Precision Functional Mapping - A biomarker platform for neuropsychiatric drug development

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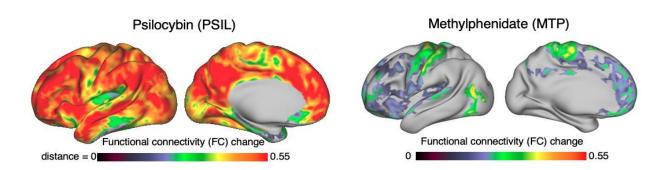
Why: In CNS drug development, rodent models are poor, pivotal trials are expensive, success rates are low. Reliable phase 1 biomarkers are <u>critical</u>. fMRI failed because good resolution is shot by group averaging.

Precision Functional Mapping fMRI: Define brain circuits in individuals, use within-subject design + data cleaning + fMRI advances + repeated sampling to assess activity/connectivity change.

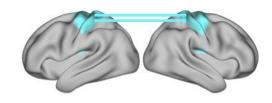
Article

Psilocybin desynchronizes the human brain

https://doi.org/10.1038/s41586-024-07624-5 Received: 24 October 2023 Joshua S. Siegel^{1⊠}, Subha Subramanian², Demetrius Perry¹, Benjamin P. Kay³, Evan M. Gordon⁴, Timothy O. Laumann¹, T. Rick Reneau⁴, Nicholas V. Metcalf³, Ravi V. Chacko⁵, Caterina Gratton⁶, Christine Horan³, Samuel R. Krimmel³, Joshua S. Shimony⁴, Julie A. Schweiger¹, Dean F. Wong⁴



What we did: We compared a predefined resting fMRI biomarker for stimulants (\$\frac{1}{2}\$ somato-motor FC) across different datasets and methods.



What you found: conventional fMRI yields Cohen's D = 0.36. Precision Functional Mapping design (dense sampling, individual-defined areas, longitudinal/cross-over design) yielded Cohen's D = 2.32. The sample size needed to detect an effect drops from N = 336 to N = 4!

	Data Cleaning	ME + Dense Sampling	Within-subject design	Individual- defined regions	Cohen's D	N to achieve 95% Power:
1: ABCD Dataset	-	-	-	-	0.36	336
2: ABCD Dataset	+	-	-	-	0.44	226
3: Psil-PFM Dataset	+	+	-	-	1.16	34
4: Psil-PFM Dataset	+	+	+	-	1.92	5
5: Psil-PFM Dataset	+	+	+	+	2.32	4

Precision Functional Mapping can provide much more sensitive biomarkers in early-phase clinical development.