5,196 females in snap trapping studies about 2 km fro the CMR grid); \( s_1 \) is the survival rate from newly born to sub-adults, assumed to take place in one month and assumed to be 0.5; \( s_2 (P) \) is the monthly survival rate of sub-adults; \( \phi_2(P) \) is the maturation rate from sub-adult to adult; and \( s_3 (P) \) is the monthly survival rate of adults; \( P \) and \( N \) refer to the precipitation and density categories, respectively. We implemented the model in Stella II (High Performance Systems; Hanover, NH) using one-month time steps. Predictions (adults, sub-adults and half of the juveniles) from the population dynamics model were compared with estimates obtained in another CMR study, at the same site, between March 1994 and November 1996 (8,796 captures of 3,331 individuals), using the actual rainfall data for this period (Fig. 1b). Other simulation runs used either stochastic monthly rainfall values (bootstrapped for each particular month among the observed values for that month in 1981–1995) or non-stochastic seasonal rainfall (mean monthly rainfall values for 1981–1995; no variation among years). We investigated the forecast of the density-dependent function in the mathematical model by changing the slope, in 200 steps, of the linearly decreasing segment of the density-dependent function. We changed the slope by \( 1^\circ \) decreasing the interval between the lower- and higher-density cutoffs between which density dependence is linear, or \( 2^\circ \) increasing the higher, respectively decreasing the lower, demographic parameter estimates by adding or subtracting from 0 to 3 standard errors. In the latter case, we constrained variation so that parameter values never became negative and survival and maturation rates never became larger than 1. The model was run for 1,000 cycles at each slope and the values obtained during the last 50 cycles were plotted, resulting in numerical analogues of bifurcation diagrams.

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**Functional relevance of cross-modal plasticity in blind humans**

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Functional imaging studies of people who were blind from an early age have shown that their primary visual cortex can be activated by Braille reading and other tactile discrimination tasks. Other studies have also shown that visual cortical areas can be activated by somatosensory input in blind subjects but not those with sight. The significance of this cross-modal plasticity is unclear, however, as it is not known whether the visual cortex can process somatosensory information in a functionally relevant way. To address this issue, we used transcranial magnetic stimulation to disrupt the function of different cortical areas in people who were blind from an early age as they identified Braille or embossed Roman letters. Transient stimulation of the occipital (visual) cortex induced errors in both tasks and distorted the tactile perceptions of the blind subjects. In contrast, occipital stimulation had no effect on tactile performance in normal-sighted subjects, whereas similar stimulation is known to disrupt their visual performance. We conclude that blindness from an early age can cause the visual cortex to be recruited to a role in somatosensory processing. We propose that this cross-modal plasticity may account in part for the superior tactile perceptual abilities of blind subjects.

Invasive10 and non-invasive11–15 cortical stimulation can transiently disrupt specific cognitive functions, such as naming objects. Trains of stimuli are more effective than single stimuli in inducing these effects11–15. Task disruption by focal stimulation has been interpreted as a sign that the stimulated region is functionally important for performance. When applied to occipital regions in subjects with normal sight, transcranial magnetic stimulation (TMS) can transiently suppress visual perception of letters and extrafoveal targets16, an effect thought to occur by interference with visual calcineur17 and association cortical areas at depths of 1.5–2.25 cm below the scalp surface. We have applied TMS to different scalp locations (Fig. 1a) to interfere with the function of different cortical areas during tactile identification of Braille letters and...
embossed Roman letters in early-blind subjects (EBR, EBs) and of embossed Roman letters in sighted volunteers (SVRs).

Five early-blind subjects who are experienced Braille readers (Table 1) were given strings of 'grade I' non-contracted, non-word Braille letters to read, and five sighted volunteers and four of the early-blind subjects were given a tactile discrimination task requiring identification of embossed Roman letters. Letters were presented with a specially designed device in a window of 6.4 x 1.9 cm (Fig. 1b). Subjects were asked to identify and read aloud letter by letter as quickly and accurately as possible. Phonographic recordings of voice and electromyographic recordings from hand muscles involved in the reading task were monitored (Fig. 1c). Overall accuracy in reading performance before TMS was 94 ± 4.6% for the EBs group, 95.0 ± 3.0% for EBR group, and 95.5 ± 2.0% for the SVRs group (Wilcoxon tests, non-significant).

In the EBR and SVRs groups there was a significant effect of stimulated scalp position on the error rate (P = 0.001). In the EBR group, mid-occipital stimulation induced more errors than the control condition (stimulation in the air) (P = 0.001, odds ratio (OR) = 2.95, confidence interval (CI) = (1.96, 4.45) (Fig. 2). In addition, stimulation of occipital positions occasionally elicited distorted somatosensory perceptions. Blind subjects reported a combination of negative ("missing dots", "dots felt faded"), positive ("phantom dots", "extra dots"), and confusing sensations ("dots don't make sense"). When comparing error rates in the EBR and SVRs groups (blind and sighted subjects performing the same task) a logistic regression analysis showed a significant effect of group (OR = 3.55, CI = (2.17, 5.74)) and position (OR = 2.38, CI = (1.63, 3.47)) (Fig. 2). In the EBR group, as with the EBs group, midoccipital stimulation induced more errors than control (stimulation in the air) (P ≤ 0.001, OR = 3.41, CI = (1.57, 7.40)). These findings support the view that the occipital cortex is functionally active despite decades of visual deafferentation20,21, and is engaged in active and meaningful processing of tactile information related but not limited to Braille reading. The results of a similar Braille-reading protocol implemented by a different subset of investigators on a different group of early-blind subjects (UVs) overall accuracy level pre-intervention, 95.4 ± 1.85%) (Table 1) also showed a significant effect of stimulated scalp position on the error rate (OR = 0.89, CI = (0.84, 0.95)). Stimulation of mid-occipital (P = 0.001, OR = 2.49, CI = (1.77, 3.51)) and contralateral occipital (P ≤ 0.001, OR = 1.84, CI = (1.30, 2.62)) positions induced more errors than the control condition (Fig. 2). The UVs group had higher error rates overall and a higher proportion of errors with stimulation of lateral occipital positions than the EBR group. These differences are probably related to the higher stimulus intensities used in the UVs group (see Methods).

Sensory processing for touch and vision seem to be segregated up to their arrival in primary reception areas (Brodmann areas 3, 1 and 2 for touch and 17 for vision). The early convergence of visual and

Table 1 Clinical characteristics of the early blind subjects

<table>
<thead>
<tr>
<th>Subject</th>
<th>Age (years)</th>
<th>Sex</th>
<th>Age of blindness</th>
<th>Cause of blindness*</th>
<th>Age of Braille reading (years)</th>
<th>Years of reading Braille</th>
<th>Visual perception</th>
<th>Daily reading (h)</th>
<th>Reading hand</th>
<th>Preferred hand</th>
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</tr>
<tr>
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<td>M</td>
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<td>39</td>
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<td>2</td>
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<td>Left</td>
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<tr>
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<td>M</td>
<td>birth</td>
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<td>29</td>
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<td>4</td>
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<td>Right</td>
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<td>63</td>
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<tr>
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<td>47</td>
<td>F</td>
<td>birth</td>
<td>Premat. retinitis</td>
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<td>41</td>
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<td>Traumatic</td>
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* Premat., premature; congen., congenital.

Figure 1 a, Schematic representation of the top of the head showing the scalp positions stimulated. The magnetic coil is shown positioned over the mid-occipital position. S-M, sensorimotor cortex; contra, contralateral; ipsi, ipsilateral. b, The index finger resting on a finger station. As the subject positioned the finger to read the first letter, the finger crossed a laser beam, triggering a 3-s period of TMS. c, Electromyographic activity from the first dorsal interosseous (FDI), which is a muscle active in tactile exploration required for the reading task, and bioeps brachii (recorded for safety monitoring purposes), and phonographic recordings indicating the latency of letter identification (N, A, V, W and J). The reading task was completed approximately 3 s after the onset of stimulation (in this example, to the mid-occipital region of a blind subject; arrow in FDI channel). The circled letters, W and J., were read incorrectly.
evoked potentials in the SV_R and 12.40 ± 3.38 in the EB_R groups) did not induce sensations of missing or extra dots in any of the subjects tested.

In the SV_R group, there was a significant effect of stimulated scalp position on the error rate. Stimulation of the occipital cortex did not affect identification of embossed Roman letters or induce abnormal somatosensory perceptions. This result, in combination with the decrease of occipital activity on positron emission tomography in subjects performing a similar task, suggests that sighted individuals do not normally use the occipital cortex for identification of embossed Roman letters as the blind do for Braille and Roman letter reading. Stimulation of the contralateral sensorimotor cortex induced more errors than in the control condition ($P \leq 0.001$, OR = 2.95, CI = (1.95, 4.48)). Because the ability to interfere with a task is likely to depend on how well learned the task is, the hand movements induced by stimulation of the contralateral sensorimotor cortex may have exerted a more disruptive effect in the less-trained sighted readers than in the highly trained blind readers. Alternatively, sighted subjects may have spent more time than blind subjects in somatosensory processing, making the task more susceptible to disruption by TMS over the contralateral sensorimotor cortex.

The finding that the occipital cortex is an important component of the network involved in Braille reading supports the idea that perceptions are dynamically determined by the characteristics of the sensory inputs rather than only by the brain region that receives those inputs, at least in the case of early blindness. These results show that cross-modal plasticity as identified electrophysiologically or by neuroimaging techniques in humans may be involved in functional compensation.

**Methods**

**Subjects.** Study protocols were approved by the Institutional Review Boards of the National Institute of Neurological Disorders and Stroke and the University of Valencia, and TMS was used under a US Food and Drug Administration investigational device exemption. Subjects gave their written informed consent for the study. Blind subjects had normal brain magnetic resonance images and no progressive neurological disease. Sighted volunteers had normal neurological examinations and visual acuity better than 20/40.

**Stimulation technique.** Each train of TMS was triggered by the reading finger crossing a laser beam (Fig. 1b) and had a fixed frequency of 10 Hz and a duration of 3 s. TMS was delivered with a magnetoelectric stimulator (Cadwell Laboratories, Kennewick, WA) and an 8-shaped23 water-cooled coil, each loop of which was 7 cm in diameter. The coil was held tangentially to the scalp with the intersection of both loops oriented sagittally. The stimulus intensity was delivered randomly to three occipital positions (midline, contralateral and ipsilateral) to the reading finger, overlying Brodmann areas 17, 18 and 19; Oz, P3 and P4), a midfrontal position (Fz) and to the primary sensorimotor area (overlying Brodmann areas 4, 3, 1 and 2)24. As a control condition, TMS was also delivered into the air (the sound of the stimulator was as loud as in actual brain stimulation, but no stimulation
reached the brain). In the sighted volunteers (SVR, mean age 51.0 ± 11.5 years, 4 right handed and 1 ambidextrous) and in the blind group reading Roman letters (EBB) TMS was delivered randomly to midline occipital (O2), contralateral parietal (P3 or P4), contralateral sensorimotor, and midfrontal (F2) positions, and into the air. In both blind and sighted groups, reading was also done in the absence of TMS.

**Reading.** Five blind subjects identified 25 Braille letters (out of 26 possible options) presented in 5 strings of 5 letters each for each scalp position stimulated. All sighted volunteers and 4 of the blind subjects identified 24 single Roman letters (out of 5 possible options) presented in 8 strings of 3 letters each for each scalp position stimulated. The question we addressed was whether the occipital activation associated with Braille reading is functionally relevant for task performance. Therefore, we included the control task in which both sighted volunteers and blind subjects identified embossed Roman letters, a task also involving form recognition of known objects. Because very few sighted subjects read Braille, a full assessment of these use visual and somatosensory input when learning Braille (an experience shared by other investigators40,41), we could not study sighted volunteers identifying Braille letters. To ensure a similar overall prestimulation accuracy level in both groups, the blind (EBB) subjects were presented with a higher number of possible letters to choose from (26 letters) than the sighted (SVR) subjects (5 letters). The reason for using strings of 3 letters in the sighted and 5 letters in the blind was that sighted subjects read at a slower rate than blind subjects. In unstimulated trials, the EBB group identified letters 1–5 in 1.0 ± 0.4, 1.6 ± 0.4, 2.1 ± 0.5, 2.7 ± 0.5 and 3.2 ± 0.6 s after reading began; the SVR group identified letters 1–3 in 1.0 ± 0.2, 2.1 ± 0.3 and 3.1 ± 0.3 s; and the EBB group in 0.9 ± 0.0, 1.7 ± 0.2 and 2.6 ± 0.3 s. There were no significant differences in the number of letters read in trials with and without TMS (Table 2). Therefore the 3 s of TMS covered most of the reading time in the three groups. To keep the total number of TMS trains the same in the EBB, EBR and SVR groups, subjects reading Roman letters were stimulated more times (8 as opposed to 5 for Braille letters at each scalp position) over fewer positions. The order of string presentations and stimulated positions were randomized across subjects. A.P.L. and M.D.C., who did not participate in testing the EB groups, used a similar protocol to study a different group of 5 early blind subjects (UVg, Table 1). This study differed from that in the EB groups in that: TMS trains lasted for 5 instead of 3 s, and the intensity was 20% above motor threshold instead of 10%; contralateral sensorimotor positions were not stimulated; and there were no trials without TMS. The parameters used in the UVg group (10 Hz, 20% above motor threshold, 5 s duration) are close to those now known to reach the brain). In the sighted volunteers (SVR, mean age 51

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**Defective platelet activation in Goαq-deficient mice**

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Platelets are small disc-shaped cell fragments which undergo a rapid transformation when they encounter vascular damage. They become more spherical and extrude pseudopodia, their fibrinogen receptors are activated, causing them to aggregate, they release their granule contents, and eventually form a plug which is responsible for primary haemostasis¹. Activation of platelets is also implicated in the pathogenesis of unstable angina, myocardial infarction and stroke²,³. Here we show that platelets from mice deficient in the α-subunit of the heterotrimeric guanine-nucleotide-binding protein Goα are unresponsive to a variety of physiological platelet activators. As a result, Goα-deficient mice have increased bleeding times and are protected from collagen and adrenaline-induced thromboembolism. We conclude that Goα is essential for the signalling processes used by different platelet activators and that it cannot be replaced by Goq or the β2 subunits of the heterotrimeric G proteins. Goq may thus be a new target for drugs designed to block the activation of platelets.

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