

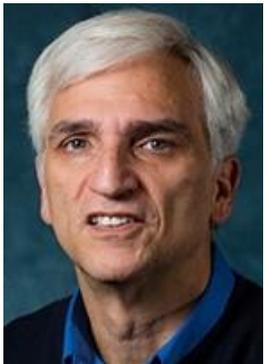


Borderline Personality Disorder: Clinical development challenges and opportunities in the current regulatory environment

Chairs:

Michael Ropacki, PhD

Gary Sachs, MD





Speakers

Michael Ropacki, PhD

Gary Sachs, MD

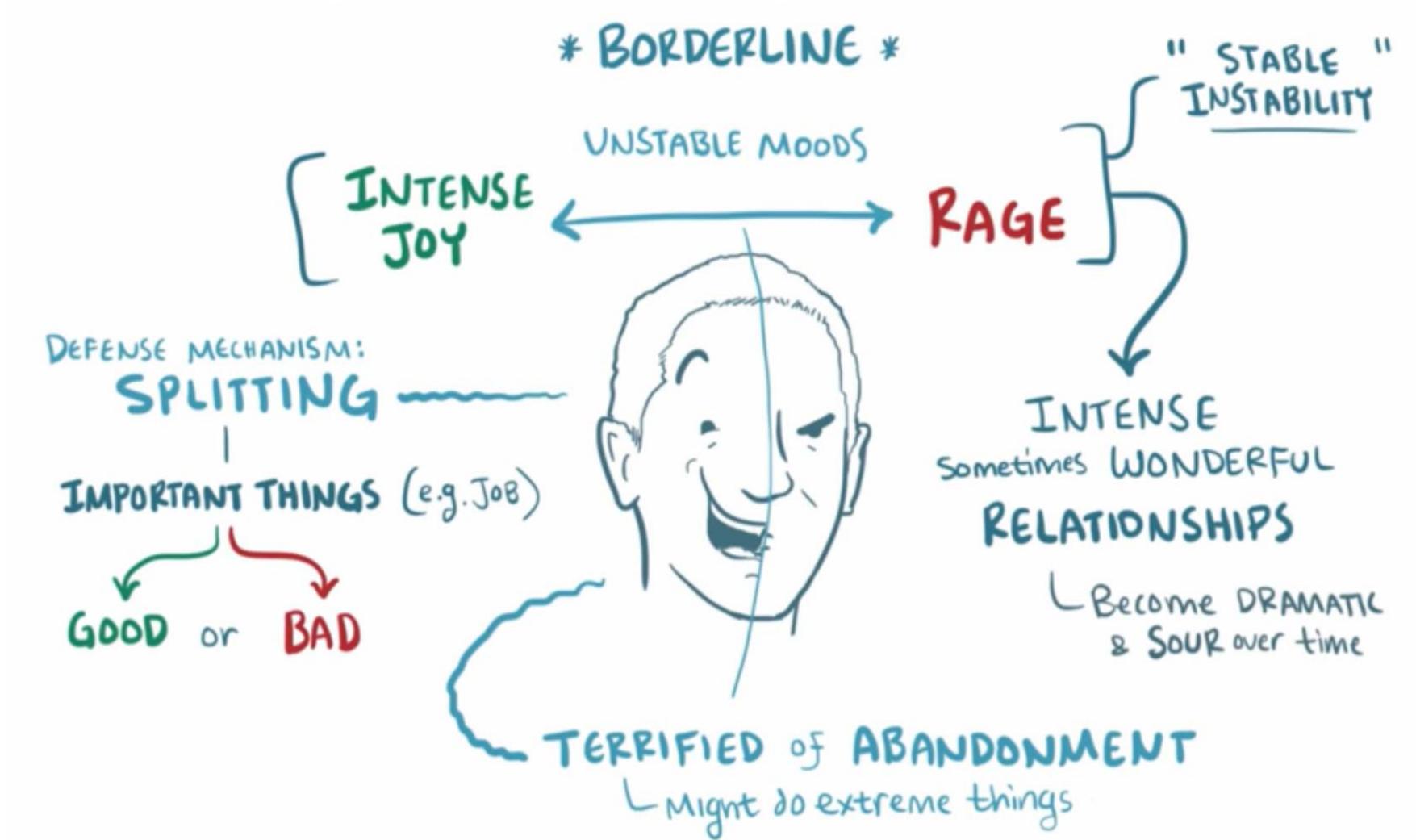
Ben Saville, PhD

Zimri Yaseen, MD

Lorenzo Guizzaro, MD

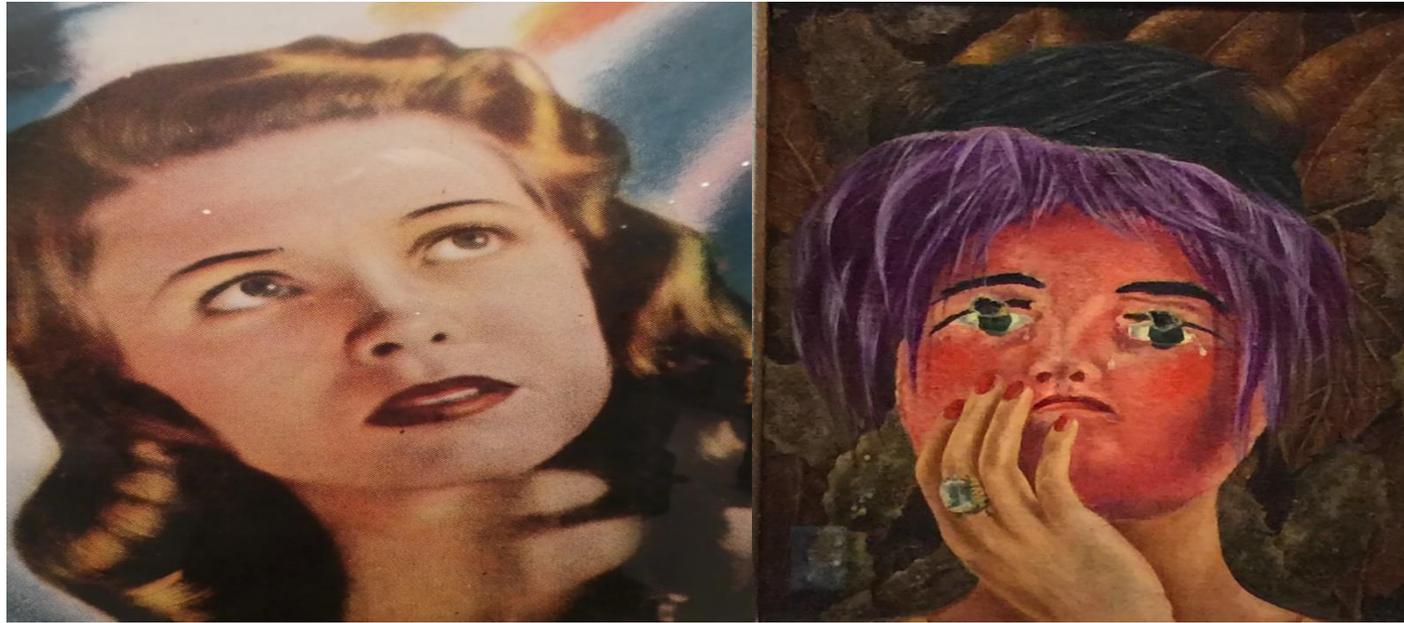
Speaker disclosures included in abstract/session info

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Q&A feature



WHAT IS BORDERLINE PERSONALITY DISORDER?

Borderline: An adjective in search of an indication?



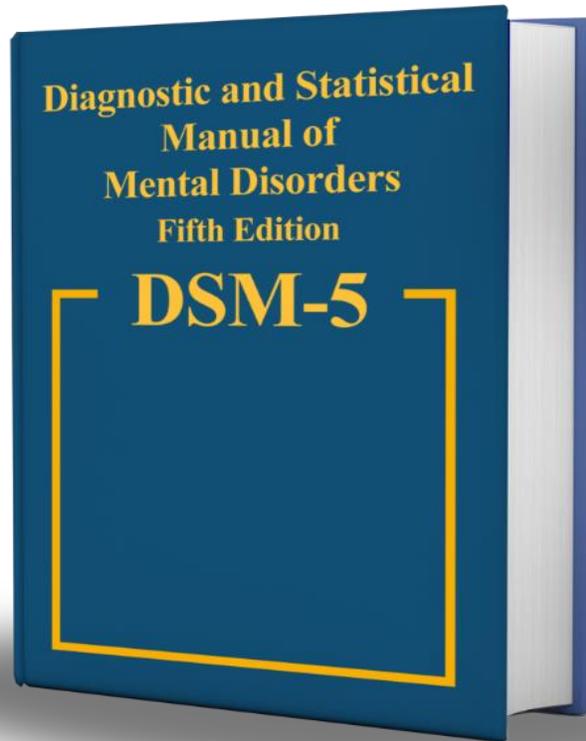
Often Confused with or co-occurring with Mood and Anxiety disorders

Core Features:

- **Inappropriate anger**
- **Paranoid ideation/ dissociation**
- **General impulsivity**
- **Affective instability**

Some accepted Eligibility Criteria and Outcome measures

Critical challenge: DSM-5 field trials show variable diagnostic reliability



DSM-5 provides criteria for:

10 Defined Personality Disorders

Cluster A: Paranoid personality disorder
Schizoid personality disorder
Schizotypal personality disorder

Cluster B: Antisocial personality disorder
Borderline personality disorder
Histrionic personality disorder
Narcissistic personality disorder

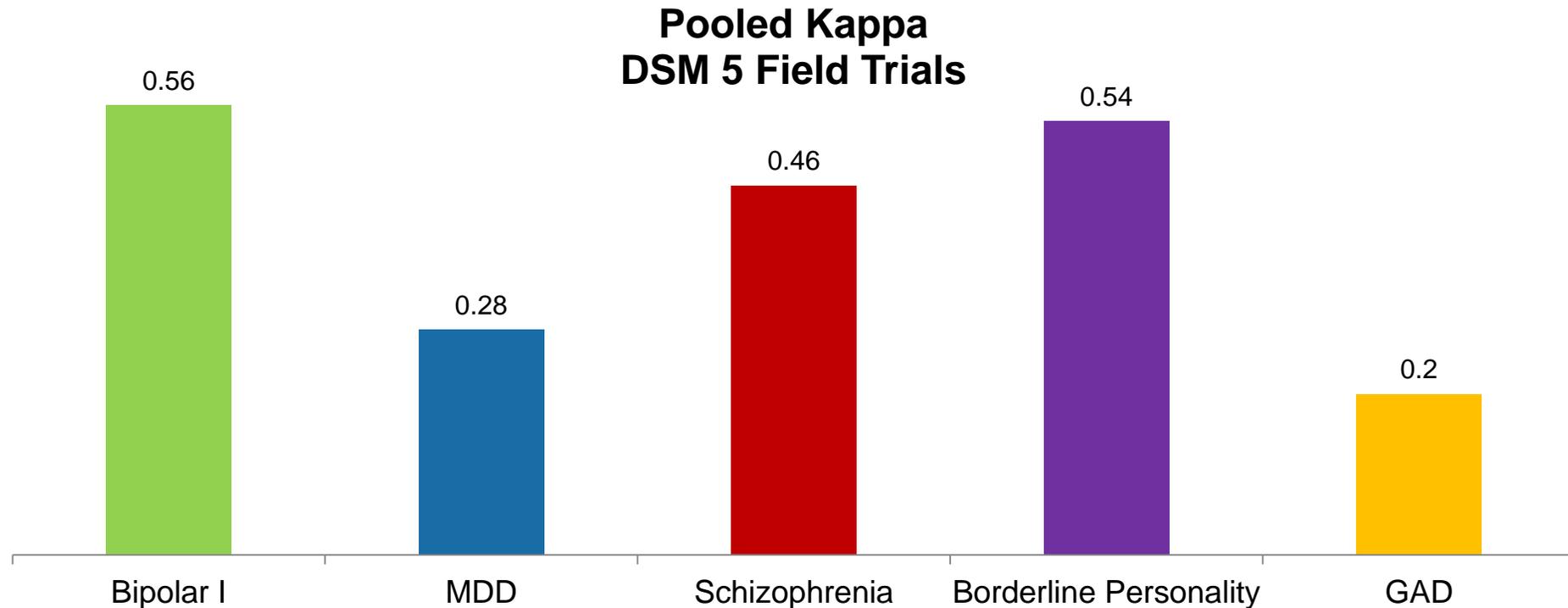
Cluster C: Avoidant personality disorder
Dependent personality disorder
Obsessive-compulsive personality disorder

+ Other

Other specified personality disorder

Best Practice Solution:
Use a structured Instrument

Reliability of BPD diagnoses is better than many other conditions



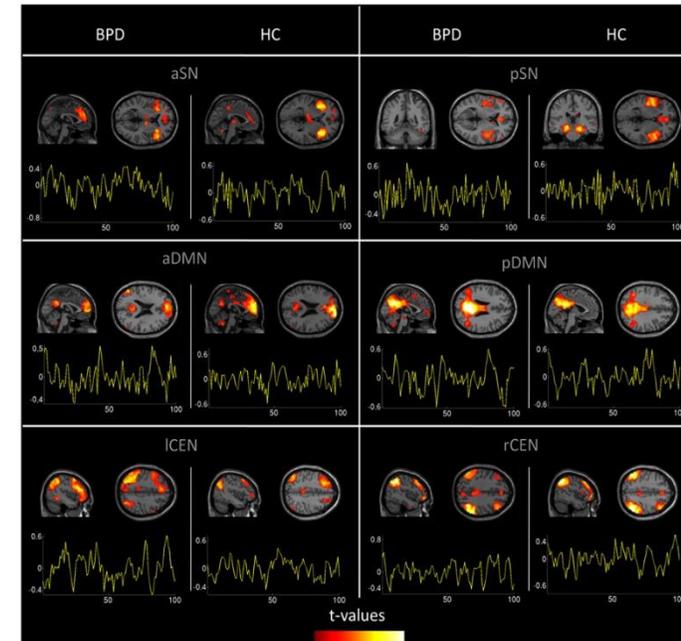
Opportunity: Maximize chance of success
by prioritizing enrolment of subjects diagnosed with high reliability.

Has the Borderline adjective found its noun?

Shifted intrinsic connectivity of central executive and salience network in borderline personality disorder

Maps and time courses are derived from independent component analysis of resting-state fMRI of subjects. SPMs are thresholded at $p < 0.05$ FDR-corrected and superimposed on a single subject high resolution T1 image.

Color coding (red > yellow) represents t -values ranging from 3 to 25. The x -axis of signal time courses reflects number of fMRI scans; the y -axis represents normalized signal amplitude. First to third row: anterior and posterior (a/p) DMN, anterior and posterior SN, left and right (l/r) CEN.



Spatial statistical parametric maps (SPM, one-sample t -tests controlled for medication) and associated time courses of intrinsic networks in healthy controls (HC) and patients with borderline personality disorder (BPD).

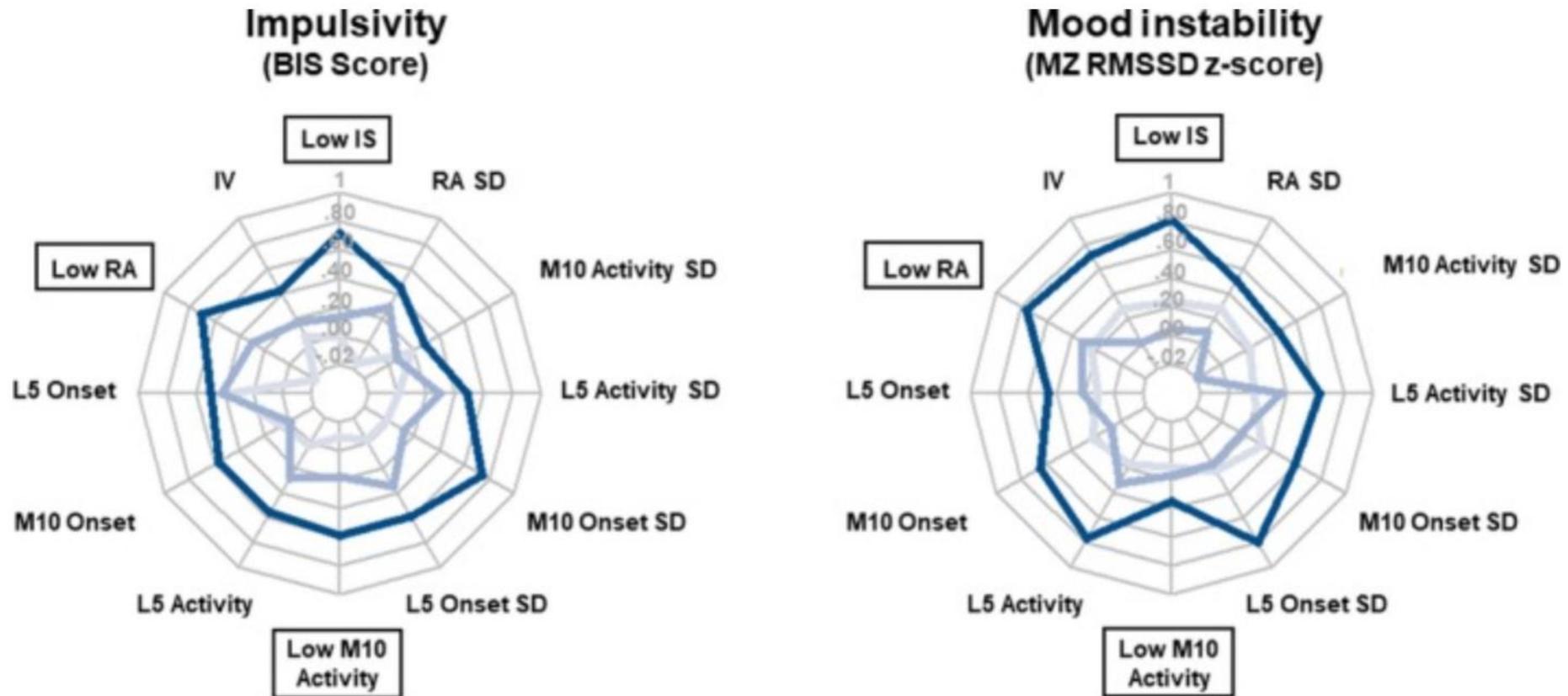
Actigraphy patterns, impulsivity and mood instability in bipolar disorder, borderline personality disorder and healthy controls

BPD stronger association between symptoms and parameters indicating perturbed and delayed rest-activity profile

Healthy Control

Bipolar Disorder

Borderline Personality Disorder



Applying modified Robins and Guze criteria : BPD vs ADHD and Bipolar

Dimension	BPD	Bipolar Disorder	ADHD
Signs and symptoms			
Impulsivity	Yes	Yes	Yes
Mood Instability	Yes	Yes	Yes
Irritability/Anger	Yes	Episodic	Yes (occasional)
Hyperactivity	No	Fluctuating circadian rhythm	All day Task demand
Sleep disturbance	No	Decreased need	Resistance
Suicidal Ideation/Self harm	Chronic	Episodic	Rare
Forgetful	No	No	Yes
Age of onset	< 18	<30	<12
Course of illness	Chronic	Episodic with durable full or partial remission	Chronic
Response of treatment (rapid)	?	+Mood stabilizers +D blockage - Stan. Antidep	+Stimulants + Alpha blockage
Family History/Biomarkers	+BPD ? HRV ? Actigraphy ? Connectivity	+ Mood ? REM onset ? Brodmann Area 25	+ADD ?qEEG

Important challenges

- Recruitment of an inherently difficult population.
- Requirement for borderline personality disorder diagnosis but exclude some of the most common co-occurring conditions.
- This may create pressure to improve recruitment by relaxing the stringency of eligibility criteria.
 - Site independent assessment can improve diagnostic confidence
 - Notably SCID 5-PD and Zan-BPD offer an opportunity for Site independent QA
- Relatively few sites have raters experienced in the administration of any BPD outcome measure.
- Collection of data from ecological momentary assessments will add to respondent burden and may increase attrition as well as missing data
- High Placebo response is a threat to signal detection
- The drug placebo difference detected in the largest of these studies was zero
- BPD and PBO response both associated with High Salience network intrinsic activity
- Resilience to potential restrictions due to COVID-19