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Supplemental Information

The Occipital Place Area Is Causally Involved in Representing Environmental Boundaries during Navigation

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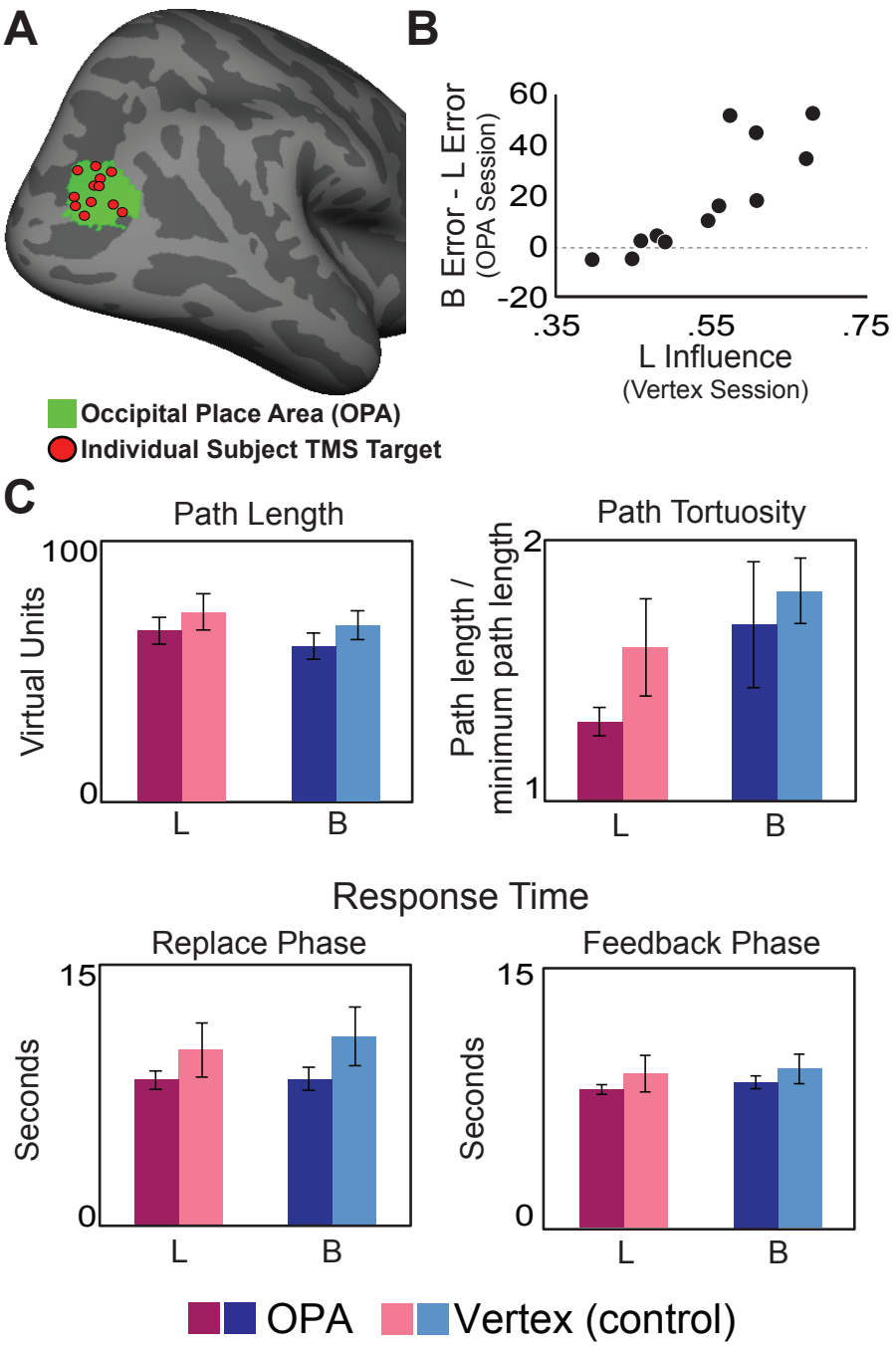

Figure S1. Supplemental Methods and Results for Experiment 1 (related to Figures 1 and 2). **A)** The group-based right Occipital Place Area (OPA) derived from a large number (42) of subjects across several studies from our laboratory, shown in green on the average cortical surface [S1]. The OPA TMS target site was defined for each participant as the OPA voxel exhibiting peak scene-selectivity. Each red dot denotes an OPA target site for a single participant in Experiment 1 (mean Talairach coordinates: [34, -77, 21]). **B**) Correlation between overall landmark influence during the Vertex session and boundary-specific memory impairment (i.e., boundary-tethered object distance error minus landmark-tethered object distance error) during the OPA session across participants. **C**) Mean path length and path tortuosity during the replace phase, and mean response time during both the replace phase and feedback phase, separately for the OPA (dark colors) and Vertex (light colors) sessions for the landmark- (*L*; in red) and boundary-related (*B*; in blue) objects (±1 SEM). Path tortuosity for each trial was computed as the path length divided by the Euclidean distance between the starting and end location of the path taken by the participant. Separate 2(object type: landmark-tethered vs. boundary-tethered) x 2(stimulation site: OPA vs. Vertex) ANOVAs revealed no significant main effects or interactions for path length, or response time during the replace or feedback phases (all $F(1,11)$s < 2.25, all ps > 0.1). Path tortuosity was marginally lower for the landmark-tethered than boundary-tethered objects ($F(1,11) = 4.15$, p=0.07), but critically there was no significant main effect of stimulation site or interaction (both $F(1,11)$s < 1.35, both ps > 0.27).

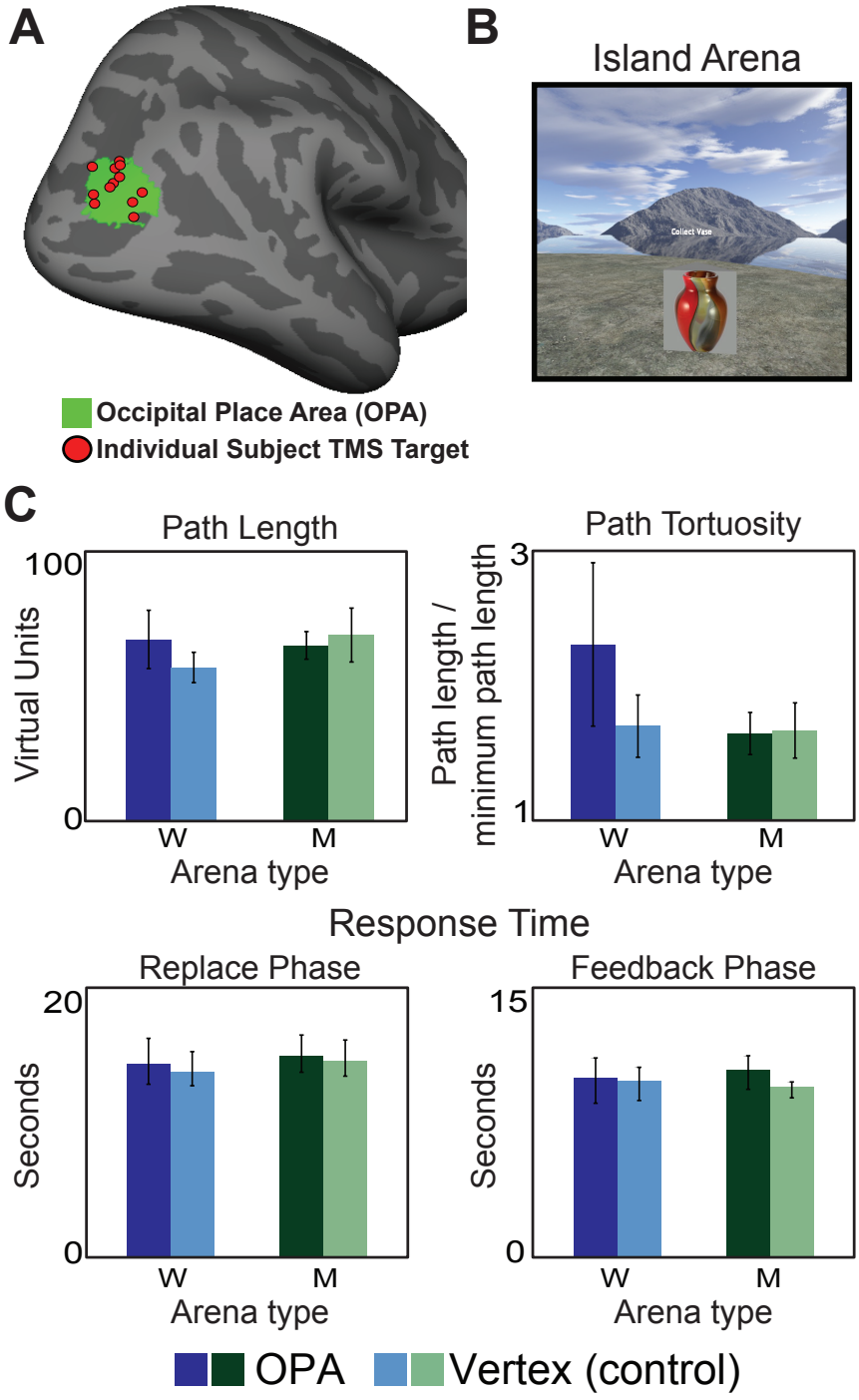

Figure S2. Supplemental Methods and Results for Experiment 2 (related to Figure 3). **A)** The group-based right Occipital Place Area (OPA) derived from a large number (42) of subjects across several studies from our laboratory, shown in green on the average cortical surface [S1]. The OPA TMS target site was defined for each participant as the OPA voxel exhibiting peak scene-selectivity. Each red dot denotes an OPA target site for a single participant in Experiment 2 (mean Talairach coordinates: [35, -79, 22]). **B)** In addition to the Wall and Mat Arenas, in Exp. 3 participants were also tested in the Island Arena. Data from the Island were inconclusive; see *Supplemental Experimental Procedures* for more information. **C)** Mean path length and path tortuosity during the replace phase, and mean response time during both the replace phase and feedback phase, separately for the OPA (dark colors) and Vertex (light colors) sessions for the Wall Arena (*W*; in blue) and Mat Arena (*M*; in green) (±1 SEM). Path tortuosity for each trial was computed as the path length divided by the Euclidean distance between the starting and end location of the path taken by the participant. Separate 2(arena: Wall vs. Mat) x 2(stimulation site: OPA vs. Vertex) ANOVAs revealed no significant main effects or interactions for path length, or response time during the replace or feedback phases (all $F(1,11)$s < 2.50, all ps > 0.14). Path tortuosity was marginally lower in the Mat than in the Wall Arena ($F(1,11)=3.62$, $p=0.08$), but critically there was no significant main effect of stimulation site or interaction (both $F(1,11)$s < 0.89, both ps > 0.35).

Table S1. Related to Figures 1 and 2. Complete results of the analyses of variance performed on data from blocks 2-3 of Experiment 1. Overall performance is analyzed in the top table and influence of the landmark in the bottom table. Significant effects ($p < 0.05$) are indicated in bold.

Performance

	df	F	Sig.	Partial Eta Squared
Object Type (Landmark-tethered vs. Boundary-tethered)	**1**	**7.086**	**.022**	**.392**
Stimulation Site (OPA vs. Vertex)	**1**	**14.755**	**.003**	**.573**
Block (2 vs. 3)	1	2.515	.141	.186
Trial (1-4)	**3**	**34.640**	**.000**	**.759**
Object Type * Stimulation Site	**1**	**10.144**	**.009**	**.480**
Object Type * Block	1	2.050	.180	.157
Stimulation Site * Block	1	.537	.479	.047
Object Type * Stimulation Site * Block	1	.223	.646	.020
Object Type * Trial	3	.680	.571	.058
Stimulation Site * Trial	3	1.127	.352	.093
Object Type * Stimulation Site * Trial	3	.937	.434	.078
Block * Trial	**3**	**3.120**	**.039**	**.221**
Object Type * Block * Trial	3	.250	.861	.022
Stimulation Site * Block * Trial	3	1.976	.137	.152
Object Type * Stimulation Site * Block * Trial	3	.127	.943	.011

Landmark Influence

	df	F	Sig.	Partial Eta Squared
Object Type (Landmark-tethered vs. Boundary-tethered)	**1**	**35.521**	**.000**	**.764**
Stimulation Site (OPA vs. Vertex)	**1**	**6.409**	**.028**	**.368**
Block (2 vs. 3)	1	.250	.627	.022
Trial (1-4)	3	2.029	.129	.156
Object Type * Stimulation Site	1	1.011	.336	.084
Object Type * Block	**1**	**12.809**	**.004**	**.538**
Stimulation Site * Block	1	1.011	.336	.084
Object Type * Stimulation Site * Block	1	.290	.601	.026
Object Type * Trial	**3**	**27.760**	**.000**	**.716**
Stimulation Site * Trial	3	.711	.552	.061
Object Type * Stimulation Site * Trial	3	2.503	.076	.185
Block * Trial	3	.714	.551	.061
Object Type * Block * Trial	**3**	**5.756**	**.003**	**.344**
Stimulation Site * Block * Trial	3	.729	.542	.062
Object Type * Stimulation Site * Block * Trial	3	2.632	.066	.193

Table S2. Related to Figure 3. Complete results of the analyses of variance performed on performance data from blocks 2-3 of Experiment 2. Significant effects ($p < 0.05$) are indicated in bold.

	df	F	Sig.	Partial Eta Squared
Arena (Wall vs. Mat)	1	0.252	.626	.022
Stimulation Site (OPA vs. Vertex)	1	0.119	.737	.011
Trial (1-3)	**2**	**5.476**	**.012**	**.332**
Arena * Stimulation Site	**1**	**5.971**	**.033**	**.352**
Arena * Trial	2	.548	.586	.047
Stimulation Site * Trial	2	.398	.676	.035
Arena * Stimulation Site * Trial	2	.548	.586	.047

Supplemental Experimental Procedures

Participants. Two groups of twelve participants gave written consent and were paid for participating in Exp. 1 (5 female, mean age 23, age range 20-28) and Exp. 2 (4 female, mean age 24, age range 19-33). Five subjects participated in both experiments, separated by roughly six months. All had normal or corrected-to-normal vision and reported to be in good health with no history of neurological disease. All subjects provided informed consent in accordance with the Institutional Review Board of the University of Pennsylvania.

fMRI Localization of the OPA. Prior to TMS, each participant completed an fMRI localizer scan to localize the right OPA. Scanning was performed at the Hospital of the University of Pennsylvania using a 3T Siemens Trio scanner equipped with a 32-channel head coil. High-resolution T1-weighted images for anatomical localization were acquired using a three-dimensional magnetization-prepared rapid acquisition gradient echo pulse sequence [repetition time (TR), 1620 ms; echo time (TE), 3.09 ms; inversion time, 950 ms; voxel size, 1 x 1 x 1 mm; matrix size, 192 x 256 x 160]. T2*-weighted images sensitive to blood oxygenation level-dependent contrasts were acquired using a gradient echo echoplanar pulse sequence (TR, 3000 ms; TE, 30 ms; flip angle 90°; voxel size, 3 x 3 x 3 mm; field of view, 192; matrix size, 64 x 64 x 44). Visual stimuli were displayed by rear-projecting them onto a Mylar screen at 1024 x 768 pixel resolution with an Epson 8100 3-LCD projector equipped with a Buhl long-throw lens. Subjects viewed the images through a mirror attached to the head coil.

During scanning, subjects completed two functional localizer scans. The localizer procedure was identical to the procedure used in prior reports (e.g, [S2]) These scans were each 5 min 21 s in length, during which subjects performed a 1-back repetition detection task on color images of faces, scenes, objects, and scrambled objects, presented in 16 s blocks with each stimulus shown for 600 ms each with a 400 ms interstimulus interval. Images subtended a visual angle of approximately 9.0° x 9.0°.

Data from the localizer scans were analyzed with the FMRIB Software Library (FSL) using the following steps. First, they were corrected for differences in slice timing by resampling slices in time to match the first slice of each volume. Second, they were corrected for subject motion by realigning to the first volume of the scan run using MCFLIRT [S3]. Third, the timecourses for each voxel were high-pass filtered to remove low temporal frequency fluctuations in the BOLD signal that exceeded lengths of 100 s. Data were then spatially smoothed with a 5 mm full-width at half-maximum Gaussian filter. A GLM consisting of a boxcar regressor convolved with a standard double gamma function was then used to model the fMRI response to each stimulus condition. The scene-selective right OPA was identified in each participant by overlaying individual scenes > objects contrast maps on high-resolution MRI scans for each participant. The anatomical location of the right OPA, near the transverse occipital and intraparietal sulci, was confirmed using standard methods [S1] (Figures S1A and S2A).

Stimulation Sites and Transcranial Magnetic Stimulation. The Brainsight system (Rogue Research, Montreal) was used to co-register MRI data with the location of the subject and the TMS coil. The OPA stimulation site was defined in each participant by selecting the voxel exhibiting peak scene-selectivity (i.e., the highest t-value from the scenes > objects contrast) in the right OPA. The Vertex control site was identified in each participant as the midpoint between the bridge of the nose and the inion, and between the temples. A Magstim Super Rapid^2 Plus^1 stimulator (Magstim; Whitland, UK) was used to deliver cTBS via a 70 mm diameter figure-eight coil. For OPA stimulation, the TMS coil handle was held pointing upwards. To calibrate the intensity of stimulation, cTBS was delivered at 80% of each participant's phosphene threshold. Each participant's phosphene threshold was determined prior to the start of the first experimental session using a standard up-down staircase procedure with stimulation to visual area V1 [S4].

For both experiments, each subject participated in two testing sessions separated by one week, one for each of the two stimulation sites (counterbalanced across subjects). In Exp. 1, stimulation was applied immediately prior to each testing block, and in Exp. 2 stimulation was applied five minutes prior to each testing block.

Virtual Reality Environments and Testing Procedure. We used Source SDK Hammer Editor (http://www.valvesoftware.com, Valve Software, Bellevue, WA) to construct a virtual reality environment that was rendered and displayed from the first person-perspective using the commercial game software Portal (http://www.valvesoftware.com, Valve Software, Bellevue, WA). The environment was displayed on a 27-inch LG monitor (resolution: 1920 x 1080) and participants were seated roughly 50 cm from the screen. In both experiments, participants learned the locations of target objects inside an arena in the virtual environment, using the learning procedure illustrated in Figure 1A. Participants moved through the arena by using their right hand to operate arrow keys to move forward or backwards and turn left or right. Responses during the replace phase were collected by participants pressing the "e" key with their left hand. Virtual heading and location were recorded every 100 ms.

In Exp. 1, participants were tested inside an arena consisting of a landmark object surrounded by a circular boundary

wall. The boundary wall was 130 virtual units (vu) in diameter, and 10 vu in height relative to a simulated eye-level of 4 vu. One virtual unit corresponds to 0.3048 real-world meters (1 foot). The landmark object was either a trashcan or a metal ball, counterbalanced across TMS target sites. The complete set of target objects was either [coffee table, propane tank, barrel, traffic cone] or [radiator, lamp, oil drum, cake], counterbalanced across TMS target sites. The target objects for each trial were selected in pseudo-random order. Prior to the start of the first replace phase during block 1, but not blocks 2-3, participants collected each target object in pseudo-random order twice (i.e., performed the feedback phase twice per target object) in order to learn the locations of the objects.

In Exp. 2, participants were tested in two different circular arenas: Wall and Mat. The Wall Arena surrounded by a wall as in Exp. 1. The Mat Arena consisted of a visual texture (or "mat") drawn on the ground. Both the Wall and Mat arenas had the same visual texture drawn on the ground; thus, the Wall and Mat arenas were visually identical except for the presence of the boundary. The Wall and Mat Arenas had the same diameter as the Exp. 1 arena. The boundary wall in the Wall Arena was 4 vu in height, which is shorter than the boundary wall in Exp. 1 so that the visibility of the distal cues were better matched between the Wall and Mat Arenas. Participants could walk beyond the edge of the mat in the Mat Arena, and were instructed that they could do so. However, participants only spent an average of 4.7% of the total testing time beyond the edge of the mat, and there was no difference in time spent outside the mat edge between the OPA and Vertex sessions ($t(11)= 0.20$, $p > 0.5$). The complete set of target objects in the Wall Arena was either [basketball, hairdryer, arm chair, refrigerator] or [cooler, binoculars, computer monitor, hat]. The complete set of target objects in the Mat Arena was either [washer, calculator, bench, cabinet] or [vacuum, bowling ball, cell phone, stapler]. Target object sets were counterbalanced across TMS target sites for each arena. The target objects for each trial were selected in pseudo-random order. Prior to the start of the first replace phase in each arena, participants collected each target object in pseudo-random order twice (i.e., performed the feedback phase twice per target object).

In addition to the Wall and Mat Arenas in Exp. 2, participants were also tested in a third arena: the Island (Figure S2B). The Island consisted of a circular island surrounded by "water" that impeded movement. This arena was included to examine if the OPA codes boundaries defined solely by their impediment to movement, and not just surface boundaries. Prior to testing in the Island arena, participants were informed that they could not walk beyond the island edge. The complete set of target objects in the Island Arena were [bottle, piano, football, coffee maker] or [treadmill, vase, soccer ball, sofa], counterbalanced across TMS target sites. In the Island, we observed no difference in overall performance between the OPA and Vertex sessions ($t(11)=0.10$, $p > 0.5$). However, performance in this arena was confounded with response time: participants took significantly more time to replace the objects following OPA stimulation than after stimulation of Vertex ($t(11) = 2.36$, $p < 0.05$). Further, 10 out of 12 participants took longer to collect the target objects during the feedback phase following OPA stimulation compared to Vertex ($p < 0.05$, sign-test), although one participant went strongly in the opposite direction. Thus, results from this experiment were ambiguous: on the one hand, the absence of an accuracy difference suggests that OPA might *not* be involved in processing boundaries that are defined by an obstacle at ground level rather than a wall; on the other hand, the fact that response times were longer after OPA stimulation suggests that an impairment in accuracy may have been masked by a speed-accuracy tradeoff. Because of the ambiguity of the results, data from the Island were omitted from further analyses.

Supplemental References

S1. Julian J., Fedorenko E., Webster J., & Kanwisher N. (2012). An algorithmic method for functionally defining regions of interest in the ventral visual pathway. Neuroimage *60*, 2357-2364.

S2. Marchette S.A., Vass L.K., Ryan J., & Epstein R.A. (2015). Outside Looking In: Landmark Generalization in the Human Navigational System. The Journal of Neuroscience *35*, 14896-14908.

S3. Jenkinson M., Bannister P., Brady M., & Smith S. (2002). Improved optimization for the robust and accurate linear registration and motion correction of brain images. Neuroimage *17*, 825-841.

S4. Kammer T. & Beck S. (2002). Phosphene thresholds evoked by transcranial magnetic stimulation are insensitive to short-lasting variations in ambient light. Experimental brain research *145*, 407-410.