Brain network dynamics underlying visuospatial judgment: an fMRI connectivity study

ADDITIONAL ONLINE MATERIAL

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ADDITIONAL METHODS

Figure S1 provides an idea of slice coverage. For each individual participant the slices were oriented obliquely, so as to cover the entire brain, particularly the parietal and frontal cortices, leaving out only the temporal pole and parts of the cerebellum.

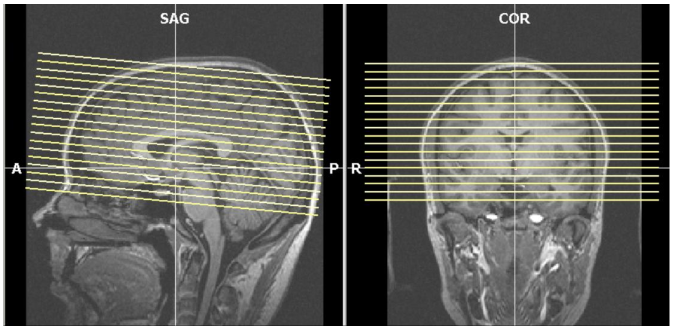


Figure S1: slice coverage
An illustration of the 18 slices positioned for the functional scan, overlaid with the anatomical scan, of one representative participant. Coverage was nearly whole-brain, cutting off only the tips of the temporal pole and the lower half of the cerebellum.

ADDITIONAL RESULTS AND DISCUSSION

POI-analysis of BOLD activation

In a post-hoc analysis, we performed additional POI-based RFX GLM contrast tests (ANGLE vs COLOR). The reasons for performing this analysis, over and above the whole-brain vertex-based analysis, were: first, because the t- and p-values in the POI-based contrasts between task give an indication of relative strengths of the contrasts and thus relative task-specificity (of clusters revealed and not revealed in the whole-brain GLM), second, because in our opinion it is potentially interesting to compare in more depth the results on visuospatial network regions yielded by GLM, versus the results yielded by GCM. POI-based GLM is more sensitive than whole-brain GLM, and indeed there were some indications that visuospatial-specific regions as identified by GCM also were more active during ANGLE than during COLOR, as shown by POI-based GLM. This convergence seems worth reporting in the interest of completeness.

POIs were defined on the cortex-based aligned group average brain, by decreasing the threshold of the whole-brain GLM below statistical significance ($P < 0.05$), to locate additional regions of interest. For each POI, the time courses of the vertices in the POI were averaged to create a POI time course. Since the POIs were thus defined and located, and without further correction for multiple comparisons, these results should be interpreted with caution.

A few additional regions showed ANGLE-specific responses and might therefore be considered part of the visuospatial network. Table 1 lists the relevant POIs with corresponding Talairach coordinates and t- and p-values. More active during the ANGLE condition, in addition to previously identified regions, were two occipital-temporal (OT) clusters, postcentral gyrus (PCG), and INS. These POIs correspond to regions also found in GCM analysis, discussed in the main text.

Table S1

Talairach coordinates of regions analyzed in ROI-based RFX GLM contrast A>C, N=10

	X	Y	Z	t-value	p-value
Occipital Cortex (OC)	29	73	21	4,08	0,003
Posterior Parietal Cortex (PPC)	20	-72	45	3,62	0,006
Middle Frontal Gyrus (MFG)	45	-3	32	3,77	0,004
Occipital-Temporal Cortex (OT)1	50	-48	-12	3,03	0,014
Occipital-Temporal Cortex (OT)2	44	-55	-10	3,07	0,013
Postcentral Gyrus (PCG)	55	-25	36	3,36	0,008
Superior Frontal Sulcus (SFS)	25	-5	53	1,66	>0,05
Insula (INS)	29	20	5	1,85	>0,05
Superior Frontal Gyrus (SFG)	25	42	28	-6,39	0,000
ant. Middle Frontal Gyrus (aMFG)	39	18	43	-6,92	0,000
Superior Marginal Gyrus (SMG)	53	-45	34	-5,18	0,001

Task modulation of effective connectivity to PPC

Figure 3 in the main text shows the task-specific effective connectivity maps to seed region PPC. The figure makes clear that several regions project to PPC during the ANGLE task, while none do so during the COLOR task to a statistically significant level. However, such differences are always relative, particularly in an experimental design as we adopted with frequent task switching and therefore probable task interference. To provide further information about the locations and extent of task-modulation of connectivity, we include supplementary figure S2.

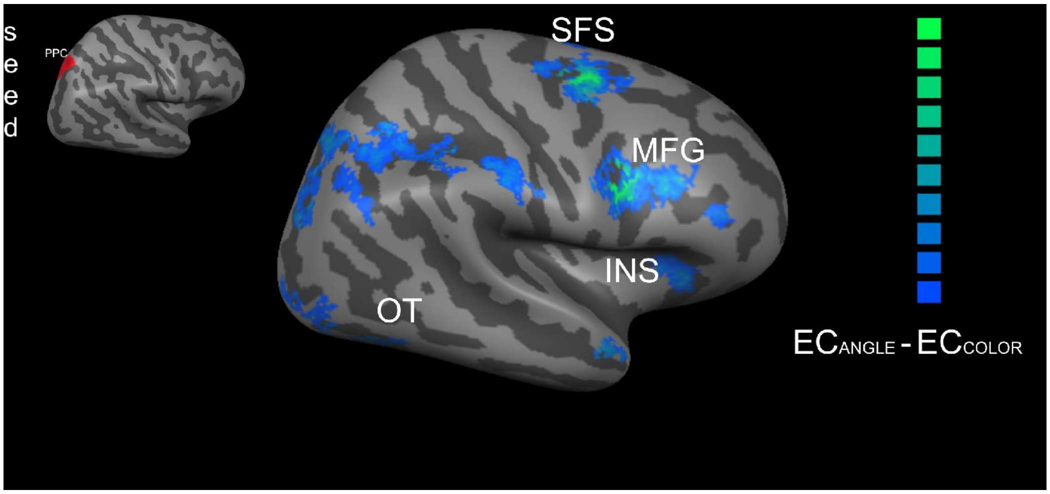


Figure S2: task-modulated difference map of effective connectivity to PPC
The red region on the upperleft inset signifies the seed region PPC. In blue-green are shown the vertices where task-modulation of effective connectivity was greatest. In other words, the blue-green regions showed stronger effective connectivity to PPC in the ANGLE task, than in the COLOR task.

Figure S2 illustrates a mean GCM difference map projected onto the cortex-based aligned group average brain. By subtracting the GCM values for each vertex for both conditions (ANGLE – COLOR, thus: ANGLE GCM value minus COLOR GCM value) a modulation index is obtained for each vertex. The map thus obtained is shown in Figure S2, where blue-green vertices project more strongly to PPC in ANGLE than in COLOR. Also shown is the PPC seed region (the same as in Figure 4 of the main text).

It becomes clear from the difference map that the strongest task modulation occurs in MFG and SFS. The strong modulation in SFS is interesting, because SFS projections to PPC were not found to be statistically significant for ANGLE, indicated by the absence of this region in Figure 4 of the main text, although a statistical tendency for effective connectivity to PPC was found (see main text). Apparently, SFS interactions with PPC were more important during the ANGLE task as compared to the COLOR task, processing aspects of the visual information or engaging in mental operations that were visuospatial in nature. We hypothesize this to be related to visuospatial working memory, as is supported by previous literature and discussed at length in the main text (see Discussion). Region OT shows less task-modulation of effective connectivity. Apparently this region in the network is involved in the processing of visual information or mental operations that are more common to the ANGLE and COLOR task. We hypothesize this to be related to the processing of object properties, as we explain in the main text.

Differential connectivity patterns for closely neighboring clusters in functional network nodes: recurrent processing

As presented in Figure 6A and discussed in the main text, closely neighboring clusters in functional regions including PPC, OT, and MFG, were differentially connected to PPC. As illustrated in Figure 6B, a post-hoc GCM analysis seeding these projecting (to PPC) and receiving (from PPC) clusters revealed opposite connectivity patterns: the projecting clusters sent influence not only to PPC, but to various other brain regions involved in visuospatial processing (see main text), while the receiving clusters received influence not only from PPC, but also from other brain regions involved in visuospatial processing (see main text). Moreover, several of the same regions that were influenced by a projecting cluster, subsequently projected back to that cluster's neighbor; the receiving cluster. This finding may support a form of recurrent processing in higher order cognitive processes, as we discuss in the main text (see Discussion).

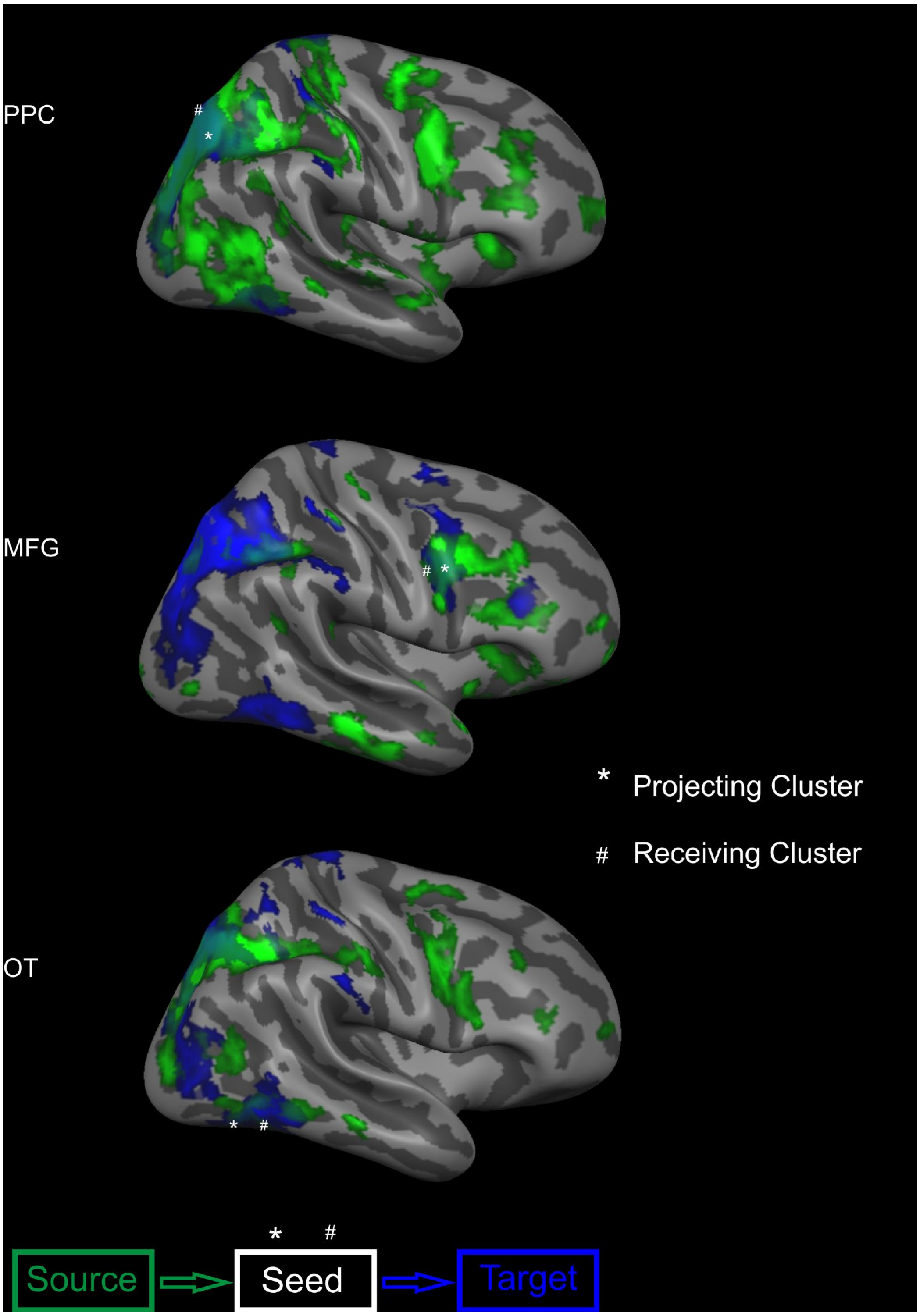
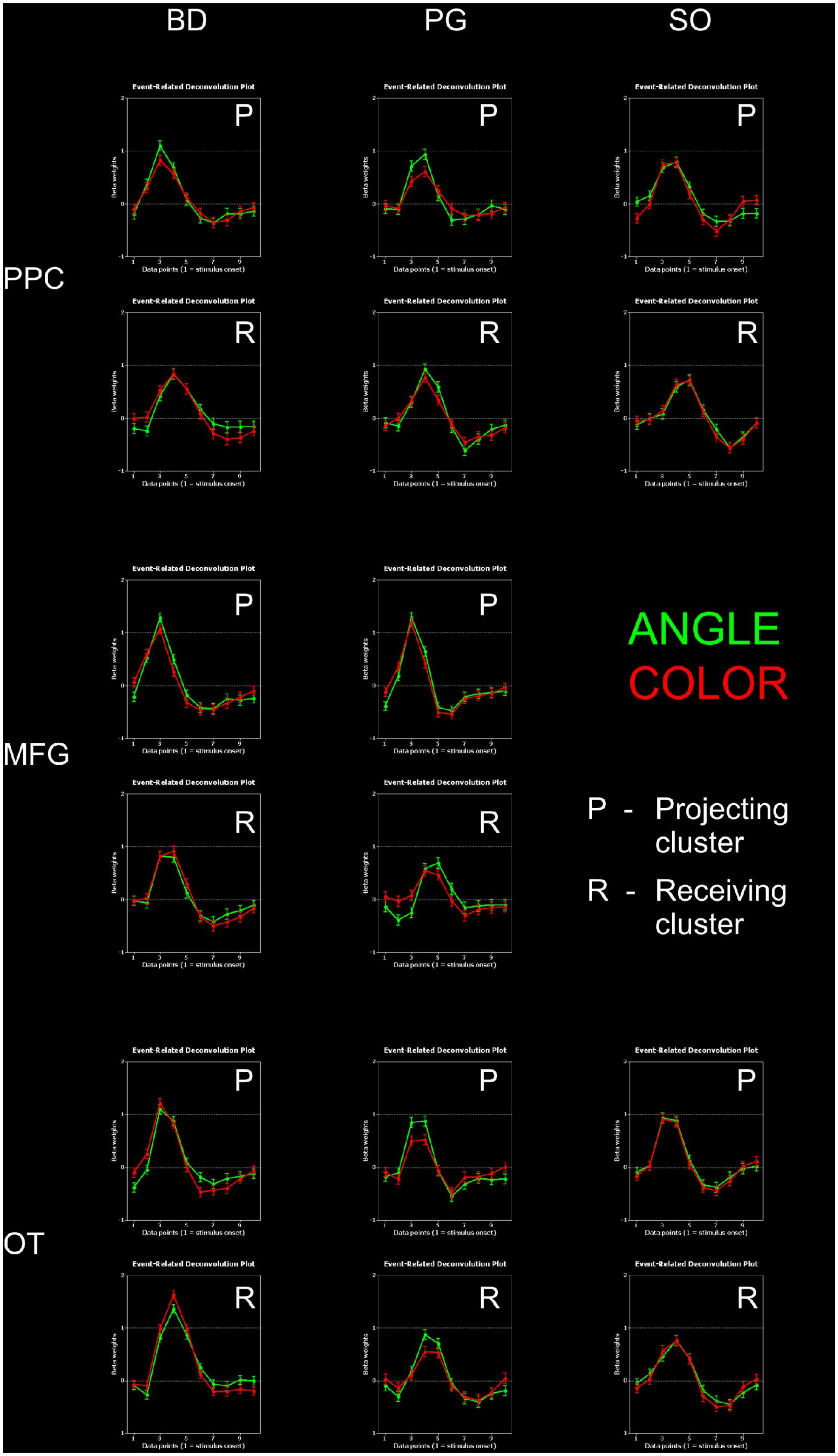

PPC
MFG
OT
* Projecting Cluster
# Receiving Cluster
Source
Seed
Target

Figure S3: Recurrent interactions in the visuospatial network
These maps are nothing more than overlays of the GCM results for the projecting clusters (left in Figure 6B) and the receiving clusters (right in Figure 6B). Green regions received information from the projecting cluster in the region (PPC for the uppermost rendered brain, MFG for the middle one, OT for the lowest one), blue regions sent information to the receiving cluster in the region. An overlap of green and blue signifies that the overlapping region first received information from one cluster, only to subsequently project back to the neighboring cluster, thereby engaging in a form of recurrent processing.

To visualize which regions may engage in such recurrent processing, Figure S3 has overlaid the maps shown on the left and on the right of Figure 6B. For regions PPC, MFG, OT, green regions on the map received influence from the projecting cluster therein (indicated by *), whereas blue regions on the map sent influence to the neighboring receiving cluster therein (indicated by #). For the PPC clusters, overlap in connectivity maps was found in surrounding PPC, occipital cortex, and OT. For the MFG clusters, only a rather small amount of overlap was found in PPC and a region above SMG. For the OT clusters, substantial overlap was found in PPC.

Figure S4 depicts the deconvolved BOLD time courses of three randomly selected participants for projecting and receiving neighboring clusters, showing that the projecting clusters were consistently involved earlier than the receiving clusters. Although no time course is shown here for the ‘intermediate’ region in the hypothesized recurrent loop (which is, however, shown in Figure 4 for PPC), this consistent pattern of earlier BOLD responses/peaks for projecting clusters, as compared to receiving clusters, may be perceived as support for, or at the very least as compatible with, a back-and-forth recurrent loop mechanism underlying visuospatial processing. It is because of these time courses that one may justifiably state that the projecting cluster was a relatively “early” cluster, whereas the receiving cluster was relatively “late”. This supports the notion of recurrent processing with a spatiotemporally defined order. See main text for further discussion.



BD
PG
SO
PPC
MFG
OT
Event-Related Deconvolution Plot
P
R
Beta weights
Data points (1 = stimulus onset)
ANGLE
COLOR
P - Projecting cluster
R - Receiving cluster

Figure S4: Time courses of neighboring receiving and projecting clusters
This matrix of event-related deconvolved BOLD time courses shows that, for each out of three randomly selected participants ("BD", "PG", "SO"; columns), and for each region (PPC, MFG, OT; rows), the BOLD response/peak was earlier for the projecting cluster (signified with a "P" within the graph) than for its neighboring receiving cluster ("R"). ANGLE task curves are shown in green, COLOR task curves are shown in red. This consistent pattern of earlier responses in projecting clusters supports the notion that these clusters were "early", and the receiving clusters "late", thereby supporting the proposed mechanism of recurrent (at least back-and-forth) processing.

Thalamic projections to PPC: BOLD time courses

Figure 4 in the main text shows the event-related deconvoluted time courses of the MFG and PPC clusters, revealing that MFG is involved earlier than PPC after stimulus onset. Figure S5 provides the same graphic depiction for the thalamic cluster in the right hemisphere, and PPC. Again, the thalamic cluster shows an earlier BOLD response/peak than the PPC cluster, in line with, though not required for or equivalent to, the GCM results obtained.

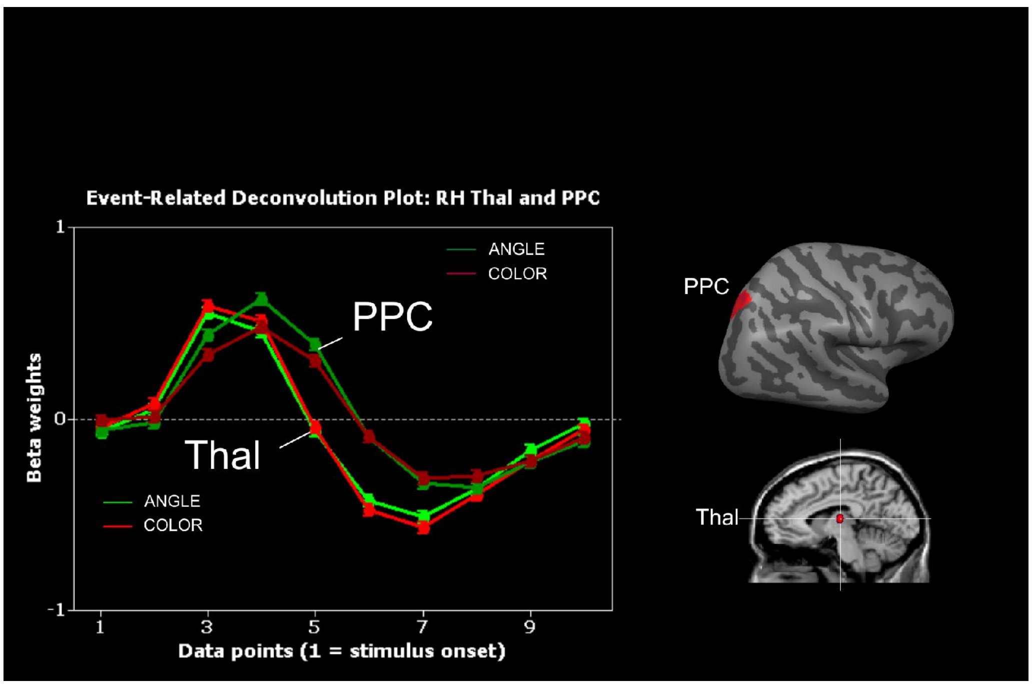


Figure S5: Time courses of thalamus and PPC
Analogous to Figure 4B in the main text, this figure displays the event-related deconvolved BOLD time courses for PPC and for the right hemispheric thalamic cluster, possibly the mediodorsal nucleus, both shown in red in the insets. The BOLD response/peak is evidently earlier in the thalamic cluster than in the PPC.