Appendix 1 to Williams LM, Whitford TJ, Gordon E, et al. Neural synchrony in patients with a first episode of schizophrenia: tracking relations with grey matter and symptom profile. *J Psychiatry Neurosci* 2009;34:21–9.

Supplementary methods

Study population

Of the 35 patients recruited into the study, 25 completed Gamma synchrony testing at first contact and follow-up, and 23 completed magnetic resonance imaging (MRI) at both sessions. The reasons for noncompletion of testing are summarized below in Table S1:

Table S1: Summary of subjects who did not complete Gamma synchrony or MRI testing sessions, and resulting final numbers in first-episode schizophrenia group

	No. of participants completing Gamma synchrony at first contact and follow-up			
No. recruited	Noncompletion (no.)	Reason for noncompletion (no.)		Final no. of complete datasets
35	Gamma (10)	"No-show" for follow-up testing, despite repeated rescheduling	(3)	25 with Gamma
		Unable to contact for follow-up testing	(2)	
		Could not complete testing	(3)	
		Artifact in data prevented its inclusion	(2)	
	MRI (12)	"No-show" for follow-up testing, despite repeated rescheduling	(3)	23 with MRI
		Unable to contact for follow-up testing	(2)	
		Could not complete follow-up testing	(3)	
		Movement artifact in data prevented its inclusion	(2)	

MRI = magnetic resonance imaging.

Of the 25 complete Gamma synchrony datasets and 23 complete MRI datasets, a total of 13 had complete datasets for both Gamma synchrony and MRI measures.

Methodologic issues in Gamma synchrony

Previous studies have investigated whether Gamma synchrony might reflect contributions from electromyography and volume conduction. Investigations of button press results have revealed negligible contamination of electroencephalography above 30 Hz.[1] Volume conduction has been found to fall off sharply at distances beyond 2 cm, which are particularly relevant to the long-range synchrony measured in our study.[2,3] Furthermore, interhemispheric synchrony has been found to disappear with corpus callosum transaction, indicating that it cannot be caused by volume conduction.[4,5] A detailed investigation of the oddball task used in our study has also indicated that muscle contamination and volume conduction are unlikely to contribute to Gamma synchrony within the 37.15–41.06 Hz frequency bin.[6] The distribution of Gamma synchrony has been found to differ from that of Gamma power over cortical regions, in contrast to the volume conduction model, which posits that a single deep generating source would result in a similar topography such that regions of high activity produce high synchrony.

Definition of MRI-search regions of interest

We parcellated grey matter images for both baseline and follow-up testing sessions into regions of interest (ROIs) in Talairach space, using the automatic anatomical labelling masks.[7] These ROIs have been established previously[8] and correspond to those for Gamma frontal, temporal, parietal and occipital cortices in both the left and right hemispheres. We defined the frontal cortical regions (left and right) in the axial plane as all cerebrum anterior to the central sulcus and superior to the sylvian fissure (and excluded the corpus callosum and insula). We defined the parietal cortical regions (left and right) in the sagittal plane as all cerebrum superior and anterior to the parieto-occipital sulcus, posterior to the central sulcus and superior to the corpus callosum. We defined the occipital cortical regions (left and right) as posterior to the following boundaries: the anterosuperior border (parieto-occipital and temporo-occiptal sulci), lateral to the midline (from where the parieto-occipital sulcus and horizontal ramus of the superior temporal sulcus) and posteroinferior border (anterior calcarine sulcus, collateral sulcus and posterior transverse collateral sulcus). The temporal cortical regions included the superior, middle and inferior gyri, with borders determined by

the sylvian fissure, occipito-temporal sulcus, superior temporal sulcus and the lateral border of the parahippocampal gyrus.[8] We quantified volumes for these grey matter search regions in terms of the sum of the values of the constituent voxels.

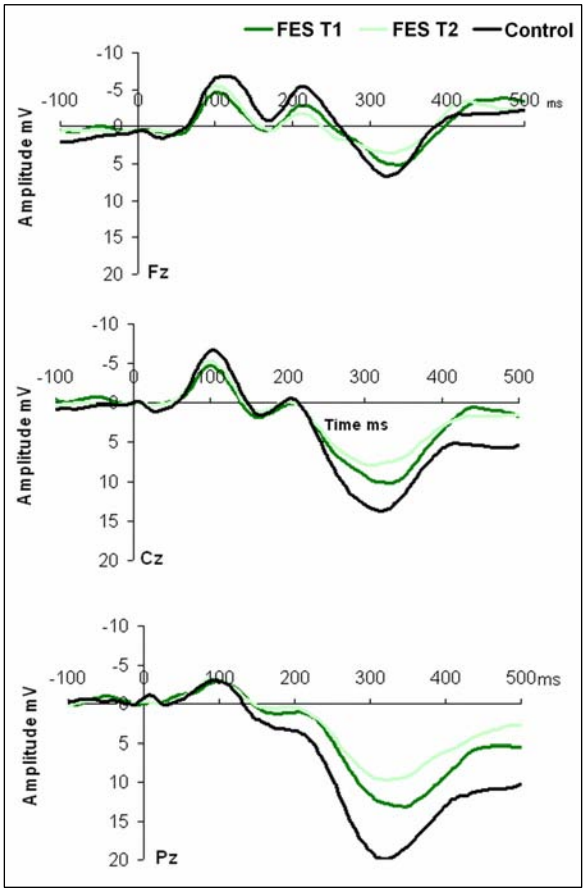

Fig. S1. Event-related potential for the midline frontal (Fz), central (Cz) and parietal (Pz) sites elicited over the 0 to 500 ms time course in which Gamma synchrony was also quantified. These event-related potentials show the expected reduction in the P300 potential peaking around 300 ms poststimulus in first contact schizophrenia patients relative to the healthy control subjects. This reduction persisted and was more pronounced at follow-up relative to both first contact and to healthy controls.

Supplementary Results

To provide a broader context for the interpretation of synchrony data, the corresponding event-related potentials across the time course of 0–500 ms were derived for patients with a first episode of schizophrenia at first contact relative to healthy controls (Fig. S1).

Confirming the consistency with previous research, first contact patients showed a marked reduction in the P300 potential peaking around 300 ms post-stimulus compared with controls, and this reduction persisted and was exacerbated at follow-up retesting (Fig. S1).

Gamma synchrony: time-frequency plots

To confirm the Gamma frequency bin of primary interest (namely the 37.15–41.06 Hz indicated in previous research[9]) we also undertook time-frequency plots across the range of the Gamma band: for frequency bins centred at 31.28 (29.33–33.24) Hz, 35.19 (33.24–37.15) Hz, 39.10 (37.15–41.06) Hz, 43.01 (41.06–44.97) Hz and 46.92 (44.97–48.88) Hz within the broad range of the Gamma band. These plots showed the changes in synchrony for each bin across the time course of 0–500 ms post-stimulus, at 50-ms intervals. Figure S2 (A–C) displays the plots for the right frontal, left temporal and left parieto-occipital regions, which showed significant effects in patients with schizophrenia at first contact versus controls in the focal analyses (see main text, Results). Phase is quantifed in these plots as the inverse of circular variance (or 1 minus circular variance) such that a value of 1 represented maximum synchrony.

These plots confirmed that group differences (patients with schizophrenia at first contact versus controls) in synchrony were particularly apparent for the 37.15–48.88 Hz frequency bin within the Gamma band (Fig. S2), which is consistent with previous evidence that the oddball task elicits significant effects within this frequency bin.[9]

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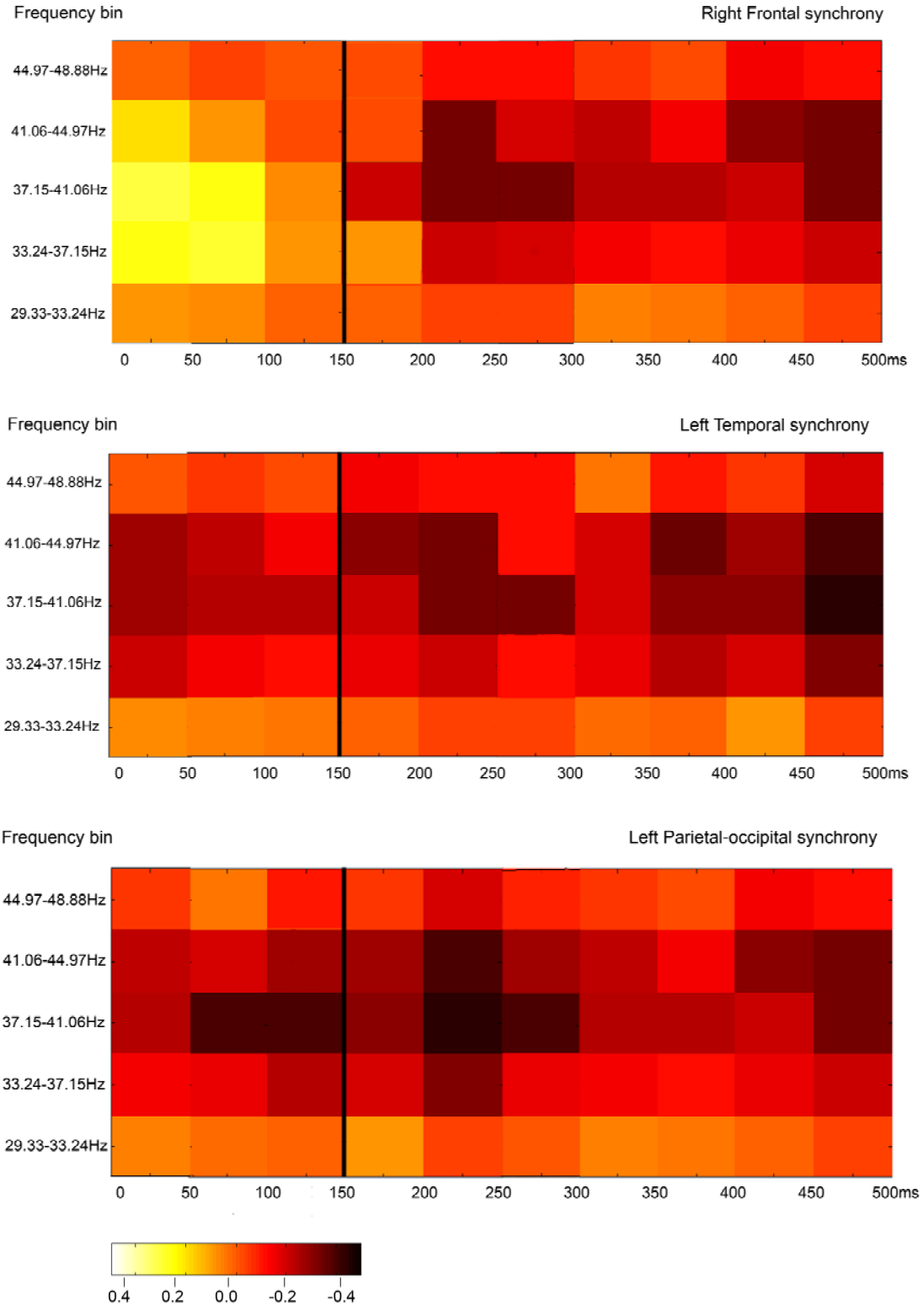

Fig. S2. Time-frequency plots for the magnitude of the difference in synchrony in first episode schizophrenia patients relative to healthy controls across frequency bins centred at 31.28 (29.33–33.24Hz), 35.19 (33.24–37.15Hz), 39.10 (37.15–41.06Hz), 43.01 (41.06–44.97Hz) and 46.92 (44.97–48.88Hz) within the range of the Gamma band. These plots are shown for the right frontal (A), left temporal (B) and left parietal-occipital (C) regions in which first episode schizophrenia patients had significant deficits in synchrony at first contact. Schizophrenia patients showed a reduction (indicated by darker shading) across the time course of 0–500ms in these regions; the black vertical line indicates the demarcation of "early" synchrony (0–150 ms) from "late" synchrony (200–500 ms). The threshold for a significant ($p < 0.05$) reduction in schizophrenia was a magnitude of –0.2; reductions of –0.4 or greater were significant at $p < 0.01$.

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References

1. Slobounov S, Rearick M, Chiang H. EEG correlates of finger movements as a function of range of motion and pre-loading conditions. *Clin Neurophysiol* 2000;111:1997-2007.
2. Rodriguez E, George N, Lachaux JP, et al. Perception's shadow: long-distance synchronization of human brain activity. *Nature* 1999;397:430-3.
3. Nunez PL, Srinivasan R, Westdorp AF, et al. EEG coherency. I: statistics, reference electrode, volume conduction, Laplacians, cortical imaging, and interpretation at multiple scales. *Electroencephalogr Clin Neurophysiol* 1997;103:499-515.
4. Kiper DC, Knyazeva MG, Tettoni L, et al. Visual stimulus-dependent changes in interhemispheric EEG coherence in ferrets. *J Neurophysiol* 1999;82:3082-94.
5. Munk MH, Nowak LG, Nelson JI, et al. Structural basis of cortical synchronization. II. Effects of cortical lesions. *J Neurophysiol* 1995;74:2401-14.
6. Haig AR. Missing links: the role of phase synchronous gamma oscillations in normal cognition and their dysfunction in schizophrenia [thesis]. Sydney (Australia): Department of Psychological Medicine, University of Sydney; 2001.
7. Tzourio-Mazoyer N, Landeau B, Papathanassiou D, et al. Automated anatomical labeling of activations in SPM using a macroscopic anatomical parcellation of the MNI MRI single-subject brain. *Neuroimage* 2002;15:273-89.
8. Whitford TJ, Rennie CJ, Grieve SM, et al. Brain maturation in adolescence: concurrent changes in neuroanatomy and neurophysiology. *Hum Brain Mapp* 2007;28:228-37.
9. Haig AR, Gordon E, Wright JJ, et al. Synchronous cortical gamma-band activity in task-relevant cognition. *Neuroreport* 2000;11:669-75.