Supplemental Figure 1

Axial and coronal T1-weighted anatomical MRI scans at the approximate level of maximum infarct volume (indicated by red region) for each patient. For two cases, images are flipped so that all lesions appear on the right side.
Supplemental Figure 2

Cortical stimulation site

(a) Example of the position of the fiducial markers attached to the MR-compatible TMS coil for one participant, with the centre of the coil indicated in blue. (b, c) Individual stimulation locations. Each white cross indicates the MNI coordinate of the derived stimulation site for a single patient, with a summary shown on a sagittal view of the mean structural image at right, and example coronal slices at left. The group mean stimulation point was (mean ± std) x = -29 ± 4, y = -9 ± 5, z = 65 ± 4. Coronal and sagittal sections of the mean T1-weighted structural scans (averaged across all patients) are shown. AH: affected hemisphere (shown on right in each coronal example); cs: central sulcus.
Supplemental Figure 3

Average grip peak-force, duration and onset time for each patient, shown separately for TMS$\text{low}$ (blue bars) or TMS$\text{high}$ (pink bars) trials, with adjacent bars for each patient. Data are presented as means ± SD. For peak force, the dotted line indicates the required force level. For grip onset, the dotted line represents the period of TMS pulse application. Note that TMS did not significantly affect any of these grip parameters during scanning in any patient. MVC: maximum voluntary contraction.

Supplemental Figure 2
**Supplemental Discussion**

An alternative (though not necessarily incompatible) interpretation of the present findings might involve a change in the effective timing of cPMd-iM1 interhemispheric interplay after stroke. In this case, a fixed interval between the application of paired TMS pulses might in effect probe different phases of the interhemispheric influence for different patients: at different temporal latencies between paired TMS pulses, inhibition might then have been observed in the facilitatory cases of our patient group. But even if this were the case, the present results would still indicate that physiological changes in interhemispheric interactions have a systematic relationship to residual motor function (and also to the remote BOLD activity changes demonstrated in the fMRI experiment).

Local spread of the conditioning stimulus from cPMd to iM1 seems very unlikely to have occurred here as the stimulation intensity was determined in relation to motor thresholds within the contralesional hemisphere, which are not raised after unilateral subcortical stroke (Byrnes et al., 2001; Shimizu et al., 2002). Moreover, altered intracortical excitability has been reported in both the ipsilesional (Manganotti et al., 2008; Cicinelli et al., 2003) and contralesional (Butefisch et al., 2003; Swayne et al., 2008) hemispheres. Stimulation thresholds for activating the neuronal populations mediating the interhemispheric PMd-M1 influence could thus be altered in stroke patients. We adjusted the test stimulus intensity individually according to the amplitude of the unconditioned MEP, to circumvent the expected reduction of corticospinal excitability in the ipsilesional hemisphere.
Indeed, the paired-coil cPMD-iM1 TMS measure did not correlate with resting motor thresholds, and the correlation with combined clinical scores remained significant even when motor thresholds were taken into account. This suggests that the observed relationship reflects genuine change in the strength of the cPMD-iM1 influence rather than merely differences in the degree of corticospinal hypoexcitability. Moreover, the relationship between cPMD-iM1 changes and the combined clinical score remain significant even when accounting for rMTs and MEP size. Thus, systematic floor / ceiling effects of raised motor thresholds or reduced MEP amplitudes are unlikely to explain the observed relationship between greater motor impairment and a more facilitatory PMd-M1 interaction, which we interpret as reflecting abnormal effective connectivity in these pathways.

The relationship of the BOLD interaction (between task (grip or rest) and TMS intensity) to residual motor function and to the interhemispheric cPMD-iM1 influence measured with paired-coil TMS cannot be trivially explained by a systematic effect of high versus low intensity TMS on behavior during scanning, as no such influence was found. Comparison of the $TMS_{\text{high}}$ and $TMS_{\text{low}}$ conditions did not reveal any differential effect of TMS intensity on mean peak force, grip onset, or grip duration. We suggest that the relationships to TMS intensity in the fMRI data instead reflect genuine state-dependent influences of cPMD on ipsilesional posterior sensorimotor cortex during impaired hand movement in our more impaired patients, consistent with the involvement of these regions for hand grip and manual object manipulation in healthy subjects (Binkofski et al., 1999; Ehrsson et al., 2001; Jenmalm et al., 2006).
References:


