Automatically Generated Report

Conducted via Brain Researcher MCP and Codex

Multiverse Robustness of Resting-State Network Segregation in Cocaine Use Disorder

Same-Data Meta-Analysis with Generalized Least Squares across 36 Analytical Specifications

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Executive Summary

This report updates and supersedes the earlier local Brain Researcher case-study PDF by using the current GitHub checkout, the README and source tree, the corrected result tables and scripts, and the full neuroimaging pipeline PDF. The core scientific story is a two-stage one. First, a single Schaefer-400 plus Tian Scale III pipeline reported strong positive associations between addiction severity and system segregation in Default, Striatum, Control, and HippAmyg networks. Second, the multiverse robustness layer asks whether the pre-specified findings survive plausible changes in atlas, motion threshold, and confound strategy.

The confirmatory robustness answer is negative: 0 rows in the confirmatory SDMA summary survive SDMA-GLS FDR correction. This means the original single-pipeline effects should be framed as analytically fragile findings, not as stable cocaine-use-disorder biomarkers.

The refreshed upstream repository is stricter than the earlier local draft: it incorporates a critical SDMA C-matrix correction, updates the figures and README, and now ships a tracked all-network SDMA table documenting a null exploratory screen. The README reports a maximum positive exploratory Z of 2.18; the tracked table's largest absolute Z is 2.62, with minimum recomputed BH q = 0.524. The revised claim boundary is therefore robust evidence for specification sensitivity, without presenting exploratory all-network candidates as FDR-surviving repo-backed findings.

What Changed Since the Earlier Case Report

The older case-study PDF should be treated as historical context, not the current scientific claim surface. It described exploratory candidate signals after the initial local render. The current upstream artifacts and README now support a complete null: no confirmatory SDMA-GLS row and no all-network exploratory row survives FDR correction.

Updated surface	Current behavior	Scientific implication
C matrix missingness	mean-impute per feature	The upstream fix replaces zero filling of missing Z values, which had biased inter-specification correlations toward independence.
GLS stability	pseudoinverse plus variance floor	brain_figure_sdma.py now matches the main SDMA implementation by using pinv and a 1e-12 variance floor for near-singular C matrices.
Confirmatory Z values	all below 1.30	The corrected SDMA table lowers the most inflated SalVentAttn employment estimate from 1.79 to 0.61 and strengthens the null interpretation.
SLURM wrappers	entrypoints fixed	run_phase1.sh and run_phase2.sh now call scripts/multiverse/multiverse_fc.py, multiverse_phase2.py, and sdma_spec_curve.py.
Exploratory artifacts	tracked null table	The current upstream tree ships sdma_all_networks.tsv for the 70 network-by-outcome screen; recomputed BH q values give 0/70 FDR-surviving rows.
Citations	expanded and corrected	The current README cites fMRIPrep, XCP-D, rapidtide, Schaefer/Tian/Gordon/Glasser atlases, multiverse-analysis precedents, GSR interpretation, and ASI.

The current confirmatory table contains six rows: the originally emphasized effects plus an additional Control-system employment row tracked in the refreshed SDMA output. All six have FDR q values above 0.58. For the 70-row exploratory screen, q values are not stored in `results/brain\_figures/sdma\_all\_networks.tsv`, so this report recomputes two-sided p values from the stored GLS Z values and applies Benjamini-Hochberg correction for display; this yields 0/70 surviving rows.

Study Origin and Sample

The pipeline report identifies the source dataset as SUDMEX-CONN, OpenNeuro ds003346: a Mexican resting-state fMRI cohort including individuals with cocaine use disorder and healthy controls. The raw dataset is described as 144 BIDS subjects acquired on a 3T Siemens scanner at the National Institute of Psychiatry in Mexico City.

Quantity	Value	Interpretation
Raw BIDS dataset	144 subjects	SUDMEX-CONN / OpenNeuro ds003346.
Manual exclusions	4 subjects	Pre-processing exclusions for fieldmap failure or missing functional data.
Failed QC	6 subjects	Motion or coverage failures in the pipeline report.
Final analytic sample	134 subjects	Pipeline report final sample before analysis-specific missingness.
Groups on cover page	CUD 71, HC 63	Pipeline report cover summary.
Demographics table	CUD 71, HC 62	The same PDF table reports one fewer HC; this discrepancy is preserved here rather than silently resolved.
Multiverse result tables	max n = 138	The cloned result tables report n_subjects = 138 across analysis rows.

The Addiction Severity Index (ASI) is the key clinical predictor family for the dimensional CUD-only analyses. The pipeline report lists psychiatric, medical, family/social, drug, legal, and employment domains; the multiverse result table contains seven analysis labels: CUD-vs-HC plus six ASI-related labels. Because the local artifacts disagree on exact sample counts, this report preserves those differences and treats the present work as a rendered evidence synthesis rather than a new subject-level audit.

Repository Evidence Surface

The repository itself is part of the scientific evidence because it records what is executable, what is only summarized, and which artifacts are derived outputs. The local clone points to the public GitHub remote, but this report uses the checked-out files rather than assuming that the remote web view and local tree are identical.

Source	Status	What it contributes
Local git source	a2e57d9: Add back GSR citation (Murphy & Fox 2017)	The report is regenerated from the checked-out repository under docs/BR-multiverse-cocaine-mri.
README.md	scientific contract	States the primary conclusion: 36-spec SDMA-GLS robustness audit; no confirmatory findings survive multiverse correction.
requirements.txt	6 packages	numpy, pandas, scipy, statsmodels, matplotlib, and nilearn are the declared lightweight analysis dependencies.
scripts/preprocessing/	10 shell scripts	HPC preprocessing surface: fMRIPrep, fMRIPrep CIFTI, QC, Rapidtide, and XCP-D 36P/24P/aCompCor variants.
scripts/multiverse/	8 Python scripts	FC/SyS extraction, Phase-2 confound strategies, SDMA/specification curves, brain figures, and original Matplotlib report.
scripts/slurm/	2 shell scripts	Batch wrappers for the phase-1 and phase-2 multiverse jobs.

Commit	Subject
a2e57d9	Add back GSR citation (Murphy & Fox 2017)
c50ad9f	Fix rapidtide citation (Korponay et al. 2024), remove GSR citation
c263b82	Fix multiverse citation: Silberzahn 2018 -> Steegen 2016
a5c0037	Expand citations in README: atlases, multiverse, GSR, clinical measures
a243473	Add updated BR scientific report (complete null, all fixes applied)

The README is more than packaging text: it states the user-facing claim boundary. The primary claim is the confirmatory null across the 36-specification SDMA-GLS audit. Current HEAD also tracks the all-network exploratory table, where the README reports 0 of 70 combinations survive FDR correction, so this report keeps that boundary explicit.

Pipeline and Atlas

The original pipeline is not just a statistical table. It starts from BIDS data and proceeds through fMRIPrep, Rapidtide, and XCP-D before extracting parcellated time series and connectivity features. This context matters because the original single-specification findings are tied to a specific denoising and parcellation workflow.

Stage	Version / setting	Role
fMRIPrep	24.0.0	Minimal preprocessing, MNI152NLin2009cAsym 2 mm output, fsLR CIFTI output, FreeSurfer reconstruction, confound TSVs.
Rapidtide	2.9.6	Systemic low-frequency oscillation estimation and removal using gray-matter restricted lagged regressors.
XCP-D	0.7.4	Nuisance regression, CIFTI processing, FD censoring, smoothing, and parcellated time series.
Base denoising	36P plus sLFO	36-parameter model with global signal regression plus Rapidtide custom confound.
Sensitivity denoising	24P and aCompCor	Additional confound strategies introduced for the multiverse robustness layer.

Component	Value	Scientific role
Cortex	Schaefer-400	Yeo-7 cortical network labels.
Subcortex	Tian Scale III	50 validated subcortical regions, including striatum, thalamus, hippocampus, and amygdala subdivisions.
Combined single-spec atlas	450 ROIs	Pipeline report concatenates Schaefer-400 and Tian Scale III time series.
Multiverse atlases	6 atlas choices	Schaefer-200/Tian III; Schaefer-400/Tian III; Schaefer-600/Tian III; Schaefer-400/HCP; Gordon/Tian III; Glasser/Tian III.

The pipeline report emphasizes Tian Scale III because it separates subcortical systems that are relevant to addiction, including nucleus accumbens shell/core, putaminal zones, thalamic nuclei, and hippocampal/amygdala subdivisions. The multiverse layer later broadens this atlas decision into six atlas specifications.

Execution component	Setting	Repository detail
Environment	fmripnet / analysis env	README expects numpy, pandas, scipy, statsmodels, matplotlib, and nilearn; setup_env pins nilearn 0.10.4, nibabel 5.2.1, numpy 1.24.4, scipy 1.11.4, pandas 2.0.3, statsmodels 0.14.1.
Subject arrays	1-144	fMRIPrep, fMRIPrep CIFTI, Rapidtide, and XCP-D scripts are written as 144-subject SLURM arrays.
QC gates	FD below 0.5; retained at least 150; no more than 50 percent censored	fMRIPrep QC writes work/fmriprep_qc_summary.tsv and included_subjects.txt; sub-003, sub-004, sub-006, and sub-061 are manually excluded.

Execution component	**Setting**	**Repository detail**
Rapidtide bridge	sLFO custom confound	The Rapidtide script extracts the final refined moving-regressor column as a TSV named for XCP-D custom-confounds ingestion.
XCP-D variants	36P, 24P, aCompCor	36P is the base GSR pipeline; 24P and aCompCor are no-GSR variants introduced for confound-strategy sensitivity.
Multiverse outputs	spec_*.tsv -> master tables -> SDMA	Per-specification OLS rows are concatenated into master_summary_all.tsv, then SDMA-GLS/Stouffer summaries and figures are generated.

Feature and Model Definitions

For each subject, the pipeline report describes a combined FC matrix and three feature families. System segregation is the central readout in the multiverse report because it turns within- and between-network connectivity into one interpretable network self-containment score.

Feature family	Count	Definition
Functional connectivity	55 features	10 within-network and 45 between-network Fisher-z-averaged correlations.
System segregation	10 features	One SyS value per network: within-network connectivity minus between-network connectivity, normalized by absolute between-network connectivity.
Graph theory	14 features	Top-20-percent thresholded FC graph summarized with modularity, global efficiency, clustering, and participation metrics.

The single-pipeline statistical model is an OLS regression for each feature: outcome feature as a function of predictor, age, sex, and mean framewise displacement. A1 uses binary CUD-vs-HC group; A3 uses continuous ASI composite scores within CUD participants. Benjamini-Hochberg FDR correction is applied within each feature set and analysis.

Original Single-Pipeline Findings

The pipeline report's core result is not a null result. Under the original Schaefer-400 plus Tian Scale III, 36P plus Rapidtide/XCP-D workflow, the A3 dimensional ASI analyses find five FDR-significant positive SyS associations. Higher addiction severity is interpreted as greater network self-containment.

Analysis	**Network**	**Beta**	**t**	**p**	**pFDR**	**Circuit**
ASI medical	Default	+74.53	5.13	.000003	.000032	Self-referential / DMN
ASI medical	Striatum	+18.57	3.39	.001	.006	Reward / habit
ASI medical	Control	+13.36	2.92	.005	.016	Cognitive control
ASI family	Default	+83.56	3.87	.0003	.003	Self-referential / DMN
ASI drug	HippAmyg	+1.33	3.06	.003	.033	Memory / cue reactivity

The strongest original signal is Default Mode Network segregation with ASI medical severity ($t = 5.13$, pFDR = .000032). The pipeline interpretation links DMN hyper-segregation to drug-focused rumination and somatic/interoceptive burden; Striatum to reward/habit circuitry; Control to frontoparietal regulation; and HippAmyg to memory, emotional context, and cue reactivity.

Multiverse Robustness Design

The multiverse combines atlas, framewise-displacement threshold, and confound-regression choices. Each specification estimates systemic segregation for network-outcome pairs and then aggregates specification-level Z statistics with Same-Data Meta-Analysis using Generalized Least Squares.

Dimension	Options in bundle
Atlas	Schaefer-200/Tian III; Schaefer-400/Tian III; Schaefer-600/Tian III; Schaefer-400/HCP; Gordon/Tian III; Glasser/Tian III
Motion threshold	Documented SDMA subset uses FD 0.3 mm and FD 0.5 mm; master table also contains 36P FD 0.4 rows.
Confound strategy	36P with global signal regression; 24P without GSR; aCompCor without GSR
Outcome family	7 analysis labels x 10 systemic-segregation features
SDMA matrix C	36 x 36; off-diagonal mean 0.164, min -0.295, max 0.938

The local master table has 42 specification IDs and 2940 rows because it includes six additional 36P FD=0.4 specifications. The documented 36-specification SDMA subset has 36 specification IDs and 2520 rows. This distinction is important: the repo contains more rows than the named 36-specification report, but the SDMA figures and summary table are aligned to the 36-specification subset.

Artifact	Observed size	Interpretation
master_summary_all.tsv	2940 rows; 42 spec IDs	Contains 96 specification-level FDR-significant rows before SDMA aggregation.
Documented SDMA subset	2520 rows; 36 spec IDs	Excludes the six 36P FD=0.4 rows; contains 82 specification-level FDR-significant rows.
Analysis family	7 analyses x 10 networks	CUD-vs-HC plus six ASI subscales over seven cortical and three subcortical systems.
inter_spec_correlation.tsv	36 x 36	Off-diagonal mean 0.164, min -0.295, max 0.938.
sdma_summary.tsv	6 confirmatory rows	Local table includes the five named confirmatory effects plus Cont SyS ~ ASI Employment.
brain_figures/	2 PNG files plus all-network TSV	Current HEAD ships confirmatory_figure.png, stability_map.png, and sdma_all_networks.tsv; the older all-network comparison PNG is not tracked.

Confirmatory Robustness Verdict

Across the confirmatory summary table, 0 rows have SDMA-GLS FDR q below 0.05. This is the central robustness result: the originally reported single-pipeline associations fail to survive multiverse aggregation.

Outcome	GLS Z	p	FDR q	Stouffer Z	Stouffer p	Sig specs
DMN SyS ~ ASI Medical (CUD)	1.05	0.293	0.585	1.36	0.174	4/36
DMN SyS ~ ASI Family (CUD)	1.13	0.260	0.585	0.73	0.465	3/36
HippAmyg SyS ~ ASI Drug (CUD)	1.23	0.217	0.585	2.00	0.045	7/36
DMN SyS ~ CUD vs HC	-0.10	0.923	0.923	0.31	0.757	0/36
SalVentAttn SyS ~ ASI Employment (CUD)	0.61	0.543	0.794	2.03	0.042	4/36
Cont SyS ~ ASI Employment (CUD)	0.44	0.662	0.794	2.18	0.029	2/36

Outcome	36P sig	24P sig	aCompCor sig
DMN SyS ~ ASI Medical (CUD)	2/12	2/12	0/12
DMN SyS ~ ASI Family (CUD)	3/12	0/12	0/12
HippAmyg SyS ~ ASI Drug (CUD)	4/12	2/12	1/12
DMN SyS ~ CUD vs HC	0/12	0/12	0/12
SalVentAttn SyS ~ ASI Employment (CUD)	0/12	2/12	2/12
Cont SyS ~ ASI Employment (CUD)	0/12	2/12	0/12

This section changes the scientific interpretation of the original result. The single-pipeline analysis remains useful as the motivating discovery, but the multiverse layer says the five pre-specified findings are not stable enough to be treated as validated biomarkers.

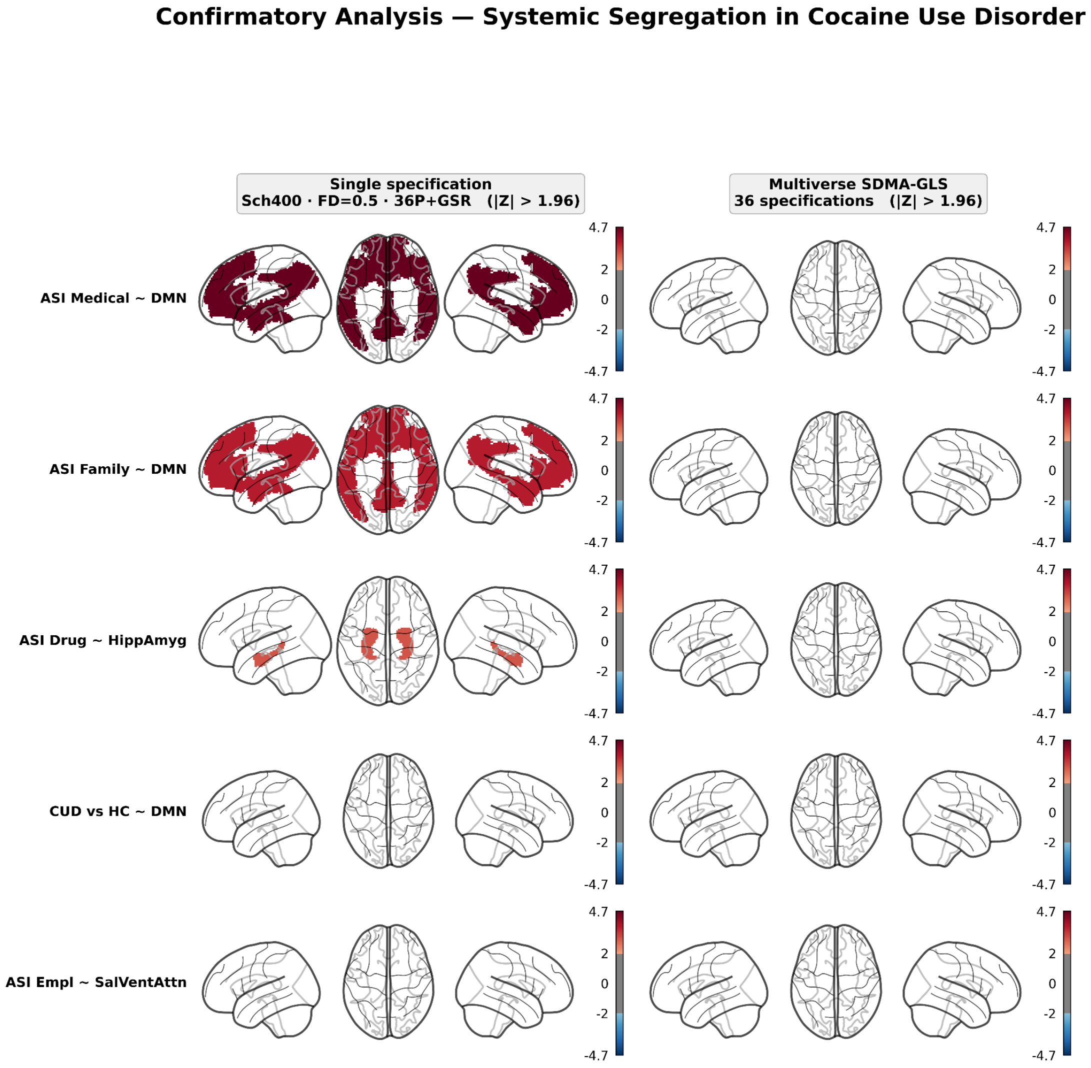

Figure 1: Confirmatory figure from the cloned artifact bundle. The top row reflects the original single specification; the SDMA-GLS row shows that the confirmatory effects do not survive the multiverse aggregation.

Stability Map and Sensitivity

The stability map is the current repository's main sensitivity visualization beyond the confirmatory brain figure. It shows every network-outcome Z score across the 36 documented specifications, sorted by confound strategy. The visual point is that nominal single-specification signals concentrate in particular preprocessing choices rather than appearing uniformly across the multiverse.

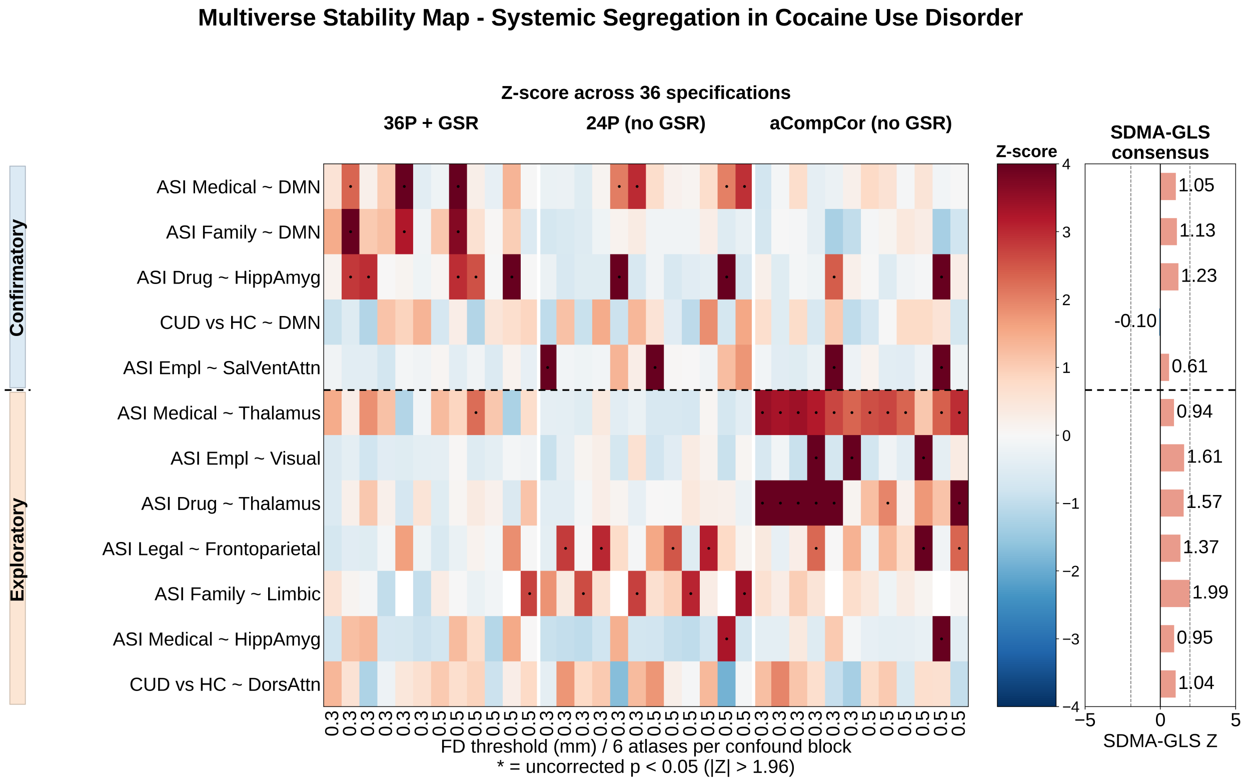

Figure 2: Stability map showing specification-level Z scores across network-outcome pairs. Columns are sorted by confound strategy, making the original GSR sensitivity visible.

The current repository includes the all-network exploratory SDMA table at `results/brain\_figures/sdma\_all\_networks.tsv`. It contains 70 network-by-outcome rows, with 0 FDR-surviving exploratory rows, maximum positive GLS Z of 2.18, maximum absolute GLS Z of 2.62, and minimum recomputed BH q of 0.524. The older all-network comparison figure is not tracked in current HEAD. The code path in `scripts/multiverse/brain\_figure\_sdma.py` can regenerate SDMA maps from `results/master\_summary\_all.tsv` and `results/inter\_spec\_correlation.tsv`, but the present evidence bundle should frame the exploratory screen as null rather than as a source of candidate biomarkers.

Analysis	**Network**	**GLS Z**	**p**	**BH q**	**Specs**
A3_ASI_medical_sys	sys_Vis	-2.62	0.009	0.524	36
A3_ASI_psychiatric_sys	sys_Limbic	2.18	0.029	0.524	30
A3_ASI_medical_sys	sys_Limbic	2.12	0.034	0.524	30
A1_CUD_vs_HC_sys	sys_HippAmyg	2.08	0.038	0.524	36
A3_ASI_family_sys	sys_Limbic	1.99	0.047	0.524	30
A3_ASI_legal_sys	sys_Limbic	1.94	0.052	0.524	30
A3_ASI_family_sys	sys_SomMot	1.84	0.066	0.524	36
A3_ASI_psychiatric_sys	sys_Default	1.83	0.067	0.524	36

Interpretation

The strongest interpretation is methodological. Resting-state CUD brain-behaviour associations can look convincing in a single atlas/denoising/motion configuration, but the direction and strength of the result can shift materially when plausible preprocessing and analysis choices are varied.

The biological interpretation should be layered. The original pipeline suggests a coherent Default-Striatum-Control-HippAmyg hyper-segregation story for addiction severity. The robustness audit does not prove that story false; it shows that the specific pre-specified effects are not stable enough across the multiverse. Under the current upstream artifact set, the report should stop at that confirmatory robustness conclusion unless additional exploratory outputs are rerun and explicitly added back to the evidence bundle.

The role of global signal regression remains central. The README and stability map emphasize that the original confirmatory effects cluster in the 36P/GSR block and vanish without GSR. That pattern supports a methodological conclusion about preprocessing sensitivity rather than a simple biological claim that GSR alone creates or removes every possible CUD association.

Limitations and Artifact Boundaries

This BR-template report was regenerated from files present in the cloned repository. The raw SUDMEX imaging data and XCP-D derivatives are not included, so this step verifies report rendering and table consistency, not a full neuroimaging rerun.

There are source-level inconsistencies that matter for scientific framing: the pipeline PDF reports 144 raw subjects, 134 after QC, and group counts that differ slightly between the cover and demographics table; the multiverse tables report 138 subjects in the subject-count field. The pipeline PDF reports a 450-ROI Schaefer-400 plus Tian Scale III construction, while some text in the feature extraction section refers to a 456 x 456 matrix. The repository report is also a derived-result bundle, not a complete BIDS derivatives release.

The local source tree adds two more provenance caveats. First, one atlas setup helper builds a Schaefer-400 plus Tian Scale II 432-parcel NIfTI, whereas the multiverse scripts and reports refer to Tian Scale III and the XCP-D atlas labels used in the result tables. Second, some historical script headers and SLURM status strings retain older names or 18/54-spec language. The latest upstream commits fixed the executable SLURM entrypoints, but the current checked-out Python scripts and result tables still define the reported 36-specification SDMA surface.

These inconsistencies do not invalidate the robustness conclusion, but they should prevent overclaiming. A publication-grade handoff should reconcile sample counts, analysis-specific missingness, exact atlas dimensionality, and whether each multiverse specification was recomputed from raw derivatives or from post-hoc reparameterized outputs.

Reproducibility Bundle

Path	Shape/status	Role
README.md	repo overview	Documents design, result interpretation, usage, citation, and acknowledgement.
requirements.txt	dependency list	Lightweight Python analysis dependency contract.
master_summary_all.tsv	2940 rows	All specification-level tests and covariates.
sdma_summary.tsv	6 rows	Confirmatory SDMA-GLS/Stouffer summary table.
inter_spec_correlation.tsv	36 x 36	Inter-specification correlation matrix C.
brain_figures/confirmatory_figure.png	figure	Primary confirmatory brain summary.
brain_figures/stability_map.png	figure	Z-score stability map across specifications.
brain_figures/sdma_comparison_all.png	not in current HEAD	Older all-network comparison figure is no longer a tracked result artifact.
brain_figures/sdma_all_networks.tsv	70 rows	Tracked all-network SDMA-GLS table for the 70 network-by-outcome exploratory screen.
Brain_Researcher_case2_Cocaine_Use.pdf	23 pages	Earlier BR scientific report containing the core multiverse interpretation.
14_pipeline_report (2).pdf	12 pages	Pipeline report from BIDS through fMRIPrep, Rapidtide, XCP-D, FC, SyS, and original single-specification results.
scripts/preprocessing/*.sh	10 scripts	BIDS-to-XCP-D operational pipeline skeleton.
scripts/multiverse/*.py	8 scripts	Multiverse, SDMA, brain-figure, and report generation code.
scripts/slurm/*.sh	2 scripts	Cluster batch wrappers for multiverse phase runs.

Generated outputs are `results/Brain\_Researcher\_case2\_Cocaine\_Use.tex`, `results/Brain\_Researcher\_case2\_Cocaine\_Use.pdf`, and `results/combined\_report.pdf`. The current upstream repo deletes tracked combined/source report PDFs, so `results/combined\_report.pdf` is regenerated as a compatibility copy of the current BR-template scientific report. It does not append the original Matplotlib multiverse report or local source PDFs, avoiding duplicate report sections in the final handoff artifact.

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