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## Single Case Report

# In a case of longstanding low vision regions of visual cortex that respond to tactile stimulation of the finger with Braille characters are not causally involved in the discrimination of those same Braille characters

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## ABSTRACT

Braille reading and other tactile discrimination tasks recruit the visual cortex of both blind and normally sighted individuals undergoing short-term visual deprivation. Prior functional magnetic resonance imaging (fMRI) work in patient 'S', a visually impaired adult with the rare ability to read both highly magnified print visually and Braille by touch, found that foveal representations of S's visual cortex were recruited during tactile perception, whereas peripheral regions were recruited during visual perception. Here, we test the causal nature of tactile responses in the visual cortex of S by combining tactile and visual psychophysics with repetitive transcranial magnetic stimulation. First, we replicate the previous fMRI findings in S. Second, we demonstrate that transient disruption of S's foveal visual cortex has no measurable impact on S's tactile processing performance compared to that of healthy controls – a pattern not predicted by the fMRI results. Third, stimulation of foveal visual cortex maximally disrupted visual processing performance in both S and controls, suggesting the possibility of preserved visual processing within S's foveal representation. Finally, stimulation of somatosensory cortex induced the expected disruption to tactile processing performance in both S and controls. These data suggest that tactile responses in S's foveal representation reflect unmasking of latent connections between visual and somatosensory cortices and not behaviourally relevant cross-modal plasticity.

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Unlike studies in congenitally blind individuals, it is possible that the absence of complete visual loss in S has limited the degree of causally impactful cross-modal reorganisation.

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## 1. Introduction

Whether or not human visual cortex reorganises functionally following deprived visual input is a crucial question in visual neuroscience (Baseler et al., 2011; Cheung et al., 2009; Haak et al., 2015; Sadato et al., 1996). In blind individuals, fMRI studies highlight visual cortex activity during somatosensory tasks (Burton et al., 2002; Sadato et al., 1996) (e.g. Braille reading) and short-term visual deprivation can lead to increased recruitment of visual cortex during somatosensory tasks in normally sighted individuals (Kauffman et al., 2002; Merabet et al., 2007, 2008). Further, somatosensory and auditory task-related activity has been reported in the lesion-projection-zone (LPZ) of patients with macular degeneration (Masuda et al., 2021). Collectively, these fMRI data suggest that some form of cross-modal plasticity is possible in visual cortex.

Whilst transient disruption of visual cortex via TMS impairs Braille reading performance in blind individuals (Cohen et al., 1997), its detrimental impact appears to depend on the onset of blindness, with little impact on Braille reading performance of individuals whose blindness occurred after ~14 years of age (Cohen et al., 1997, 1999). Thus, despite considerable fMRI evidence suggesting visual cortex is capable of cross-modal plasticity, whether or not such activity is causally related to cross-modal performance is less clear and may depend on plasticity of the brain that is only present early in life.

Prior fMRI work (Cheung et al., 2009), capitalised on the rare case of ‘patient S’, who despite being visually impaired, is capable of both reading highly magnified print visually and Braille by touch. In S, tactile processing (e.g. Braille reading) selectively recruited the foveal representation of visual cortex whereas visual processing (e.g. viewing letter strings) recruited more peripheral representations. There was no evidence of central-visual field loss in S, despite the loss of visual responses in the foveal representation. The fact that the foveal representation was recruited during Braille reading in S was interpreted as reflecting retinotopically specific cross-modal plasticity. Although it was argued that in S, such reorganisation was optimal - since only those parts of visual cortex that were not critical for S’s remaining low-vision were recruited during somatosensory processing - whether or not this somatosensory activity plays a causal role in S’s tactile processing ability is unclear.

Here, we tested this prediction directly in S by pairing both tactile and visual psychophysics with repetitive transcranial magnetic stimulation (rTMS) of the foveal representation of visual cortex (occipital pole [OP]), somatosensory cortex (S1) and an occipital lobe control region (OC). First, our fMRI experiment replicated prior work in S by demonstrating preferential recruitment of the foveal and peripheral

representations of visual cortex during tactile and visual stimulation, respectively (Cheung et al., 2009). Second, we report that despite the pattern of fMRI data in S, transient disruption of OP via repetitive TMS does not alter tactile performance beyond that observed in normally sighted controls. The somatosensory-related activity within the foveal representation of visual cortex of S likely reflects unmasked latent connections with somatosensory cortex rather than reflecting causally relevant cross-modal reorganisation.

## 2. Materials and methods

We report how we determined the sample size of the control group, all data exclusions (if any), all inclusion/exclusion criteria, whether inclusion/exclusion criteria were established prior to data analysis, all manipulations, and all measures in the study. The conditions of our ethics approval do not permit public archiving of anonymised fMRI study data. Readers seeking access to the data should contact the lead author Prof. Tony Morland. Access will be granted to named individuals following completion of a formal data sharing agreement and in accordance with ethical procedures governing the reuse of sensitive data.

### 2.1. Participants

We report fMRI and behavioural measurements from 1 participant with ‘low-vision’ (Patient S; see [Case Description](#)) and three control participants with normal vision and no prior Braille reading experience (C1-3; 2 male and 1 female; ages 21–35). Recruitment of low-vision patients who can still read visual print and are also expert Braille readers for basic research is difficult. Prior work, on which this study is based (Cheung et al., 2009) focused on a case study of Patient S and compared fMRI response in S to those of 4 healthy controls. In the current case study of S, we have therefore adopted similar methods that enable us to perform measurements of single participants. All procedures adhered to protocols based upon the declaration of Helsinki ethical principles for research involving human participants. The ethics committees at the York Neuroimaging Centre and the Department of Psychology at the University of York approved these experiments. All participants provided written informed consent to participate in the experiment.

### 2.2. Case Description

S (male, aged 60 at time of testing) had normal visual development and acuity until approximately six years of age. It is assumed this resulted in typically developed retinotopic organisation in early visual areas, which can be disrupted by

inherited visual deficits (Baseler et al. 2002; Hoffmann et al., 2003). Post six years of age, S developed severe bilateral corneal opacification, secondary to Stevens-Johnson syndrome. S has low-vision, but no evidence of nystagmus and no evidence of central visual field loss (Cheung et al., 2009). Prior work reported Snellen acuity of 20/1000 and Pelli-Robson contrast sensitivity of 1.00 log unit in S. We were unable to test S's visual and Braille reading speeds directly, but prior work (Cheung et al., 2009) report visual reading speeds of 40–100 words per minute and Braille reading at 110 words per minute. S's Braille reading speed is slightly slower than the median reading speeds of a large group of visually disabled Braille readers [ $n = 44$ , median Braille reading = 124 words per minute], (Legge et al., 1999).

### 2.3. MR tactile and visual stimuli

Tactile stimuli in the form of Braille letters [(a, l, q or x)] were delivered via piezoelectric stimulator (maximum pedestal level, 300 ms). Eight presentations occurred during each 12s block. Visual stimuli consisted of 5 100% contrast reversing ring patterns extending to 15° eccentricity (radial frequency .16 cycles per degree, reversal rate 6 Hz). Each run consisted of 10 cycles of 12s on 12s off stimulation using an interleaved paradigm (Visual, rest, Tactile, rest), (see inset of Fig. 1 for stimulus schematics). Presentation code for the visual experiment was standard within the mrVista distribution (<https://web.stanford.edu/group/vista/cgi-bin/wiki/index.php/MrVista>). Experimental code for the tactile experiment can be accessed via the Open Science Framework page for this project (DOI 10.17605/OSF.IO/N87F6).

### 2.4. Scanning procedure

All MRI data were acquired on a 3.0 T GE Sigma HD Excite scanner housed at the York Neuroimaging Centre (YNiC). For structural data, two multi-average, whole-head T1-weighted anatomical volumes were acquired for each subject (repetition time = 7.8 ms, echo time = 3 ms, TI = 450 ms, field of view = 290 × 290 × 176, 256 × 256 × 176 matrix, flip angle = 20°, 1.13 × 1.13 × 1.0 mm<sup>3</sup>). For functional data, gradient recalled echo pulse sequences were used to measure T2\* blood oxygen level-dependent data (repetition time = 2,000 ms, echo time = 30 ms, field of view = 192 cm, 64 × 64 matrix, 39 contiguous slices, voxel size = 3 mm<sup>3</sup>). Images were read-out using an echo planar imaging (EPI) sequence. Magnetisation was allowed to reach a steady state by discarding the first five volumes.

### 2.5. fMRI data analysis and visualisation

All anatomical and functional data were pre-processed and analysed using the Analysis of Functional NeuroImages (AFNI) software (Cox, 1996) (RRID: SCR\_005927). All images were motion-corrected to the first volume of the first run (using the AFNI function *3dVolreg*). Following motion correction, images were detrended (*3dDetrend*) and spatially smoothed (*3dmerge*) with a 3 mm full-width-half-maximum smoothing kernel. Signal amplitudes were then converted into percent signal change (*3dTstat*). To analyse the functional data, we employed

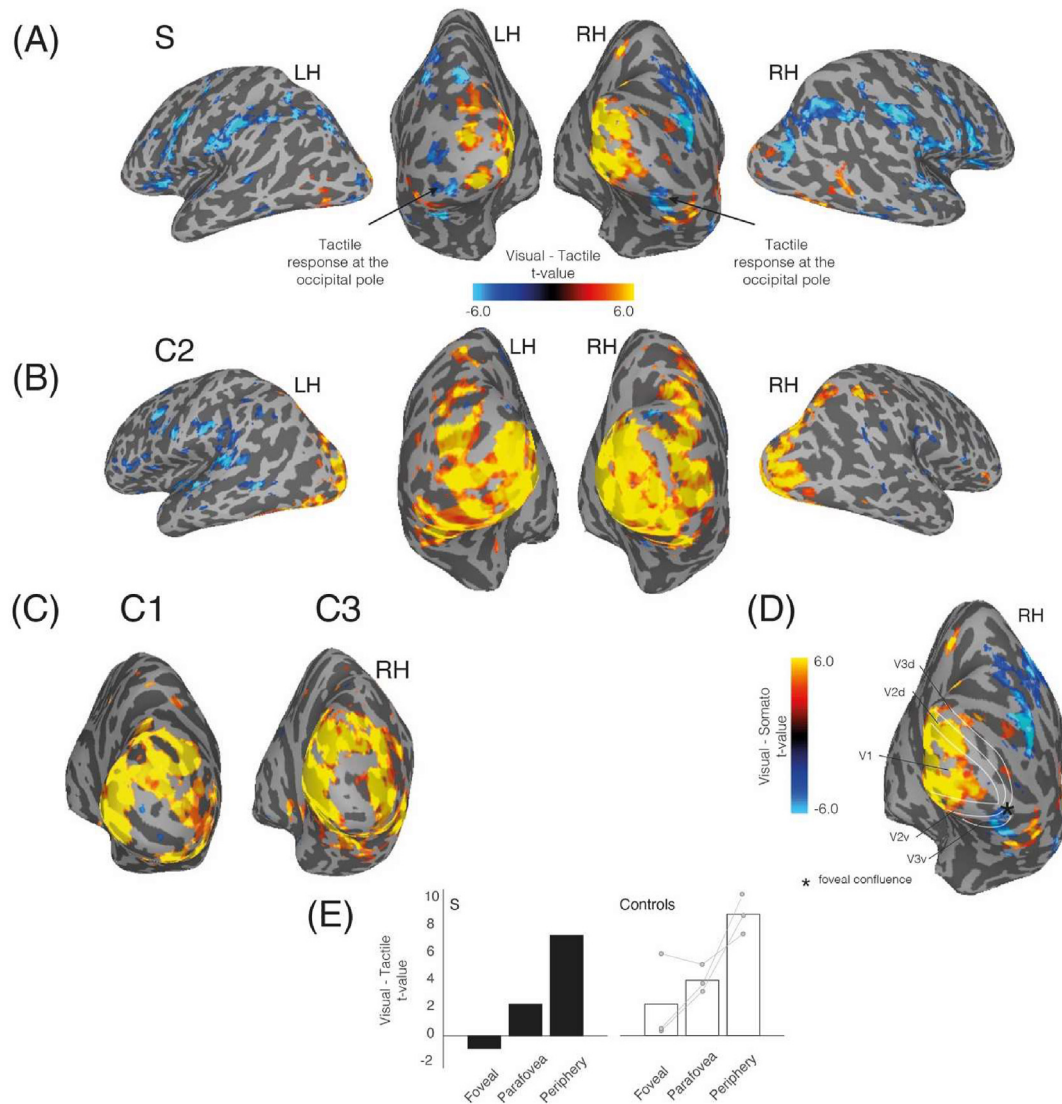
a general linear model implemented in AFNI (*3dDeconvolve*, *3dREMLfit*). The data at each time point were treated as the sum of all effects thought to be present at that time and the time-series was compared against a Generalized Least Squares (GSLQ) model fit with REML estimation of the temporal auto-correlation structure. Responses were modelled by convolving a standard gamma function with a 12s square wave for each stimulus block (Visual, Tactile). Estimated motion parameters were included as additional regressors of no-interest and fourth-order polynomials were included to account for slow drifts in the MR signal over time. To derive the response magnitude per condition, t-tests were performed between the condition-specific beta estimates and baseline. The corresponding statistical parametric maps were aligned to the T1 obtained within the same session by calculating an affine transformation (*3dAllineate*) between the motion-corrected EPIs and the anatomical image and applying the resulting transformation matrices to the T1. In each participant, the pre-processed functional data were projected onto surface reconstructions (*3dvol2surf*) of each individual participant's hemispheres derived from the Freesurfer4 autorecon script (<http://surfer.nmr.mgh.harvard.edu/>) using the Surface Mapping with AFNI (SUMA) software (Saad & Reynolds, 2012).

### 2.6. TMS target localisation

TMS target locations were defined in each participant individually. The occipital pole [OP] target was defined according to the T1-weighted anatomical scan. The occipital control [OC] target was defined as a fixed distance (~1 cm) dorsal and anterior of that participants' OP target. The S1 target site was defined as the voxel showing the largest response to tactile stimulation within the appropriate portion of the somatosensory cortex.

### 2.7. Psychophysical tasks and stimuli

Tactile and visual thresholds were established in each individual participant prior to rTMS sessions. Note that due to S's low-vision the size of the visual stimuli differed from controls. **Tactile threshold:** Braille letters (a, l, q or x) were delivered via piezoelectric stimulator. Each stimulus comprised all 6 pins, which were raised to a minimum pedestal level of 2250 (max available 4095) units. All pins were raised for 100 ms, before a subset of these 6 pins were further raised to represent the Braille letter. Participants had to detect the target letter as the pins raised above the background pedestal. Using a 4AFC paradigm with a 1 up 2 down staircase, the maximum pin displacement was reduced while the pedestal pin amplitude was held constant to establish a 71% correct threshold for letter detection. Note that S used the index finger of his left hand, whereas C1–C3 used the index fingers of their right hand. Participants were not blindfolded during the tactile task. **Visual threshold:** Maximum luminance visual letters (white, A, L, Q or X) were presented on a black background (15° for S, 4° for controls). Using a 4AFC paradigm with a 1 up 2 down staircase, the background luminance was increased while the letter luminance was held constant to establish a 71% correct threshold for letter detection.



**Fig. 1 – Tactile responses in foveal cortex of S. (A)** Tactile and visual stimuli presented during fMRI are displayed inset. The contrast of Visual - Tactile is overlaid onto lateral and posterior partially inflated surface reconstructions of both hemispheres in S (LH = left hemisphere, RH = right hemisphere). Hot-colours represent visually evoked responses, cold-colours represent tactile evoked responses ( $P < .0001$ , uncorrected). Tactile responses are evident at the occipital pole in both hemispheres. Note, S used the index finger of his left hand. **(B)** Same as (A) but for a representative control (C2). No tactile responses are evident within visual cortex, but robust tactile activity is observed in S1 of the left hemisphere (C2 used index finger of right hand) with some tactile responses also present in right S1. **(C)** The contrast of Visual - Tactile is overlaid onto posterior views of the right hemisphere in the additional control participants (C1, C3). No tactile responses are evident at the occipital pole or within visual cortex. **(D)** The contrast of Visual - Tactile is overlaid onto S's right hemisphere. The borders of V1–V3 are overlaid in white. \* Denotes the foveal confluence of V1–V3. Tactile responses at the occipital pole overlap the confluence of V1–V3. **(E)** Bars represent the mean response (t-value) within foveal, parafoveal and peripheral portions of V1 in S (black bars) and the average of controls (white bars). Individual data points are plotted and linked for each control. Negative values represent larger responses during tactile processing, positive values represent larger responses during visual processing. In S, foveal cortex responds more to tactile over visual processing with the opposite pattern evident in parafoveal and peripheral portions. In controls, all portions show the anticipated larger responses during visual processing.

## 2.8. TMS protocol

A train of four biphasic (equal relative amplitude) TMS pulses, separated by 50 ms (20 Hz) at 70% of the maximum stimulator output (2.6 T) were applied to the participants' scalp using a

figure-of-eight coil (50-mm external diameter of each ring) connected to a Magstim Rapid2 stimulator (Magstim). Participants were seated in a purpose-built chair with chin rest and forehead support. The coil was secured mechanically and placed directly above each cortical target (occipital pole [OP],

occipital control [OC], somatosensory cortex [S1]) with the handle oriented parallel with the floor. The position of the coil was monitored and tracked in real time allowing the displacement between the intended and actual site of rTMS delivery to be measured. Each participant underwent eight sessions [2 tasks  $\times$  (3 TMS sites + 1 no TMS)]. Each TMS session contained 35 trials (5 training). Stimuli (both Tactile and Visual) were presented according to each participants' specific threshold. rTMS pulses were delivered concurrently with the presentation of the test stimulus. This temporal configuration was identical to that used in previous studies from our laboratory where induced functional deficits were found to be maximized when rTMS was delivered coincident with the stimulus onset.

### 2.9. Resampling of rTMS data

Our study lacked the power to compare S' behavioural performance to the average of the controls as is commonplace in other case studies. Instead, we adopted a bootstrapping and resampling procedure to quantify that the impact of OP stimulation in S was not different from an expected distribution of controls. For each control participant and session, we randomly sampled 80% of the experimental data (24/30 trials) and calculated the proportion of correct responses. This procedure was then repeated 10,000 times before averaging these values across control participants. Distributions of the difference between conditions (e.g. S1 - OP tactile performance) were then created and compared with the same calculation in S.

### 2.10. Regions of interest

To divide V1 into foveal (<4 deg), parafoveal (>4 & <8 deg) and peripheral (>8 deg) portions we made use of an independent group-based eccentricity map derived from the average of pRF mapping conducted in twelve participants (Silson et al., 2015). In brief, 12 participants underwent pRF mapping scans at 3.0 T in which a bar aperture traversed through the visual field (20 deg diameter). From these data a group-averaged eccentricity map was defined and applied to the current data.

## 3. Results

### 3.1. Foveal recruitment during somatosensory processing in S

First, blood-oxygen-level-dependent (BOLD) fMRI was employed to localise tactile and visual responses in S and three normally sighted controls (C1–C3). Fig. 1, shows the contrast of Visual versus Tactile overlaid onto surface reconstructions of both hemispheres for S (Fig. 1A) and a representative control (C2, Fig. 1B). In S, tactile responses are evident at the occipital pole in both hemispheres and throughout somatosensory cortex, whereas visual responses are restricted to more anterior portions of visual cortex that represent the periphery (Wandell et al., 2007). No such somatosensory related activity was observed in the visual cortex of C2. Indeed, visual and tactile responses were restricted to

visual and somatosensory cortices, respectively - a pattern replicated in C1 and C3 (Fig. 1C).

Fig. 1D shows the contrast of Visual versus Tactile in S with the borders of V1–V3 overlaid in white. Tactile responses can be seen at the confluence of V1–V3, which represents the fovea. To confirm the replication of prior findings (Cheung et al., 2009), three contiguous regions of interest (ROIs) were defined that divided primary visual cortex (V1) into foveal (<4 deg eccentricity), parafoveal (>4 < 8 deg) and peripheral (>8 deg) portions using eccentricity data from an independent group-average dataset derived from 12 healthy volunteers (Silson et al., 2015). Fig. 1E shows the median response (given by the t-value for Visual versus Tactile) within each ROI for S and all three controls. In S, foveal responses are negative, reflecting tactile recruitment with both parafoveal and peripheral responses becoming increasingly positive (visual recruitment). In contrast, all three controls show positive responses, reflecting visual recruitment in all ROIs that increase in magnitude with increasing eccentricity.

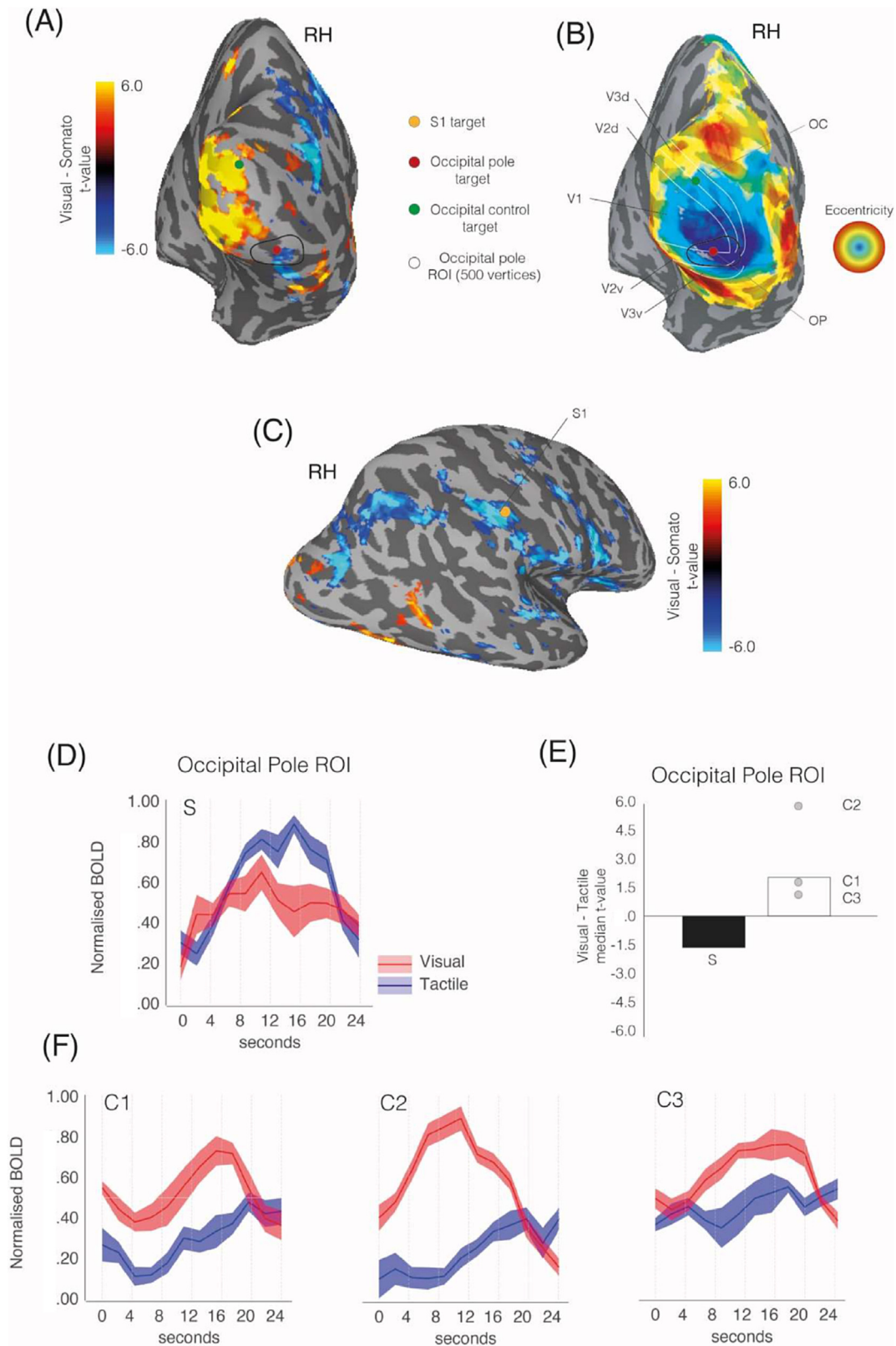
### 3.2. TMS target locations

Fig. 2A shows the three TMS target locations in S, overlaid onto posterior and lateral partially inflated surface reconstructions of the right hemisphere, along with the contrast of Visual versus Tactile. The OP target site (black dot), which was defined according to the T1-weighted anatomical scan, can be seen to overlap the tactile responses (at the selected statistical threshold). Comparing the OP target with group-based eccentricity data confirm that the OP ROI falls within the foveal confluence of V1–V3. The OC target (green dot) was defined as a fixed distance (~1 cm) dorsal and anterior of our OP target. Comparing this location with a freely available probabilistic retinotopic atlas (Wang et al., 2015) indicates our OC target falls at the border of retinotopic maps V2d/V3d. Our team has previously employed a similar approach in order to define close proximity control locations relative to our primary target sites (Silson et al., 2013; Strong et al., 2017). The S1 target site (yellow dot) was defined as the voxel showing the largest response to tactile processing.

To confirm that our anatomically defined OP target was within tactile responding cortex in S, we defined a region-of-interest (ROI) around the OP target site (500 vertices) and calculated the mean response from this ROI across all 10 tactile and visual fMRI blocks. Fig. 2B shows the mean response (plus s.e.m) and highlights the preferential recruitment of this region during tactile processing in S. Fig. 2C shows the median response (t-value) from this OP ROI for both S and all three controls. Whereas in S, a negative response is observed, reflecting tactile recruitment, the opposite pattern is observed in each control. Thus, the pattern of fMRI responses not only confirm prior work in S (Cheung et al., 2009), but also, highlight that responses in the foveal representation of S are the opposite to those observed in normally sighted controls.

### 3.3. rTMS of OP has no measurable impact on Braille character discrimination in S

Examples of the tactile and visual stimuli used in the psychophysical and rTMS sessions are shown in Fig. 3A and B.



**Fig. 2** – TMS target sites in S and fMRI responses from the occipital pole in S and controls. **(A)** Posterior and lateral views of the right hemisphere of S are shown with the contrast of Visual - Tactile overlaid ( $p < .0001$ , uncorrected). The occipital pole [OP] target site (black dot) can be seen to overlap tactile responses. The occipital control [OC] target site (green dot) is located dorsal and anterior of the OP. Probabilistic retinotopic mapping data suggest the OC target sites is located on the border of retinotopic maps V2d/V3d. The OP ROI encompassing the OP target site is shown by the black outline. **(B)** Group-based eccentricity map overlaid onto the same surface as (A). The borders of V1–V3 are overlaid in white. The OP ROI can be seen

Fig. 3C shows tactile performance in S and controls for all four conditions. These data reveal a strikingly similar pattern of performance across conditions in S and controls - not predicted on the basis of the fMRI data. In S, tactile performance was maximally impaired (relative to noTMS baseline) following rTMS of S1 and to a lesser extent OC. Critically however, rTMS of OP had little to no detrimental impact on S's tactile performance compared to the noTMS condition. On average controls showed a largely similar pattern with tactile performance maximally impaired following S1 stimulation but no clear detrimental impact of either OP or OC stimulation. Bootstrapping analyses indicate the impact of OP relative to S1 stimulation on tactile performance in S fell within the expected distribution of results in controls [control range =  $-.50$  to  $-.10$ ;  $S = -.40$ ] (Fig. 3D). Similarly, the impairment in tactile processing induced by TMS of S1 in S relative to noTMS baseline was of a similar magnitude to what could be expected from controls [control range =  $-.50$  to  $-.10$ ;  $S = -.43$ ] (Fig. 3E).

#### 3.4. Impact of TMS on visual processing performance in S and controls

Fig. 3F shows visual performance in S and controls for all four conditions. In S, visual performance was impaired slightly (relative to noTMS baseline) following rTMS of both OP and OC, but not S1 (which caused a slight increase in performance). In controls, performance was severely impaired following OP stimulation with much smaller decreases following stimulation of OC and S1, respectively - as was predicted for foveally presented small letter stimuli. Bootstrapping analyses indicate that the effect of OP stimulation on S's visual performance is smaller than what could be expected compared to both stimulation of OC [control range =  $-.50$  to  $-.10$ ;  $S = -.06$ ] (Fig. 3G) and the noTMS baseline [control range =  $-.60$  to  $-.30$ ;  $S = -.10$ ] (Fig. 3H). The differential impact of OP stimulation on visual performance between S and controls likely reflects the fact that in S visual stimuli were required to be very large ( $\sim 15$  deg) extending much further into the periphery, whereas the targeted OP region by definition represents foveal visual field positions.

## 4. Discussion

Our measurements suggest that the somatosensory related responses within the foveal representation of visual cortex of S play little to no causal role in S's tactile processing

performance, and more likely reflects unmasking of latent connections between the somatosensory and visual cortices that are typically suppressed in normally sighted individuals (Masuda et al., 2021).

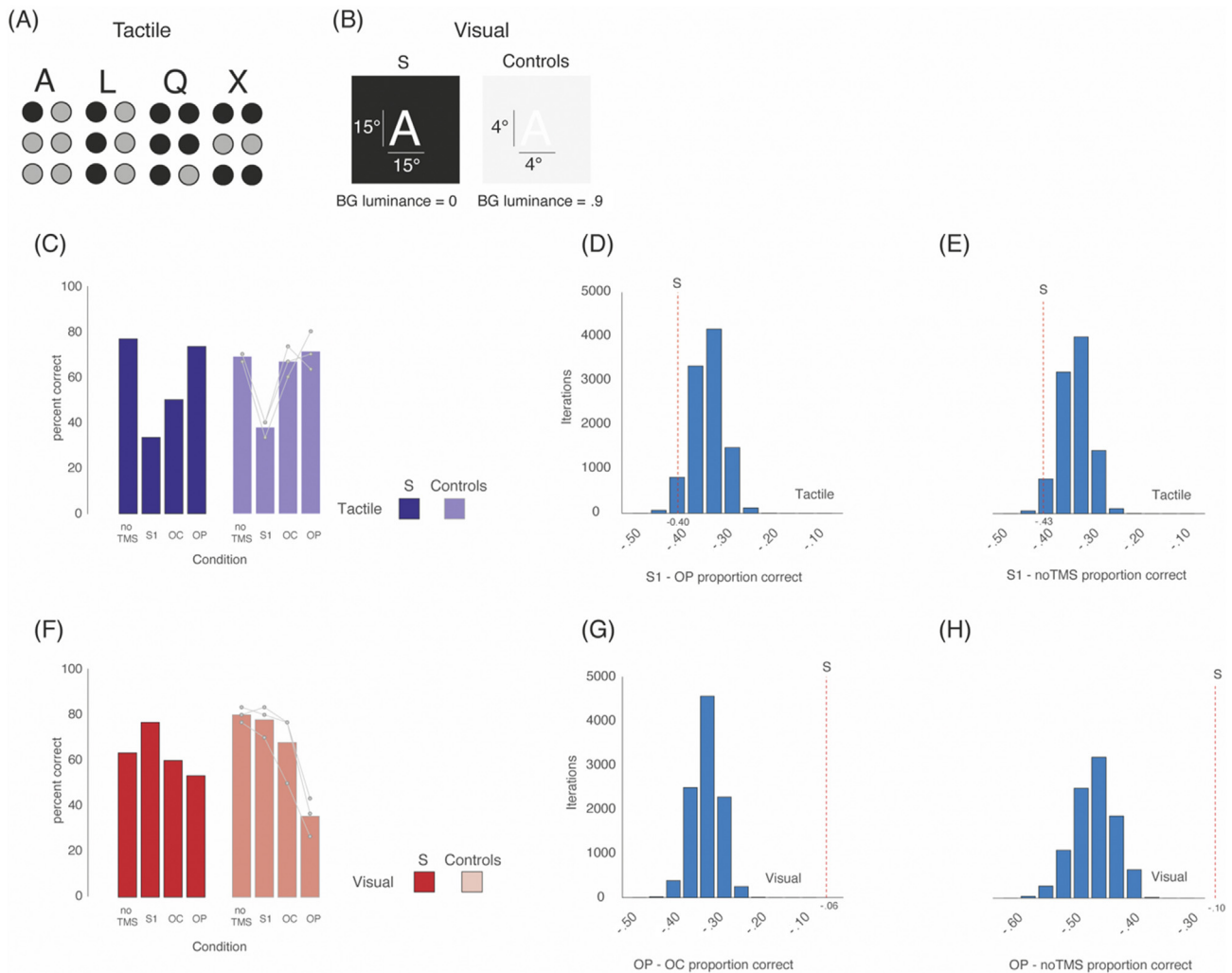
The patterns of TMS results in S during Braille letter discrimination were largely indistinguishable from those of the control participants, with stimulation of S1 inducing the largest detrimental impact to somatosensory processing in both S and controls. Critically, OP stimulation in S did not induce the reduction in tactile performance predicted on the basis of the fMRI experiments (employing the same somatosensory task) conducted here and in prior work (Cheung et al., 2009). That the foveal confluence of S preferentially responds to tactile over visual information was confirmed and yet the TMS data suggest that such activity is not causally related to tactile performance. In this regard, the pattern of TMS results in S are consistent with those of individuals with late-onset blindness (Cohen et al., 1999). This prior work demonstrated that TMS of occipital cortex induced tactile deficits in both congenitally blind (Cohen et al., 1997) and early-blind individuals but not those whose blindness occurred after  $\sim 14$  years of age (Cohen et al., 1999), suggesting a critical time-frame in which functionally relevant reorganisation of visual cortex occurs. Although S's loss of visual function began at approximately six years of age, and thus within that timeframe, he nevertheless retains visual function. Indeed, S has a full visual field with no evidence of a central scotoma despite the very low-resolution central vision (Cheung et al., 2009). It is possible that this preserved peripheral visual function or his age when he lost vision has prevented the foveal representation in visual cortex taking on a causal role in tactile discriminations as is clearly the case in congenitally and early-onset blind individuals (Cohen et al., 1997, 1999; Sadato et al., 2002).

The finding that tactile responses in the foveal representation of S play little to no causal role in S's tactile performance on our Braille letter discrimination task offers the possibility that such cortical resources remain capable of high-resolution visual analysis even in the absence of such input from the retinogeniculate pathway (Cheung et al., 2009). It is possible therefore that S's foveal representation could revert back to processing high-resolution visual information if such retinogeniculate inputs could be restored (Fine et al., 2003) - although prior sight-restoration studies offer mixed encouragement for this possibility (Fine et al., 2003; Ostrovsky et al., 2006).

Recent work in patients with macular degeneration (Masuda et al., 2021) highlights the presence of both somatosensory and auditory related activity within the LPZ during a one-back task, but not a passive condition. Such activity in the

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to fall within the large foveal confluence of V1–V3. (C) The somatosensory [S1] target site (yellow dot) can be seen to overlap tactile responses within the hand-representation of somatosensory cortex. (D) Lines represent the mean (plus s.e.m) response within the occipital pole ROI across all tactile (blue-line) and visual (red-line) fMRI blocks in S. The OP ROI selectively responds to tactile over visual processing. (E) Bars represent the mean response within the OP ROI in S (black bar) and the average of controls (white bars). Individual data points are plotted and labelled for each control. Whereas in S, the OP ROI shows a negative response reflecting selective recruitment during tactile processing, all three controls show the opposite pattern, reflecting the expected selective recruitment during visual processing. (F) Lines represent the mean (plus s.e.m) response within the occipital pole ROI across all tactile (blue-line) and visual (red-line) fMRI blocks in each control (C1, C2, C3).



**Fig. 3 – Impact of TMS on tactile and visual performances in S and controls. (A) Examples of the Braille letters presented during both psychophysics and rTMS sessions. (B) Schematic of visual stimuli presented during both psychophysics and rTMS sessions. During S's rTMS sessions, letters were highly magnified (15 dva), white and presented on a black background (BG luminance = 0). In controls, letters were smaller (4 dva), and presented on a background luminance determined through psychophysical testing. Note, the figure indicates a BG luminance of .9 for illustrative purposes only (see [Supplementary data](#) for BG luminance thresholds in C1–C3). (C) Bars represent tactile performance (proportion correct) across conditions (noTMS, S1, OC & OP) in S (solid bars) and the average of controls (faded bars). Individual data points are plotted and linked for each control. The pattern of results is strikingly similar across S and controls. In both, performance is maximally disrupted (relative to noTMS baseline) following TMS of S1, as expected. In S, rTMS of OC caused a slight drop in performance, but crucially rTMS of OP had little to no impact on tactile performance in either S or controls. (D) Distribution represents the bootstrapped difference in performance between TMS of S1 - OP in controls (negative values represent a larger drop in performance following rTMS of S1). The red-dashed line indicates the same difference in S. Crucially, this difference falls not only within the distribution of expected differences from controls, but also towards the left-hand edge of the distribution (i.e. the maximum difference that could be expected in controls). This reflects the fact that the impact of OP stimulation in S on tactile performance is as small as could be reasonably anticipated in controls (E) Same as (D) but for S1 - noTMS baseline. Again, the result in S falls within that expected from controls. (F) Bars represent visual performance (% correct) across conditions (noTMS, S1, OC & OP) in S (solid bars) and the average of controls (faded bars). Individual data points are plotted and linked for each control. Unlike tactile performance, the pattern of results is more varied between S and controls. In both, performance is maximally disrupted (relative to noTMS baseline) following TMS of OP, but the magnitude of this disruption is larger for controls than for S. In S, rTMS of S1 caused an increase in performance, but had little to no impact in controls. (G) Distribution represents the bootstrapped difference in performance between TMS of OP - OC in controls (negative values represent a larger drop in performance following rTMS of OP). The red-dashed line indicates the same difference in S. The difference observed in S falls beyond that expected in controls. (H) Same as (G) but for OP - noTMS baseline. Again, the result in S falls outside that expected from controls.**

LPZ is considered to be mediated by task-related feedback signals, rather than feedforward visual input. The pattern of fMRI results in S could be interpreted in a similar manner, in that tactile responses within the foveal representation could reflect task-related feedback from S1 (although distinguishing feedforward from feedback signals definitively with fMRI is challenging due to the sluggishness of the fMRI response). Nevertheless, it is possible that the reduced retinal input to foveal representations in both S and patients with macular degeneration leads to an unmasking of pre-existing connections between visual and other sensory cortices that are suppressed during normal vision (Cheung et al., 2009; Masuda et al., 2021). Similarly, the somatosensory related activity within the foveal representation of S could be interpreted as reflecting altered cross-modal responses due to S' extensive experience with Braille stimuli, rather than cross-modal plasticity per se. Indeed, increased recruitment of V1 during tactile discrimination is present in Mah-Jong experts over novices, in the absence of any accompanying visual loss (Saito et al., 2006).

Importantly, only one form of tactile perception (i.e. Braille letter discrimination) was measured here, and although the pattern of rTMS results is striking, it is nevertheless possible that some other form of tactile function (e.g. texture perception, tactile acuity) might benefit from the tactile recruitment of foveal visual cortex. For example, visual cortex in the congenitally blind is recruited during language and numerical processing (Bedny et al., 2017) and TMS of visual cortex in the congenitally blind is reported to disrupt verb generation (Amedi et al., 2004). Occipital stroke in congenitally blind can also lead to deficits in Braille letter and word recognition (Hamilton et al., 2000). On the one hand, it remains possible that TMS of S's foveal representation could disrupt performance on these and other non-visual tasks, yet on the other hand, it is important to recognise that S's performance is similar to individuals with late-onset blindness (Hamilton et al., 2000), in which TMS of occipital cortex was shown to not alter tactile processing (Cohen et al., 1999). Further, the type of Braille letter discrimination employed here is different from Braille reading of entire words or sentences (Burton et al., 2002; Kim et al., 2017). It remains to be seen whether transient disruption of S's foveal representation would impact more complex Braille reading paradigms or whether, as we report here, such stimulation would be commensurate with that expected in healthy controls.

At first glance, it may appear surprising that TMS of OP during visual processing induced a much smaller decrement to performance in S than in controls. We believe however that this is accounted for by considering the size of the visual stimuli presented to S with respect to the foveal visual field representation of the targeted OP region. Placed in this context, it is not altogether surprising that rTMS of S's OP resulted in a weaker deficit than TMS of OP in controls. It is likely that were it possible to stimulate peripheral parts of V1 in S, a similar drop in performance would be observed to that of OP stimulation in controls during visual perception. Additionally, we considered whether differences in the accuracy of rTMS delivery could provide an alternative explanation for the pattern of results reported here in S, and the critical finding that rTMS of OP does not impact tactile processing, in

particular. To rule out this possibility, we analysed coil-displacement data acquired during each rTMS trial - an index of stimulation error. We found no evidence for significant variation in displacement as a function of either task or site. Thus, the lack of a detrimental impact on tactile processing following rTMS of OP in S cannot be attributed to poor precision during rTMS delivery.

Our TMS protocol delivered TMS pulses coincident with the visual/tactile stimulation and was consistent with our groups prior TMS work (McKeefry et al., 2008; Silson et al., 2013). However, prior TMS work (Bola et al., 2019) indicated an early time window (120–220 ms) for early visual cortex TMS during Braille reading in normally sighted individuals. Given that our TMS pulses were delivered at 0, 50, 100 & 150 ms post stimulus onset, it is possible that the impact of only the last two pulses (or one) on Braille letter discrimination performance were maximised. Future work could look to confirm our findings in S using a more temporally targeted approach.

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## 5. Conclusions

In summary, our study of S demonstrates that whilst the foveal representation in visual cortex responds preferentially to tactile over visual stimulation, such activity does not causally influence tactile processing performance. Although prior work interpreted S's responses in the foveal representation as reflecting an optimal redistribution of cortical resources (Cheung et al., 2009), our data suggests this pattern likely reflects the unmasking of latent connections between visual and somatosensory cortex that are normally suppressed by the feedforward visual input provided to foveal cortex of normally sighted individuals (Masuda et al., 2021). We add weight to the view that cortical responses in individuals with visual deficits that differ from those obtained from controls are not always a signature of functional reorganisation (Wandell & Smirnakis, 2009; Morland, 2015).

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## Contribution statement

Antony Morland & Gordon Legge: Conceptualization. Andre Gouws, Antony Morland & Edward Silson: Data curation, Writing - Original draft preparation. Edward Silson, Andre Gouws, Antony Morland & Gordon Legge: Writing - Reviewing and Editing.

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## Data availability

Data will be made available on request.

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'S' is author G.E.L. Note, no part of the study procedures or analyses was pre-registered prior to the research being conducted. Behavioural data can be accessed via the Open Science Framework page for this project <https://dx.doi.org/10.17605/OSF.IO/N87F6>.

## Supplementary data

Supplementary data to this article can be found online at <https://doi.org/10.1016/j.cortex.2022.07.012>.

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