

Cognition and Depression

Summary

Overview

Andy Nierenberg, Barbara Sahakian, Catherine Harmer, Michael Green

- Hot vs Cold cognition : Cognitive bias vs cognitive deficit.
- Hot cognitive changes preceding mood changes in RCTs
- MATRICS - Process for achieving consensus on process (practicality, test-retest, int'l approach)

Take home: Holistic approach w pt engagement (studies in the real world), Stratification important, Cognition as a surrogate biomarker, Hot cognition as a new target

State of the Science

Amit Etkin, Diego Pizzagalli, Rich Keefe, Chris Bowie

- Does Rx depression improve cognition?
- How do you know if cognition improved?
- Cognitive deficits as main variable (not hot cognition) – changes precede mood deficits and remain after Rx in remitters
- Meta-analyses underwhelming but limited by heterogeneity, different designs, varied assessments, and loose relationship to function

Take home: Use of cognitive measures to stratify, focusing on early phases of illness, consider combination protocols

Design and Assessment

Madhukar Trivedi, Maurizio Fava, Phil Harvey, Pat Arean

Partial overlap between sub and obj (40% - 55% have either before or after Rx), cog deficits = greater illness, independently related to fcnl deficits

Use of adjunctive design vs comparing 2 drugs

Need for assessments sensitive to change

Performance based outcomes UPSA may be both valid and sensitive

Milieu based assessment – consumers care about sleep, social, ability to do more

Take home: Self report not good enough, outcome needs to be clinically meaningful

Regulatory Issues

Tom Laughren, Tiffany Farchione, Carlos Pena, Maria Isaacs

How do we define cog dysfunction in MDD? How do we measure change? What population?

For both drugs and devices, involve FDA early

EMA – centralized evaluation for qualification guidelines

Is change in cognition clinically relevant?

Is cognitive impairment in dep caused by antidepressants?

Can CI be a target across DSM?

Questions

- Cognitive assessment (bias vs deficit; hot vs cold; standard vs novel, reliable vs sensitive to change)?
- Exptl design - population (early vs late, mechanistic vs outcome based, stratification)?
- What is success (symptoms vs function, statistical vs clinical significance, subjective vs objective)?
- Pseudo-specificity? (present before and after; may be in subgroup; so this may be resolved)
- Holistic approaches?

Take Homes

- Depression is not the right term
- Consensus about cognitive assessments still needed – standardized measures that are valid, reliable, and sensitive to change
- Regulatory considerations sooner rather than later
- Think beyond single Rx, single assessment

Thank you!
Clare Stroud and Annalyn Welp
All Speakers
And You!

“We didn’t lose, we just ran out of time.”

Vince Lombardi