

Are acute rapid onset anti-depressant results valid, or just a
consequence of functional unblinding?

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Disclosures- S Brannan

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 - Forum
 - Takeda
 - Novartis
 - Cyberonics
 - Eli Lilly

RAAD Development

- In 2006, labs at NIMH explored ketamine infusions and their findings spawned both excitement and a number of new “targets”
- Several companies and “compounds” are currently making their way through the system
- These “compounds” behave differently from traditional antidepressants and thus may not ideally fit the “traditional” tools and systems for development

Unresolved Problems in Neuroscience Drug Development:

Are Patients with Suicidal Ideation or Behavior Acceptable for Inclusion in Clinical Trials?

Are Acute Rapid Onset Anti-depressants Results Valid or Just a Consequence of Functional Unblinding?

Summary of Points Discussed

- Mark Opler

- Esketamine has shown a rapid benefit in depressive Sx (IV & nasal)
- “Unblinding” Dissociative sx are not driving the benefit because:
 - Dissociative Sx only explain a small part of the variance
 - Glyx-13 (w/o dissociative Sx) also showed rapid benefit in depressive Sx
 - Use of blinded independent raters correlates quite well with site ratings

- Torsten Madsen

- RAAD like Rx has been pursued before with sleep deprivation, ECT, etc
 - The correct durations and outcome measures still have not yet been developed and are unlikely to be simply the standard antidepressant outcomes
- Unblinding is always an important element in trials and frequently appears to favor a treatment
 - Thus extra efforts are required for ensuring results are valid

Issues requiring Further Discussion

- Were the study designs and outcome measures “fit for purpose” for these NCEs that are different from more traditional development targets?
- How important is unblinding
 - What measures need to be taken to mitigate problems
- What else have these discussants missed that you believe is important??