Replication of a neuroimaging biomarker for striatal dysfunction in schizophrenia

Supplementary Information

Table S1. Sample characteristics

HCP psychosis dataset (n=152)			**ZHH treatment response cohort (n=97)**	
	Early phase psychosis	Healthy controls		First episode psychosis
N	n= 101	n= 51		n= 97
Female (n,%)	n=38, (37.62%)	n=19, (37.25%)	Female (n,%)	n=44, (45.36%)
Age (mean,sd)	22.49, (3.54)	24.83, (4.23)	Age (mean,sd)	24.3, (5.9)
White (n,%)	n=52, (51.49%)	n=37, (72.55%)	White (n,%)	n=32, (32.99%)

Table S2. Effect sizes of differences between patients and controls in FSA and intrinsic connectivity values of canonical networks

Connectivity measure	Phase encoding and GSR	Cohens d	lower bound 95%CI	upper bound 95%CI
FSA	AP GSR	0.88	0.53	1.23
FSA	AP No GSR	0.86	0.51	1.21
FSA	PA GSR	0.91	0.56	1.26
FSA	PA No GSR	0.80	0.45	1.15
Cognitive control network	AP GSR	0.01	-0.32	0.35
Cognitive control network	AP No GSR	0.24	-0.10	0.58
Cognitive control network	PA GSR	0.11	-0.22	0.45
Cognitive control network	PA No GSR	0.25	-0.09	0.58
Default mode network	AP GSR	-0.25	-0.59	0.09
Default mode network	AP No GSR	0.35	0.01	0.68
Default mode network	PA GSR	-0.19	-0.52	0.15
Default mode network	PA No GSR	0.10	-0.23	0.44
Dorsal attention network	AP GSR	-0.52	-0.86	-0.18
Dorsal attention network	AP No GSR	0.06	-0.28	0.39
Dorsal attention network	PA GSR	-0.48	-0.82	-0.14
Dorsal attention network	PA No GSR	-0.01	-0.34	0.33
Salience network	AP GSR	-0.28	-0.62	0.06
Salience network	AP No GSR	-0.05	-0.39	0.29
Salience network	PA GSR	-0.11	-0.45	0.23
Salience network	PA No GSR	0.25	-0.09	0.59
Somatosensory network	AP GSR	0.03	-0.31	0.37
Somatosensory network	AP No GSR	0.28	-0.06	0.62
Somatosensory network	PA GSR	0.16	-0.18	0.49
Somatosensory network	PA No GSR	0.41	0.07	0.75
Visual network	AP GSR	0.03	-0.31	0.36

Visual network	AP No GSR	0.18	-0.16	0.52
Visual network	PA GSR	0.12	-0.22	0.45
Visual network	PA No GSR	0.22	-0.11	0.56

Table S3. Effect of potential confounders on FSA (p Values)

Measure	p Value Age	p Value Sex	p Value Race	p Value mean FD	p Value Age*Group	p Value Sex*Group	p Value Race*Group	p Value mean FD*Group	p Value PANSS Total (SZ only)	p Value CPZ eq (SZ only)	p Value PANSS Negative (SZ only)
FSA PA GSR	0.72	0.69	0.07	0.88	0.13	0.49	0.23	0.26	0.17	0.29	0.42
FSA PA No GSR	0.44	0.09	0.01	0.49	0.18	0.83	0.13	0.44	0.12	0.09	0.20
FSA AP GSR	0.97	0.86	0.74	0.72	0.66	0.25	0.50	0.90	0.30	0.11	0.04*
FSA AP No GSR	0.64	0.73	0.85	0.19	0.44	0.40	0.81	0.35	0.30	0.22	0.05

*no longer significant after multiple comparisons correction. CPZ eq: Chlorpromazine equivalents. FD: Framework Displacement. SZ: Schizophrenia

Table S4. Predictive performance of the FSA discriminating individuals with psychosis from healthy controls

Entire cohort						
FSA measure	Sensitivity	Specificity	Optimal discrimination cutoff	AUC	Lower bound 95%CI	Upper bound 95%CI
FSA AP GSR	0.76	0.66	-1.04	0.74	0.65	0.81
FSA AP No GSR	0.65	0.75	-0.45	0.73	0.64	0.81
FSA PA GSR	0.82	0.65	-1.06	0.75	0.67	0.83
FSA PA No GSR	0.78	0.65	-0.73	0.75	0.66	0.83
Non-affective psychosis as cases only						
FSA measure	Sensitivity	Specificity	Optimal discrimination cutoff	AUC	Lower bound 95%CI	Upper bound 95%CI
FSA AP GSR	0.76	0.73	-1.04	0.76	0.68	0.85
FSA AP No GSR	0.65	0.77	-0.45	0.74	0.65	0.82
FSA PA GSR	0.82	0.73	-1.06	0.80	0.72	0.88
FSA PA No GSR	0.80	0.72	-0.74	0.78	0.69	0.86
Affective psychosis as cases only						
FSA measure	Sensitivity	Specificity	Optimal discrimination cutoff	AUC	Lower bound 95%CI	Upper bound 95%CI
FSA AP GSR	0.86	0.39	-1.37	0.65	0.52	0.78
FSA AP No GSR	0.43	0.96	-0.08	0.70	0.57	0.82

FSA PA GSR	0.82	0.39	-1.06	0.59	0.45	0.73
FSA PA No GSR	0.55	0.70	-0.52	0.63	0.49	0.76

Table S5. Predictive performance of the FSA discriminating in individuals with psychosis between response and non-response to a prospective trial of antipsychotic drugs

Entire cohort						
FSA measure	Sensitivity	Specificity	Optimal discrimination cutoff	AUC	Lower bound 95%CI	Upper bound 95%CI
FSA AP GSR	0.72	0.41	-1.47	0.49	0.34	0.66
FSA AP No GSR	0.72	0.35	-0.98	0.52	0.36	0.68
FSA PA GSR	0.35	0.88	-0.54	0.56	0.40	0.71
FSA PA No GSR	0.35	0.88	-0.02	0.53	0.38	0.69
Non-affective psychosis only						
FSA measure	Sensitivity	Specificity	Optimal discrimination cutoff	AUC	Lower bound 95%CI	Upper bound 95%CI
FSA AP GSR	0.67	0.50	-1.47	0.52	0.34	0.70
FSA AP No GSR	0.42	0.71	-0.64	0.50	0.32	0.67
FSA PA GSR	0.31	0.93	-0.54	0.56	0.39	0.71
FSA PA No GSR	0.31	0.93	-0.02	0.48	0.33	0.64

Figure S1. Receiver operating characteristic curves for prediction of treatment response by FSA score at baseline

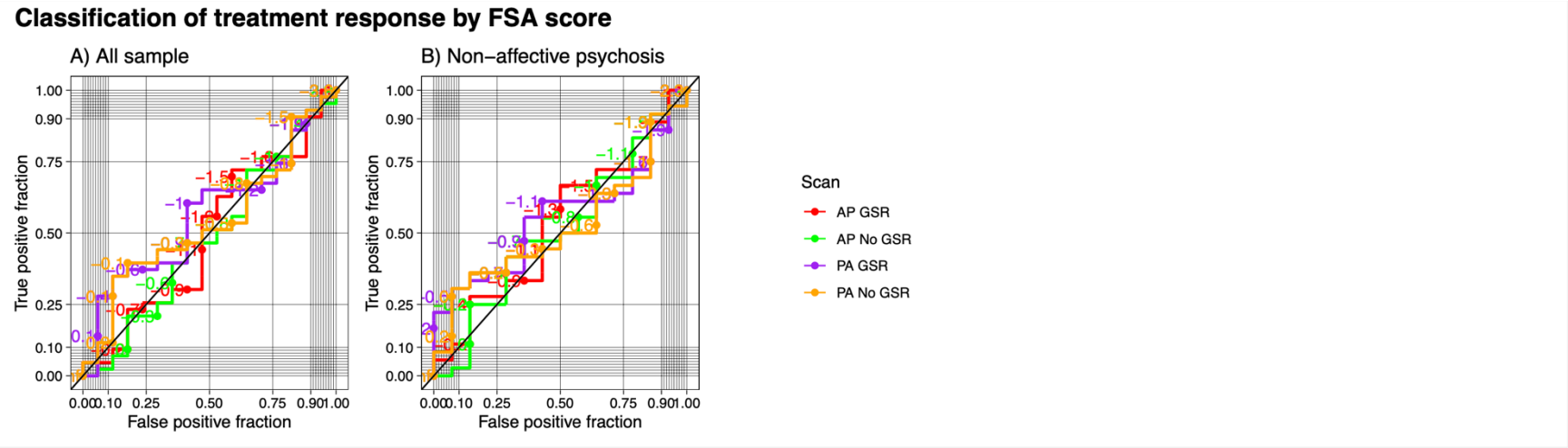

Table S6. Intraclass correlation coefficients of test-restest reliability of FSA and network intrinsic connectivity

Biomarker	**GSR_phase**	**Participant type**	**ICC**	**lower bound 95%CI**	**upper bound 95%CI**
FSA	AP GSR	Entire sample	0.42	0.28	0.55
FSA	AP GSR	Control	0.24	-0.04	0.48
FSA	AP GSR	Patient	0.42	0.24	0.57
FSA	AP NoGSR	Entire sample	0.48	0.35	0.60
FSA	AP NoGSR	Control	0.46	0.21	0.65
FSA	AP NoGSR	Patient	0.41	0.23	0.56
FSA	PA GSR	Entire sample	0.28	0.13	0.42
FSA	PA GSR	Control	0.20	-0.08	0.45
FSA	PA GSR	Patient	0.20	0.01	0.38
FSA	PA NoGSR	Entire sample	0.22	0.06	0.37
FSA	PA NoGSR	Control	0.28	0.00	0.51
FSA	PA NoGSR	Patient	0.10	-0.10	0.29
Cognitive control network	AP GSR	Entire sample	0.50	0.37	0.61
Cognitive control network	AP GSR	Control	0.47	0.23	0.66
Cognitive control network	AP GSR	Patient	0.53	0.37	0.65
Cognitive control network	AP NoGSR	Entire sample	0.37	0.22	0.50
Cognitive control network	AP NoGSR	Control	0.34	0.07	0.56
Cognitive control network	AP NoGSR	Patient	0.39	0.21	0.54
Cognitive control network	PA GSR	Entire sample	0.35	0.21	0.48
Cognitive control network	PA GSR	Control	0.25	-0.03	0.49
Cognitive control network	PA GSR	Patient	0.40	0.22	0.55
Cognitive control network	PA NoGSR	Entire sample	0.30	0.15	0.44
Cognitive control network	PA NoGSR	Control	0.23	-0.05	0.47

Cognitive control network	PA NoGSR	Patient	0.35	0.16	0.51
Default mode network	AP GSR	Entire sample	0.34	0.19	0.47
Default mode network	AP GSR	Control	0.36	0.09	0.57
Default mode network	AP GSR	Patient	0.32	0.14	0.49
Default mode network	AP NoGSR	Entire sample	0.25	0.10	0.40
Default mode network	AP NoGSR	Control	0.14	-0.13	0.40
Default mode network	AP NoGSR	Patient	0.30	0.11	0.46
Default mode network	PA GSR	Entire sample	0.35	0.20	0.48
Default mode network	PA GSR	Control	0.11	-0.17	0.37
Default mode network	PA GSR	Patient	0.45	0.28	0.59
Default mode network	PA NoGSR	Entire sample	0.27	0.11	0.41
Default mode network	PA NoGSR	Control	0.13	-0.15	0.39
Default mode network	PA NoGSR	Patient	0.32	0.13	0.48
Dorsal attention network	AP GSR	Entire sample	0.46	0.33	0.58
Dorsal attention network	AP GSR	Control	0.35	0.08	0.57
Dorsal attention network	AP GSR	Patient	0.48	0.31	0.61
Dorsal attention network	AP NoGSR	Entire sample	0.30	0.15	0.44
Dorsal attention network	AP NoGSR	Control	0.26	-0.01	0.50
Dorsal attention network	AP NoGSR	Patient	0.33	0.15	0.50
Dorsal attention network	PA GSR	Entire sample	0.39	0.25	0.52
Dorsal attention network	PA GSR	Control	0.23	-0.05	0.47
Dorsal attention network	PA GSR	Patient	0.44	0.26	0.58
Dorsal attention network	PA NoGSR	Entire sample	0.26	0.11	0.41
Dorsal attention network	PA NoGSR	Control	0.23	-0.05	0.47
Dorsal attention network	PA NoGSR	Patient	0.29	0.10	0.46
Salience network	AP GSR	Entire sample	0.34	0.20	0.48
Salience network	AP GSR	Control	0.26	-0.02	0.50
Salience network	AP GSR	Patient	0.38	0.20	0.54

Salience network	AP NoGSR	Entire sample	0.29	0.14	0.43
Salience network	AP NoGSR	Control	0.29	0.02	0.52
Salience network	AP NoGSR	Patient	0.29	0.11	0.46
Salience network	PA GSR	Entire sample	0.30	0.15	0.44
Salience network	PA GSR	Control	0.40	0.14	0.61
Salience network	PA GSR	Patient	0.27	0.08	0.44
Salience network	PA NoGSR	Entire sample	0.07	-0.09	0.22
Salience network	PA NoGSR	Control	0.00	-0.27	0.27
Salience network	PA NoGSR	Patient	0.10	-0.10	0.29
Somatosensory network	AP GSR	Entire sample	0.18	0.02	0.33
Somatosensory network	AP GSR	Control	0.20	-0.08	0.45
Somatosensory network	AP GSR	Patient	0.18	-0.02	0.36
Somatosensory network	AP NoGSR	Entire sample	0.35	0.21	0.49
Somatosensory network	AP NoGSR	Control	0.16	-0.12	0.42
Somatosensory network	AP NoGSR	Patient	0.48	0.32	0.62
Somatosensory network	PA GSR	Entire sample	0.26	0.11	0.41
Somatosensory network	PA GSR	Control	0.15	-0.13	0.41
Somatosensory network	PA GSR	Patient	0.33	0.14	0.49
Somatosensory network	PA NoGSR	Entire sample	0.26	0.10	0.40
Somatosensory network	PA NoGSR	Control	0.17	-0.10	0.43
Somatosensory network	PA NoGSR	Patient	0.29	0.10	0.46
Visual network	AP GSR	Entire sample	0.25	0.10	0.40
Visual network	AP GSR	Control	0.20	-0.08	0.45
Visual network	AP GSR	Patient	0.28	0.09	0.45
Visual network	AP NoGSR	Entire sample	0.22	0.06	0.36
Visual network	AP NoGSR	Control	0.25	-0.03	0.49
Visual network	AP NoGSR	Patient	0.22	0.02	0.40
Visual network	PA GSR	Entire sample	0.33	0.18	0.46

Visual network	PA GSR	Control	0.25	-0.02	0.49
Visual network	PA GSR	Patient	0.38	0.20	0.53
Visual network	PA NoGSR	Entire sample	0.27	0.12	0.41
Visual network	PA NoGSR	Control	0.31	0.04	0.54
Visual network	PA NoGSR	Patient	0.26	0.07	0.43

Table S7. Intraclass correlation coefficients of phase encoding direction reliability (i.e., AP vs PA) of FSA and network intrinsic connectivity

Biomarker	**Participant type**	**ICC**	**lower bound 95%CI**	**upper bound 95%CI**
FSA	Entire sample	0.51	0.42	0.59
FSA	Patient	0.54	0.43	0.63
FSA	Control	0.23	0.04	0.40
Cognitive control network	Entire sample	0.83	0.79	0.86
Cognitive control network	Patient	0.84	0.80	0.88
Cognitive control network	Control	0.81	0.73	0.86
Default mode network	Entire sample	0.76	0.71	0.80
Default mode network	Patient	0.75	0.68	0.80
Default mode network	Control	0.79	0.70	0.85
Dorsal attention network	Entire sample	0.86	0.82	0.88
Dorsal attention network	Patient	0.85	0.81	0.89
Dorsal attention network	Control	0.86	0.80	0.91
Salience network	Entire sample	0.76	0.71	0.80
Salience network	Patient	0.73	0.66	0.79
Salience network	Control	0.82	0.75	0.88
Somatosensory network	Entire sample	0.75	0.70	0.80
Somatosensory network	Patient	0.75	0.68	0.80
Somatosensory network	Control	0.76	0.66	0.83
Visual network	Entire sample	0.80	0.76	0.84
Visual network	Patient	0.83	0.78	0.87
Visual network	Control	0.76	0.66	0.83