Visual experience shapes functional connectivity between occipital and non-visual networks

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Abstract

Comparisons of visual cortex function across blind and sighted adults reveals effects of experience on human brain function. Since almost all research has been done with adults, little is known about the developmental origins of plasticity. We compared resting state functional connectivity of visual cortices of blind adults (n = 30), blindfolded sighted adults (n = 50) to a large cohort of sighted infants (Developing Human Connectome Project, n = 475). Visual cortices of sighted adults show stronger coupling with non-visual sensory-motor networks (auditory, somatosensory/motor), than with higher-cognitive prefrontal cortices (PFC). In contrast, visual cortices of blind adults show stronger coupling with higher-cognitive PFC than with nonvisual sensory-motor networks. Are infant visual cortices functionally like those of sighted adults? Alternatively, do infants start like blind adults, with vision required to set up the sighted adult pattern? Remarkably, we find that, in infants, secondary visual cortices are more like those of blind adults: stronger coupling with PFC than with nonvisual sensory-motor networks, suggesting that visual experience establishes elements of the sighted-adult long-range connectivity. Infant primary visual cortices are in-between blind and sighted adults i.e., equal PFC and sensory-motor connectivity. The lateralization of occipital-to-frontal connectivity in infants resembles the sighted adults, consistent with reorganization by blindness. These results reveal instructive effects of vision and reorganizing effects of blindness on functional connectivity.

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Introduction

Relative to sighted adults, visual cortices of adults born blind show enhanced responses during non-visual tasks, such as reading braille and localizing sounds as well as distinctive patterns of long-range functional connectivity with non-visual networks (Abboud & Cohen, 2019; Bedny et al., 2011; Burton et al., 2012, 2014; Butt et al., 2013; Collignon et al., 2011; Deen et al., 2015; Kanjlia et al., 2016, 2021; Lane et al., 2015; Liu et al., 2007; Sadato et al., 1996; Striem-Amit et al., 2015; Watkins et al., 2012). Since almost all research thus far has been done with adults, a key outstanding question concerns the developmental origins of these experience-based differences.

One possibility is that at birth, infant visual cortices start out in the 'prepared' sighted adult state and blindness leads to functional reorganization. Alternatively, infant visual cortices may start out functionally similar to those of blind adults and lifetime visual experience establishes the sighted adult pattern. To distinguish between these possibilities, we compare the function of visual cortices across blind adults, sighted adults and a large cohort of 2-week-old sighted infants (Developing Human Connectome Project, dHCP, n = 475). We examined functional connectivity using resting state data, which provide a common measure of cortical function across these diverse populations.

To our knowledge no prior studies have compared infants to multiple populations of adults with different sensory experiences. Previous studies comparing sighted infants to sighted adults have largely reported similarity across groups (Barttfeld et al., 2018; Doria et al., 2010; Fransson et al., 2009; Gao et al., 2009; Liu et al., 2008; Zhang et al., 2019). However, these studies focused on whether large scale functional networks are present in infancy e.g., stronger connectivity of regions within the visual network, than between visual and auditory regions. Studies comparing blind and sighted adults find differences across groups in which non-visual networks are most strongly coupled with the visual system i.e., visual cortices of sighted adults show stronger coupling with non-visual sensory-motor networks (i.e., auditory, somatosensory/motor) than higher-cognitive systems; by contrast, in blind adults, visual cortex coupling is stronger with higher-cognitive prefrontal cortices (PFC) than with non-visual sensory-motor networks (Abboud & Cohen, 2019; Bedny et al., 2011; Burton et al., 2014; Deen et al., 2015; Kanjlia et al., 2021; Liu et al., 2007; Qin et al., 2013; Striem-Amit et al., 2015; Watkins et al., 2012; Yu et al., 2008). In the current study, we compare this experience-sensitive functional signature across infants, sighted and blind adults.

We measured the connectivity profile of four occipital 'visual' areas that show cross-modal plasticity in blindness, i.e., respond to non-visual tasks in blind people: Three secondary visual areas (located in lateral, dorsal and parts of the ventral occipital cortex) and the primary visual cortex (V1).

The three secondary visual areas have been found to respond to different non-visual tasks in blind people: language tasks, numerical reasoning tasks and executive control tasks respectively. Enhanced coupling with PFC in blindness is observed across all of three occipital regions. However, in blind people each region shows preferential coupling with distinct subregions of PFC with analogous functional profiles (e.g., language responsive occipital areas are more coupled with language responsive PFC) (Kanjlia et al., 2016, 2021; Lane et al., 2015). The precise visual functions of these secondary visual regions in sighted people are not known. Anatomically, these regions correspond roughly to the location of areas such as motion area V5/MT+, the lateral occipital complex (LO), V3a and V4v in sighted people (Tootell et al., 1997; Van Essen et al., 2001).

We also examined connectivity of anatomically defined primary visual cortex (V1), which likewise shows altered task-based responses and functional connectivity in congenitally blind adults (Amedi et al., 2003; Bedny et al., 2011; Burton et al., 2014; Butt et al., 2013; Lane et al.,

2015; Raz et al., 2005; Sadato et al., 1996; Striem-Amit et al., 2015; Yu et al., 2008). Since many previous studies have found that blindness alters the balance of connectivity between visual cortex and higher-order prefrontal as opposed to sensory-motor regions, this was our primary outcome measure. We also examined changes in connectivity lateralization – i.e., the balance of between vs. within hemisphere connectivity.

To preview the results, we find that, in infants, the long-range functional connectivity profile of secondary visual areas resembles that of blind adults, whereas V1 falls between blind and sighted adult populations. Relative to sighted adults, both blind adults and infants show stronger coupling between visual cortices and PFC and weaker coupling between visual cortices and non-visual sensory-motor networks. This suggests that vision plays an instructive role in setting up the balance of connectivity between occipital cortex and non-visual networks. In contrast, connectivity lateralization patterns appear to reflect blindness-related reorganization.

Results

Connectivity profile of secondary visual cortices in sighted infants is more similar to that of blind than sighted adults

We first examined the long-range functional connectivity of (three) secondary visual areas with sensory-motor areas on the one hand, and higher-order PFC networks on the other. In sighted adults, all three secondary visual areas showed stronger functional connectivity with non-visual sensory-motor areas (primary somatosensory and motor cortex, S1/M1, and primary auditory cortex, A1) than with higher-cognitive prefrontal cortices (PFC). By contrast, in blind adults, all secondary visual regions showed stronger functional connectivity with PFC than with non-visual sensory-motor areas (S1/M1 and A1) (group (sighted adults, blind adults) by ROI (PFC, non-visual sensory) interaction effect: $F_{(1,\ 78)} = 148.819$, $p < 0.001$; post-hoc Bonferroni-corrected paired *t*-test, sighted adults: non-visual sensory > PFC: $t_{(49)} = 9.722$, $p < 0.001$; blind adults: non-visual sensory < PFC: $t_{(29)} = 8.852$, $p < 0.001$; Fig. 1).

Like in blind adults, in sighted infants, secondary visual areas showed higher connectivity to PFC than to non-visual sensory-motor areas (S1/M1 and A1) (non-visual sensory < PFC paired *t*-test, $t_{(474)} = 20.144$, $p < 0.001$) (Fig. 1). The connectivity matrix of sighted infants was more correlated with that of blind than sighted adults, but strongly correlated with both adult groups (secondary visual, PFC and non-visual sensory areas: sighted infants correlated to blind adults:

$r = 0.721$, $p < 0.001$; to sighted adults: $r = 0.524$, $p < 0.001$; difference between correlations of infants to blind vs. to sighted adults: z = 3.77, $p < 0.001$; see Supplementary Figure S1 for the connectivity matrices).

These results suggests that vision is required to set up elements of the sighted adult functional connectivity pattern, i.e., vision enhances occipital cortex connectivity to non-visual sensory-motor networks and dampens connectivity to higher-cognitive prefrontal networks.

We checked the robustness of these results in a number of ways. We first compared the effects across the three secondary visual regions and observed the same pattern across all. (Supplementary results and Supplementary Figure S2). Next, to check the robustness of the findings in infants we randomly split the infant dataset into two halves and did split-half cross-validation. Across all comparisons the results of the two halves were highly similar, suggesting the effects are robust (see Supplementary Figure S3 and S4). We performed this validation procedure for all analyses reported below with similar results.

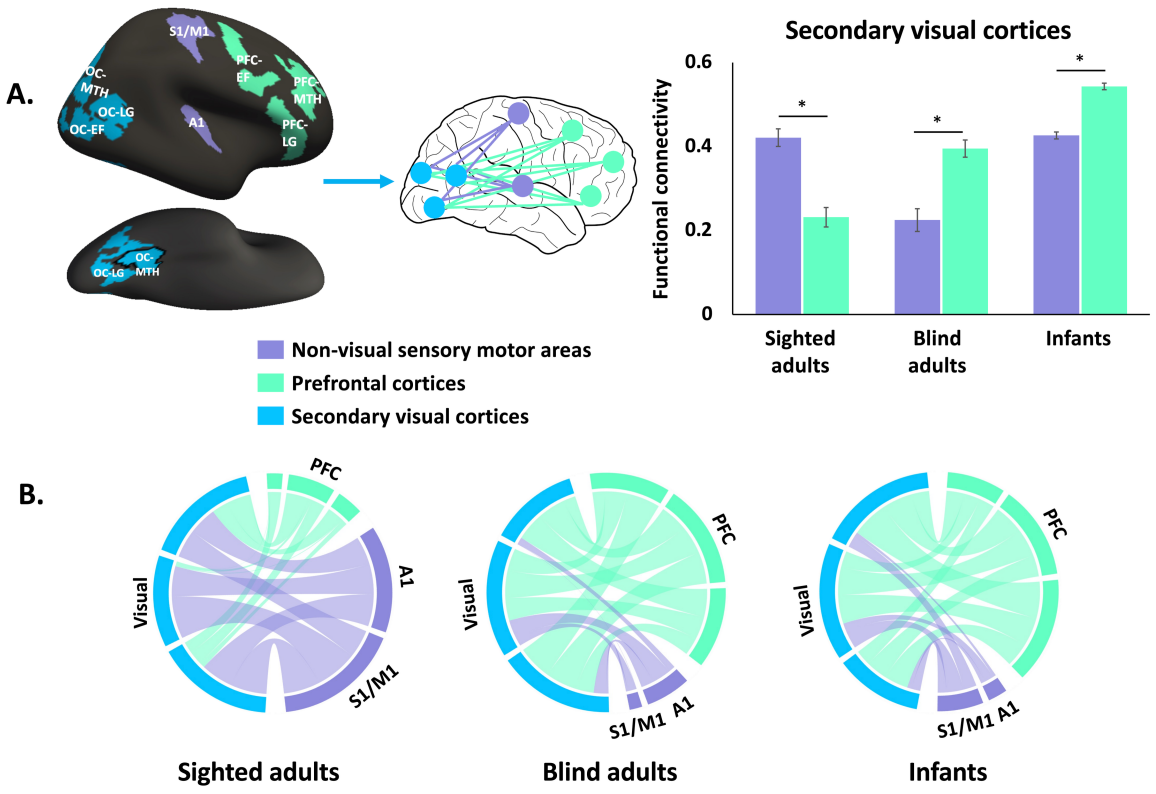


Figure 1 Functional connectivity of secondary visual cortices. (A) Bar graph shows functional connectivity (r) of secondary visual cortices (blue) to non-visual sensory motor areas (purple) and prefrontal cortices (green), averaged across occipital, PFC and sensory-motor ROIs (A1 and S1/M1) in sighted adults, blind adults and sighted infants. Regions of interest (ROI) displayed on the left. Note that regions extend to ventral surface, not shown.

See Supplementary Figure S5 for the full views of three occipital ROIs. **(B)** Circle plots represent the connectivity of secondary visual cortices to non-visual networks, min-max normalized to [0,1], i.e., as a proportion. OC: occipital cortices; MTH: math-responsive region; LG: language-responsive region; EF: executive function-responsive (response-conflict) region. Asterisks (*) denote significant Bonferroni-corrected pairwise comparisons ($p < .05$).

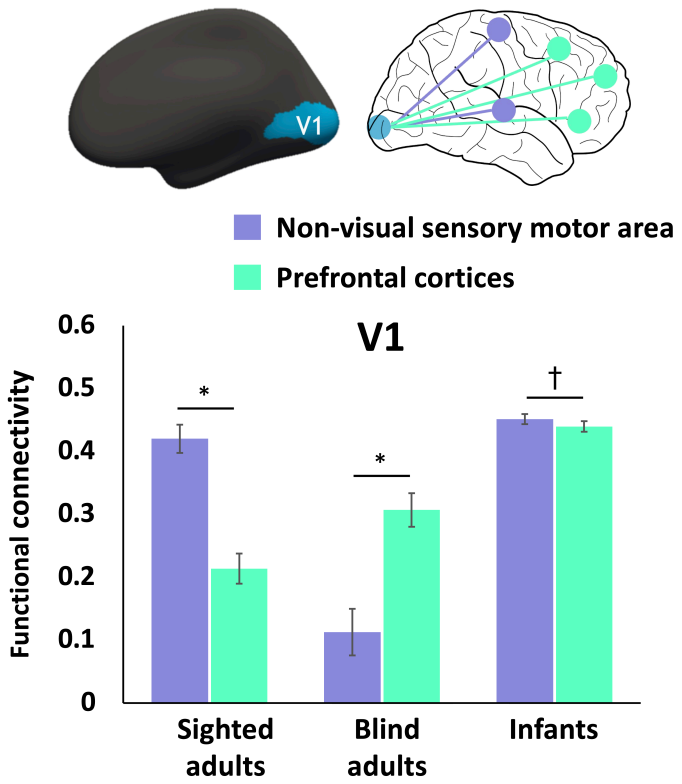
The connectivity pattern of V1 is influenced by early visual experience and blindness

V1 showed the same dissociation between sighted and blind adults as secondary visual areas: in sighted adults, V1 has stronger functional connectivity with non-visual sensory-motor areas than with PFC. By contrast, in blind adults, V1 shows stronger connectivity with PFC than with non-visual sensory areas (group (sighted adults, blind adults) by ROI (PFC, non-visual sensory) interaction: $F_{(1, 78)} = 125.775$, $p < 0.001$; post-hoc Bonferroni-corrected paired *t*-test, sighted adults non-visual sensory > PFC: $t_{(49)} = 9.404$, $p < 0.001$; blind adults non-visual sensory < PFC: $t_{(29)} = 7.128$, $p < 0.001$; Fig. 2).

The pattern for sighted infants in V1 fell between that of sighted and blind adults. The connectivity matrix of sighted infants (V1, PFC, and non-visual sensory) was equally correlated with blind and sighted adults (infants correlated to blind adults: $r = 0.654$, $p < 0.001$; to sighted adults: $r = 0.594$, $p < 0.001$; correlation of infants with blind vs. with sighted adults: $z = 0.832$, $p = 0.406$; see Supplementary Figure S1 for the connectivity matrices). The difference in connectivity strength between V1 to PFC and V1 to non-visual sensory regions was weaker in sighted infants than in sighted or blind adults (group (sighted adults, infants) by ROI (PFC, non-visual sensory) interaction effect: $F_{(1, 523)} = 92.21$, $p < 0.001$; group (blind adults, infants) by ROI (PFC, non-visual sensory) interaction effect: $F_{(1, 503)} = 57.444$, $p < 0.001$). V1 of sighted infants showed marginally stronger connectivity to non-visual sensory regions (S1/M1 and A1) than PFC (non-visual sensory regions > PFC, paired *t*-test, $t_{(474)} = 1.95$, $p = 0.052$; Fig.2).

The dHCP cohort included both full-term neonates and preterm infants, scanned at their equivalent gestational age. Visual exposure therefore varied somewhat in duration across infants (from 0 to 19.71 weeks), with slightly longer exposure in preterm babies. This variation did not affect connectivity patterns either in V1 or secondary visual cortices (V1: $r = 0.06$, $p = 0.192$; secondary visual: $r = 0.004$, $p = 0.923$; see Supplementary Figure S6). We also compared the connectivity patterns of preterm ($n = 90$) and full-term infants ($n = 385$) and

171 found no difference from each other or from the all-infant dataset (see Supplementary Figure
172 S7). A few weeks of vision after birth is therefore insufficient to influence connectivity.



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174 **Figure 2 Functional connectivity of primary visual cortices (V1).** Regions of interest
175 (ROI) displayed on the upper. Bar graph shows functional connectivity (*r*) of V1 to non-
176 visual sensory motor areas (purple) and prefrontal cortices (green), averaged across three
177 PFC ROIs and sensory-motor ROIs (S1/M1 and A1). Asterisks (*) denote significant
178 Bonferroni-corrected pairwise comparisons ($p < .05$). Cross (†) denote marginal difference in
179 Bonferroni-corrected pairwise comparisons ($0.05 < p < 0.1$).

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181 Evidence for blindness-related reorganization in laterality of 182 occipito-frontal connectivity

183 Compared to sighted adults, blind adults exhibit a stronger dominance of within-hemisphere
184 connectivity over between-hemisphere connectivity. That is, in people born blind, left visual
185 networks are more strongly connected to left PFC, whereas right visual networks are more
186 strongly connected to right PFC. By contrast, in sighted adults, this cross-hemisphere
187 difference is weak or absent. This difference between adult groups is observed for both V1 and
188 secondary visual cortices (group (blind adults, sighted adults) by lateralization (within

hemisphere, between hemisphere) interaction in secondary visual cortices: $F_{(1, 78)} = 131.51$, $p < 0.001$). Secondary visual cortices showed a significant within > between difference in both groups, with a lager effect in the blind group (post-hoc tests, Bonferroni-corrected paired: *t*-test: sighted adults within hemisphere > between hemisphere: $t_{(49)} = 7.441$, $p = 0.012$; blind adults within hemisphere > between hemisphere: $t_{(29)} = 10.735$, $p < 0.001$; V1: $F_{(1, 78)} = 87.211$, $p < 0.001$). In V1, only the blind group showed a significant within > between hemisphere effect (post-hoc Bonferroni-corrected paired: *t*-test: sighted adults within hemisphere < between hemisphere: $t_{(49)} = 3.251$, $p = 0.101$; blind adults within hemisphere > between hemisphere: $t_{(29)} = 7.019$, $p < 0.001$).

With respect to laterality, infants resembled sighted more than blind adults (Fig. 3). For secondary visual cortices, there was a significant difference between blind adults and sighted infants and no difference between sighted adults and sighted infants (group (blind adults, infants) by lateralization (within hemisphere, between hemisphere) interaction effect: $F_{(1, 503)} = 303.04$, $p < 0.001$); (group (sighted adults, infants) by lateralization (within hemisphere, between hemisphere) interaction effect: $F_{(1, 523)} = 2.244$, $p = 0.135$). A similar group by laterality interaction were observed for V1 (group (blind adults, infants) by lateralization (within hemisphere, between hemisphere) interaction: $F_{(1, 503)} = 123.608$, $p < 0.001$; group (sighted adults, infants) by lateralization (within hemisphere, between hemisphere) interaction effect: $F_{(1, 523)} = 2.827$, $p = 0.093$). This suggests that the enhancement of within over between hemisphere long-range connectivity is related to blindness-driven reorganization.

Task-based fMRI studies find that cross-modal responses in occipital cortex colateralize with fronto-parietal networks with related functions (e.g., language, response selection) (Kanjlia et al., 2021; Lane et al., 2017). For example, language-responsive occipital areas collateralize with language responsive prefrontal areas across individuals (Lane et al., 2017). Recruitment of visual cortices by cross-modal tasks (e.g., spoken language) may enhance within-hemisphere connectivity in people born blind (Kanjlia et al., 2021; Lane et al., 2017; Tian et al., 2022). Together, this evidence supports the hypothesis that, starting from the less lateralized infant state, blindness increases lateralization of occipital long-range connectivity.

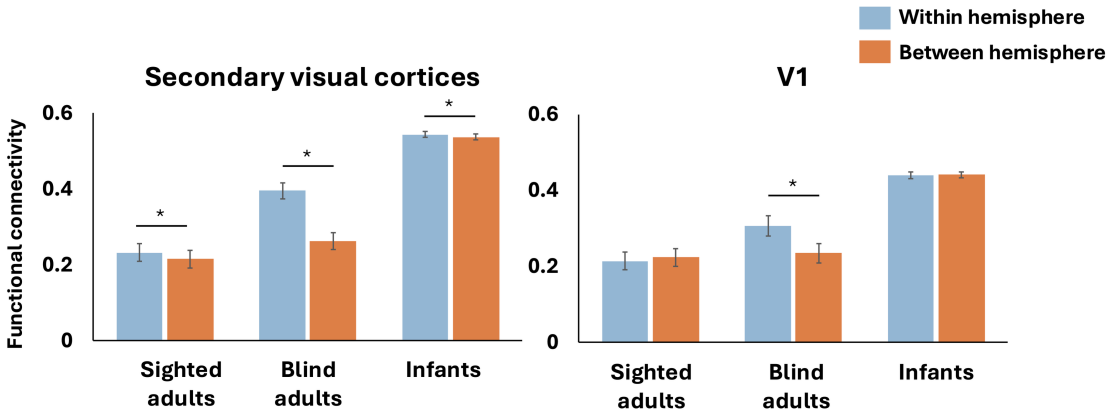

Figure 3 Within hemisphere vs. between hemisphere functional connectivity. Bar graph shows within hemisphere (blue) and between hemisphere (orange) functional connectivity (r coefficient of resting state correlations) of secondary visual (left) and V1 (right) to prefrontal cortices in sighted adults, blind adults, and sighted infants. Blind adults show a larger difference than any of the other groups. Asterisks (*) denote significant Bonferroni-corrected pairwise comparisons ($p < .05$).

Specialization of connectivity across different fronto-occipital networks: present in adults, absent at birth

In blind adults, different occipital areas show enhanced connectivity patterns with distinct subregions of PFC and this specialization is aligned with the functional specialization observed in task-based data (Bedny et al., 2011; Kanjlia et al., 2016, 2021). For example, language-responsive subregions of occipital cortex show strongest functional connectivity with language-responsive sub-regions of PFC, whereas math-responsive occipital areas show stronger connectivity with math-responsive PFC. This pattern is most pronounced in blind people but can be seen weakly even in sighted participants (Fig. 4) (Bedny et al., 2011; Kanjlia et al., 2016, 2021; Lane et al., 2015). Is this fronto-occipital connectivity specialization present in infancy, potentially enabling the task-based cross-modal specialization?

We compared connectivity preferences across three prefrontal and three occipital regions previous shown to activate preferentially in language (sentences > math), math (math > sentences) and response-conflict (no-go > go with tones) (Kanjlia et al., 2016, 2021; Lane et al., 2015). For ease of viewing, Fig. 4 shows results from two of the three regions, math and language. See Supplementary Figure S8 for all three regions. Note that the statistical analyses included all three areas.

Contrary to the hypothesis that specialization of functional connectivity across different prefrontal/occipital areas is present from birth, sighted infants showed a less differentiated fronto-occipital connectivity pattern relative to both blind and sighted adults (Group (sighted adults, blind adults, sighted infants) by occipital regions (math, language, response-conflict) by PFC regions (math, language, response-conflict) interaction $F_{(8,\ 2208)} = 16.323$, $p < 0.001$). Unlike in adults, in infants, all the occipital regions showed stronger correlations with math- and response-conflict related prefrontal areas than language-responsive prefrontal areas (Fig. 4 and Supplementary Figure S8). However, the preferential correlation with math responsive PFC was strongest in those occipital areas that go on to develop math responses in blind adults (occipital regions (math, language, response-conflict) by PFC regions (math, language, response-conflict) interaction in infants $F_{(4,\ 1896)} = 85.145$, $p < 0.001$, post-hoc Bonferroni-corrected paired *t*-test see Supplementary Table 1).

Note that findings of reduced regional specialization in infants need to be interpreted with caution. First, we do not know whether the same specialization of prefrontal sub-regions seen in adults is present in infants, although, prior evidence suggests some prefrontal specialization is already present (Raz & Saxe, 2020). Second, the more fine-grained comparisons across occipital/frontal regions are more vulnerable to potential anatomical alignment issues between adult and infant brains. In other words, lack of specialization in infants could reflect the different location of the areas in this population.

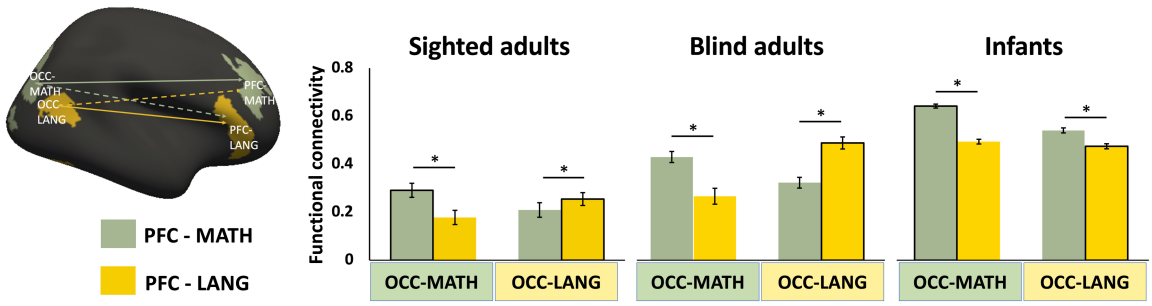

Figure 4 Occipito-frontal functional connectivity. Bar graph shows across functional connectivity of different sub-regions of prefrontal (PFC) and occipital cortex (OCC) in sighted adults, blind adults, and sighted infants. Sub-regions (regions of interest) were defined based on task-based responses in a separate dataset of sighted (frontal) and blind (frontal and occipital) adults (Kanjlia et al., 2016, 2021; Lane et al., 2015). PFC/OCC-MATH: math-responsive regions were more active when solving math equations than comprehending sentences. PFC/OC-LANG: language-responsive regions were more active when comprehending sentences than solving math equations (Kanjlia et al., 2016, 2021; Lane et al., 2015). In blind adults these regions show biases in connectivity related to their function i.e., language-responsive PFC is more correlated with language responsive OCC. No such pattern is observed in infants. Asterisks (*) denote significant Bonferroni-corrected pairwise comparisons ($p < .05$). See Supplementary Figure S9 for connectivity matrix.

Discussion

The present results provide insight into the developmental process of experience-based functional specialization in human cortex. We find independent effects of visual experience and blindness on the development of visual networks. Aspects of the sighted adult connectivity pattern require visual experience to become established. This is particularly striking for secondary visual cortices, where, connectivity with nonvisual networks in sighted infants resemble blind more than sighted adults. Both in infants and blind adults, secondary occipital areas showed stronger functional connectivity with higher-order prefrontal cortices than with other sensory-motor networks (S1/M1, A1). Consistent with this observation, one previous study with a small sample of infants found strong connectivity between lateral occipital and prefrontal areas, although there was no comparison to blind adults in that study (Barttfeld et al., 2018). In V1, infants fell somewhere in between sighted and blind adults, suggesting an effect both of vision and of blindness on functional connectivity.

The present results reveal the effects of experience on development of functional connectivity between infancy and adulthood, but do not speak to the precise time course of these effects. Infants in the current sample had between 0 and 20 weeks of visual experience. Comparisons across these infants suggests that several weeks of postnatal visual experience is insufficient to produce a sighted-adult connectivity profile. The time course of development could be anywhere between a few months and years and could be tested by examining data from children of different ages.

We propose that vision, as well as temporally coordinated multi-modal experiences contribute to establishing the sighted adult connectivity profile in visual cortices. For example, coordinated visuo-motor activity during development may enhance connectivity

between visual and motor networks. Supporting this idea, evidence shows that in infants, motor competence and early experience predict coupling between occipital and motor networks (Colomer et al., 2023).Despite these insights, many questions remain regarding the neurobiological mechanisms underlying experience-based functional connectivity changes and their relationship to anatomical development. Long-range anatomical connections between brain regions are already present in infants—even prenatally—though they remain immature (Huang et al., 2009; Kostović et al., 2019, 2021; Takahashi et al., 2012; Vasung, 2017). Functional connectivity changes may stem from local synaptic modifications within these stable structural pathways, consistent with findings that functional connectivity can vary independently of structural connection strength (Fotiadis et al., 2024). Moreover, functional connectivity has been shown to outperform structural connectivity in predicting individual behavioral differences, suggesting that experience-based functional changes may reflect finer-scale synaptic or network-level modulations not captured by macrostructural measures (Ooi et al., 2022). Prior studies also suggest that, even in adults, coordinated sensory-motor experience can lead to enhancement of functional connectivity across sensory-motor systems, indicating that large-scale changes in functional connectivity do not necessarily require corresponding changes in anatomical connectivity (Guerra-Carrillo et al., 2014; Li et al., 2018). Another possibility is some connectivity changes are mediated by 'third-party' regions, including subcortical mechanisms such as those involving the thalamus (Vega-Zuniga et al., 2025).

The current findings reveal both effects of vision and effects of blindness on the functional connectivity patterns of the visual cortex. A further open question is whether visual experience plays an instructive or permissive role in shaping neural connectivity patterns. An instructive role suggests that specific sensory experiences or patterns of neural activity directly shape and organize neural circuitry. In contrast, a permissive role implies that sensory experience or neural activity merely facilitates the influence of other factors—such as molecular signals—on the formation and organization of neural circuits (Crair, 1999; Sur et al., 1999). Studies with animals that manipulate the pattern or informational content of neural activity while keeping overall activity levels constant could distinguish between these hypotheses (Crair, 1999; Roy et al., 2020; Stellwagen & Shatz, 2002).

A further key question concerns the behavioral relevance of the connectivity signatures observed in the current study. The capacity of occipital cortices to support visual and

multimodal behavior in sighted people may depend not only on local visual cortex function but also on the capacity of the visual system to coordinate its function with non-visual networks. Does enhanced connectivity between visual and non-visual sensory motor networks facilitate multimodal integration for sighted people e.g., when catching a ball? Potentially consistent with this possibility, recent evidence suggests that people who grew up blind but recover sight in adulthood show multimodal integration deficits (Ashtari, 2020; Badde et al., 2020; Guerreiro et al., 2015; Putzar et al., 2007) and distinct occipital oscillations (Pant et al., 2023).

Conversely, for people who remain blind throughout life, visual-PFC connectivity could enable recruitment of visual cortices for higher-order non-visual functions, such as language and executive control. Habitual activation of occipital networks during higher cognitive tasks in early development could intern enhance connectivity and specialization of visual networks for non-visual functions.

In the current study, the clearest evidence for functional change driven by blindness was observed for laterality. Connectivity lateralization in sighted infants resembles that of sighted adults, in both V1 and secondary visual cortices. Relative to both sighted infants and sighted adults, blind adults show more lateralized connectivity patterns between occipital and prefrontal cortices. Previous studies suggest that in people born blind occipital and non-occipital language responses are co-lateralized (Lane et al., 2017). We speculate that habitual activation of visual cortices by higher-cognitive tasks, such as language, which are themselves highly lateralized, contributes to this biased connectivity pattern of occipital cortex in blindness.

Materials and methods

Participants

Fifty sighted adults and thirty congenitally blind adults contributed the resting state data (sighted: n = 50; 30 females; mean age = 35.33 years, standard deviation (SD) = 14.65; mean years of education = 17.08, SD = 3.1; blind: n = 30; 19 females; mean age = 44.23 years, SD = 16.41; mean years of education = 17.08, SD = 2.11; blind vs. sighted age, $t_{(78)} = 2.512$, $p < 0.05$; blind vs. sighted years of education, $t_{(78)} = 0.05$, $p = 0.996$). Since blind participants were on average older, we also performed analyses in an age-matched subgroups of sighted controls ($n = 29$) and found similar results to the full sample (see Supplementary Figure S10). Blind and sighted participants had no known cognitive or neurological disabilities (screened

through self-report). All adult anatomical images were read by a board-certified radiologist, and no gross neurological abnormalities were found. All the blind participants had at most minimal light perception from birth. Blindness was caused by pathology anterior to the optic chiasm (i.e., not due to brain damage). All participants gave written informed consent under a protocol approved by the Institutional Review Board of Johns Hopkins University.

Neonate data were from the third release of the Developing Human Connectome Project (dHCP) (*n* = 783) (https ://www.developing connectome.org). Ethical approval was obtained from the UK Health Research Authority (Research Ethics Committee reference number: 14/LO/1169). After quality control procedures (described below), 475 subjects were included in data analysis, with one scan per subject. The average age from birth at scan = 2.79 weeks (SD = 3.77, median = 1.57, range = 0 – 19.71); average gestational age at scan = 41.23 weeks (SD = 1.77, median = 41.29, range = 37 – 45.14); average gestational age at birth = 38.43 weeks (SD = 3.73, median = 39.71, range = 23 – 42.71). We only included infants who were full-term or scanned at term-equivalent age if preterm, while not being flagged by the dHCP project team as not passing quality control for functional MRI (fMRI) images (*n* = 634). Infants with more than 160 motion outliers were exclude (*n* = 116 dropped). Motion-outlier volumes were defined as DVARS (the root mean square intensity difference between successive volumes) higher than 1.5 interquartile range above the 75th centile, after motion and distortion correction. Infants with signal drop-out in regions of interest (ROI) were also excluded (*n* = 43 dropped). To identify signal dropout, we first averaged blood oxygen level-dependent (BOLD) signal intensity for all time point, for each subject, in each of 100 parcel defined by Schaefer's atlas (Schaefer et al., 2018). For each ROI (*n* = 18 ROIs) in the current study, signal dropout was then identified as BOLD intensity lower than -3 standard deviations, where the mean and standard deviations were identified across all 100 cortical parcels. Participants were excluded if any of the ROIs showed a signal dropout. The infants' structural images were reviewed by a pediatric neuroradiologist from the dHCP team, who assigned scores on a scale from 1 to 5. A score of 1 indicated a normal appearance for the subject's age, while scores of 4 or 5 suggested potential or likely clinical significance, or both clinical and imaging relevance. We repeated our analysis after excluding infants with a radiology score of 4 or 5, and the results remained consistent (see Figure S11).

Image acquisition

Blind and sighted adult MRI anatomical and functional images were collected on a 3T Phillips scanner at the F. M. Kirby Research Center. T1-weighted anatomical images were collected using a magnetization-prepared rapid gradient-echo (MP-RAGE) in 150 axial slices with 1 mm isotropic voxels. Resting state fMRI data were collected in 36 sequential ascending axial slices for 8 minutes. TR = 2 s, TE = 0.03 s, flip angle = 70°, voxel size = 2.4 × 2.4 × 2.5 mm, inter-slice gap = 0.5 mm, field of view (FOV) = 192 × 172.8 × 107.5. Participants completed 1 to 4 scans of 240 volume each (average scan time = 710.4 second per person). During the resting state scan, participants were instructed to relax but remain awake. Sighted participants wore light-excluding blindfolds to equalize the light conditions across the groups during the scans.

Infants (dHCP) Anatomical and functional images were collected on a 3T Phillips scanner at the Evelina Newborn Imaging Centre, St Thomas' Hospital, London, UK. A dedicated neonatal imaging 219 system including a neonatal 32-channel phased-array head coil was used. T2w multi-slice fast spin-echo images were acquired with in-plane resolution 0.8x0.8 mm^2 and 1.6 mm slices overlapped by 0.8 mm (TR = 12000 ms, TE = 156 ms, SENSE factor 2.11 axial and 2.6 sagittal). In infants, T2w images were used as the anatomical image because the brain anatomy is more clearly in T2w than in T1w images. Fifteen minutes of resting state fMRI data were collected using a used multiband 9x accelerated echo-planar imaging (TR = 392 ms, TE = 38 ms, 2300 volumes, with an acquired resolution of 2.15 mm isotropic). Single-band reference scans were acquired with bandwidth-matched readout, along with additional spin-echo acquisitions with both AP/PA fold-over encoding directions.

Data analysis

Resting state data were preprocessed using FSL version 5.0.9 (Smith et al., 2004), DPABI version 6.1 (Yan et al., 2016), FreeSurfer (Dale et al., 1999), and in-house code (https://github.com/NPDL/Resting-state_dHCP). The functional data for all groups were linearly detrended and low-pass filtered (0.08 Hz).

For adults, functional images were registered to the T1-weighted structural images, motion corrected using MCFLIRT (Jenkinson et al., 2002), and temporally high-pass filtering (150 s). No subject had excessive head movement (> 2mm) or rotation (> 2°) at any timepoint. Resting state data are known to include artifacts related to physiological fluctuations such as cardiac pulsations and respiratory-induced modulation of the main magnetic field. A component-based

method, CompCor (Behzadi et al., 2007), was therefore used to control for these artifacts. Particularly, following the procedure described in Whitfield-Gabrieli *et al*., nuisance signals were extracted from 2-voxel eroded masks of spinal fluid (CSF) and white matter (WM), and the first 5 principal components analysis (PCA) components derived from these signals was regressed out from the processed BOLD time series (Whitfield-Gabrieli & Nieto-Castanon, 2012). In addition, a scrubbing procedure was applied to further reduce the effect of motion on functional connectivity measures (Power et al., 2012, 2014). Frames with root mean square intensity difference exceeding 1.5 interquartile range above the 75th centile, after motion and distortion correction, were censored as outliers.

The infants resting state functional data were pre-processed by the dHCP group using the project's in-house pipeline (Fitzgibbon et al., 2020), This pipeline uses a spatial independent component analysis (ICA) denoising step to minimize artifact due to multi-band artefact, residual head-movement, arteries, sagittal sinus, CSF pulsation. For infants, ICA denoising is preferable to using CSF/WM regressors. Because it is challenging to accurately define anatomical boundaries of CSF/WM due to the low imaging resolution comparing with the brain size and the severe partial-volume effect in the neonate (Fitzgibbon et al., 2020). Like in the adults, frames with root mean square intensity difference exceeding 1.5 interquartile range above the 75th centile, after motion and distortion correction, were considered as motion outliers. Out from the 2300 frames, a subset of continuous 1600 with minimum number of motion outliers was kept for each subject. Motion outliers were censored from the subset of continuous 1600, and a subject was excluded from further analyses when the number of outlier exceeded 160 (10% of the continues subset) (Hu et al., 2022). While infant connectivity estimates may be less robust at the individual level compared to adults due to shorter scan durations and higher motion, our cohort's large sample size (n=475) and rigorous motion censoring mitigate these limitations for group-level analyses. Substantial differences between the groups exist in this study, including the number of subjects, brain sizes, imaging parameters, and data preprocessing, all of which are likely to have an impact on the overall signal quality. To address this concern, we compared the split-half noise ceiling across the groups (infants, sighted adults, and blind adults). For each participant, we first split the rs-fMRI time series into two halves, then calculated the ROI-wise rsFC pattern from the two splits. The split-half noise ceiling was estimated according to Lage-Castellanos et al (Lage-Castellanos et al., 2019). The noise ceilings of the three groups (infants: 0.90 ± 0.056, blind adults: 0.88 ± 0.041, sighted

adults: 0.90 ± 0.055) showed no significant difference (One-way ANOVA, F (2,552) = 2.348, p = 0.097). Therefore, overall signal quality is unlikely to impact our results.

For both groups of adult and infants, we performed a temporal low-pass filter (0.08 Hz low-pass cutoff) and a linear detrending. ROI-to-ROI connectivity was calculated using Pearson's correlation between ROI-averaged BOLD timeseries (ROI definition see below). The All *t*-tests and *F*-tests are two-sided. The comparison of correlation coefficients was done using cocor software package and Pearson and Filon's z (Diedenhofen & Musch, 2015; Pearson & Filon, 1898).

ROI definition

Frontal and secondary visual ROIs were defined functionally based on data from a separate task-based fMRI experiments with blind and sighted adults (Kanjlia et al., 2016, 2021; Lane et al., 2015). Three separate experiments were conducted with the same group of blind and sighted subjects (sighted n=18; blind n=23). The language ROIs in the occipital and frontal cortices were identified by sentence > nonwords contrast in an auditory language comprehension task (Lane et al., 2015). The math ROIs were identified by math > sentence contrast in an auditory task where participants judged equivalence of pairs of math equations and pairs of sentences (Kanjlia et al., 2016). The executive function ROIs were identified by no-go > frequent go contrast in an auditory go/no-go task with non-verbal sounds (Kanjlia et al., 2021). All ROI files are available at openICPSR (https://doi.org/10.3886/E198832V1).

Occipital secondary 'visual' ROIs were defined based on group comparisons blind > sighted in a whole-cortex analysis (Figure 1, Figure S5.) The occipital language ROI was defined as the cluster that responded more to auditory sentence than auditory nonwords conditions in blind, relative to sighted, in a whole-cortex analysis, likewise the occipital math ROI was defined as math>sentences, blind>sighted interaction and the occipital executive ROI as no-go > frequent go, blind>sighted. All three occipital ROIs were defined in the right hemisphere. Left-hemisphere occipital ROIs were created by flipping the right-hemisphere ROIs to the left hemisphere. Each functional ROI spans multiple anatomical regions and together the secondary visual ROIs tile large portions of lateral occipital, occipito-temporal, dorsal occipital and occipito-parietal cortices. In sighted people, the secondary visual occipital ROIs include the anatomical locations of functional regions such as motion area V5/MT+, the lateral occipital complex (LO), category specific ventral occipitotemporal cortices and dorsally, V3a and V4v.

The occipital ROI also covers the middle of the ventral temporal lobe. Dorsally, it extended to the intraparietal sulcus and superior parietal lobule.

The frontal PFC ROIs were defined functionally, based on a whole-cortex analysis which combined all blind and sighted adult data. The frontal language ROI was defined as responded more auditory sentence than auditory nonwords conditions across all blind and sighted subjects, constrained to the prefrontal cortex. Likewise, math responsive PFC was defined as math>sentences and executive no-go > frequent go. For frontal ROIs, the language ROI was defined in the left, and the math and executive function ROI were defined in the right hemisphere, then flip to the other hemisphere.

The V1 ROI was defined from a previously published anatomical surface-based atlas (PALS-B12) (Van Essen, 2005). The primary somatosensory and motor cortex (S1/M1) ROI was selected as the area that responds more to the go than no-go trials in the auditory go/no-go task across both blind and sighted groups, constrained to the hand area in S1/M1 search-space from neurosynth.org (term “hand movements”) (Kanjlia et al., 2021). The primary auditory cortex (A1) ROI was defined as the transverse temporal portion of a gyral-based atlas (Desikan et al., 2006; Morosan et al., 2001).

All the ROIs were defined in standard space and then transformed into each subject’s native space. For adults this was done by employing the deformation field estimated by FreeSurfer. For infants, the ROIs were transformed into each subject’s native space using a two-step approach. First, the ROIs were converted from the adult's MNI space into the 40-week dHCP template (Bozek et al., 2018). ANTS, previously shown to be effective in pediatric studies (Avants et al., 2014; Cabral et al., 2022; Jain et al., 2012; Lawson et al., 2013), was utilized to estimate the deformation field between these two spaces. In this step, the infant’s scalp and cerebellum were masked, as these structures in the infant brain greatly differ from those in the adult and can introduce bias into the registration process, as outlined in a study by Cabral *et al* (Cabral et al., 2022). Secondly, the ROIs were further transformed from the 40-week template space into each individual’s native spaces, employing the deformation field provided by the dHCP group. Nearest neighbor interpolation was applied in both steps (Examples of the resulting ROI alignment on individual brains are shown in Supplementary Figure S12). For both adults and infants, any overlapping voxels between ROIs were removed and not counted toward any ROIs.

Data availability

Neonate data were from the second and third release of the Developing Human Connectome Project (https://www.developing connectome.org). The de-identified blind and sighted adults' data were posted on openICPSR (https://doi.org/10.3886/E198832V1).

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Competing interests

The authors report no competing interests.

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