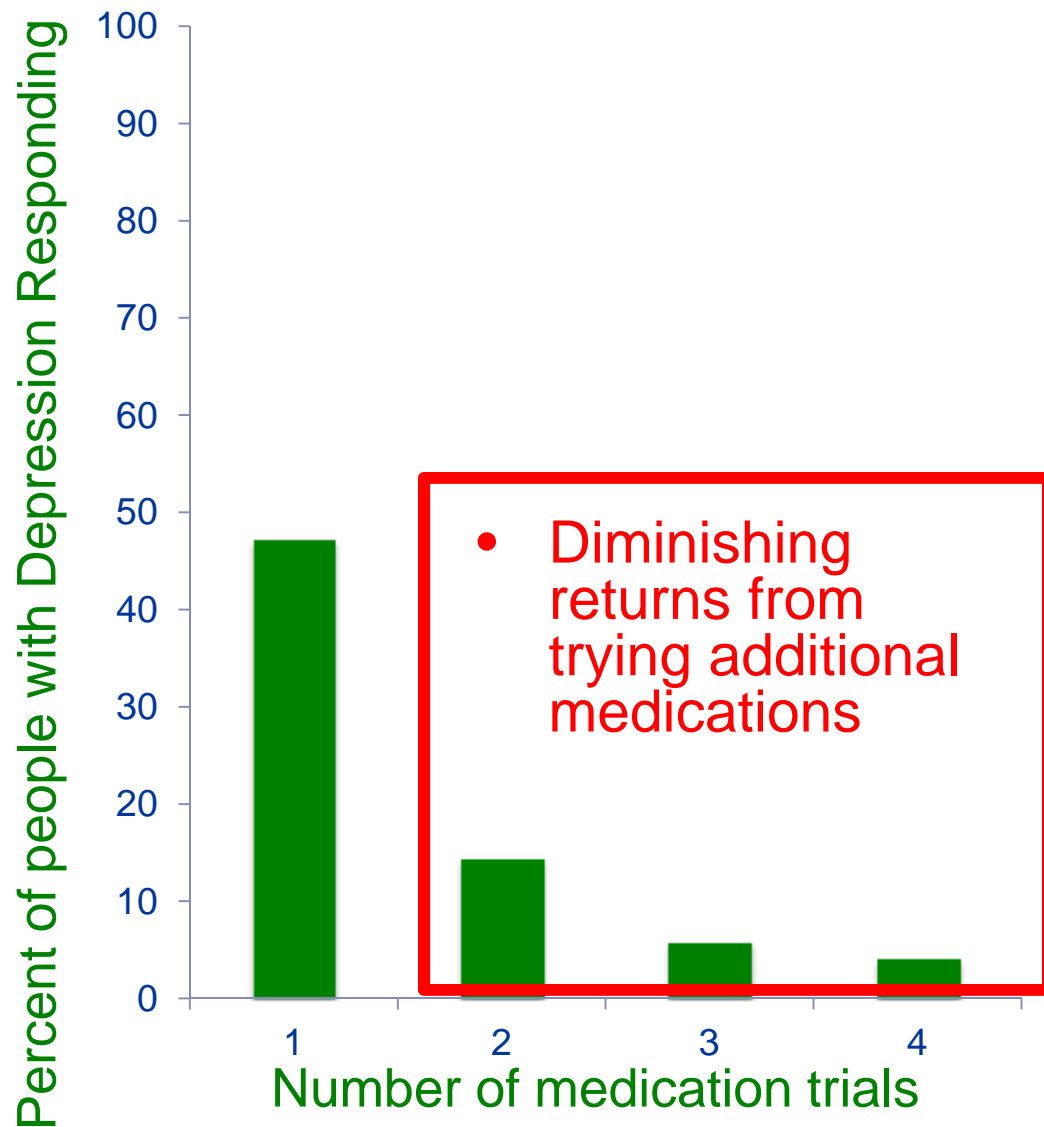
- N=176,347 persons in Denmark born 1955-1991
- Followed from first mental health contact



NIH National Institute of Mental Health

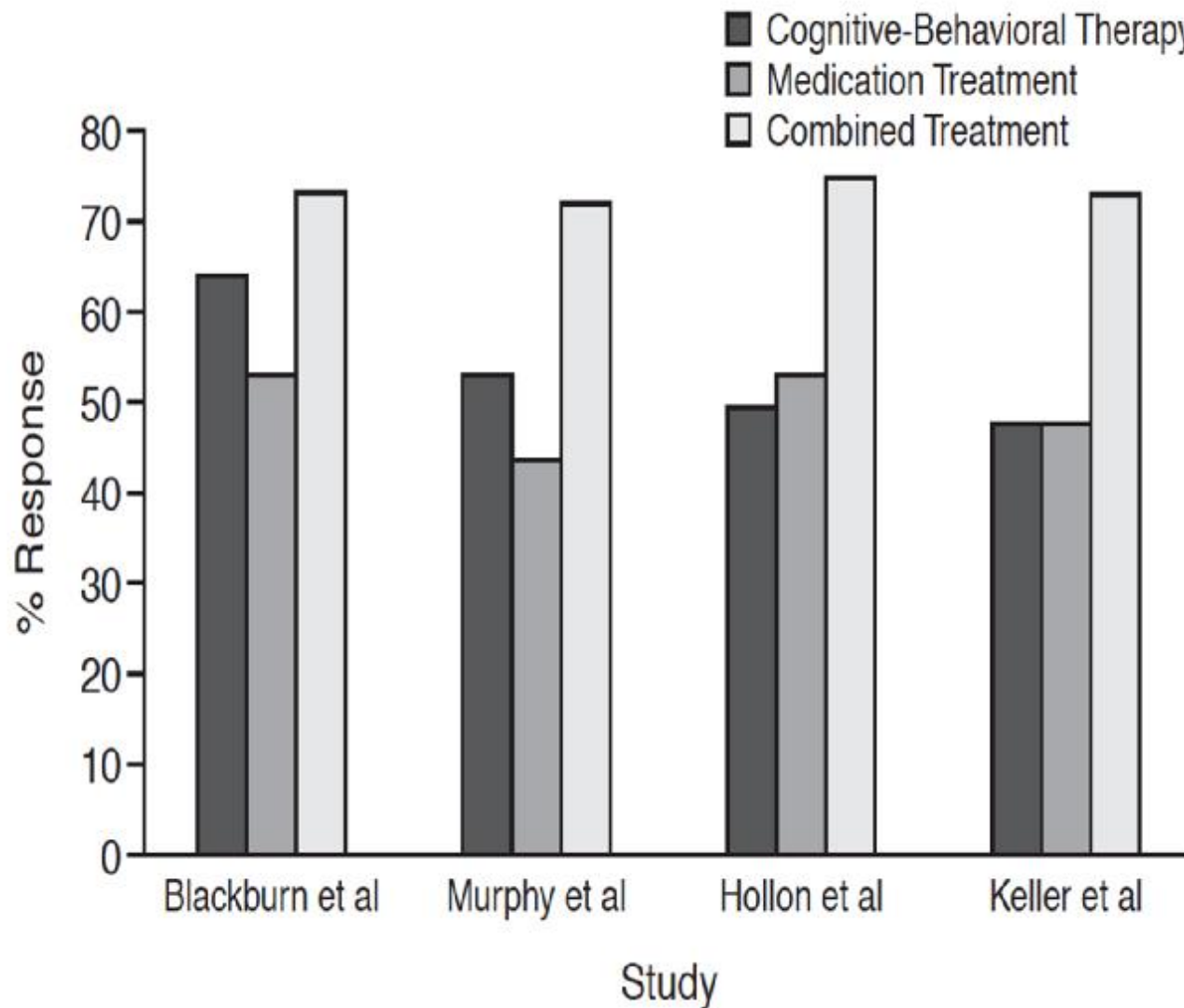
Limited Efficacy of Mono-Therapy in Depression

Source: STAR-D Trial



- Highlights need for more effective approaches to bend the curve for serious mental illness and suicide prevention
- Role for multi-modal therapies
- Reflects standard of care in psychiatry today, but rarely studied systematically

Combo-Therapy Standard of Care for Depression



- Combining 2 treatments with comparable efficacy, but which address different aspects of the illness
- Recommended in practice guidelines

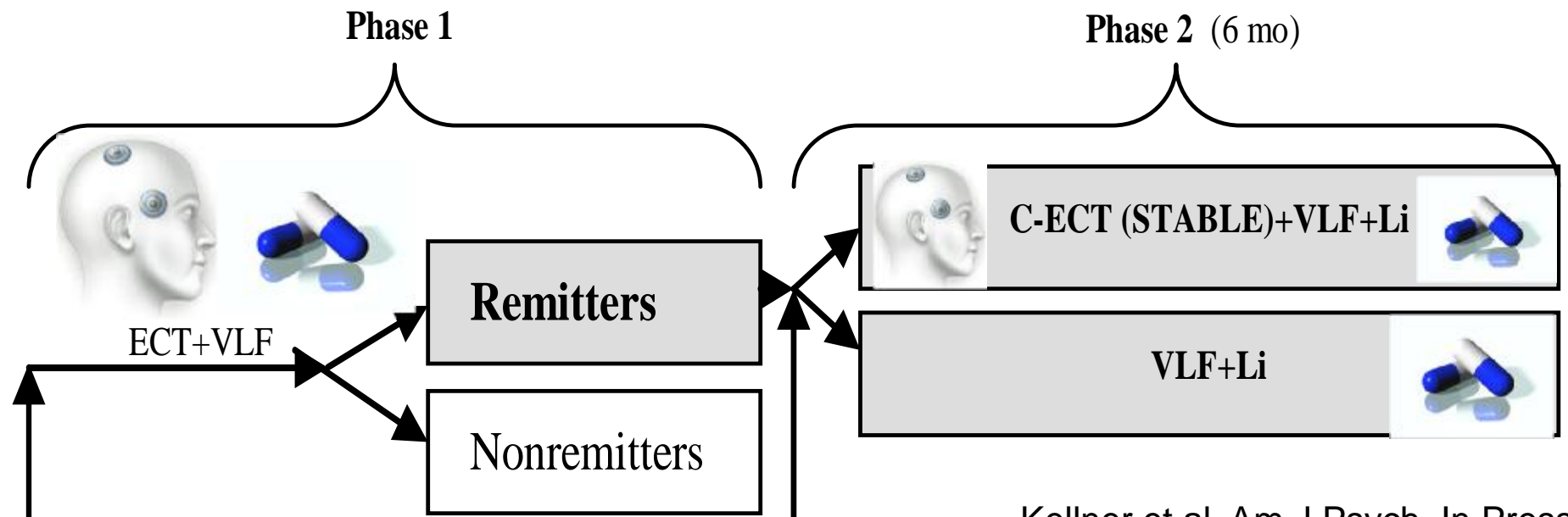
Hollan et al. J Clin Psych 2005

ECT + Combination Pharmacotherapy in Depressed Elders

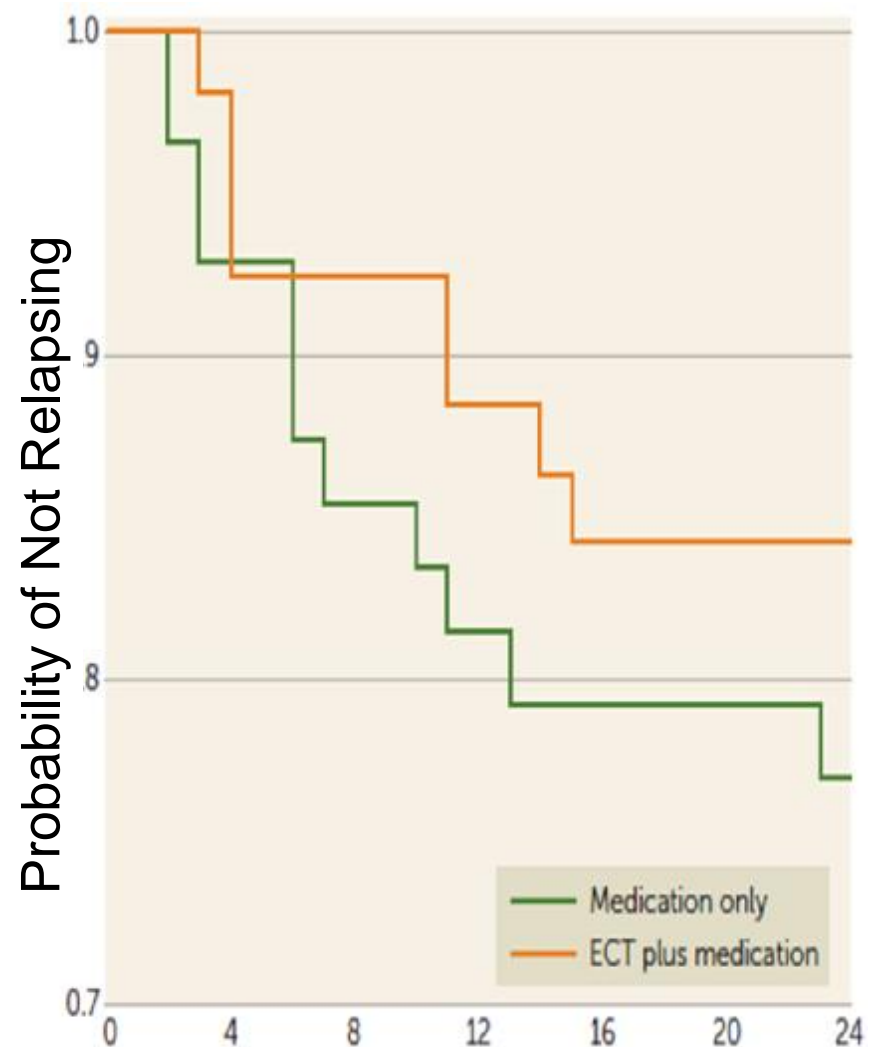
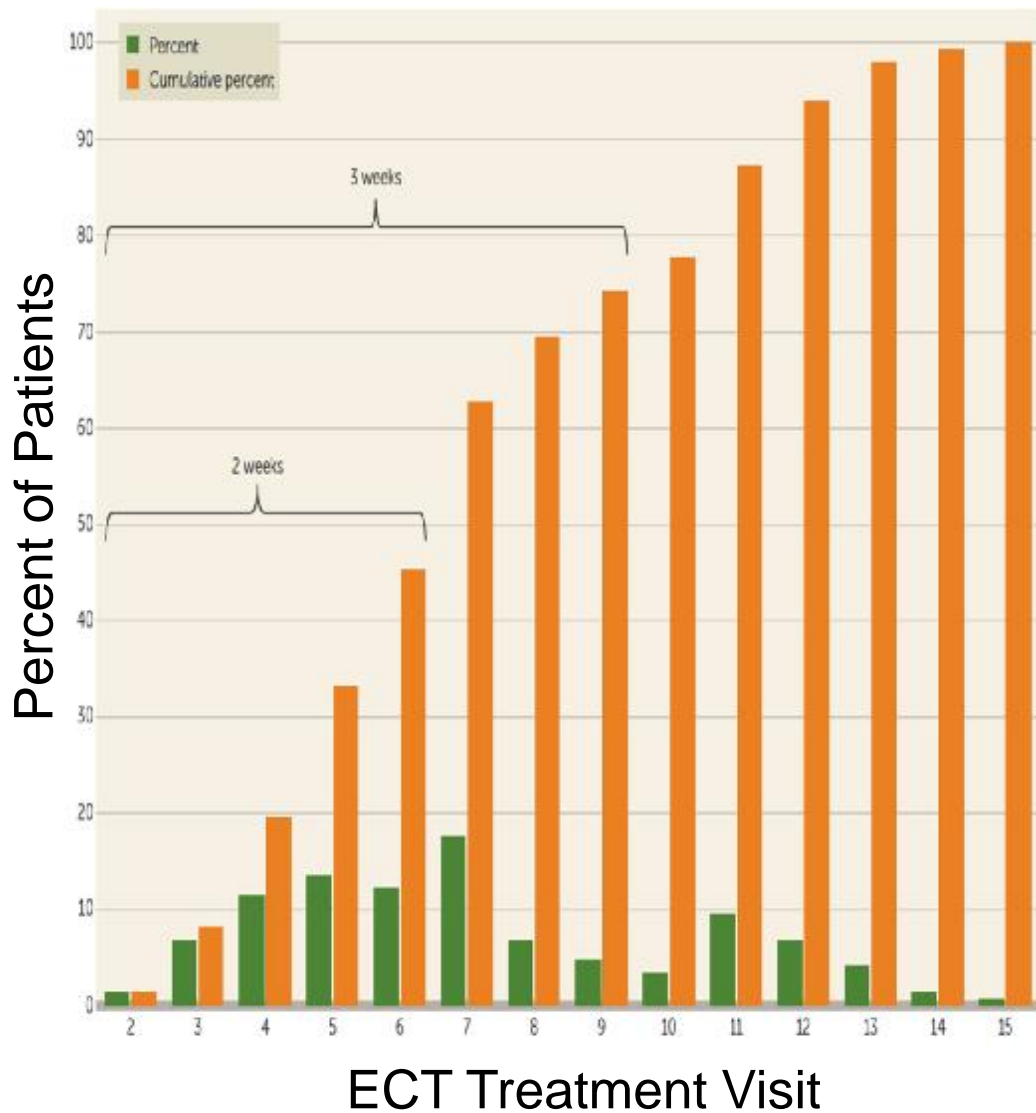
- Prolonging Remission in Depressed Elders (PRIDE)
 - NIMH-funded U01 (PIs: Lisanby and Kellner)
 - 8 centers across the country
 - 1,326 patients screened, 240 enrolled
 - Mean age 70 ± 8 yrs, 58% female

ECT + Combination Pharmacotherapy in Depressed Elders

- Prolonging Remission in Depressed Elders (PRIDE)
- Aims: To compare efficacy and tolerability of 2 post-ECT continuation treatment strategies:
 - PHARM - venlafaxine (VLF) + Li
 - STABLE - Symptom titrated algorithm based longitudinal ECT



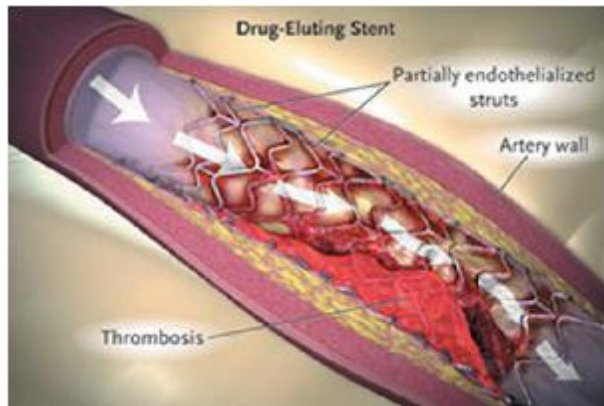
ECT + Combination Pharmacotherapy in Depressed Elders



Kellner et al. Am J Psych. In Press

Additional Definitions

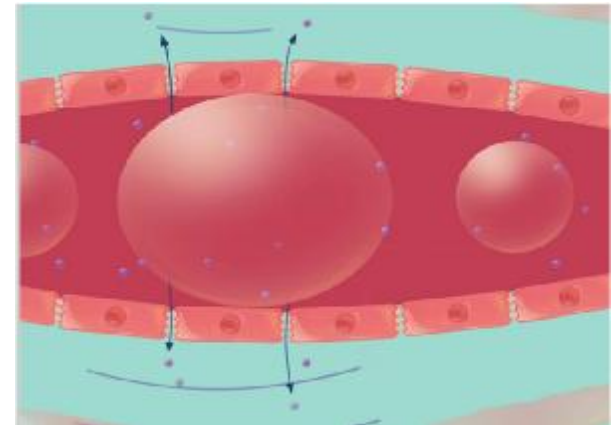
- Delivery Device
 - Device used to deliver a medication or a cognitive intervention



Drug-eluting stent



Mobile device-administered cognitive/behavioral intervention



Focused ultrasound Blood-Brain Barrier disruption for drug delivery

Additional Definitions

- Delivery Device
- Paired Associative Stimulation (PAS)
 - Simultaneous activation of a neural circuit via central and peripheral neuromodulation to induce Hebbian plasticity

Interventional paired stimulation

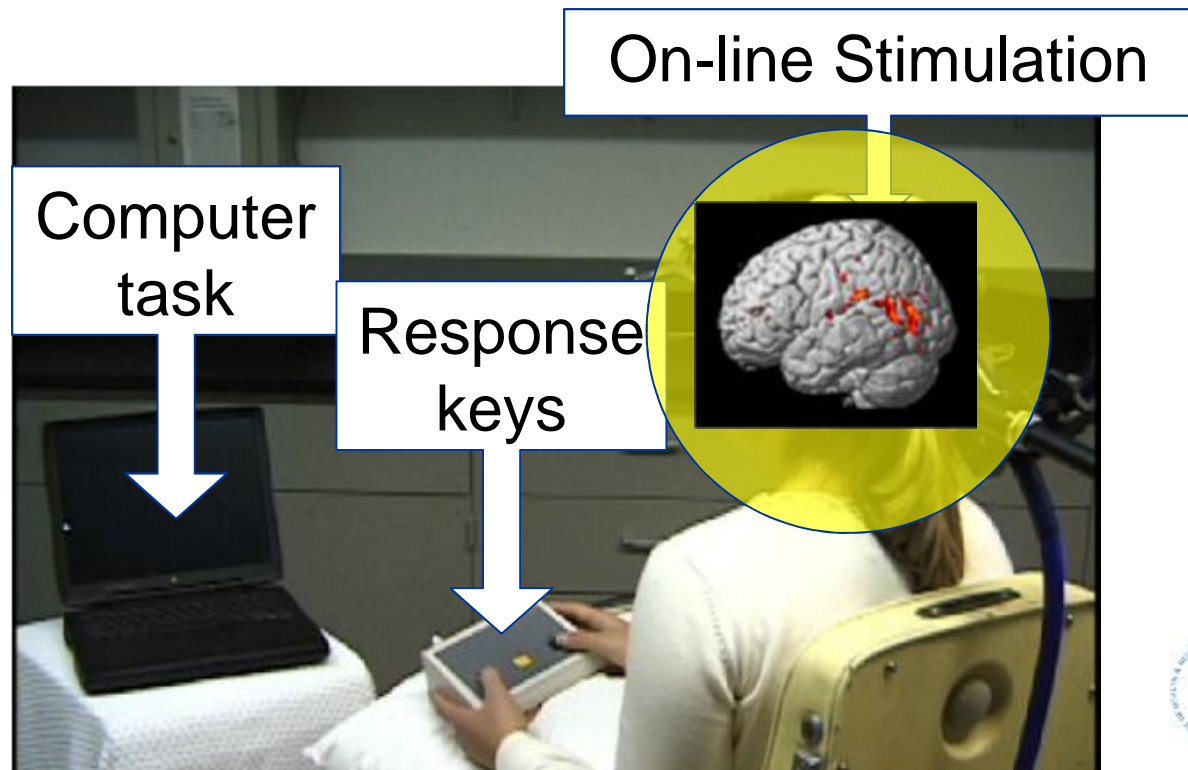


90 pairs
ISI 25 ms

Stefan et al. 2000; Ridding et al. 2001

Additional Definitions

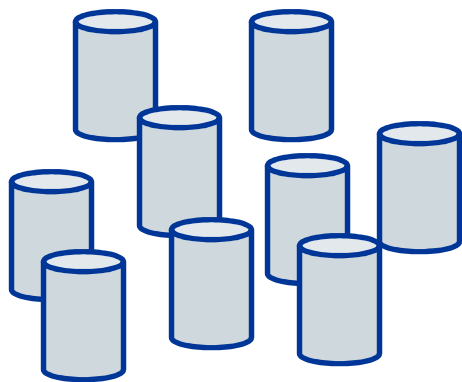
- Delivery Device
- Paired Associative Stimulation (PAS)
- Cognitive Paired Associate Stimulation (C-PAS)
 - Simultaneous activation of a neural circuit via cognitive task performance and central neuromodulation



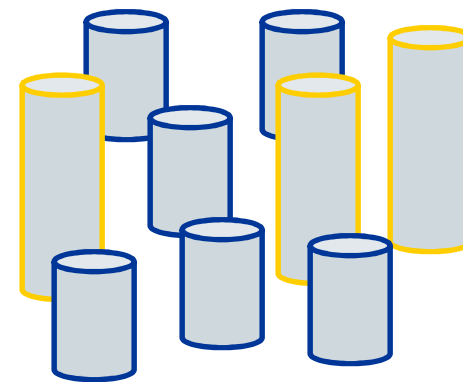
Alternative Pairing Mechanism: Behavioral Activation of Neural Ensembles

Slide Credit: Radman

neural ensemble at "rest"

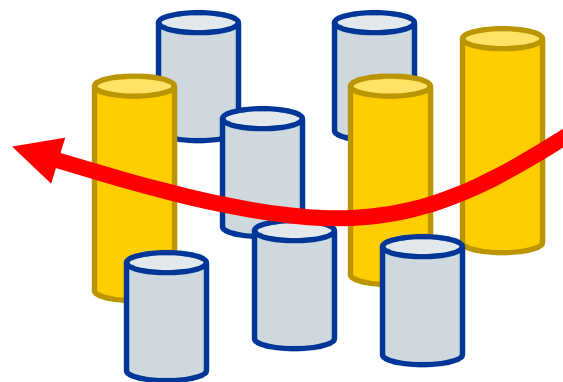


neural ensemble activation via behavior



Represents means of providing a "functional focality" to nonfocal interventions, such as tDCS or dTMS

Neurostim effects maximized at activated neurons



Stimulate the circuit while it's activated

The Therapeutic Context

Multi-Modal Therapies



The Therapeutic Context

Neuromodulation
Therapy



Multi-
Modal
Treatment
Paradigms



Psycho-
social therapy



Pharmaco-
therapy