Appendix 1 to Fukuda Y, Katthagen T, Deserno L, et al. Reduced parieto-frontal effective connectivity during working memory in people with high delusional ideation *J Psychiatry Neurosci* 2019.

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Supplement

Reduced prefrontal-parietal effective connectivity during working memory in individuals with high delusional ideation

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Supplemental Information

The supplement contains the following analyses: additional information on the working memory task, behavioural and FMRI data analyses and dynamic causal modeling (model spaces), tables of BMA parameters, correlational analysis between DCM parameters and PDI scores, and the results of Baysian Model Selection (BMS) for all 16 models within each family.

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S1 Working memory task

The numeric working memory task was similar to (6, 37) and consisted of two conditions: "2-back" (WM condition) and "0-back" (control condition) which alternated in blocks. One block consisted of 22 numbers with 3 targets. In total, 6 "2-back" and 6 "0-back" conditions alternated separated by rest periods within the experiment with a total duration of 10 min. In the (1) "2-back condition" participants were instructed to press a button whenever they saw a number that was identical to the number they saw two numbers before (working memory condition). (2) In the "0-back" condition participants were told to press the button whenever they saw the number zero (control condition).

S2 Behavioural analysis

To analyze behavioral performance the sensitivity index *d*' was calculated for the 2-back as well as for 0-back condition using the following equation from Wickens et al. (1):

$$d' = z(\text{ probability(hits)}) - z(\text{ probability(false alarms)})$$

For each subject, the percentage of correct hits (hits / all targets) and false alarms were transformed into *z*-scores using the inverse cumulative distribution function in Matlab (icdf). This computation allows a better distinction between signal and noise, thus providing a more sensitive measurement of the participant's performance. High level of accuracy in the current task is indicated by a high *d'*.

S3 FMRI data analysis

To correct for inter-scan movements the volumes were realigned to a mean image of the EPIs after the first realignment. Each individual's T1 weighted anatomical image was co-registered to the un-warped mean EPI image. All T1 weighted images were segmented and normalized using default tissue probability maps of grey matter images provided by the Montreal Neurological Institute (MNI). The normalization parameters were then applied to all EPIs, which were subsequently smoothed with a Gaussian kernel of 6 mm full-width at half maximum.

The two-level approach of the general linear model was applied for statistical analysis. On the first single-subject level, the 2-back and 0-back condition as well as the instruction cues were modelled and convolved with the canonical hemodynamic response function. Furthermore, the 6 movement (3 translational and 3 rotational) parameters, the first temporal derivative of the translational movement parameters and an additional regressor marking scans with 1 mm scan-to-scan movement were included as regressors of no interest in the design matrix. Serial correlations were removed using a first-order autoregressive model and a high-pass filter (128s) was applied to remove low-frequency noise.

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S4 Dynamic causal modeling

Time series extraction and model space Based on previous studies of WM processing the DLPFC and the parietal cortex were included as regions of interest in the model space. In addition, the primary visual cortex was included as the input region as experimental stimulation was visual, resulting in three bi-directionally connected regions yielding 6 intrinsic connections that could be modulated by the experimental stimuli. According to Deserno et al. (2), three families of models were defined according to the direction of the WM effect on the prefrontal-parietal connectivity: the unidirectional influence from the parietal cortex (PC) to DLPFC was defined as the forward model, from DLPFC to PC as the backward model, and the bidirectional influence between DLPFC and PC as the bidirectional model. In addition, the model space was extended to further models that considered potential unidirectional and bidirectional experimental effects on connections between the primary visual cortex, the DLPFC and the PC, respectively. Thus, for each family, 16 models were defined resulting in a total of 48 models for each hemisphere. Time series were extracted from each subject's individual peak voxel surrounded with 4mm spheres. Individual peak voxel were identified within the DLPFC and PC masks for the contrast 2-back > 0-back and within visual mask (derived from the WFUPick Atlas toolbox defined as BA 17) for a visual contrast using a 4mm sphere. The visual contrast compared all visual stimuli (2-back, 0-back and instruction cue) to baseline.

We assessed the evidence for the different models and estimated model parameters using a one-state, bilinear, deterministic DCM. We corrected for differences in slice time acquisition between the three areas during estimation of the DCMs as suggested by Kiebel et al. (3).

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Table S1: DCM parameters of the left hemisphere are reported for individuals with low and high delusional ideation. The standard deviations are reported in brackets. One-sample t-test was used to test for within-group effects and two-sample t-tests for group comparison. Significant effects are indicated by the asterisk (*).

	Individuals with low delusional ideation	Individuals with high delusional ideation	2 test for group comparison	
			t-value	*p*-value
Modulatory effects				
2b on VC → DLPFC	0.398 (1.065)	0.889 (1.854)*	-1.125	0.268
2b on VC → PC	1.095 (1.811)*	0.470 (1.743)	1.217	0.230
2b on PC → VC	0.085 (0.410)	0.075 (0.357)	0.091	0.928
2b on PC → DLPFC	0.989 (1.087)*	0.044 (1.208)	2.850	0.007*
2b on DLPFC → VC	-0.124 (0.349)*	0.201 (0.615)	-2.246	0.031*
2b on DLPFC → PC	0.415 (0.950)	0.249 (1.086)	0.567	0.574
Intrinsic effects				
VC → DLPFC	-0.096 (0.468)	-0.030 (0.545)	-0.448	0.656
VC → PC	0.370 (0.406)*	0.332 (0.405)*	0.324	0.747
PC → DLPFC	0.195 (0.315)*	0.309 (0.219)*	-1.452	0.154
PC → VC	-0.859 (0.088)*	-0.734 (0.399)*	-1.493	0.148
DLPFC → VC	0.188 (0.323)*	0.398 (0.254)*	-2.501	0.016*
DLPFC → PC	-0.055 (0.405)	-0.057 (0.439)	0.013	0.989

Table S2: Parametric correlation analysis between PDI scores and DCM parameters of the left hemisphere. Significant effects are reported at a threshold of $p < 0.05$ (*).

	r – value	***p* – value**
Modulatory effects		
2b on VC → DLPFC	0.130	0.378
2b on VC → PC	-0.248	0.089
2b on PC → VC	-0.037	0.801
2b on PC → DLPFC	-0.304	0.035*
2b on DLPFC → VC	0.213	0.147
2b on DLPFC → PC	-0.059	0.690
Intrinsic effects		
VC → DLPFC	0.073	0.624
VC → PC	-0.016	0.914
PC → DLPFC	0.169	0.251
PC → VC	0.184	0.210
DLPFC → VC	0.350	0.015*
DLPFC → PC	-0.119	0.422

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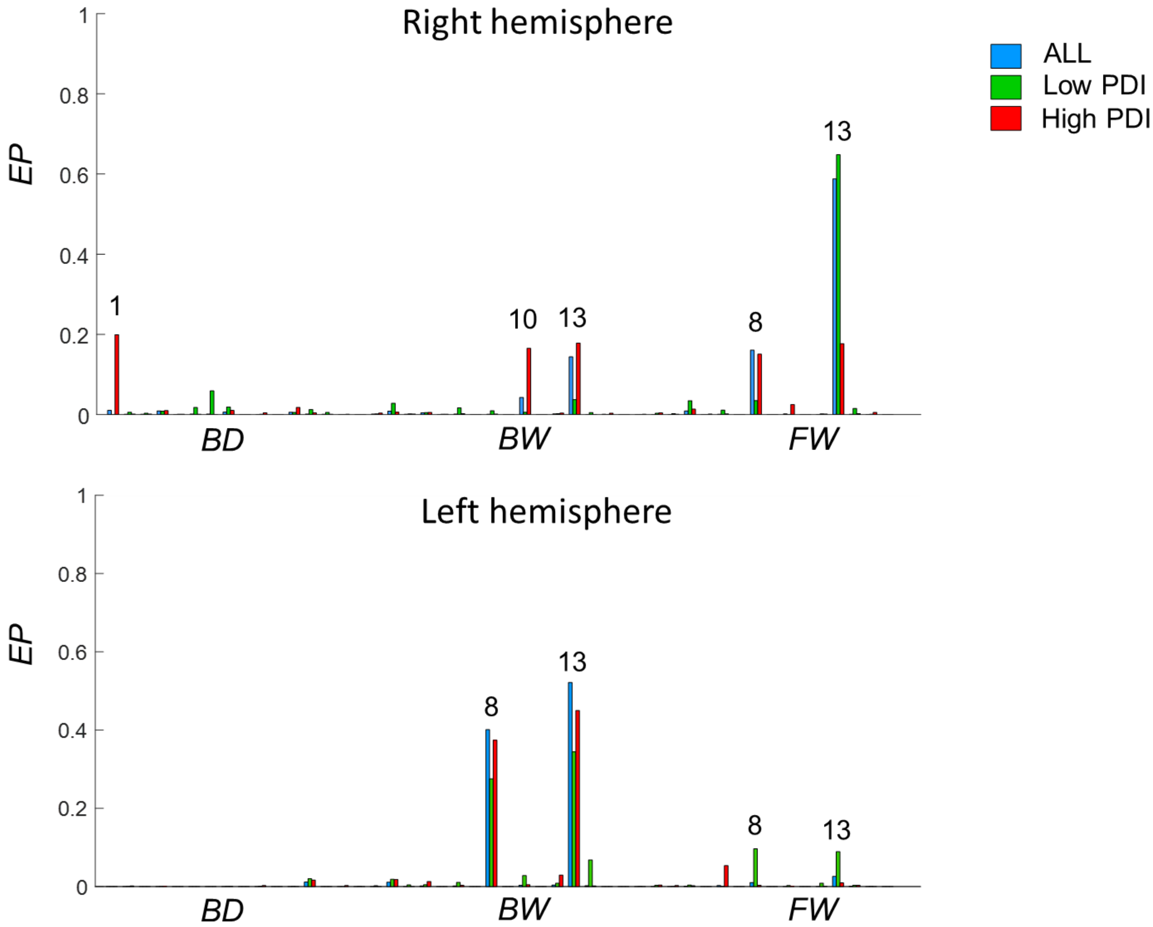

Figure S1: Model selection for all 16 models within each family for the left and right hemisphere, resulting in 48 models. For detailed description of all models including the number of each model please see **Figure 1** in the manuscript.

References:

1. Wickens TD (2002) Elementary signal detection theory (Oxoford UP, Oxford, New York)

2. Deserno L, Sterzer P, Wustenberg T, et al. Reduced prefrontal-parietal effective connectivity and working memory deficits in schizophrenia. J Neurosci. 2012;32(1):12-20.

3. Kiebel SJ, Kloppel S, Weiskopf N, et al. Dynamic causal modeling: a generative model of slice timing in fMRI. Neuroimage. 2007;34(4):1487-96.