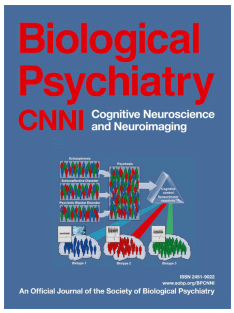


Comparing neural correlates of consciousness: from psychedelics to hypnosis and meditation

Flora F. Moujaes, Nathalie M. Rieser, Christophe Phillips, Nuno M.P. de Matos, Mike Brügger, Patricia Dürler, Lukasz Smigielski, Philipp Stämpfli, Erich Seifritz, Franz X. Vollenweider, Alan Anticevic, Katrin H. Preller

PII: S2451-9022(23)00174-X

DOI: https://doi.org/10.1016/j.bpsc.2023.07.003

Reference: BPSC 1110

To appear in: *Biological Psychiatry: Cognitive Neuroscience and Neuroimaging*

Received Date: 6 February 2023

Revised Date: 23 May 2023

Accepted Date: 7 July 2023

Please cite this article as: Moujaes F.F., Rieser N.M., Phillips C., de Matos N.M.P., Brügger M., Dürler P., Smigielski L., Stämpfli P., Seifritz E., Vollenweider F.X., Anticevic A. & Preller K.H., Comparing neural correlates of consciousness: from psychedelics to hypnosis and meditation *Biological Psychiatry: Cognitive Neuroscience and Neuroimaging* (2023), doi: https://doi.org/10.1016/j.bpsc.2023.07.003.

Comparing neural correlates of consciousness: from psychedelics to hypnosis and meditation

Neural correlates of altered states of consciousness

Flora F. Moujaes†,[1,2], Nathalie M. Rieser†,[1,*], Christophe Phillips[3], Nuno M.P. de Matos[4], Mike Brügger[4], Patricia Dürler[1], Lukasz Smigielski[1a], Philipp Stämpfli[1b], Erich Seifritz[1], Franz X. Vollenweider[1], Alan Anticevic[2], Katrin H. Preller[1]

[1]Department of Psychiatry, Psychotherapy and Psychosomatics, Psychiatric Hospital, University of Zurich, Switzerland.

[1a]Department of Child and Adolescent Psychiatry and Psychotherapy, Psychiatric University Hospital Zurich, University of Zurich, Switzerland

[1b]MR-Center, Psychiatric University Hospital, University of Zurich, Switzerland.

[2]Department of Psychiatry, Yale University School of Medicine, New Haven, United States.

[3]GIGA Cyclotron Research Centre in vivo imaging, University of Liège, Belgium.

[4]Clinic of Cranio-Maxillofacial and Oral Surgery, Center of Dental Medicine, University of Zurich, Switzerland.

† Nathalie M. Rieser and Flora F. Moujaes contributed equally to this paper.

*Corresponding author: Nathalie M. Rieser, nathalie.rieser@bli.uzh.ch

Keywords: consciousness | psilocybin | LSD | hypnosis | meditation | rsfMRI functional connectivity

Abstract

Background: Pharmacological and non-pharmacological methods of inducing altered states of consciousness (ASC) are becoming increasingly relevant in the treatment of psychiatric disorders. While comparisons between them are often drawn, to date no study has directly compared their neural correlates. Methods: To address this knowledge gap we directly compared two pharmacological methods: psilocybin (n=23, dose=0.2mg/kg p.o.) and LSD (n=25, dose=100µg p.o.) and two non-pharmacological methods: hypnosis (n=30) and meditation (n=29) using resting state functional connectivity magnetic resonance imaging (rs-fcMRI), and assessed the predictive value of the data using a machine learning approach. Results: We found that (i) no network reaches significance in all four ASC methods; (ii) pharmacological and non-pharmacological interventions of inducing ASC show distinct connectivity patterns that are predictive at the individual level; (iii) hypnosis and meditation show differences in functional connectivity when compared directly, and also drive distinct differences when jointly compared to the pharmacological ASC interventions; (iv) psilocybin and LSD show no differences in functional connectivity when directly compared to each other, but do show distinct behavioral-neural relationships. Conclusion: Overall, these results extend our understanding of the mechanisms of action of ASC and highlight the importance of exploring how these effects can be leveraged in the treatment of psychiatric disorders.

Introduction

As altered states of consciousness (ASC) become increasingly relevant in the treatment of psychiatric disorders (1–4), comparisons between different altered states are often drawn (5–7). However, these comparisons are limited by the lack of plentiful and rigorous data that directly compares the neural correlates of different ASC. Furthermore, the whole-brain data-driven effects of many ASC methods (e.g., hypnosis, meditation) have not yet been explored, and the link between the behavioral and neural effects of ASC have been largely ignored.

To address this, we will directly compare two pharmacological (psilocybin, LSD) and two non-pharmacological (hypnosis, meditation) ASC interventions. While there is evidence of overlap in the phenomenology of pharmacologically and non-pharmacologically induced ASC, prior work has not tested whether there is also overlap at the neural level (8–14). By elucidating the common and distinct acute effects of pharmacologically and non-pharmacologically induced ASC in healthy controls, and their predictive value, we hope to inform the development of biomarkers for patient stratification that predict individual differences in response to the ASC interventions, including clinical efficacy and possible side-effects (15; 16).

Psilocybin and LSD are classic hallucinogens that have been shown to alter perception and experience of the self (17). While psilocybin is a preferential 5-HT2A and 5-HT1A agonist and LSD stimulates serotonin and dopamine receptors (18–21), their experiential effects are both widely attributed to their agonist activity at the 5-HT2A receptor (22; 23). Recent neuroimaging studies are starting to uncover the neural mechanisms underlying psychedelic-induced ASC, pointing to the importance of altered information integration in sensory and associative brain regions (17; 23).

Hypnosis and mediation are terms that both incorporate a wide range of mental techniques. In this study, we refer to a specific form of hypnosis termed ‘Esdaile’, in which instructions are used to induce a visualization. This results in a state of deep physical relaxation and mental absorption, distortions of the

perception of time and space, and altered bodily sensations. By meditation we refer to 'open awareness' meditation, which involves the non-judgmental, non-attached observation of salient thoughts and feelings and aims to cultivate meta-awareness (24). Research into the neural correlates of both hypnosis and meditation has implicated regions known to be involved in the top-down regulation of lower-level brain structures; however, such studies are limited by their use of seed-based approaches as: (i) the selections of seed regions is subjective; and (ii) the selection of different seeds makes it difficult to compare findings (9; 25–36).

To directly explore the common and distinct features of pharmacologically and non-pharmacologically induced ASC, we will utilize four existing datasets ideally suited for comparison - they were collected at the same site, used the same MRI scanner and eyes-closed resting-state paradigm, and all included an appropriate within-person control condition. We aim to: (i) establish the neural correlates of each ASC intervention using a whole-brain data driven approach; (ii) assess the differences between the pharmacological and non-pharmacological ASC intervention methods; (iii) assess the predictive value of the rs-fcMRI effects; and (vi) conduct a preliminary analysis exploring the relationship between ASC-induced changes in behavior and neural correlates. We hypothesize that pharmacological and non-pharmacological ASC intervention methods show distinct changes in rs-fcMRI, and that changes in rs-fcMRI are predictive at the individual level.

Methods and Materials

Experimental Design

The data were collected as part of four separate studies. Detailed information about the study procedures are described in the corresponding papers and the supplement (psilocybin: n=23, dose=0.2mg/kg p.o. (37), LSD: n=25, dose=100µg p.o. (38), meditation: n=29 (39); hypnosis: n=30 (Fig. S1)). A final sample of N=107 (female=51, male=56; ethnicity=Caucasian (100%)) was included (Table S1). Detailed description and subjective experience of each ASC are reported in the supplementary methods and Figure S2. The groups differed in age and gender. Therefore, we used each participant's individual intervention vs. control contrast as the input for all analysis. For direct comparison of the intervention scans, controlling for age and gender, see Figure S3-S6.

Imaging analysis

For details on neuroimaging data acquisition, fMRI preprocessing, and exclusion criteria for flagged frames see supplementary methods and Table S2. ROI-to-ROI functional connectivity analysis was conducted using the Conn19c-toolbox (www.nitrc.org/projects/conn, RRID:SCR_009550). For each participant and condition, ROI-to-ROI connectivity (RRC) matrices were generated between the 132 Conn-default ROIs derived from a combination of FSL Harvard-Oxford atlas cortical and subcortical areas and AAL atlas cerebellar areas. The 132 ROIs were categorized into 22 networks (Table S3). Each value in an RRC matrix represents a Fisher-transformed bivariate correlation coefficient between a pair of ROI BOLD time series.

For second-level statistics, three analyses were conducted. First, RRC matrices for the psilocybin, LSD, hypnosis, meditation and their respective control conditions were entered into a 2x2 ANOVA with pharmacological (psilocybin and LSD) and non-pharmacological (meditation and hypnosis) intervention as between-subject and intervention vs. control as within-subject factors. This analysis maps the differences between pharmacologically-induced and non-pharmacologically induced changes in RRC

with respect to each participant's control condition. Next, to characterize differences between conditions, changes induced by each intervention with respect to its control condition were compared with each other. To investigate changes induced by each intervention individually, we compared each condition to its respective control condition separately. For both analyses, 'Threshold Free Cluster Enhancement' (TFCE) was used and statistical results were thresholded at $p<0.05$ (FWE-corrected). Finally, as a quality check, we also confirmed there were no correlations between mean hypo-/hyperconnectivity difference (intervention-control) and difference in motion (framewise displacement) or sleepiness (Fig. S7&S8). Using global signal regression (GSR) as a denoising step is still subject to ongoing debate. Therefore, we additionally report the results without GSR in the supplement (Fig. S9- S16). Lastly, the preliminary behavioral-neural analysis is described in the supplementary methods.

Machine learning classification analyses

Next, we investigated whether the ASC condition could be predicted based on the RRC matrices. The RRC matrices for each contrast (intervention-control) were therefore transformed into nifti images (https://github.com/CyclotronResearchCentre/Matrix_to_NIfTI). Each ROI was given equal weighting. Only the lower half of the symmetrical 132x132 matrix was used. These nifti images were fed into a binary support vector machine (SVM) classifier as implemented in the Pattern Recognition for Neuroimaging Toolbox ((PRoNTo), (40); http://www.mlnl.cs.ucl.ac.uk/pronto) to discriminate between pharmacologically and non-pharmacologically induced ASC at an individual subject level. To discriminate between all four interventions, a multiclass Gaussian Process Classification (GPC) was used. The accuracy and generalizability of the classifications were assessed with leave-one-subject-out cross-validation procedure. Hyper-parameter estimation relied on a nested 5-fold cross-validation scheme. The soft-margin parameter for the SVM was optimized using 5 values between .01 and 100, as powers of 10 from -2 to 2 (41). In a last step, a binary SVM was used to distinguish between psilocybin vs. LSD and hypnosis vs. meditation. For each classification, a 5000-times permutation test was used to test statistical significance of these accuracy measures. To avoid the risk of overfitting, we used kernel-based

approaches (42). In addition, for the SVM we explicitly optimized the hyper-parameter controlling for the regularization of the classifier.

Reported outcomes consist of total accuracy, balanced accuracy, class accuracy, and Area Under the curve (AUC). Total accuracy is calculated as the number of correctly classified test samples divided by the overall number of test samples. Average class (balanced) accuracy considers the number of samples in each class and weights their accuracy equally. Class accuracy shows the model's preference for some classes. AUC provides a scale-invariant measure of performance across classifications.

Results

Behaviorally, all four interventions induced an ASC (as reported previously: psilocybin (37); LSD (38); meditation (39); hypnosis (Fig. S1)). Psilocybin and LSD resulted in a significant increase in all 5D-ASC subscales ($p<0.05$) (Fig. S2A) (43), meditation resulted in a significant increase in all MEDEQ subscales ($p<0.05$) (Fig. S2B) (44), and all participants in the hypnosis condition reported reaching sufficient hypnotic depth (Fig. S2C). When comparing the pharmacological interventions, we found no differences in the 5D-ASC subscales between psilocybin and LSD ($p>0.05$) (Fig. S2A). A direct behavioral comparison of the non-pharmacological interventions was not possible due to the different scales used.

Psilocybin, LSD, hypnosis, and meditation each induce distinct changes in rs-fcMRI

To investigate the neural correlates of each ASC, each intervention was first compared to its control condition using a paired t-test (Fig. 1). Both psilocybin and LSD induced: (i) increased connectivity between regions involved in sensory and associative networks; (ii) decreased connectivity between regions involved in different associative networks; and (iii) decreased connectivity within sensory networks. Meanwhile, hypnosis induced: (i) decreased connectivity within the primary visual (V1) network; and (ii) increased connectivity between the V1 network and the somatomotor, superior temporal gyrus (STG), anterior default mode network (DMN), and limbic/anterior parahippocampal cortex (aPaHC) networks (Fig. 1). Finally, meditation induced decreased connectivity between the posterior DMN and secondary visual networks (V2) (Fig. 1).

Pharmacological and non-pharmacological ASC intervention methods induce distinct rs-fcMRI changes that are predictive at the individual level

We hypothesized that pharmacological and non-pharmacological ASC interventions have distinct rs-fcMRI patterns. The main effect of pharmacological vs. non-pharmacological ASC interventions on RRC revealed 22 significantly correlated cluster pairs ($p<0.05$ TFCE) (Fig. 2). Compared to non-pharmacological ASC methods, pharmacological ASC methods showed: (i) decreased connectivity between and within different

associative networks (e.g., DMN, STG); ii) increased connectivity between the V1 and associative networks (e.g., inferior temporal gyrus (ITG), dorsal attention network (DAN)); and (iii) decreased connectivity between the V1 and associative networks (e.g., somatomotor).

In addition, we hypothesized that rs-fcMRI changes induced by pharmacological and non-pharmacological ASC intervention methods are predictive at the individual level. We found that a binary SVM was able to predict pharmacological and non-pharmacological interventions with a total accuracy of 85.05% (balanced accuracy=84.89%, p=0.0002; class accuracy: pharmacological interventions=83.33%, p=0.0002, non-pharmacological interventions=86.44%, p=0.0002) (Fig. 2). Furthermore, the weights matrix (Fig. S17) showed that this multivariate machine learning analysis reflects the univariate ROI-to-ROI analysis in Figure 2 (e.g., negatively weighted connections between the V1 and somatomotor networks).

Hypnosis and meditation show distinct differences when compared to pharmacological interventions

Each pair of individual ASC intervention methods was compared directly using a series of 2x2 mixed ANOVAs with a between-subjects factor of ASC intervention method (intervention 1 vs. intervention 2) and within-subjects factor of State (intervention vs. control) (Fig. 3). Directly comparing each of the pharmacological interventions to hypnosis revealed a consistent pattern. Compared to hypnosis, both psilocybin and LSD induced: increased connectivity between regions involved in sensory and associative networks; and decreased connectivity between regions involved in sensory networks (Fig. 3A&C). Meanwhile, directly comparing each of the pharmacological interventions to meditation revealed one common change in connectivity: decreased connectivity within V1 (Fig. 3B&D).

As hypothesized, directly comparing psilocybin and LSD revealed no significant differences in RRC (Fig. 3E). In contrast, directly comparing the non-pharmacological conditions showed that hypnosis induced decreased connectivity within V1 compared to meditation (Fig. 3F).

rs-fcMRI changes are predictive at the individual level when comparing hypnosis and meditation, but not psilocybin and LSD

We hypothesized that hypnosis and meditation have distinct rs-fcMRI patterns, while psilocybin and meditation do not. To investigate this, we trained a multiclass Gaussian Process Classification (GPC) with four classes: psilocybin, LSD, hypnosis, and meditation. The multiclass GPC demonstrated no clear classification between all four interventions (class accuracy: psilocybin=39.13%, p=0.07; LSD=40.00%, p=0.23; hypnosis = 66.67%, p=0.01; meditation=44.83%, p=0.16) (Fig. 4A). This confusion matrix indicates that the model's inaccuracy may be due to similarities between psilocybin and LSD. To further investigate this, we trained a binary SVM with two classes, psilocybin and LSD. The model was unable to distinguish the two pharmacological groups from each other as the model had a classification accuracy of 47.92% (balanced accuracy=47.91%, p=0.46; class accuracy: psilocybin=47.83%, p=0.36, LSD=48.00%, p=0.73, Receiver Operating Characteristic=50%) (Fig. 4B). In contrast, a binary SVM was able to successfully distinguish between hypnosis and meditation, with a classification accuracy of 66.03% (balanced accuracy=66.03%, p=0.02; class accuracy: hypnosis=70%, p=0.03; meditation=62.07%, p=0.07; AUC=0.50) (Fig. 4C).

ASC-induced changes in rs-fcMRI are directly related to behavioral changes

To explore whether ASC-induced changes in rs-fcMRI are related to behavioral changes, we conducted a preliminary analysis regressing ASC-induced changes in behavior onto changes in rs- fcMRI for psilocybin, LSD, and meditation. We were unable to include hypnosis in this analysis as no in-depth behavioral data was collected. We found that two 5D-ASC subscales, 'experience of unity' and 'insightfulness', resulted in significant ($p<0.05$) clusters in the psilocybin condition (Fig. 5A-B), while one 5D-ASC subscale, 'elementary imagery', resulted in a significant ($p<0.05$) cluster in the LSD condition (Fig. 5C). Furthermore, the meditation depth questionnaire (MEDEQ) subscale 'essential quality' resulted in two borderline significant (p=0.06) clusters in the meditation condition (Fig. 5D).

Discussion

This study closes major knowledge-gaps regarding the neurobiology of ASC by showing that: (i) no network reaches significance in all four ASC methods; (ii) pharmacological and non-pharmacological interventions of inducing ASC show distinct connectivity patterns that are predictive at the individual level; (iii) hypnosis and meditation show differences in functional connectivity when compared directly, and also drive distinct differences when jointly compared to the pharmacological ASC interventions; (iv) psilocybin and LSD show no differences in functional connectivity when directly compared to each other, but do show distinct behavioral-neural relationships.

Psilocybin and LSD show overlap in their neural correlates, while hypnosis and meditation are distinct

We used a whole-brain data-driven approach to establish the neural correlates of each ASC method and found that: (i) no network reached significance in all four interventions (Fig. 1); and (ii) while there is overlap in the neural correlates of the pharmacological methods, there is no overlap in the non-pharmacological methods (Fig. 3). The lack of a common network in all four ASC methods is striking given the observed overlap in the phenomenology (45; 46; 38; 37; 11; 8–10; 12–14). In addition, the lack of overlap between hypnosis and mediation is of particular interest, as to date the whole-brain data-driven effects of hypnosis and meditation have not yet been explored, limiting comparisons between studies.

Comparing hypnosis to its control, we found that all changes involved V1, which may reflect the importance of visual imagery in hypnosis. More specifically, we found that hypnosis induced decreased connectivity within V1, and increased connectivity between V1 and associative networks (e.g., aDMN, pSTG, limbic, and somatomotor) (Fig. 1C). This finding is in line with previous studies showing that both hypnotic and mental imagery rely on activation of the visual cortex via top-down mechanisms (26; 27). In addition, a recent meta-analysis of 15 hypnosis neuroimaging studies found that hypnotic responses correlate most highly with activation in the lingual gyrus, a key V1 region (28).

Comparing meditation to its control showed that meditation induced decreased connectivity between regions of V2 (fusiform cortex) and pDMN (precuneus, posterior cingulate) (Fig. 1D). Interestingly, the fusiform cortex is an area that has come up consistently in the meditation literature but has been largely ignored (47; 35; 48–50). Though historically the fusiform cortex has most commonly been linked to the perception of faces, it has also been linked to visual imagery (51–53). Thus, one possible explanation for why meditation involves decreased connectivity between the fusiform cortex and the DMN is that visual imagery commonly accompanies mind wandering, which is typically reduced during meditation and involves alterations in the DMN (54). This finding is in line with the literature: one of the most consistent findings is that open awareness-related meditation techniques lead to changes in the functional dynamics of the DMN (34; 47; 48; 55).

In contrast to the non-pharmacological ASC methods, psilocybin and LSD show an overlap in their neural correlates as both induced: (i) decreased connectivity between regions involved in different associative networks (e.g., aDMN and STG); (ii) decreased connectivity within sensory networks (e.g., V1, V2); and (iii) increased connectivity between regions involved in V1 and DAN (Fig. 1A-B). This general pattern of results is of interest as it replicates previous publications that used the same data but (i) different preprocessing pipelines (QuNex vs. Conn Toolbox), (ii) different levels of analysis (dense vs. parcellated), and (iii) different analysis methods (GBC vs. ROI-to-ROI functional connectivity) (38; 37). We also observed several differences between psilocybin and LSD. For example, only LSD induced increased connectivity between V1 and the frontoparietal, language, and ITG networks, while only psilocybin induced increased connectivity between STG and the DAN/ superior lateral occipital cortex (sLOC) networks (Fig. 1A-B).

<u>Pharmacological and non-pharmacological ASC intervention methods induce distinct changes in rs-fcMRI that are predictive at the individual level</u>

Comparing changes in RRC between pharmacological and non-pharmacological methods revealed widespread differences within and between neural networks. Compared to non-pharmacological ASC

methods, pharmacological ASC methods showed: (i) decreased connectivity between and within different associative networks; ii) increased connectivity between the V1 and associative networks; and (iii) decreased connectivity between the V1 and associative networks (Fig. 2). This neural connectivity pattern mainly reflects that observed when comparing psilocybin and LSD to their own control (Fig. 1A&B). Our machine learning analysis confirmed that pharmacological and non-pharmacological methods of inducing ASC have distinct neural correlates, as a binary SVM was able to successfully classify pharmacological and non-pharmacological interventions using functional connectivity data (Fig. 2). This demonstrates that the ROI-to-ROI functional connectivity results are predictive at the individual level.

Hypnosis and meditation show distinct differences when compared to pharmacological interventions

To further investigate the contrast between pharmacological and non-pharmacological ASC methods we then compared each pair of ASC methods directly. This revealed that: (i) the decreased connectivity between and within different associative networks in Figure 2 is primarily driven by the differences between psilocybin and meditation (Fig. 3B); (ii) the increased connectivity between the V1 and associative networks in Figure 2 is primarily driven by differences between the pharmacological and hypnosis (Fig. 4A&C); and (iii) the decrease in connectivity between the V1 network and the somatomotor network is primarily driven by differences between the pharmacological interventions and hypnosis (Fig. 4A&C). Overall, this supports our finding that hypnosis and meditation are distinct, as not only do they show significant differences in connectivity when compared directly, but they also show distinct differences when compared with the pharmacological conditions (Fig. 4A-F). This conclusion is further supported by the fact that a binary SVM was able to successfully classify hypnosis and meditation using the functional connectivity matrices, while it was unable to distinguish between psilocybin and LSD (Fig. 4).

The decrease in connectivity between V1 and the somatomotor network (Fig. 2) is of particular interest as it is the only significant connection where pharmacological and non-pharmacological interventions show

opposite effects: LSD shows decreased connectivity between V1 and the somatomotor network (Fig. 1B) while hypnosis shows increased connectivity (Fig. 1C). This connection is also highlighted by the machine learning analysis, as the weights matrix for the binary support vector comparing pharmacological to non-pharmacological conditions shows that one of the most discriminative ROI-to-ROI connections is the one between V1 and the somatomotor network (Fig. S12). The contrast in connectivity patterns may reflect the different origins of psychedelic and hypnotic visual perceptual alterations: in hypnosis, visual perceptual alterations are believed to be the result of mental representations that are then translated into perceptual states via top-down regulation; in psychedelics, visual perceptual alterations have been shown to be the result of an amplification of internally-driven excitation of the visual pathway (8; 9). However, causal influences cannot be derived from RRC, as it is a measure of functional rather than effective connectivity.

Similarities between pharmacological methods and hypnosis may be linked to visual alterations

Directly comparing hypnosis to meditation reveals reduced connectivity within V1 (Fig. 3F). This finding is of particular interest as it may reflect the fact that hypnosis involves guided visual imagery, while meditation does not involve visual imagery, but instead a self-instigated strengthened awareness of the present moment (Fig. 3F). This interpretation is supported by the fact that psilocybin and LSD, which both involve visual alterations, also show: (i) reduced connectivity within V1 when each intervention is compared to its own control (Fig. 1A&B); and (ii) reduced connectivity within V1 when each intervention is compared to meditation (Fig. 3B&D). In addition, neither psilocybin nor LSD show a difference in connectivity within the V1 cortex when compared to hypnosis (Fig. 3B&D). Overall, these findings highlight that not only are hypnosis and meditation distinct, but there are similarities between the pharmacological conditions and hypnosis, which may be linked to visual alterations.

Behavior-neural analysis uncovers further distinctions between psilocybin and LSD

As outlined above, at these specific doses psilocybin and LSD show no significant behavioral or neural differences when compared directly to each other (Fig. S2, Fig. 3E). However, we also observed that different behavioral 5D-ASC subscales correlate with different rs-fcMRI changes in the psilocybin and LSD conditions. For example, in the psilocybin condition both 'experience of unity' and 'insightfulness' correlate with decreased connectivity between regions in the DAN/aSMG and the language networks (Fig. 5A&B). In contrast, in the LSD condition 'elementary imagery' correlates with decreased connectivity between regions in the DAN and the lDMN/aDMN/ITG networks (Fig. 5C). Although we were not able to assess the relationship between behavioral and rs-fcMRI changes in hypnosis as no in-depth behavioral data was collected, we did find that meditation depth correlated with decreased connectivity between the fusiform cortex and several other regions (Fig. 5D).

Implications for clinical use and consciousness research

When considering the clinical implications of our results, it is important to note that we focus on acute effects. However, it is currently unclear how the acute ASC state translates into prolonged clinical improvements, though there is some preliminary evidence that in psychedelics, the acute experience may be related to treatment response (56). Understanding this relationship is of vital importance given that: (i) there is substantial variability in the acute response which may help understand the variability in treatment response (15; 57); and (ii) we are able to shape the acute experience (e.g., the psychedelic experience can be shaped by an individual's set, setting, and dose) (58; 59). Furthermore, by establishing the acute neural correlates of different ASC methods in healthy controls, we hope to contribute to the development of clinical biomarkers and the mapping of specific mechanisms of action of each ASC intervention to either a disease area or individual patients. In addition, given that we show pharmacological and non-pharmacological engage in distinct brain circuits, they may have synergistic properties that could prolong or augment therapeutic effects.

Limitations

These findings should be interpreted in light of the following limitations. First, we combined datasets that used different scan parameters and showed significant differences in age, which we tried to account for by: (i) using a within-subject design; and (ii) conducting an additional analysis including age as a co-factor (Fig. S3-S6). Secondly, meditation study had a shorter scan time that may reduce the data's test–retest reliability (60). Furthermore, the test-retest reliability of the four ASC methods is currently unknown. Thirdly, we were unable to directly compare subjective effects as no consistent behavioral measure was used across datasets and no in-depth behavioral data was collected for hypnosis. Fourthly, we were unable to correct for physiological noise due to lack of data (see supplementary discussion for further details). Finally, the use of GSR remains an unresolved issue in the field (see supplementary discussion for further details).

Conclusion

Overall, these results deepen our understanding of the mechanisms of action of ASC and highlight the importance of exploring how these effects can be leveraged in the treatment of psychiatric disorders. In addition, they show that care must be taken when drawing comparisons between different methods of inducing ASC, especially given the differences we observed between the non-pharmacological ASC methods, and to a lesser extent the pharmacological ASC methods. However, such categorizations may still prove useful given we found that when comparing pharmacological and non-pharmacological ASC methods, changes in rs-fcMRI are predictive at the individual level. Our results also highlight the need for more whole-brain data-driven approaches in the hypnosis and meditation literature to obtain a more cohesive picture of their neural correlates. Finally, our findings demonstrate the importance of linking behavioral and rs-fcMRI data, as doing so revealed distinctions between psilocybin and LSD that are not apparent when evaluating the behavioral and rs-fcMRI results in isolation.

Acknowledgments

Swiss National Science Foundation under the framework of Neuron Cofund (Grant No. 01EW1908) (FXV)

Heffter Research Institute (Grant No.1-190420) (FXV)

Swiss Neuromatrix Foundation (Grant No. 2016-0111) (FXV)

Swiss National Science Foundation (P2ZHP1\161626) (KHP)

Fonds de la Recherche Scientifique – FNRS, Belgium (CP)

Funding by University of Zurich and Hypnose.NET GmbH/OMNI Hypnosis International (MB)

Heffter Young Investigator Fellowship Award (Grant No. HYIFA-2022-01) (NMR)

Author contributions:

Conceptualization: KHP, NMR, FFM, CP

Methodology: NMR, FFM, KHP, CP, ES

Investigation: PD, LS, KHP, FXV, NMP, MB, PS

Visualization: NMR, FFM, KHP

Supervision: KHP, CP, AA

Writing—original draft: NMR, FFM, KHP

Writing—review & editing: CP, AA, FXV, PD, LS, NMP, MB, PS, ES

Data has been presented as a poster at ECNP 2021 and at OHBM 2022.

Financial Disclosures

Katrin Preller is employed as principal clinical biomarker lead at Boehringer Ingelheim GmbH & Co KG.

All other authors report no biomedical financial interests or potential conflicts of interest.

References

1. Alladin A (2012): Cognitive hypnotherapy for major depressive disorder. *The American journal of clinical hypnosis* 54: 275–293.
2. Carhart-Harris RL, Bolstridge M, Rucker J, Day CMJ, Erritzoe D, Kaelen M, *et al.* (2016): Psilocybin with psychological support for treatment-resistant depression: an open-label feasibility study. *The Lancet Psychiatry* 3: 619–627.
3. Gasser P, Holstein D, Michel Y, Doblin R, Yazar-Klosinski B, Passie T, *et al.* (2014): Safety and efficacy of lysergic acid diethylamide-assisted psychotherapy for anxiety associated with life-threatening diseases. *The Journal of nervous and mental disease* 202: 513–520.
4. Hilton L, Hempel S, Ewing BA, Apaydin E, Xenakis L, Newberry S, *et al.* (2017): Mindfulness Meditation for Chronic Pain: Systematic Review and Meta-analysis. *Annals of behavioral medicine : a publication of the Society of Behavioral Medicine* 51: 199–213.
5. Millière R, Carhart-Harris RL, Roseman L, Trautwein F-M, Berkovich-Ohana A (2018): Psychedelics, Meditation, and Self-Consciousness. *Frontiers in psychology* 9: 1475.
6. Lemercier CE, Terhune DB (2018): Psychedelics and hypnosis: Commonalities and therapeutic implications. *Journal of psychopharmacology (Oxford, England)* 32: 732–740.
7. Lifshitz M, Cusumano EP, Raz A (2014): Meditation and Hypnosis at the Intersection Between Phenomenology and Cognitive Science. In: Schmidt S, Walach H. *Meditation – Neuroscientific Approaches and Philosophical Implications*. Cham: Springer International Publishing, pp 211–226.
8. Kometer M, Vollenweider FX (2018): Serotonergic Hallucinogen-Induced Visual Perceptual Alterations. *Current topics in behavioral neurosciences* 36: 257–282.
9. Landry M, Lifshitz M, Raz A (2017): Brain correlates of hypnosis: A systematic review and meta-analytic exploration. *Neuroscience and biobehavioral reviews* 81: 75–98.

10. Lebedev AV, Lövdén M, Rosenthal G, Feilding A, Nutt DJ, Carhart-Harris RL (2015): Finding the self by losing the self: Neural correlates of ego-dissolution under psilocybin. *Human brain mapping* 36: 3137–3153.

11. Kihlstrom JF (2005): Is hypnosis an altered state of consciousness or what? *Contemp. Hypnosis* 22: 34–38.

12. Lou HC, Kjaer TW, Friberg L, Wildschiodtz G, Holm S, Nowak M (1999): A15O-H2O PET study of meditation and the resting state of normal consciousness. *Hum. Brain Mapp.* 7: 98–105.

13. Mason NL, Kuypers KPC, Müller F, Reckweg J, Tse DHY, Toennes SW, *et al.* (2020): Me, myself, bye: regional alterations in glutamate and the experience of ego dissolution with psilocybin. *Neuropsychopharmacology : official publication of the American College of Neuropsychopharmacology* 45: 2003–2011.

14. Rainville P, Price DD (2003): Hypnosis phenomenology and the neurobiology of consciousness. *The International journal of clinical and experimental hypnosis* 51: 105–129.

15. Moujaes F, Preller KH, Ji JL, Murray JD, Berkovitch L, Vollenweider FX, *et al.* (2022): Towards mapping neuro-behavioral heterogeneity of psychedelic neurobiology in humans. *Biological Psychiatry*.

16. Schmid Y, Enzler F, Gasser P, Grouzmann E, Preller KH, Vollenweider FX, *et al.* (2015): Acute Effects of Lysergic Acid Diethylamide in Healthy Subjects. *Biological Psychiatry* 78: 544–553.

17. Vollenweider FX, Preller KH (2020): Psychedelic drugs: neurobiology and potential for treatment of psychiatric disorders. *Nature reviews. Neuroscience* 21: 611–624.

18. Gregorio D de, Posa L, Ochoa-Sanchez R, McLaughlin R, Maione S, Comai S, *et al.* (2016): The hallucinogen d-lysergic diethylamide (LSD) decreases dopamine firing activity through 5-HT1A, D2 and TAAR1 receptors. *Pharmacological research* 113: 81–91.

19. Halberstadt AL, Geyer MA (2011): Multiple receptors contribute to the behavioral effects of indoleamine hallucinogens. *Neuropharmacology* 61: 364–381.

20. Pokorny T, Preller KH, Kraehenmann R, Vollenweider FX (2016): Modulatory effect of the 5-HT1A agonist buspirone and the mixed non-hallucinogenic 5-HT1A/2A agonist ergotamine on psilocybin-induced psychedelic experience. *European neuropsychopharmacology : the journal of the European College of Neuropsychopharmacology* 26: 756–766.
21. Passie T, Halpern JH, Stichtenoth DO, Emrich HM, Hintzen A (2008): The pharmacology of lysergic acid diethylamide: a review. *CNS neuroscience & therapeutics* 14: 295–314.
22. Madsen MK, Fisher PM, Burmester D, Dyssegaard A, Stenbæk DS, Kristiansen S, *et al.* (2019): Psychedelic effects of psilocybin correlate with serotonin 2A receptor occupancy and plasma psilocin levels. *Neuropsychopharmacology : official publication of the American College of Neuropsychopharmacology* 44: 1328–1334.
23. Preller KH, Herdener M, Pokorny T, Planzer A, Kraehenmann R, Stämpfli P, *et al.* (2017): The Fabric of Meaning and Subjective Effects in LSD-Induced States Depend on Serotonin 2A Receptor Activation. *Current biology : CB* 27: 451–457.
24. Vigo D, Thornicroft G, Atun R (2016): Estimating the true global burden of mental illness. *The Lancet Psychiatry* 3: 171–178.
25. Terhune DB, Cleeremans A, Raz A, Lynn SJ (2017): Hypnosis and top-down regulation of consciousness. *Neuroscience and biobehavioral reviews* 81: 59–74.
26. Deeley Q, Oakley DA, Toone B, Giampietro V, Brammer MJ, Williams SCR, *et al.* (2012): Modulating the default mode network using hypnosis. *The International journal of clinical and experimental hypnosis* 60: 206–228.
27. Demertzi A, Soddu A, Faymonville M-E, Bahri MA, Gosseries O, Vanhaudenhuyse A, *et al.* (2011): Hypnotic modulation of resting state fMRI default mode and extrinsic network connectivity. *Progress in brain research* 193: 309–322.
28. Halligan PW, Oakley DA (2013): Hypnosis and cognitive neuroscience: bridging the gap. *Cortex; a journal devoted to the study of the nervous system and behavior* 49: 359–364.

29. Hoeft F, Gabrieli JDE, Whitfield-Gabrieli S, Haas BW, Bammer R, Menon V, *et al.* (2012): Functional brain basis of hypnotizability. *Archives of general psychiatry* 69: 1064–1072.

30. Huber A, Lui F, Duzzi D, Pagnoni G, Porro CA (2014): Structural and functional cerebral correlates of hypnotic suggestibility. *PloS one* 9: e93187.

31. Jiang H, White MP, Greicius MD, Waelde LC, Spiegel D (2017): Brain Activity and Functional Connectivity Associated with Hypnosis. *Cerebral cortex (New York, N.Y. : 1991)* 27: 4083–4093.

32. Lipari S, Baglio F, Griffanti L, Mendozzi L, Garegnani M, Motta A, *et al.* (2012): Altered and asymmetric default mode network activity in a "hypnotic virtuoso": an fMRI and EEG study. *Consciousness and cognition* 21: 393–400.

33. McGeown WJ, Mazzoni G, Venneri A, Kirsch I (2009): Hypnotic induction decreases anterior default mode activity. *Consciousness and cognition* 18: 848–855.

34. Brewer JA, Worhunsky PD, Gray JR, Tang Y-Y, Weber J, Kober H (2011): Meditation experience is associated with differences in default mode network activity and connectivity. *Proceedings of the National Academy of Sciences of the United States of America* 108: 20254–20259.

35. Fox KCR, Dixon ML, Nijeboer S, Girn M, Floman JL, Lifshitz M, *et al.* (2016): Functional neuroanatomy of meditation: A review and meta-analysis of 78 functional neuroimaging investigations. *Neuroscience and biobehavioral reviews* 65: 208–228.

36. Josipovic Z, Dinstein I, Weber J, Heeger DJ (2011): Influence of meditation on anti-correlated networks in the brain. *Frontiers in human neuroscience* 5: 183.

37. Preller KH, Duerler P, Burt JB, Ji JL, Adkinson B, Stämpfli P, *et al.* (2020): Psilocybin induces time-dependent changes in global functional connectivity: Psi-induced changes in brain connectivity. *Biological Psychiatry:* 197–207.

38. Preller KH, Burt JB, Ji JL, Schleifer CH, Adkinson BD, Stämpfli P, *et al.* (2018): Changes in global and thalamic brain connectivity in LSD-induced altered states of consciousness are attributable to the 5-HT2A receptor. *eLife* 7: e35082.

39. Smigielski L, Scheidegger M, Kometer M, Vollenweider FX (2019): Psilocybin-assisted mindfulness training modulates self-consciousness and brain default mode network connectivity with lasting effects. *NeuroImage* 196: 207–215.

40. Schrouff J, Rosa MJ, Rondina JM, Marquand AF, Chu C, Ashburner J, *et al.* (2013): PRoNTo: pattern recognition for neuroimaging toolbox. *Neuroinformatics* 11: 319–337.

41. Marcot BG, Hanea AM (2021): What is an optimal value of k in k-fold cross-validation in discrete Bayesian network analysis? *Comput Stat* 36: 2009–2031.

42. Shawe-Taylor J, Cristianini N, others (2004): *Kernel methods for pattern analysis:* Cambridge university press.

43. Studerus E, Gamma A, Vollenweider FX (2010): Psychometric evaluation of the altered states of consciousness rating scale (OAV). *PloS one* 5: e12412.

44. Piron H (2022): Meditation Depth Questionnaire (MEDEQ) and Meditation Depth Index (MEDI). *Handbook of Assessment in Mindfulness Research*: Springer, pp 1–16.

45. Huels ER, Kim H, Lee U, Bel-Bahar T, Colmenero AV, Nelson A, *et al.* (2021): Neural Correlates of the Shamanic State of Consciousness. *Frontiers in human neuroscience* 15: 610466.

46. Smigielski L, Kometer M, Scheidegger M, Krähenmann R, Huber T, Vollenweider FX (2019): Characterization and prediction of acute and sustained response to psychedelic psilocybin in a mindfulness group retreat. *Scientific reports* 9: 14914.

47. Berkovich-Ohana A, Harel M, Hahamy A, Arieli A, Malach R (2016): Alterations in task-induced activity and resting-state fluctuations in visual and DMN areas revealed in long-term meditators. *NeuroImage* 135: 125–134.

48. Fujino M, Ueda Y, Mizuhara H, Saiki J, Nomura M (2018): Open monitoring meditation reduces the involvement of brain regions related to memory function. *Scientific reports* 8: 9968.

49. Garrison KA, Zeffiro TA, Scheinost D, Constable RT, Brewer JA (2015): Meditation leads to reduced default mode network activity beyond an active task. *Cognitive, affective & behavioral neuroscience* 15: 712–720.

50. Tomasino B, Fregona S, Skrap M, Fabbro F (2012): Meditation-related activations are modulated by the practices needed to obtain it and by the expertise: an ALE meta-analysis study. *Frontiers in human neuroscience* 6: 346.

51. Kanwisher N, McDermott J, Chun MM (1997): The Fusiform Face Area: A Module in Human Extrastriate Cortex Specialized for Face Perception. *J. Neurosci.* 17: 4302–4311.

52. Spagna A, Hajhajate D, Liu J, Bartolomeo P (2021): Visual mental imagery engages the left fusiform gyrus, but not the early visual cortex: A meta-analysis of neuroimaging evidence. *Neuroscience & Biobehavioral Reviews* 122: 201–217.

53. Winlove CIP, Milton F, Ranson J, Fulford J, MacKisack M, Macpherson F, *et al.* (2018): The neural correlates of visual imagery: A co-ordinate-based meta-analysis. *Cortex; a journal devoted to the study of the nervous system and behavior* 105: 4–25.

54. Fox KCR, Nijeboer S, Dixon ML, Floman JL, Ellamil M, Rumak SP, *et al.* (2014): Is meditation associated with altered brain structure? A systematic review and meta-analysis of morphometric neuroimaging in meditation practitioners. *Neuroscience and biobehavioral reviews* 43: 48–73.

55. Taylor VA, Daneault V, Grant J, Scavone G, Breton E, Roffe-Vidal S, *et al.* (2013): Impact of meditation training on the default mode network during a restful state. *Social cognitive and affective neuroscience* 8: 4–14.

56. Ross S, Bossis A, Guss J, Agin-Liebes G, Malone T, Cohen B, *et al.* (2016): Rapid and sustained symptom reduction following psilocybin treatment for anxiety and depression in patients with life-threatening cancer: a randomized controlled trial. *Journal of psychopharmacology (Oxford, England)* 30: 1165–1180.

57. Elkins G (2021): Hypnotizability: Emerging Perspectives and Research. *The International journal of clinical and experimental hypnosis* 69: 1–6.

58. Studerus E, Kometer M, Hasler F, Vollenweider FX (2011): Acute, subacute and long-term subjective effects of psilocybin in healthy humans: a pooled analysis of experimental studies. *Journal of psychopharmacology (Oxford, England)* 25: 1434–1452.

59. Johnson M, Richards W, Griffiths R (2008): Human hallucinogen research: guidelines for safety. *Journal of psychopharmacology (Oxford, England)* 22: 603–620.

60. Birn RM, Molloy EK, Patriat R, Parker T, Meier TB, Kirk GR, *et al.* (2013): The effect of scan length on the reliability of resting-state fMRI connectivity estimates. *NeuroImage* 83: 550–558.

Figure 1. Psilocybin, LSD, hypnosis, and meditation each induce distinct changes in rs-fcMRI. Paired t-tests were conducted to compare intervention vs. control for each ASC intervention method: (**A**) psilocybin (N=23), (**B**) LSD (N=25), (**C**) hypnosis (N=30), and (**D**) meditation (N=29). (**A-D**) Centre shows the cluster pairs that survived connection thresholding ($p<0.05$ TFCE type I error protected). Red = increased connection between cluster pairs induced by intervention vs. control, blue = decreased connection between cluster pairs induced by intervention vs. control. Opacity of the connections is scaled according to the TFCE statistics for visual clarity. For further details about each cluster see Table S6, Table S7, Table S8, Table S9. The three brain images at the bottom of each panel depict the same ROI-to-ROI results in the sagittal, coronal, and axial planes. Network abbreviations: DAN = dorsal attention, sLOC = superior lateral occipital cortex, Cereb Crus = cerebellar crus, FPN = fronto parietal, Lang = language, ITG = inferior temporal gyrus, l/a/p DMN = lateral/anterior/posterior default mode, aPaHC = anterior parahippocampal cortex, STG = superior temporal gyrus, Som. Motor = somatormotor. r/l denotes both the left and right hemispheres.

Figure 2. Pharmacological vs. Non-Pharmacological ASC Interventions. (**A**) A 2x2 mixed ANOVA with a between-subjects factor of ASC intervention method (pharmacological (Ph) vs. non-pharmacological (N-Ph)) and a within-subjects factor State (intervention vs. control) was conducted. Pharmacological interventions (N=48) include psilocybin and LSD; non-pharmacological interventions (N=59) include hypnosis and meditation. Centre shows the 22 cluster pairs that survived connection thresholding ($p<0.05$ TFCE type I error protected). Red = increased connection between cluster pairs induced by pharmacological vs. non-pharmacological interventions, blue = decreased connection between cluster pairs induced by pharmacological vs. non-pharmacological interventions. Opacity of the connections is scaled according to the TFCE statistic for visual clarity. The 132 ROIs used are arranged into 22 networks, and the relevant networks are displayed on the outer ring. The three brain images in the right column depict the same ROI-to-ROI connectivity results in the sagittal, coronal, and axial planes. For further details about each cluster see Table S10. (**B**) Confusion matrix showing the predicted vs. the true classifications of subjects' intervention vs. control ROI-to-ROI connectivity matrices into either pharmacological or non-pharmacological interventions. Green = correct predictions, red = incorrect predictions. (**C**) Model predictions per subject (as we used a leave-one-subject out cross-validation scheme each fold represents an individual subject). The y-axis shows each subject grouped by ASC intervention method. The x-axis shows whether the subjects were classified as having undergone the pharmacological intervention (negative function value), or non-pharmacological condition (positive function value).

Figure 3. Direct comparison of each pair of ASC Interventions. A 2x2 mixed ANOVA with a between-subjects factor of ASC intervention methods (intervention 1 (Int 1) vs. intervention 2 (Int 2)) and within-subjects factor state (intervention vs. control) was conducted to directly compare each pair of ASC intervention methods including: (**A**) Psilocybin vs. Hypnosis, (**B**) Psilocybin vs. Meditation, (**C**) LSD vs. Hypnosis, (**D**) LSD vs. Meditation, (**E**) Psilocybin vs. LSD, and (**F**) Hypnosis vs. Meditation. (**A-F**) Centre shows the cluster pairs that survived connection thresholding ($p<0.05$ TFCE type I error protected). Red = increased connection between cluster pairs in intervention 1 vs. intervention 2, blue = decreased connection between cluster pairs in intervention 1 vs. intervention 2. Opacity of the connections is scaled according to the TFCE statistic. For further details about each cluster see Table S11, Table S12, Table S13, Table S14, Table S15. Psilocybin: N=23, LSD: N=25, Hypnosis: N=30, Meditation: N=29.

Figure 4. Classification of Individual ASC Interventions. (**A**) Confusion matrix showing the predicted vs. the true classifications from the Multiclass GPC with four classes: psilocybin, LSD, hypnosis, and meditation. Green = correct predictions, red = incorrect predictions. (**B**) Left: confusion matrix showing the predicted vs. the true classifications from the binary SVM with two classes: psilocybin and LSD. Green = correct predictions, red = incorrect predictions. Right: Model predictions per subject. The y-axis depicts each subject. The x-axis shows whether the subjects were classified as psilocybin (negative function value), or LSD (positive function value). (**C**) Left: confusion matrix showing the predicted vs. the true classifications from the binary SVM with two classes: hypnosis and meditation. Green = correct predictions, red = incorrect predictions. Right: Model predictions per subject. The y-axis depicts each subject. The x-axis shows whether the subjects were classified as hypnosis (negative function value), or meditation (positive function value).

Figure 5. Regression of ASC-induced behavioral changes onto changes in rs- fcMRI. To assess the effect of behavior on the rs-fcMRI, a preliminary analysis was conducted regressing ASC-induced changes (intervention - control) in behavior onto changes (intervention - control) in rs-fcMRI for psilocybin, LSD, and meditation. For the pharmacological interventions (psilocybin and LSD), the 5D-ASC subscales were used. For meditation, the MEDEQ five subscales were used. The behavioral-neural analyses were run with hierarchical clustering and all clusters were p-FDR corrected at $p<0.05$ using an MVPA omnibus test. (**A**-**B**) The 5D-ASC subscales 'experience of unity' and 'insightfulness' showed a significant relationship to psilocybin induced rs-fcMRI change ($p < 0.05$, FDR-corrected). (**C**) The 5D-ASC subscale 'elementary imagery' showed a significant relationship to LSD induced rs-fcMRI change ($p < 0.05$, FDR-corrected). (**D**) The MEDEQ subscale 'essential quality' showed a borderline significant relationship to meditation induced rs-fcMRI change ($p = 0.06$, FDR-corrected). For further details about each cluster see Table S16, Table S17, Table S18, Table S19.

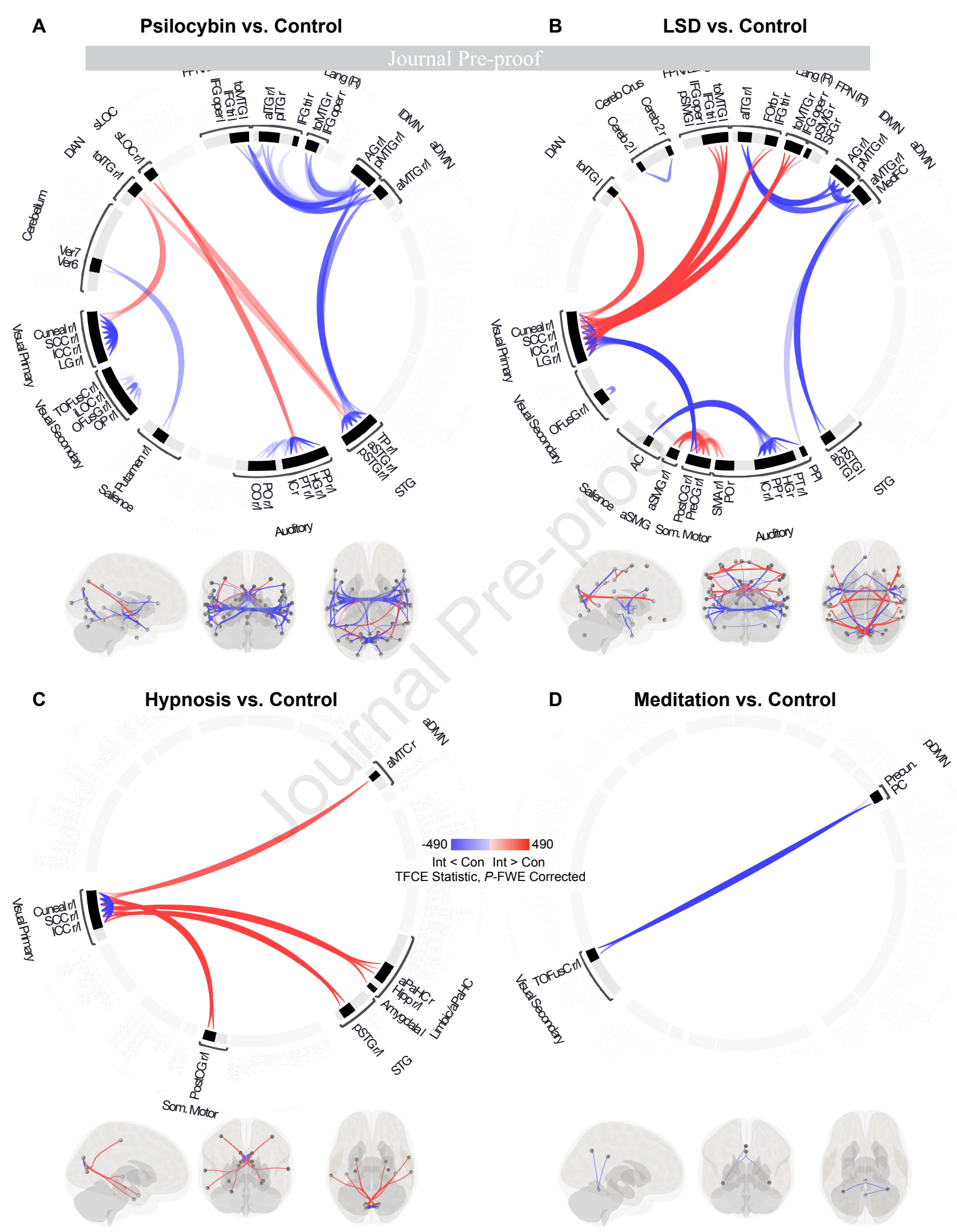
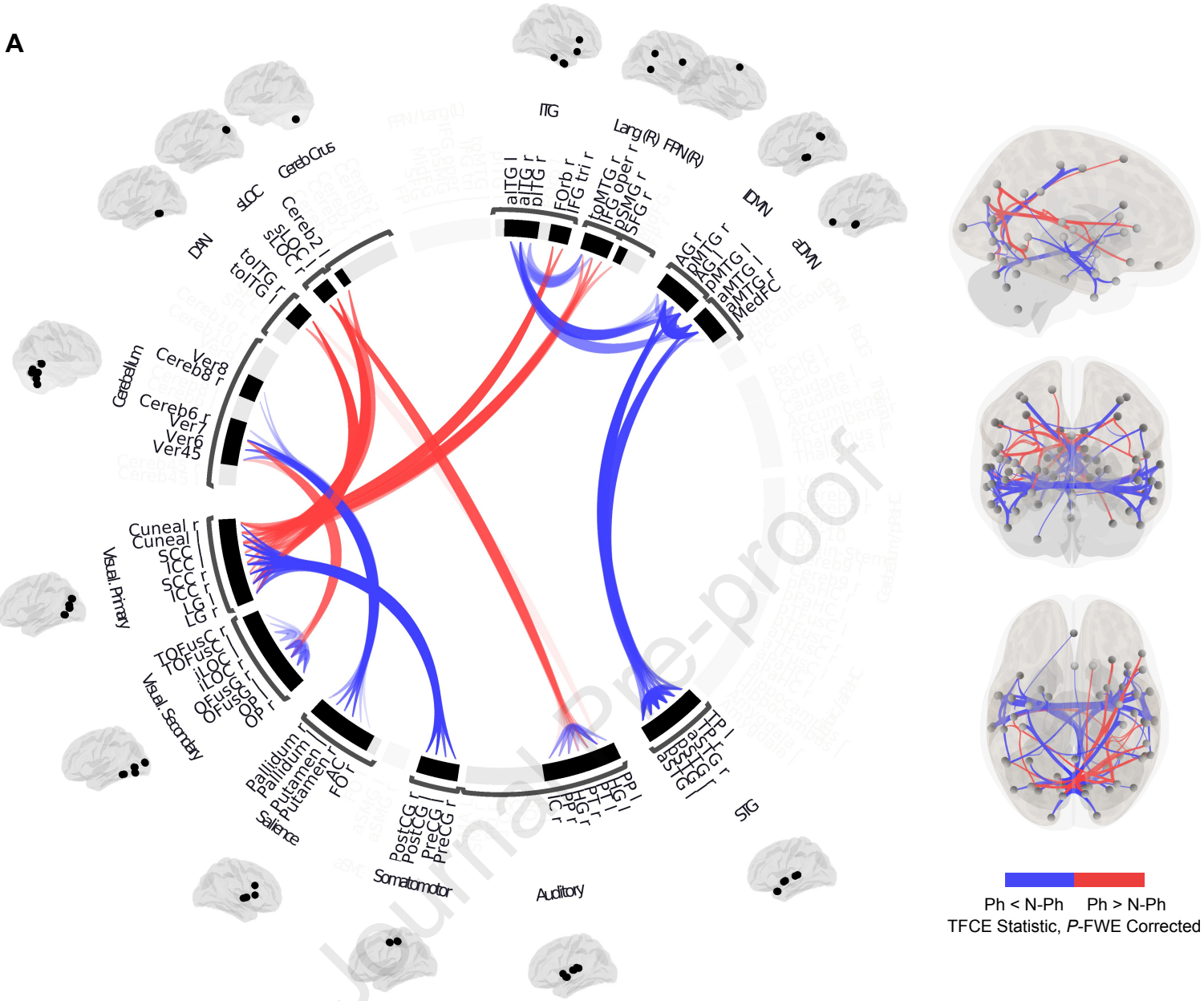
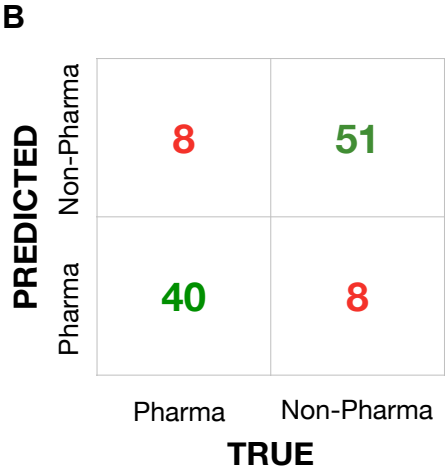
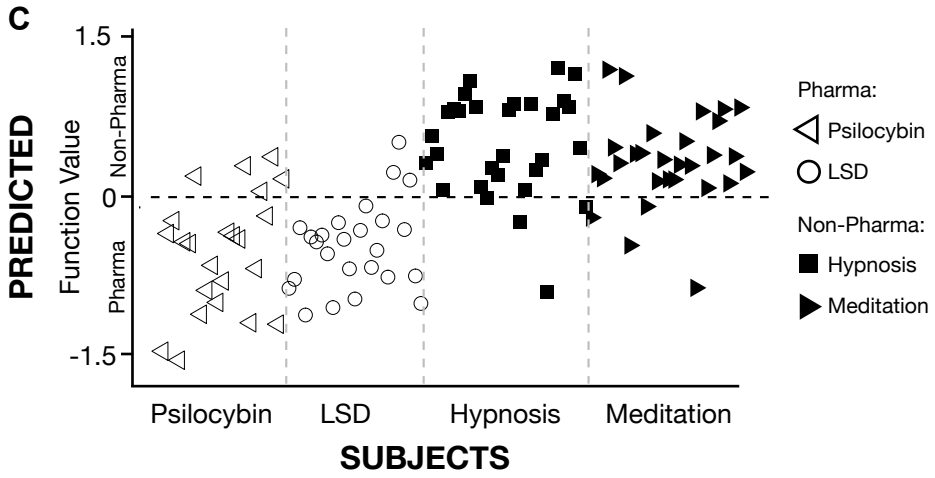
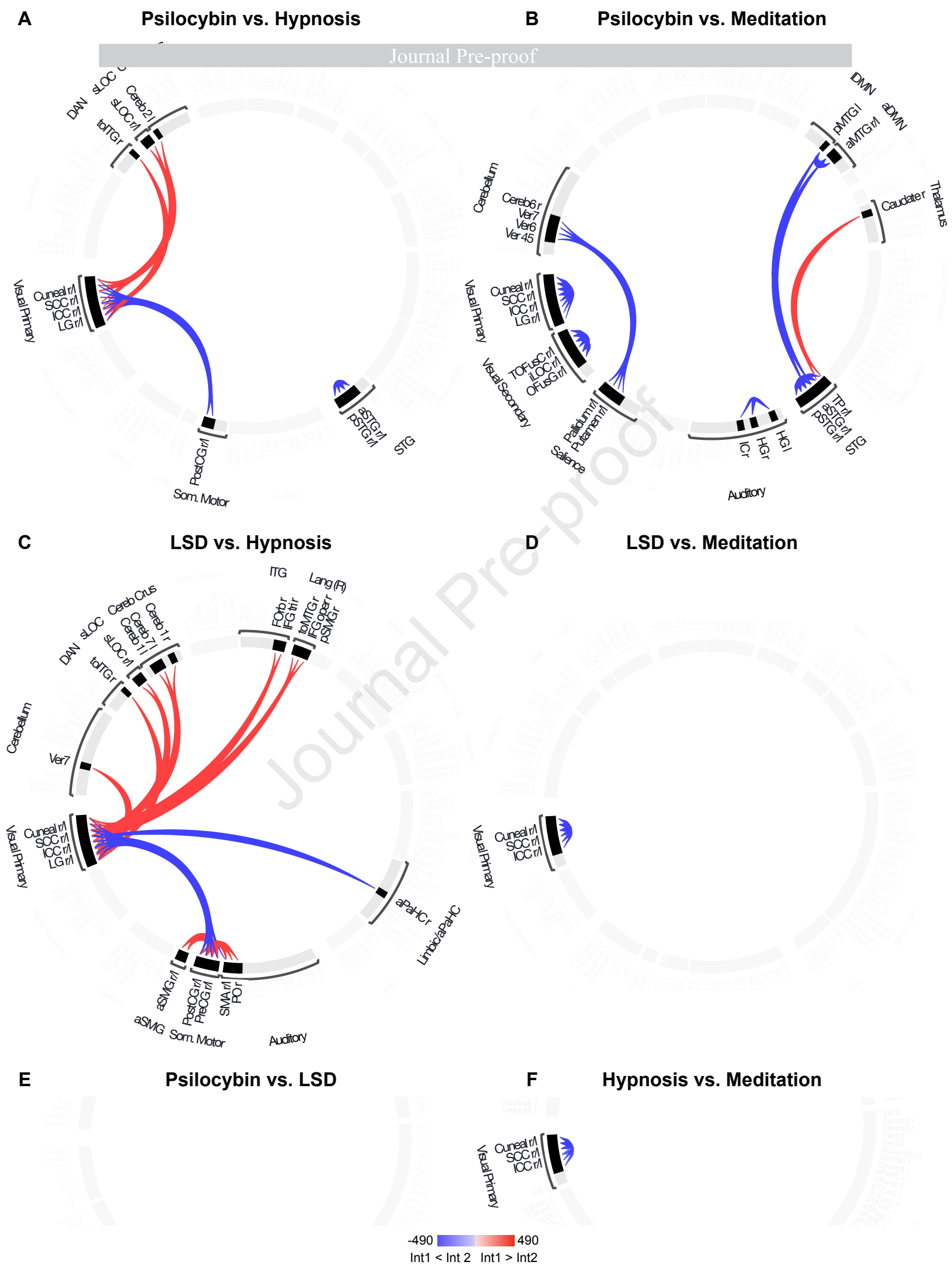


Figure 1


A
ITG
Lang(R) FPN(R)
IDMN
aDMN
DAN
sLOC
CerebCrus
Cereb2 l
sLOC l
sLOC r
tolTG l
tolTG r
Cerebellum
Cereb8 r
Ver8
Cereb6 r
Ver7
Ver6
Ver45
Cuneal r
Cuneal l
SCC r
SCC l
ICC r
ICC l
LG r
LG l
Visual Primary
TOFusC r
TOFusC l
iLOC r
iLOC l
OFusG r
OFusG l
OP r
OP l
Visual Secondary
Pallidum r
Pallidum l
Putamen r
Putamen l
ACC r
FO r
Salience
PostCG r
PostCG l
PreCG r
PreCG l
Somatomotor
PP l
HG l
PT r
PT l
HG r
PP r
IC r
Auditory
STG
aITG l
aITG r
pITG r
FOrb r
IFG tri r
IFGoper r
PrCG r
SFG r
AG r
pMTG r
pSTG l
aSTG l
pMTG l
aMTG r
MedFC
Ph < N-Ph
Ph > N-Ph
TFCE Statistic, P-FWE Corrected


B
PREDICTED
Non-Pharma
Pharma
8
51
40
8
Pharma
Non-Pharma
TRUE


C
PREDICTED
Function Value
1.5
0
-1.5
Non-Pharma
Pharma
Psilocybin
LSD
Hypnosis
Meditation
SUBJECTS
Pharma:
Psilocybin
LSD
Non-Pharma:
Hypnosis
Meditation



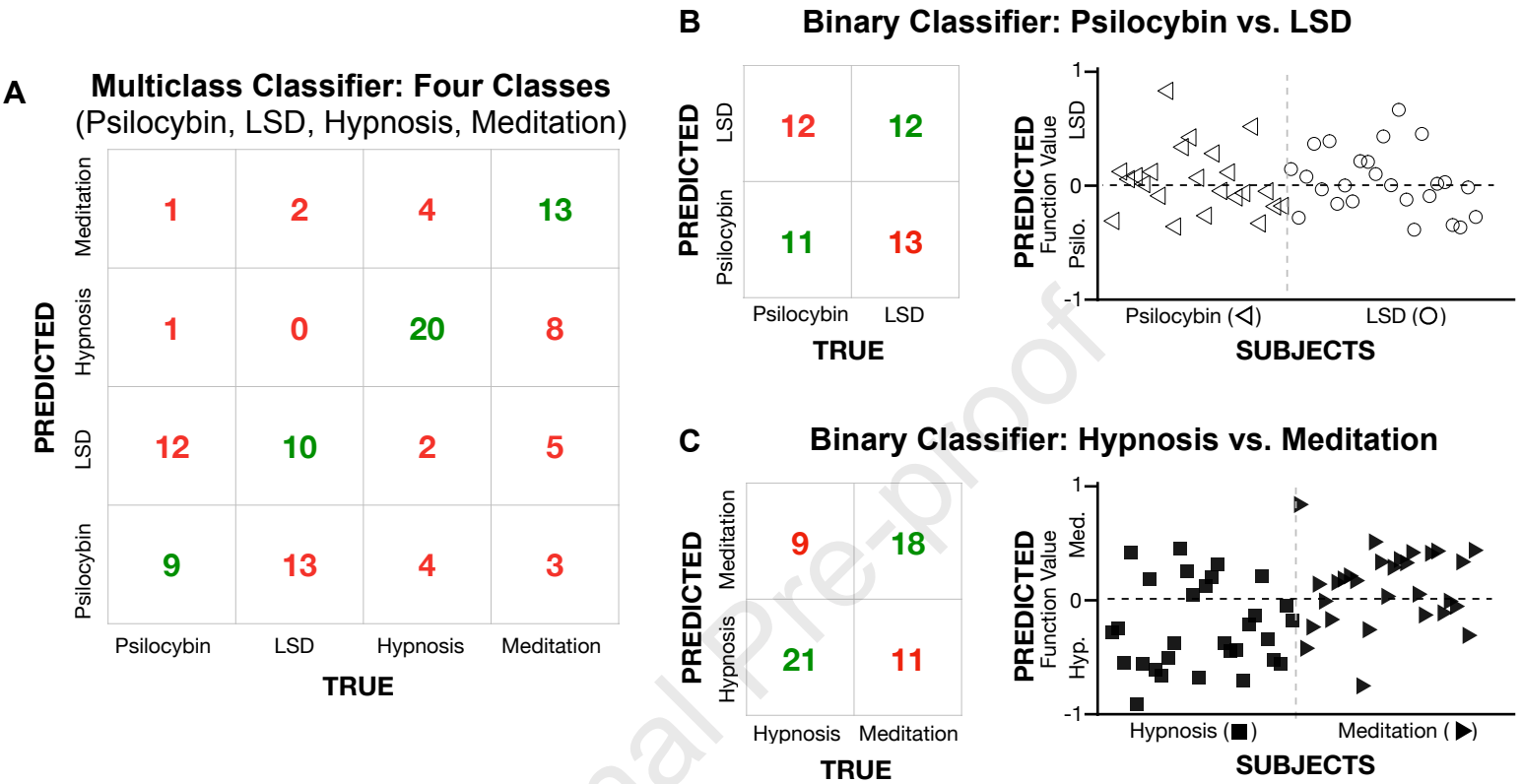


Figure 4

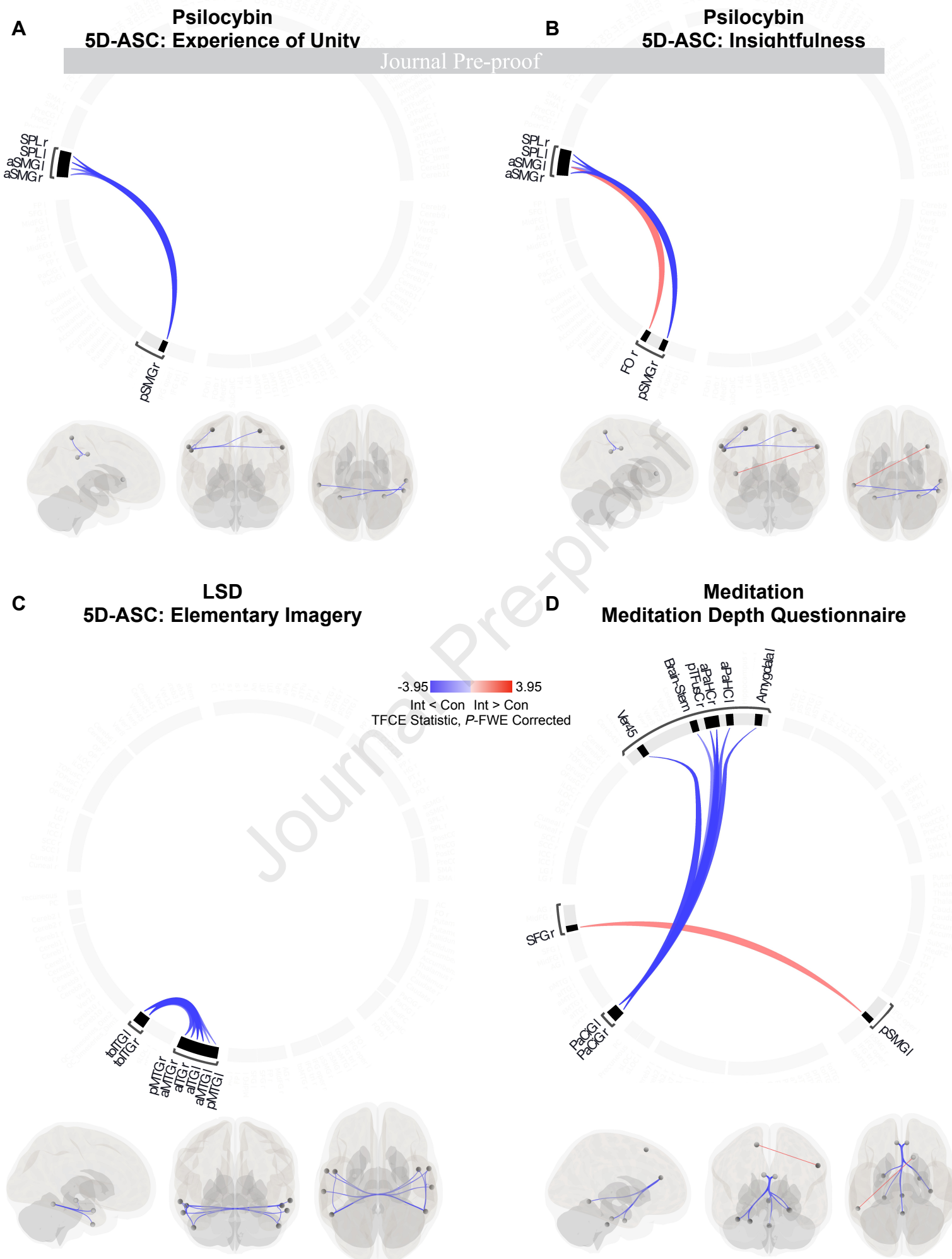


Figure 5