Grounding psychiatry in brain-based biomarkers

Amit Etkin, MD PhD

CEO

Alto Neuroscience, Inc.

Professor

Stanford University

From one-size-fits all to precision psychiatry

2008:

Prozac, used by 40m people, does not work say scientists

Analysis of unseen trials and other data concludes it is no better than placebo
**Full text: the PLoS paper**

2018:

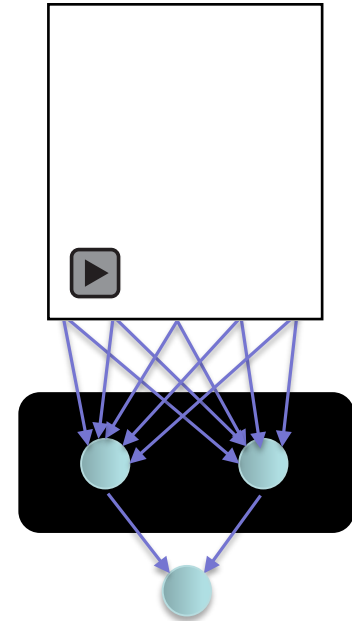**The drugs do work: antidepressants are effective, study shows**

Doctors hope study will put to rest doubts about the medicine, and help to address global under-treatment of depression
It's official: antidepressants are not snake oil or a conspiracy

EMBARC study <u>*all patients:*</u> *small effect size*

placebo (red)

sertraline (blue)

Fonzo, Nature Hum. Behav, 2019
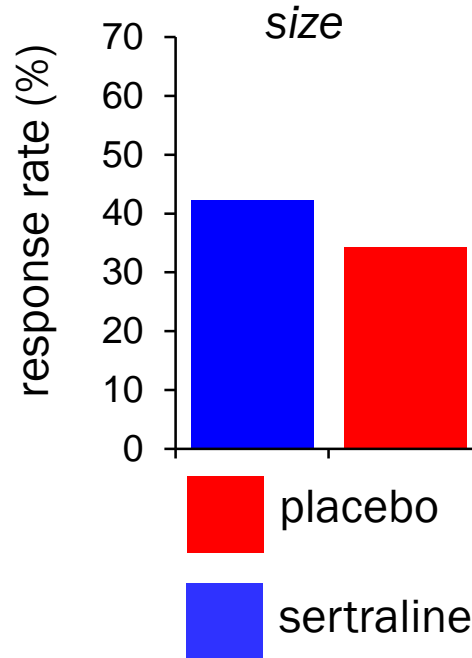
Electroencephalography (EEG)

machine learning

ALTO NEUROSCIENCE
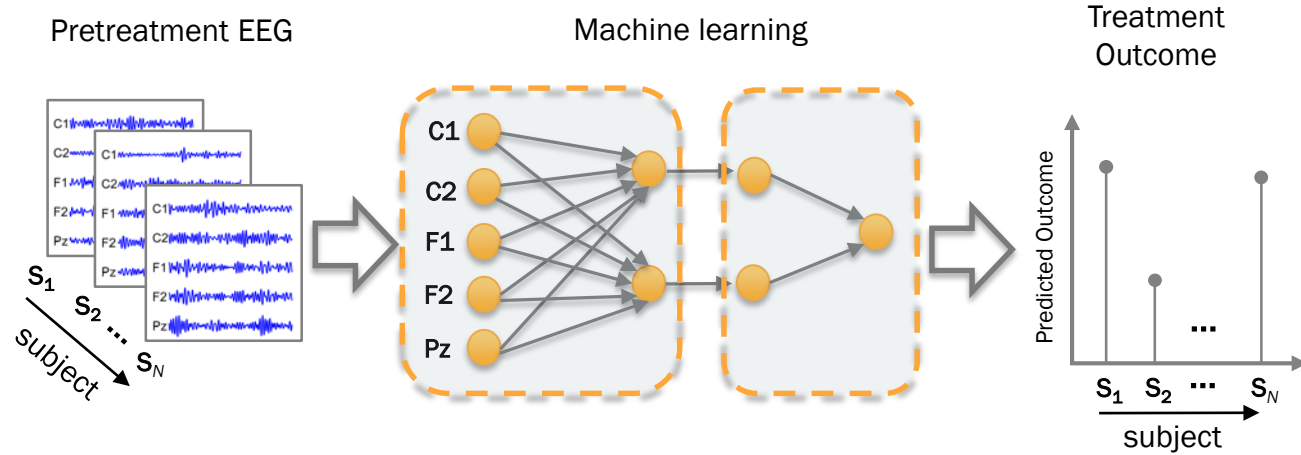
Two general approaches at machine learning

Supervised:

- Known clinical targets
- Heterogeneity in treatment outcomes

Pretreatment EEG
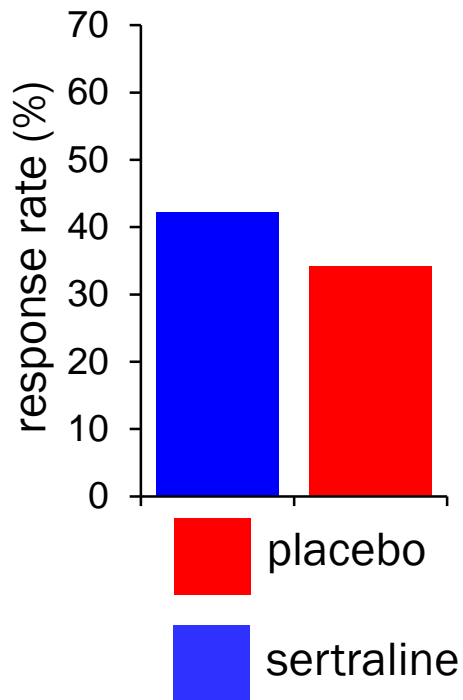
Machine learning

Treatment Outcome

Unsupervised:

- Heterogeneity in biology itself
- Challenge is aligning with clinical targets

Pretreatment EEG
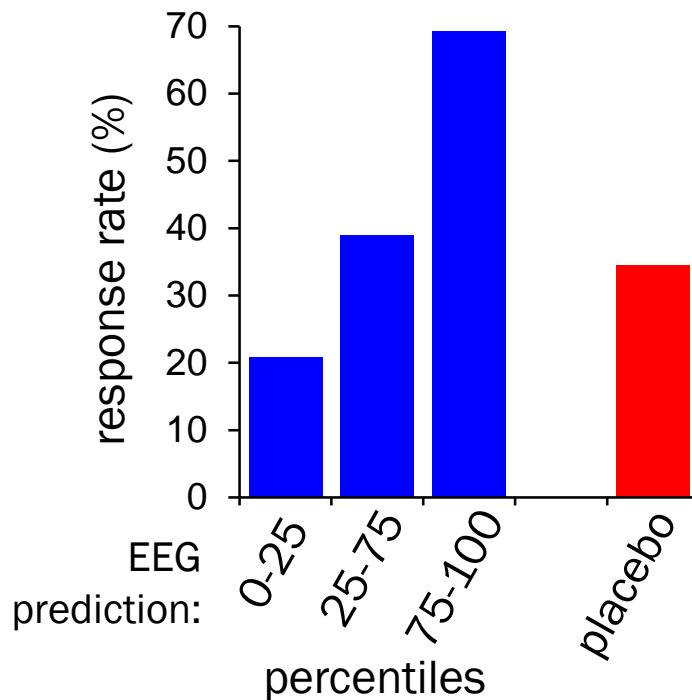
Machine learning
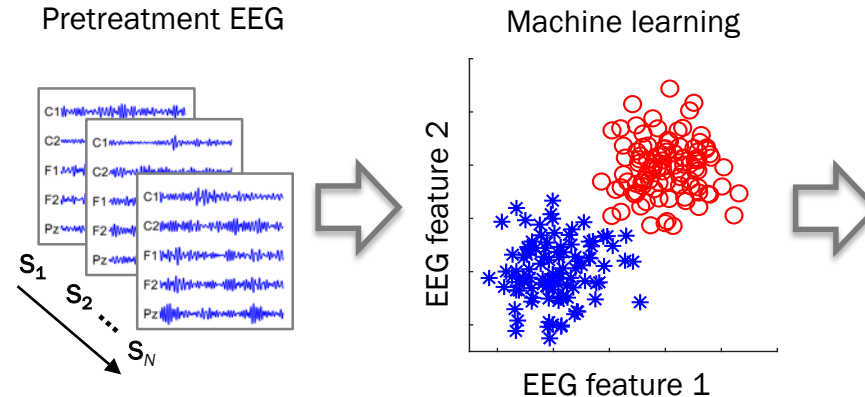
Supervised prediction of treatment outcome

all comers

split based on
sertraline EEG signature

- Independent of depression severity
- Works across EEG systems and sites

Fonzo, Nature Hum. Behav, 2019

Wu, Nature Biotechnology, 2020

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Brain connectivity networks visualized with EEG

visual:
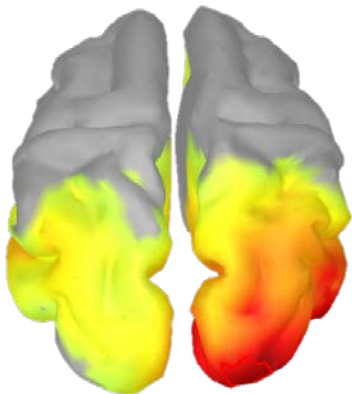
default mode:
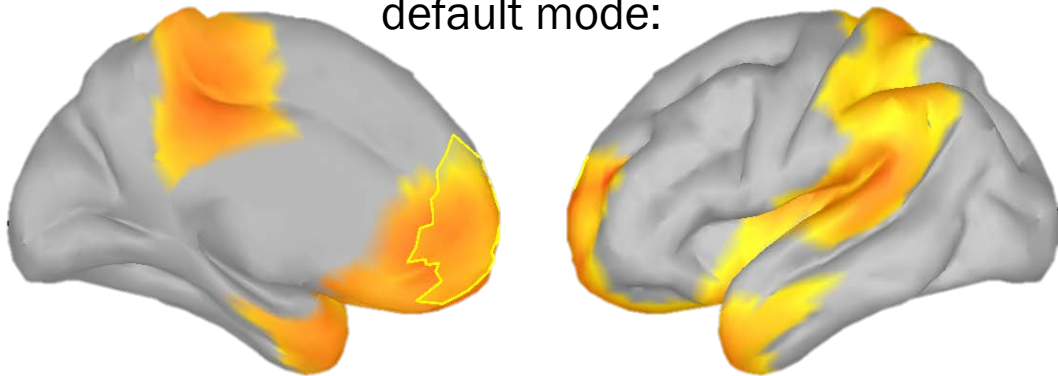
somatosensory:

frontoparietal:

Toll, Am J Psychiatry, 2020
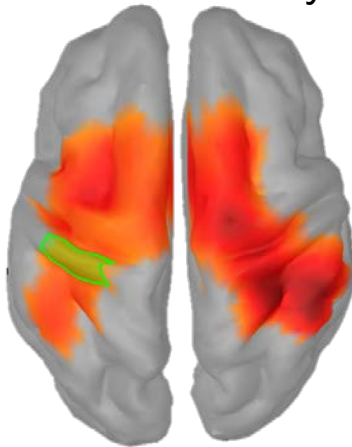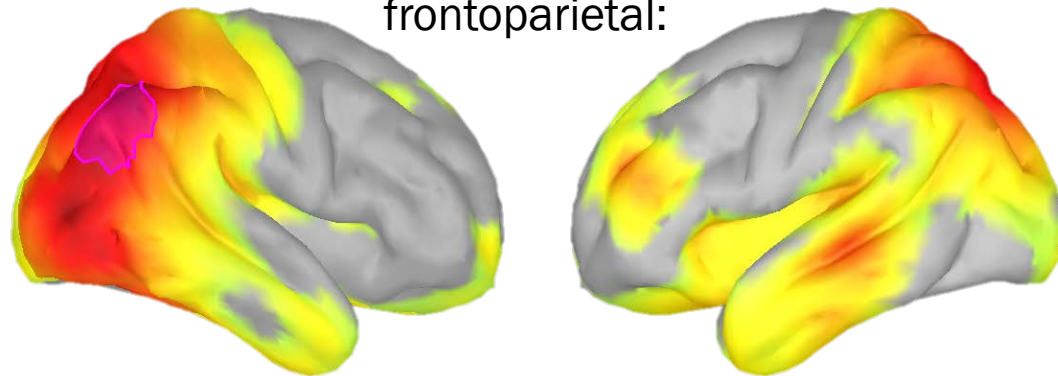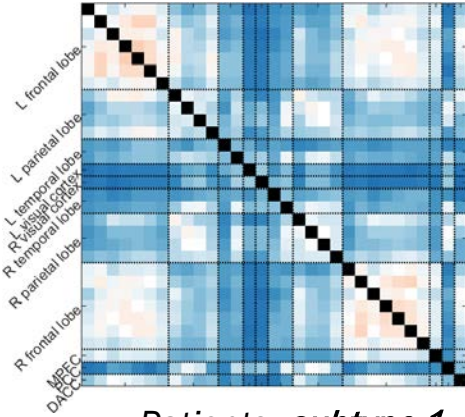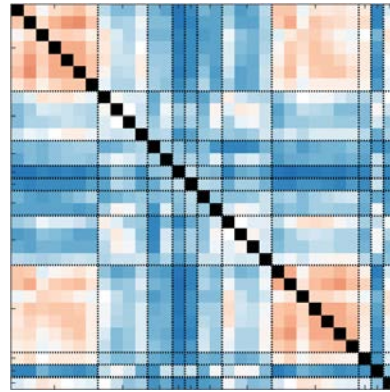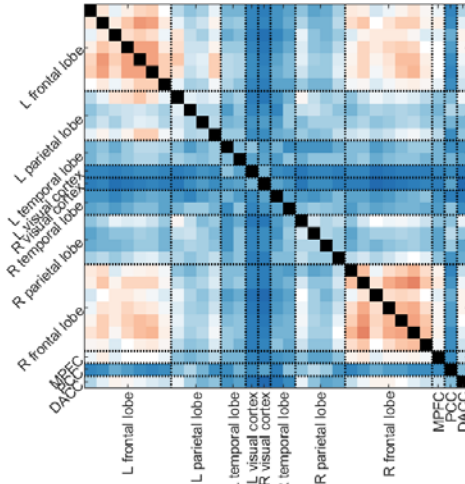
Unsupervised subtyping using only EEG
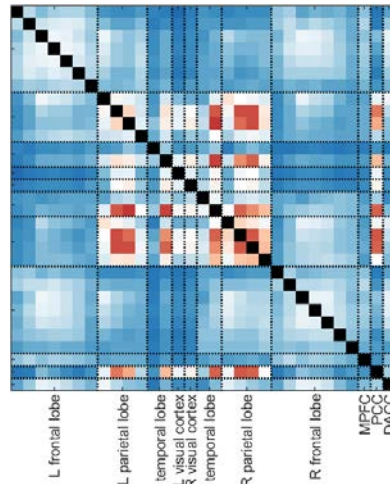

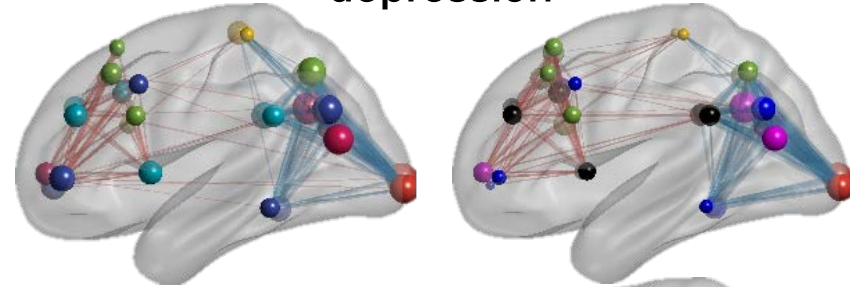*All patients*

Healthy participants
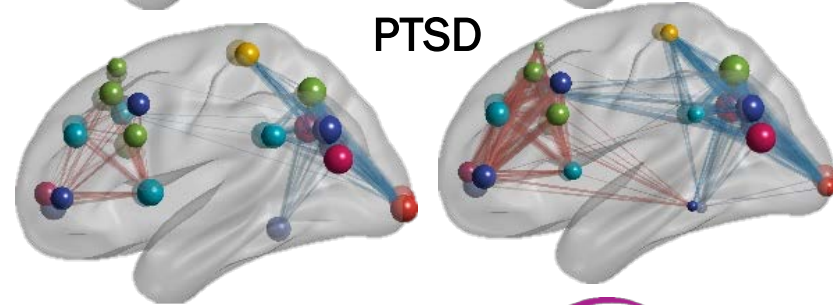
Patients: subtype 1

Patients: subtype 2

EEG subtypes identified at 90% accuracy across **four** cohorts, representing **two** disorders and **multiple** EEG systems
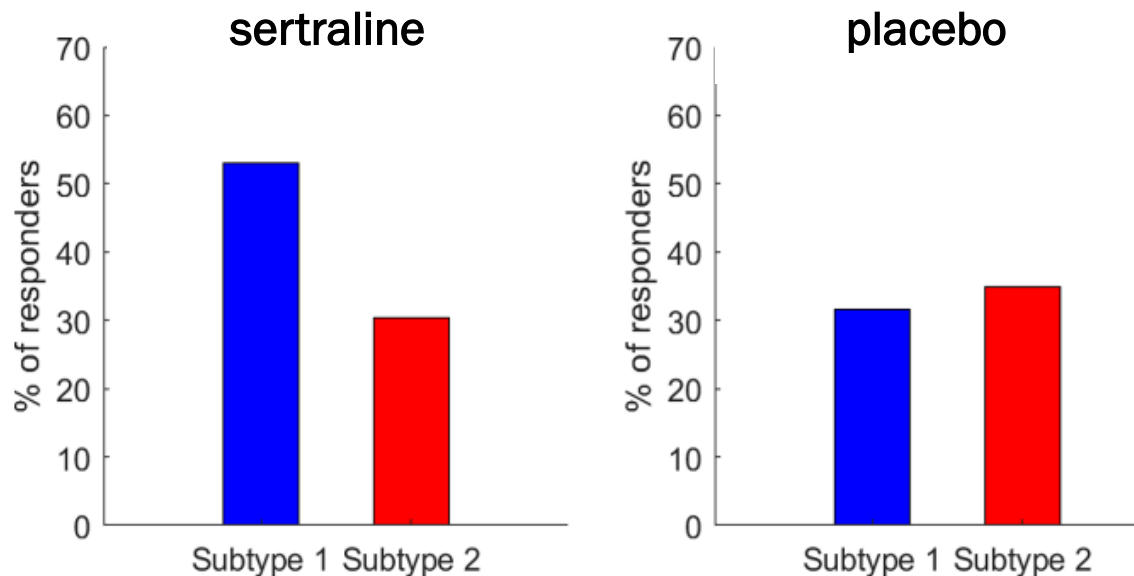
depression

PTSD

Zhang, Nature Biomed. Eng., prov. acceptance
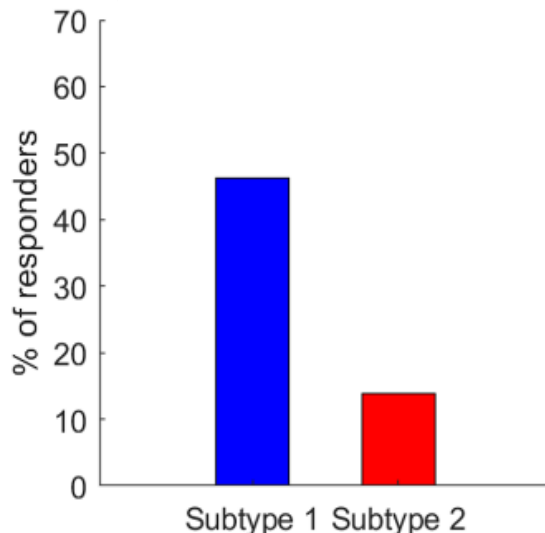
Clinical significance of EEG subtypes

Do the subtypes respond differentially to antidepressant treatment (EMBARC)?

Zhang, Nature Biomed. Eng., prov. acceptance
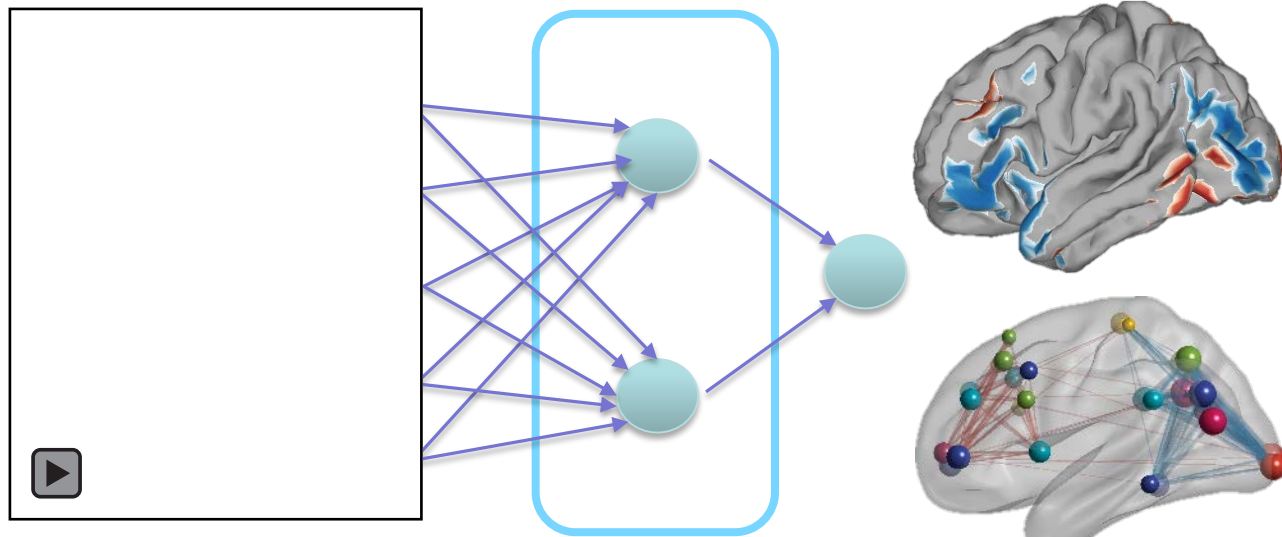
Clinical significance of EEG subtypes

Do the subtypes respond differentially to psychotherapy?
- One PTSD cohort was veterans getting therapy in VA

- Independent of type of therapy

Grounding psychiatry in brain-based biomarkers

customized
machine learning

brain
signatures

clinical
course/decisions

- Insights not possible from clinical measures
- Effective in cutting through heterogeneity
- Near-term clinical-translatable tool/test