Supplementary Online Material

for

Translating working memory into action: Behavioural and neural evidence for using motor representations in encoding visuo-spatial sequences

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Supplementary Results

Effector-independent activity differences between encoding and recall

We contrasted activity during encoding and recall to delineate areas selectively associated with either sub-process. These comparisons were based only on trials with correct reproduction and were performed across both hands and both delays. Higher activity during encoding compared to recall was found bilaterally in a cluster extending from rostral dPMC (superior frontal junction, presumably corresponding to human FEF) over rostral vPMC to IFJ and (predominantly right) posterior dorsal area 44 (Fig. S1, red-coloured voxels; Table S1). This cluster substantially overlapped with the dPMC and vPMC clusters reported above as being significantly activated during both encoding and recall (cf. Fig. 3). Encoding-specific activity was also observed in a bilateral (though left-dominant) cluster extending from pre-SMA to anterodorsal MCC (caudal area 32') as well as in a bilateral cluster covering major parts of the occipital (visual) cortex, extending dorsally to IPS (area hIP3) and SPL (areas 7A, 7PC), mid-laterally to posterior STS, and ventrally to fusiform and posterior inferior temporal gyrus. Subcortically, we found stronger encoding-related activity in bilateral medial thalamus, ventral striatum (anterior putamen and nucleus accumbens), and a cluster extending from postero-inferior pulvinar to hippocampal subiculum (area SUB).

Contrasting recall against encoding (see Fig. S1, blue-coloured voxels; Table S1) revealed bilaterally increased activity in SI/SII (predominantly areas 2, 3b, OP1, OP4) as well as adjacent SPL (areas 5L, 7A, 7PC) and TPJ (areas PFt, PFop, PF). This contrast further yielded increased activity in bilateral caudal dPMC [area 6; located posteriorly to (1) the dPMC cluster commonly activated by encoding and recall (cf. Fig. 3) and (2) the rostral dPMC cluster observed in the reverse contrast (cf. above)], in a bilateral cluster covering parts of SMA and midcingulate cortex [ventral MCC (areas a24' and p24'), located posteriorly to the pre-SMA/MCC cluster observed in the reverse contrast (cf. above)], as well as in a cluster comprising large parts of the central insula, extending medially via the claustrum to the mid-putamen and laterally to the IFG pars opercularis (area 44). Further recall-specific activity was observed in the cerebellar vermis and cerebellar lobulus VI bilaterally as well as in bilateral posterolateral putamen.

Table S1

Differences in brain activity between encoding and recalling visuo-spatial sequences

Location	Histological Assignment	Local Maximum			*t*-value
Encoding vs. recall					
Left hemisphere					
Inferior occipital gyrus	hOC4v (V4)	-42	-80	-12	23.4
Inferior occipital gyrus	hOC3v (V3v)	-30	-93	-12	22.1
Superior parietal lobule	7PC	-27	-54	50	15.4
Inferior temporal gyrus	-	-47	-56	-15	14.4
Intraparietal sulcus	hIP3	-25	-57	49	14.4
Dorsal premotor cortex	area 6	-39	-6	47	12.5
Superior parietal lobule	7A	-26	-60	53	12.4
Pulvinar	-	-20	-29	0	9.0
Superior parietal lobule	7P	-18	-78	50	8.7
Ventral premotor cortex	-	-38	5	28	8.6
Posterior superior temporal sulcus	-	-54	-47	8	7.9
Hippocampus (Subiculum)	SUB	-18	-28	-8	7.6
Putamen	-	-20	16	-10	7.6
pre-SMA	area 6	-9	0	60	7.1
Inferior frontal gyrus	area 44	-45	6	30	6.7
Nucleus accumbens	-	-11	13	-14	5.9
Medial thalamus	-	-5	-5	0	5.0

Right hemisphere

Middle occipital gyrus	hOC3v (V3v)	32	-90	2	23.8
Inferior occipital gyrus	hOC4v (V4)	42	-78	-12	22.3
Inferior temporal gyrus	-	48	-71	-6	20.4
Intraparietal sulcus	hIP3	28	-57	45	13.6
Ventral premotor cortex	-	40	6	32	11.1
Posterior superior temporal sulcus	-	54	-44	10	11.0
Inferior frontal gyrus	area 44	43	8	27	9.3
Putamen	-	19	16	-10	9.1
Hippocampus (Subiculum)	SUB	20	-30	-5	8.4
Pulvinar	-	18	-29	1	8.1
Dorsal premotor cortex	area 6	37	-6	45	7.9
Superior parietal lobule	7A	28	-64	56	7.7
Medial thalamus	-	6	-8	-1	7.4
Superior parietal lobule	7PC	28	-54	53	6.7
Nucleus accumbens	-	12	9	-9	6.6
pre-SMA	area 6	8	8	51	6.1
Caudate	-	6	12	-9	5.5
Cerebellum	vermis	2	-53	-38	5.3

Recall vs. encoding

Left hemisphere

Central insula	-	-41	0	8	15.3
SMA	area 6	0	-12	51	11.2
Parietal operculum	OP1	-62	-20	20	10.6
Midcingulate cortex	areas a24', p24'	-3	-2	42	9.9
Postcentral sulcus	area 2	-53	-26	44	9.7
Temporo-parietal junction	PFop, PF, PFt	-59	-23	30	9.5
Cerebellum	lobule VI	-23	-60	-23	8.0
Superior parietal lobule	7A	-27	-50	69	7.9
Superior parietal lobule	5L	-25	-48	66	7.7
Dorsal premotor cortex	area 6	-24	-18	68	7.0
Putamen	-	-30	0	-2	6.8
Inferior frontal gyrus	area 44	-60	6	10	5.5
Cerebellum	lobule VIII	-20	-65	-47	5.1

Right hemisphere

Central insula	-	39	3	5	12.4
Cerebellum	vermis	2	-63	-17	10.1
Parietal operculum	OP1	62	-24	27	8.3
Midcingulate cortex	areas a24', p24'	6	-2	39	8.2
Temporo-parietal junction	PF, PFt, PFop,	61	-25	29	8.0
Cerebellum	lobule VI	24	-54	-26	7.9
Dorsal premotor cortex	area 6	33	-17	62	7.4
Inferior frontal gyrus	area 44	58	8	8	7.3
Putamen	-	27	-2	-2	7.0
Superior parietal lobule	7PC	29	-51	63	6.8
Superior parietal lobule	5L	22	-54	66	6.7
Pallidum	-	27	-5	-2	6.1
Postcentral sulcus	area 2	48	-32	50	5.9
Caudate	-	18	-2	17	5.3
SMA	area 6	8	-14	69	5.0

Note (Table S1). Peak coordinates refer to MNI space. SMA = supplementary motor area;
References to histological assignments: area 2: Grefkes et al. (2001); area 6: Geyer (2004); 7A, 7P, 7PC, 5L, hIP3: Scheperjans et al. (2008); areas a24', p24': Palomero-Gallagher et al. (2008); area 44: Amunts et al. (1999); hOC3(V3v), hOC4(V4v): Rottschy et al. (2007); OP1: Eickhoff et al. (2006); Pfop, PFt, PF, PGa: Caspers et al. (2006); SUB: Amunts et al. (2005); Cerebellum: Diedrichsen et al. (2009).

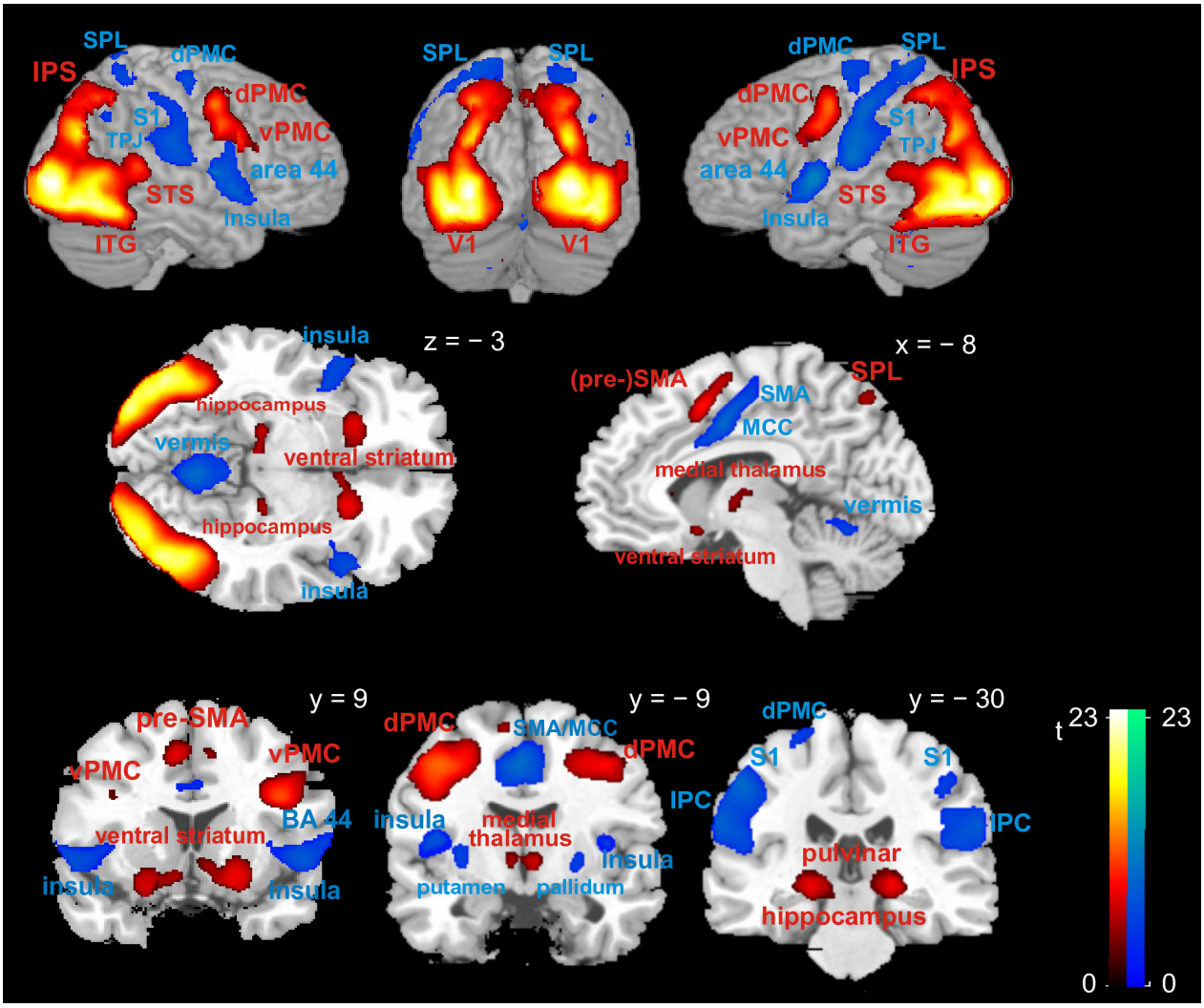

Figure S1. Differences in brain activity between encoding and correctly recalling visuo-spatial sequences, irrespective of delay length and effector side. Warm colours denote higher activity during encoding (vs. recalling) sequences; cool colours denote higher activity during recalling (vs. encoding) sequences. Section coordinates refer to MNI space.

Abbreviations: dPMC = dorsal premotor cortex; IPC = inferior parietal cortex; IPS = intraparietal sulcus; ITG = inferior temporal gyrus; MCC = midcingulate cortex; pre-SMA = pre-supplementary motor area; S1 = primary somatosensory cortex; SPL = superior parietal lobule; STS = superior temporal sulcus; TPJ = temporoparietal junction; vPMC = ventral premotor cortex.

Supplementary Discussion

The basal ganglia featured regions more specifically activated by encoding (anterior putamen and nucleus accumbens) or recall (middle and posterior putamen). This differentiation is consistent with studies on motor sequence learning in humans (Jueptner et al. 1997; Lehéricy et al. 2005; Toni et al. 1998) and animals (Miyachi et al. 2002) showing that anterior striatal activity is associated with early learning, and posterior striatal activity with overlearned responding. In our task, new sequences were presented on every trial, precluding across-trial learning. However, each encoding–reproduction cycle itself can be considered a miniature learning episode, in which encoding required a sequence to be memorised (i.e. "learned"), and recall required the memorandum (i.e. the "learned material") to be applied for manual reproduction. The anterior ventral striatum is part of a "limbic" cortico–basal ganglia loop (Alexander et al. 1986) involving afferents from the hippocampus and efferents, via the mediodorsal thalamus, to the DLPFC and anterior midcingulate cortex (cf. Turner and Desmurget 2010); it is deemed responsible for boosting the selection of action-relevant visual items and their mapping onto specific motor behaviours. We here showed specifically encoding-related activity within this entire network, which also implicates hippocampal involvement in the encoding of visuo-spatial sequence information for short-term storage, as previously suggested by animal and patient studies (for a review, see Marshuetz 2005). In contrast, the middle and posterior putamen are part of the skeletomotor loop and might, in collaboration with the "motoric" central insula (Kurth et al. 2010), support the efficient encoding and subsequent overt expression of the (memorised) motor intention.

The dorso-caudal aspect of the dPMC also showed significantly higher activity during recall than encoding. This resonates well with current concepts that in particular the caudal aspects of the dPMC are involved in lower-level motor control and hence the actual execution of movements (reviewed in Abe and Hanakawa 2009; see also Chouinard and Paus 2006; Simon et al. 2002). For instance, dPMC was found to represent the spatial targets of planned reach movements in both gaze- and body-centred reference frames (Bernier and Grafton 2010; Beurze et al. 2010;

McGuire and Sabes 2009). Therefore, it may be argued that the more pronounced increase in caudal dPMC activity during recall reflects spatial information processing for the lower-level programming of motor output for sequence reproduction.

As argued before (cf. main discussion), the mid-DLPFC may contribute to the sequencing of actions via converting a chain of task-relevant input into temporally ordered behavioural goals (during encoding) and selecting the appropriate string of goal-relevant action representations (during recall). However, this high-level translation can only be achieved by disassembling the observed temporospatial input pattern into temporally distinct units forming the basis of subsequently executable motor operations. We suggest that this process is guided by the rule that defines the mapping of the location of a given red dot onto the flexion of a specific finger, represented by dPMC activity and fed to frontomedial areas for temporal segregation. During encoding of longer sequences, the segregated sensorimotor units probably need be reassembled immediately into a manageable number of chunks, a process that most likely relies on mid-DLPFC involvement. During recall, the individual elements (or chunks) have to be implemented in the remembered order. Based on previous evidence (e.g. Hoffstaedter et al. 2013) and our own data we suggest that this memory-guided (i.e. internally triggered) initiation of temporally distinct movements relies on the anterior MCC.

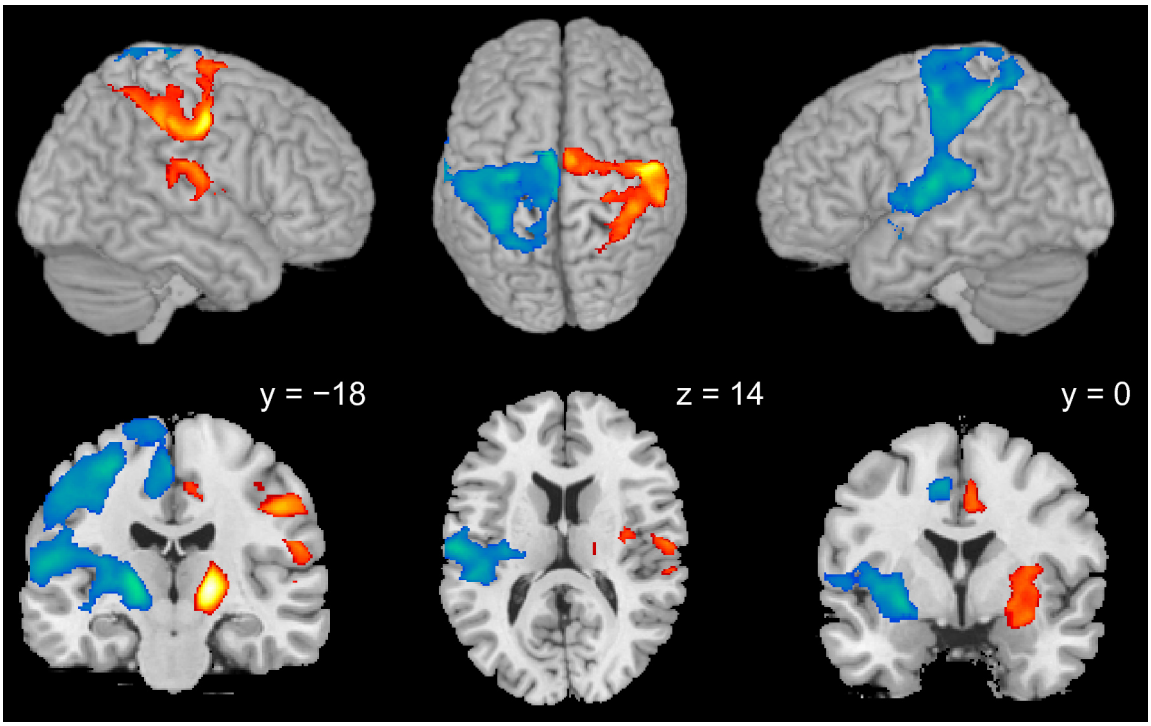

Figure S2. Effector-specific effects of delayed versus immediate recall. Warm colours denote higher activity during delayed, relative to immediate, recall of left-hand (vs. right-hand) sequences; cool colours denote higher activity during delayed, relative to immediate, recall of right-hand (vs. left-hand) sequences.

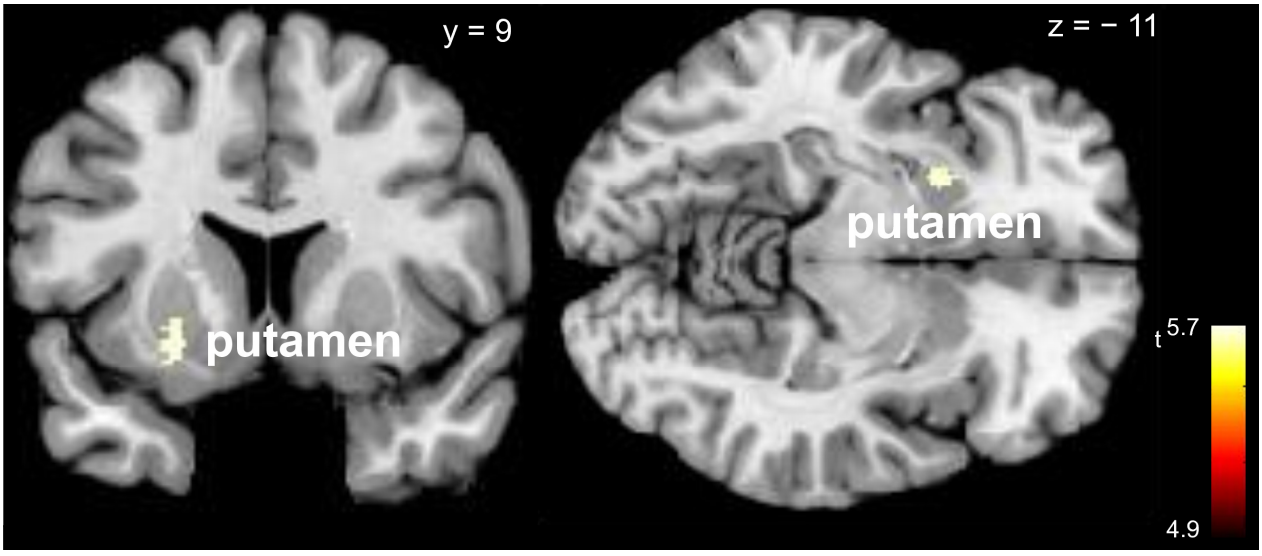

Figure S3. Encoding-related activity selectively associated with subsequent correct (vs. incorrect) recall, irrespective of delay length and effector side. Section coordinates refer to MNI space.

Table S2

Effector-specific brain activity related to delayed (vs. immediate) recall

Location	Histological Assignment	Local Maximum			*t*-value
Left- vs. right-hand sequences					
Right hemisphere					
Thalamus	-	17	-20	2	7.9
Primary motor cortex	areas 4a, 4p	53	-12	42	6.9
Pallidum	-	23	-6	5	5.5
Temporo-parietal junction	PFt, PFop, PF	57	-29	42	5.4
SMA	area 6	8	-9	59	5.1
Postcentral sulcus	area 2	42	-36	45	5.0
Dorsal premotor cortex	area 6	48	-11	51	4.6
Putamen	-	36	-5	0	4.5
Superior parietal lobule	7PC	35	-48	56	4.3
Intraparietal sulcus	hIP3	36	-45	53	4.2
Parietal operculum	OP3, OP4, OP1	36	-9	14	3.9
Central sulcus	area 3a	23	-27	47	3.9
Superior parietal lobule	7A	26	-59	60	3.5
Postcentral gyrus	areas 3b, 1	41	-27	59	3.4
Right- vs. left-hand sequences					
Left hemisphere					
Thalamus	-	-17	-15	-2	7.1
SMA	area 6	-5	-6	53	6.8
Parietal operculum	OP4, OP1, OP2	-60	-15	12	6.2
Postcentral sulcus	area 2	-33	-36	-51	6.1
Dorsal premotor cortex	area 6	-29	-18	57	6.1
Putamen	-	-27	0	-6	6.0
Superior parietal lobule	7PC	-33	-45	59	5.9
Temporo-parietal junction	PFcm, PFt	-50	-32	18	5.9
Primary motor cortex	areas 4a, 4p	-3	-26	54	5.5
Central insula	-	-36	-11	-8	5.2
Superior parietal lobule	7A	-26	-54	63	5.0
Postcentral gyrus	areas 3b, 1	-47	-20	45	5.0
Central sulcus	area 3a	-39	-21	38	5.0
Superior parietal lobule	5L	-17	-50	78	4.1
Inferior frontal gyrus	area 44	-62	3	6	3.3

Note. Peak coordinates refer to MNI space. SMA = supplementary motor area;

References to histological assignments: areas 4a, 4p: Geyer et al. (1996); area 44: Amunts et al. (1999); areas 1, 3a, 3b: Geyer et al. (1999); area 2: Grefkes et al. (2001); area 6: Geyer (2004); PFop, PF, PFt, PFcm: Caspers et al. (2006); OP1-OP4: Eickhoff et al. (2006); 7A, 7PC, 5L: Scheperjans et al. (2008).

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