Eye and Brain

Dovepress
open access to scientific and medical research

Open Access Full Text Article

REVIEW

The development of human visual cortex and clinical implications

This article was published in the following Dove Press journal:
Eye and Brain

Caitlin R Siu[1]
Kathryn M Murphy[1,2]

[1]McMaster Integrative Neuroscience Discovery and Study (MiNDS) Program, McMaster University, Hamilton, ON, Canada; [2]Department of Psychology, Neuroscience & Behaviour, McMaster University, Hamilton, ON, Canada

Abstract: The primary visual cortex (V1) is the first cortical area that processes visual information. Normal development of V1 depends on binocular vision during the critical period, and age-related losses of vision are linked with neurobiological changes in V1. Animal studies have provided important details about the neurobiological mechanisms in V1 that support normal vision or are changed by visual diseases. There is very little information, however, about those neurobiological mechanisms in human V1. That lack of information has hampered the translation of biologically inspired treatments from preclinical models to effective clinical treatments. We have studied human V1 to characterize the expression of neurobiological mechanisms that regulate visual perception and neuroplasticity. We have identified five stages of development for human V1 that start in infancy and continue across the life span. Here, we describe these stages, compare them with visual and anatomical milestones, and discuss implications for translating treatments for visual disorders that depend on neuroplasticity of V1 function.

Keywords: development, human visual cortex, amblyopia, synaptic plasticity, glutamatergic, GABAergic, receptors

Introduction

The human brain has >20 cortical areas that receive strong visually driven activity and process that information to support all aspects of our visual perceptions. Changes in any of those cortical areas can affect visual perception, and abnormal visual experience, especially in childhood, often disrupts the maturation of visual cortical circuits causing poor vision. The role of the visual cortex in processing visual perception and plasticity has been well studied in animal models,[1–9] but there are few studies about the neurobiology of human visual cortex[10–19] and even fewer examine how it develops and changes across the life span.[20–24] Brain imaging studies are beginning to address structural and functional development of the human cortex,[25] but the lack of information about cellular and molecular mechanisms has slowed the translation of biologically inspired treatments for visual disorders.

Over the past decade, our laboratory has focused on studying the neurobiology of human visual cortex by measuring the expression of molecular markers that regulate neural function and plasticity, and characterizing a series of neurobiological milestones. Perhaps the most striking finding from our studies has been the prolonged development of those markers in human primary visual cortex (V1). We have found that development of the human V1[20–22,24] mirrors the long process of visual maturation and age-related changes in perception.[26–29] In this review, we will focus on the five stages that we identified for human V1 and link them with visual and anatomical milestones.

Correspondence: Kathryn M Murphy
Department of Psychology, Neuroscience & Behaviour, McMaster University, 1280 Main Street West, Hamilton, ON L8S 4K1, Canada
Tel +1 905 525 9140 ext 24264
Email kmurphy@mcmaster.ca

submit your manuscript | www.dovepress.com
Dovepress
http://dx.doi.org/10.2147/EB.S130893

Finally, we will discuss the implications of these new findings for translation of biologically inspired neuroplasticity-based therapeutic approaches for treating visual disorders.

To study the development of human visual cortex, we chose to measure the expression of synaptic and non-synaptic proteins because these mechanisms link structure and function.[20–22,24] Imagine a Venn diagram with the anatomical structure of V1 on one side and the physiological and visual functions on the other side. The neural proteins sit at the interface joining structure with function, they regulate how synapses and circuits develop, they respond to plasticity, and they control neural communication. Furthermore, measuring neural proteins in postmortem tissue from human cortex is a robust methodology that provides high-quality reliable data about these rare and valuable human tissue samples.

Stage 1: the first year, early maturation of vision and the structure of V1 neurobiology

Visual milestones

Early visual development is characterized by progressive improvements in functions such as acuity,[30,31] contrast sensitivity,[32] orientation selectivity,[33] and motion sensitivity.[34] None of those visual abilities, however, attain adult levels at this early stage. In contrast, binocular functions such as fusion, stereopsis, and stereoacuity emerge abruptly around 3 months of age.[35] By 2 months of age, infants can discriminate some color from white light,[36] and by 3 months evidence for trichromacy emerges.[37,38] Infants develop the ability to individuate objects by shape and size by 4.5 months,[39] while the ability to integrate contours or edges emerges later around 6 months.[40,41] By 5 months most infants have fusion and stereopsis, followed by rapid development to reach adult levels by 6–7 months of age;[35] meanwhile, the development of spatial acuity continues to improve well past infancy (Figure 1).[31,42] Normal time course for the development of spatial visual functions is not preprogrammed but instead is experience-dependent and abnormal vision can have a profound effect on the maturation of these functions.[43,44] Infancy marks the onset of the sensitive period for developing amblyopia, as the average age of diagnosis is about 1.2 years.[45] Early treatment of cataracts in infancy shows rapid improvement in visual acuity even within 1 hour of cataract removal.[46] Many studies and clinical experience have shown that early treatment for amblyopia, even starting in infancy, improves the chance of developing normal acuity.[47]

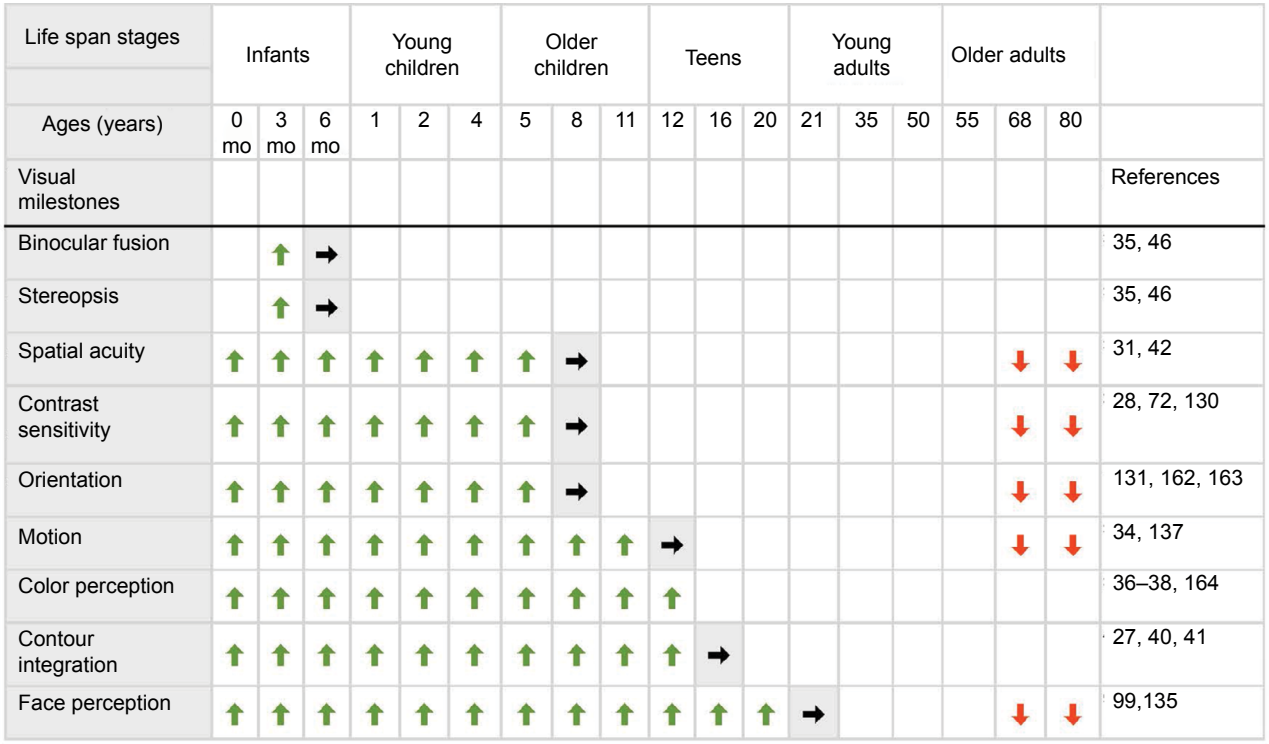


Figure 1 Summary chart for development of human visual milestones.

Notes: A summary of the development of key visual perceptual milestones across the life span. The top panel shows the stages of human development (infants, young children, older children, teens, young adults, older adults), and associated ages in months and years (as presented by Siu et al[22]). The rows below illustrate the approximate timing of onset and emergence (green arrows), adult-like levels (gray shade with black arrows), and loss of function (red arrows). References linked to each milestone are provided in the right column.

Abbreviations: V1, primary visual cortex; mo, months.

Anatomical milestones

Many of the anatomical features of human V1 develop prenatally. Neurogenesis begins around embryonic day 33 and is complete by birth,[48–50] while the thalamic input to layer 4 in V1,[51,52] bipolar, and pyramidal cells with long and thin dendritic spines forms distinct laminar patterns at around 20–30 weeks gestation.[16,53] Other aspects of cortical development that begin prenatally continue to mature after birth. Cytochrome oxidase expression is present at 26 weeks gestation, and is organized into clearly visible "puffs" by 24 days postnatal, and becomes well organized by 4 months postnatal.[19] Vertical interlaminar connections form between 26 and 29 weeks gestation, while long-range horizontal connections in layers 4B and 5 emerge at around 37 weeks gestation, and show adult-like patchiness by 8 weeks postnatal. Layer 2/3 horizontal connections emerge later at around 16 weeks postnatal and become adult-like by 15 months of age.[15] By 4 months of age, feedforward connections from V1 to extrastriate area V2 have formed mature connections, while feedback connections are still immature only reaching adult levels at around 2 years of age.[14] Synaptogenesis in human V1 increases to reach a peak between 8 months and 2 years and is followed by a longer period of synaptic pruning to reach adult levels later in childhood.[13] The number of dendritic spines in V1 follows a similar trajectory that peaks at around 5 months of age and then decreases to adult levels by 2 years.[54] Many anatomical features are already adult-like by the end of this stage (Figure 2); however, vision continues to mature well beyond the first year of life.

Neurobiological milestones

We have found that the first stage of human V1 development is characterized by rapid changes in neurobiological mechanisms that will support the emergence of visual function and synaptic plasticity. There are some early changes to both excitatory glutamatergic and inhibitory gamma-aminobutyric acid (GABA)ergic synaptic receptors (Figure 3),[22,24] and a shift toward a balance between these excitatory and inhibitory (E-I) receptors.[20] The immature $GABA_A$ receptors subunits, $GABA_A\alpha2$ and $GABA_A\alpha3$, dominate expression in the first

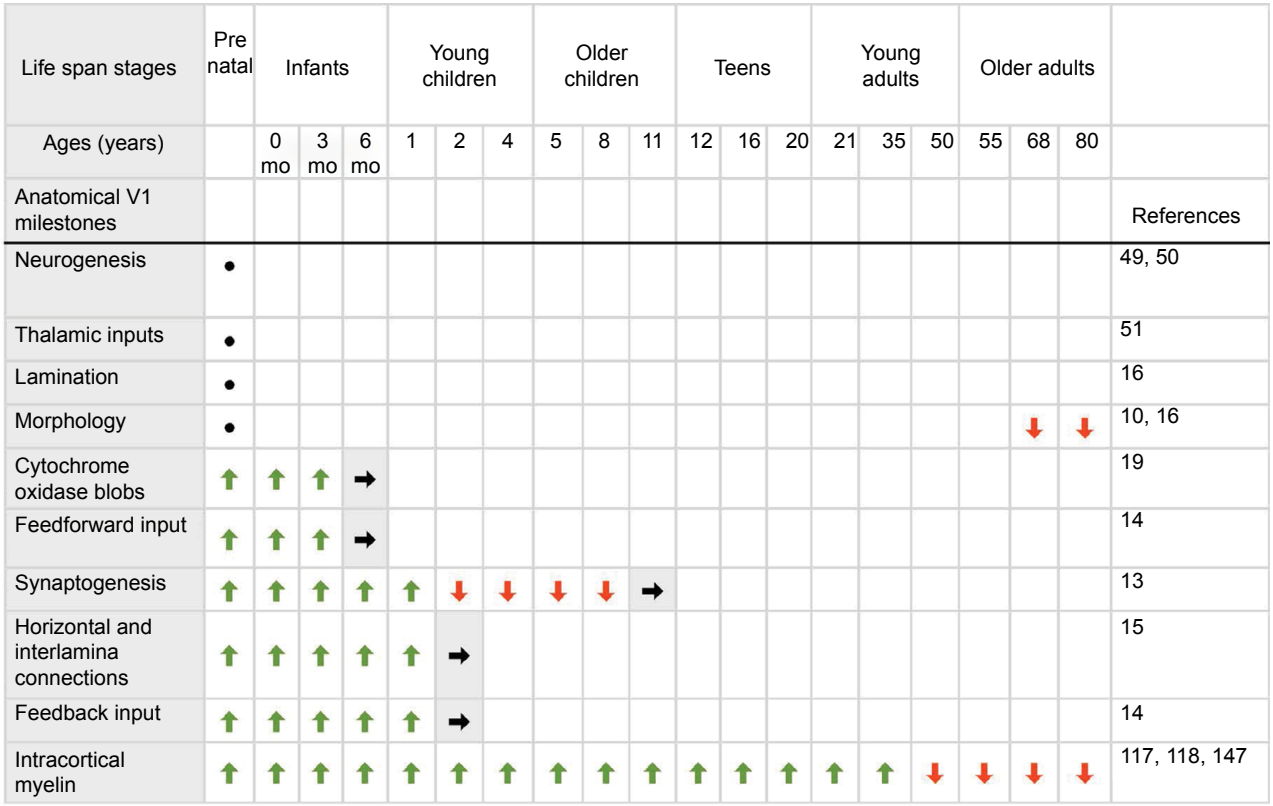


Figure 2 Summary chart for development of human V1 anatomical milestones.

Notes: A summary of the development of key neuroanatomical milestones in human V1 across the life span. The top panel shows the stages of human development (prenatal, infants, young children, older children, teens, young adults, older adults), and associated ages in months and years (as presented by Siu et al[22]). The rows below illustrate the approximate timing of onset and emergence (green arrows), adult-like levels and structure (gray shade with black arrows), and loss of expression (red arrows). Black dots refer to anatomical milestones that are completed before birth. References linked to each milestone are provided in the right column.

Abbreviations: V1, primary visual cortex; mo, months.

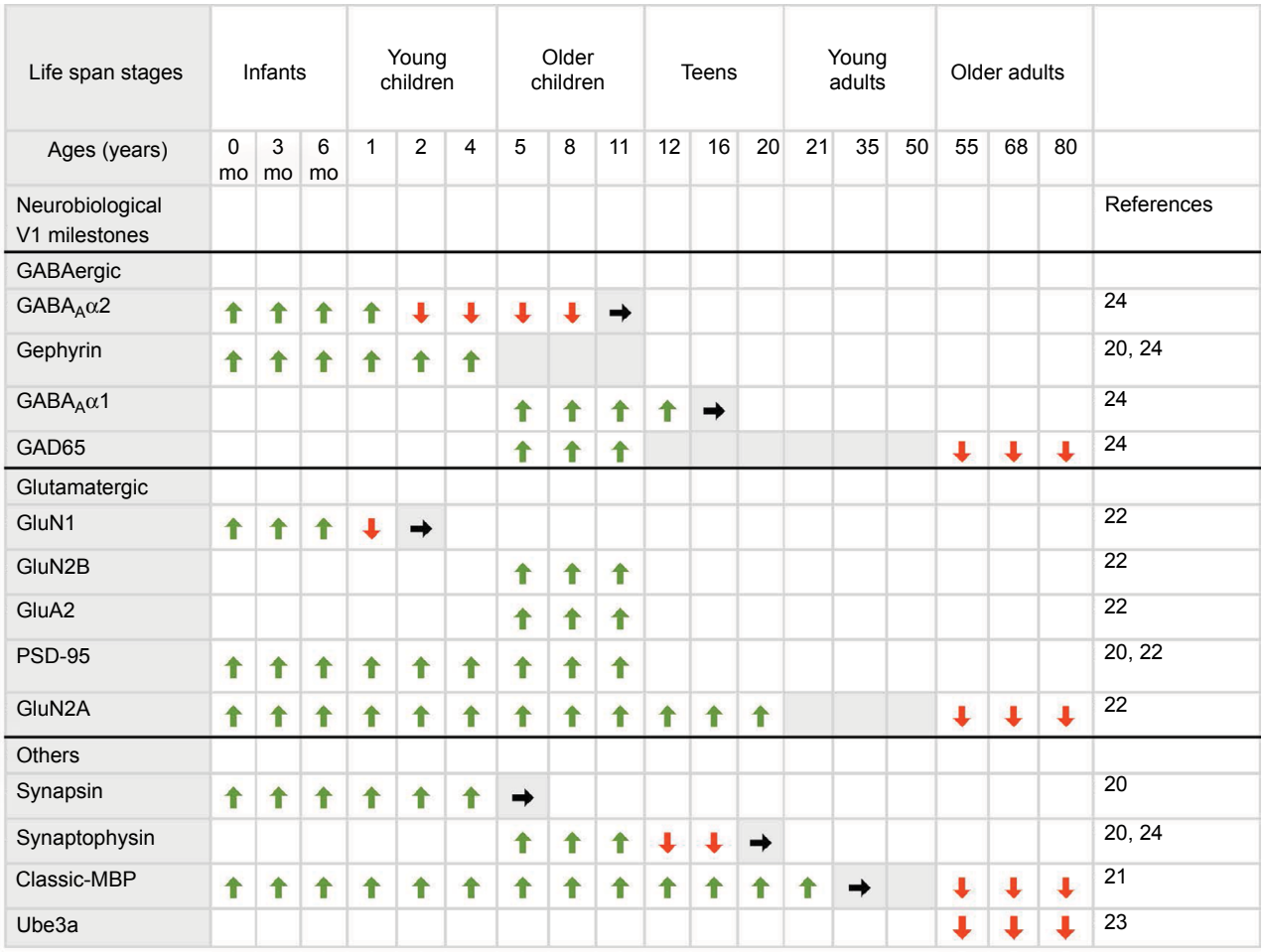


Figure 3 Summary chart for development of human V1 neurobiological milestones.
Notes: A summary of the development of key neurobiological milestones in human V1 across the life span. The top panel shows the stages of human development (infants, young children, older children, teens, young adults, older adults), and associated ages in months and years (as presented by Siu et al[22]). The rows below illustrate the approximate timing of onset and emergence (green arrows), peak expression (gray shades), adult-like levels (gray shade with black arrows), and loss of expression (red arrows). References linked to each milestone are provided in the right column.
Abbreviations: V1, primary visual cortex; mo, months; MBP, myelin basic protein.

year, but quickly show signs of maturation as those subunits are replaced by GABA$_A$α1 (Figure 4) so that there is relatively more GABA$_A$α1 by about 1 year of age, that peaks later in adolescence (Figure 3).[24] For glutamatergic synapses, the N-methyl-D-aspartate (NMDA) receptor subunit GluN1 is highly expressed at birth, then rapidly declines to reach adult levels at around 1 year. That loss is balanced by an increase in GluA2 containing AMPA receptor (AMPAR) expression, and the shift from more NMDA to more AMPA signals the loss of NMDA-dominated silent glutamatergic synapses to be replaced by active AMPA containing synapses (Figure 3).[22] The maturation of both GABA$_A$ receptor subunits and the AMPA:NMDA balance speed up responses at those receptors and trigger an environment that supports experience-dependent plasticity (Figure 4).[55–57] For example, the maturation of GABA$_A$ receptor regulates the critical period for plasticity,[56] as the mature α1 subunit is necessary for ocular dominance plasticity.[55] Moreover, the insertion of AMPAR is driven by visual experience and is an important step in initiating the critical period.[58]

Stage 2: preschool children have high variability in V1 development (1–4 years)

Visual milestones

Many aspects of visual perception continue to improve through the first few years of development (Figure 1). Young children have experience-dependent improvements in visual acuity,[42] biological motion perception,[59] and contrast sensitivity,[60,61] but those abilities are still not adult-like.[62] During the first 2 years of this stage (~1–3 years), children are most susceptible to abnormal binocular vision[63] that can cause amblyopia. Alternatively, if abnormal vision is identified and treated in children under

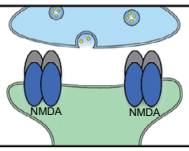
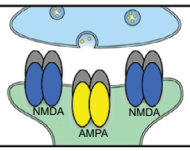
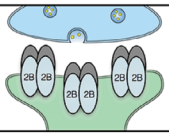
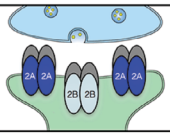
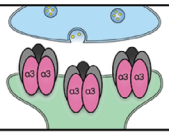
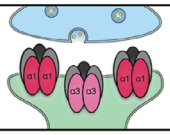
	Juvenile	Mature
NMDA: AMPA	Silent synapses (NMDAR)	Active synapses (AMPAR)
		
GluN2	GluN2B dominated	GluN2B and GluN2A
		
$GABA_A$	$GABA_A\alpha3$ dominated	$GABA_A\alpha3$ and $GABA_A\alpha1$
		
Plasticity	More	Less
Kinetics	Slower	Faster

Figure 4 Summary chart of glutamatergic and GABAergic receptor subunits.
Notes: This figure presents a summary of some key glutamate (AMPAR and NMDAR) and GABA ($GABA_A$) receptor subunit compositions that regulate neuroplasticity in the primary visual cortex. The columns represent functional significance of the balance of NMDA:AMPA (top), GluN2A:GluN2B (middle), and $GABA_A\alpha1$:$GABA_A\alpha3$ (bottom). More juvenile synapses are dominated by more NMDAR, GluN2B containing NMDAR, and $GABA_A\alpha3$ containing $GABA_A$ receptors that allow for LTP in excitatory synapses[127] and slower kinetics through the receptors. More mature synapses are dominated by more AMPAR, GluN2A containing NMDAR, and $GABA_A\alpha1$ containing $GABA_A$ receptors that allow for more LTD in excitatory synapses,[127] and faster kinetics through the receptors.
Abbreviations: GABA, gamma-aminobutyric acid; LTD, long-term depression; AMPAR, AMPA receptor; NMDAR, N-methyl-D-aspartate receptor; LTP, long-term potentiation.

5 years of age, there is the greatest likelihood for recovery,[64] for both high and low spatial frequencies.[65] For example, binocular iPad treatment for amblyopia shows improvement in visual acuity at this stage for amblyopic children.[66]

Anatomical milestones

In young children, V1 undergoes synaptic and dendritic refinement to reach adult appearance at around 2 years of age (Figure 2).[54] Other aspects of human cortical development are characterized as "adult-like" by this stage, including cortical thickness[67] and the appearance of feedback connections from extrastriate areas to V1.[14]

Neurobiological milestones

Although this period of experience-driven visual development points to significant increases in visual plasticity, we have found little evidence that neural plasticity mechanisms complete maturation during this stage (Figure 3). Instead, we found a novel aspect of human cortical development that is characterized by waves of high interindividual variability in the expression of neural plasticity markers in human V1.[20–23] Interindividual variability in human V1 can be characterized across development using the variance-to-mean ratio of protein expression across a moving window of three age-adjacent cases. Using this, we found a period of high interindividual variability, or a "wave", during young childhood for many of the synaptic proteins, but not during the other stages of development.[22] This variability may signify either interindividual differences in the rate of development, or it may identify intraindividual fluctuations in the expression of plasticity mechanisms.[22] Nevertheless, this large dynamic range in protein expression likely contributes to increased plasticity or learning for optimal behavioral performance.[68] Interestingly, this stage of interindividual variability comes just after the E-I balance has been reached in human V1.[20] Balanced excitation and inhibition in the cortex establish cortical criticality, defined as a dynamic range of spontaneous activity that maximizes the processing of input activity.[69] Thus, the waves of variability in cortical development may be an important stage of development when visual circuits "learn" complex processing by using the variability to fine-tune optimal neural circuits.[22,70]

Stage 3: experience-dependent visual development in school aged children (5–11 years)

Visual milestones

Many visual abilities finish maturation in older children (Figure 1). However, the precise age of maturation may vary significantly, and usually, depends on the type of measure

used to assess vision, or the type of patterned visual input that a child has experienced.[71] For example, visual acuity can mature between 5 and 15 years, while contrast sensitivity can mature anywhere between 6 and 19 years of age.[26,72] While some studies suggest that motion perception can mature in older children,[73–76] others suggest that it continues to improve beyond childhood into adolescence and adulthood.[34,77–79]

Children aged 6–10 years are just beyond the period of susceptibility for developing amblyopia[65,80,81] that is associated with the end of the critical period for ocular dominance plasticity in animal models.[20] Despite this, there is evidence for significant visual plasticity at this stage in both children with amblyopia and children with normal vision.[82–84] The neurobiological mechanisms that regulate this experience-dependent plasticity, including triggers proteins that promote neuroplasticity, and brakes that limit it are well studied in animal models.[5,85,86]

Neurobiological milestones

The expression of some neural plasticity mechanisms peaks during this stage of development (Figure 3). These include peaks in the expression of the glutamatergic receptor scaffolding protein PSD-95 and AMPA receptor subunit GluA2.[22] Peaks in the expression for both of these proteins have been linked with ending the critical period for experience-dependent plasticity in the visual cortex.[58,87] The maturation of those proteins is experience-dependent[87] and contributes to stabilizing synapses.[88] Furthermore, GluA2 is necessary for a form of plasticity, homeostatic synaptic scaling, which regulates synaptic strength over fluctuations in synaptic activity.[89] The homeostatic scaling up or down of AMPAR expression is dependent on synaptic activity and cooperates with NMDA-dependent Hebbian plasticity to refine cortical connectivity and promote synaptic stability during the development of V1.[90–92]

In human V1, expression of the GABA receptor scaffolding protein gephyrin also matures during late childhood development (Figure 3).[20,24] Gephyrin is directly related to the strength and stability of inhibitory synapses[93] and this peak suggests a developmental balance between excitatory (eg, PSD-95, GluA2) and inhibitory synaptic mechanisms.[20] It is interesting to note that the AMPAR subunit GluA2 is highly expressed on parvalbumin-positive (PV+) inhibitory interneurons,[94] and PV+ cell activity regulates critical period plasticity.[95] It will be important for future experiments to address the development of PV+ inhibitory interneurons in human V1 to fully understand the maturation of these plasticity mechanisms during this important stage of childhood visual development.

Stage 4: prolonged visual development in adolescence and adulthood (12–55 years)

Visual milestones

A series of studies characterizing visual development have shown that "higher-order" visual abilities continue to mature through the teen and young adult years (Figure 1). For example, global and biological motion[34,77,96–98] and spatial integration of contours[27] mature during adolescence (eg, 14–15 years of age). Face perception has an even slower pace of maturation, with continuous improvements into adulthood, as face learning and recognition improve into the third decade of life.[29,99,100] Expertise in face perception depends on visual experience, and abnormal early vision has a "sleeper effect" on the development of the neural circuits and perceptual processing that support normal face perception.[101–103]

Children older than 7 years of age are less responsive to amblyopia treatment,[104] but some forms of treatment may be effective in teens and adults and suggest that plasticity persists in the visual cortex.[105–107] For example, perceptual training for low-level perceptual abilities like contrast sensitivity and letter-recognition can improve the vision of some amblyopic patients.[108] These training-induced improvements are often small and not clinically significant.[109] Perceptual learning studies have shown that there is plasticity in adulthood that can support recovery from amblyopia.[110] Adults with amblyopia can improve visual acuity with extensive perceptual training,[111] and succeed in refining contrast sensitivity,[83] orientation selectivity,[112] stereopsis,[113] spatial discrimination,[114] and face learning.[115,116]

Anatomical milestones

Structural imaging studies of humans show that intracortical myelin in the visual cortex continues to increase well into adulthood, peaking between 30 and 40 years of age (Figure 2).[117] Anatomical analysis of postmortem human visual cortex also indicates the prolonged development of cortical myelination that continues into the third decade of life.[118] Gray matter density mapping shows a slow linear decline of cortical thickness with age in the occipital cortex,[119,120] and that regression appears to mature sequentially across the cortical areas, with primary areas maturing before higher-order association areas.[121]

Neurobiological milestones

Our studies of neuroplasticity mechanisms in human V1 provide new evidence that many aspects of V1 continue to

develop into the adult years (Figure 3). Our findings include measures of myelin expression as a brake on plasticity classic-myelin basic protein [MBP]),[122] and of the balance between NMDA receptor subunits 2A and 2B that supports plasticity when 2B dominates and reduces plasticity when 2A dominates (2A:2B) (Figure 4).[123–127] Myelin expression peaks in young adults[21] and the shift from more 2B to more 2A also ends at around 35 years of age.[22] Some GABAergic proteins also continue developing into adulthood. The enzyme that makes the on-demand pool of GABA (GAD65) and the $GABA_A\alpha1$ receptor subunit continues to increase into adulthood (Figure 3).[24] Each of these late maturing mechanisms is important for regulating neural transmission and plasticity. For example, the bidirectional regulation of the 2A:2B balance can facilitate plasticity when 2B is favored, or reduce experience-dependent plasticity when 2A is favored.[123–127] All of these findings show that the progressive shift in human V1 from a very plastic environment in childhood to a less plastic environment in adults continues into the third decade of life (Figure 3). That pace of neurobiological development is much slower than predicted by vision studies or animal research.[20–22,24]

The very slow maturation of human V1 may keep a sliver of the plasticity window open that both normal visual development and some types of vision treatments can use.

Stage 5: loss of plasticity mechanisms during aging of human V1 (>55 years)

Visual milestones

Certain visual losses in aging have been interpreted as part of normal aging that changes the receptive field properties of neurons in V1 (Figure 1).[28] During normal aging, there is an increase in the population receptive field size for neurons in V1 and in the extrastriate area V2 that serve the foveal representations.[128] These neural changes and others contribute to age-related losses of low-level visual functions like visual acuity,[129] contrast sensitivity,[130] and orientation selectivity.[131] In addition, there are age-related losses for many higher-order visual perceptions,[132] including face perception,[99,133–135] motion processing,[136–140] and reading speed.[28]

There are also acquired causes for age-related vision loss that include diseases such as diabetic retinopathy, macular degeneration, cataracts, and glaucoma. All of these diseases affect the eye and either directly or indirectly reduce retinal functioning either because the cataract has degraded the image or the disease has caused degeneration of the retina.[141] These retinal changes impact the information that is transmitted to the central visual pathway and many studies have shown changes in the visual areas of the brain.[142] Often, these eye diseases are described as neurodegeneration spreading that starts in the eye and progresses to affect the visual cortex.[143] Thus, it is likely that vision changes in normal aging and adult-acquired visual diseases may involve neurodegenerative processes in V1 in addition to optical changes.

Anatomical milestones

Aging in the visual cortex is characterized by specific microstructural changes (Figure 2). These include significant changes in the morphology of pyramidal cell bodies in human V1, a loss of dendrite number, and reduced complexity of the dendritic arborizations.[10] In primate V1, aging changes the process of cortical demyelination and remyelination so that remyelinated axons have shorter segments and the myelin sheaths are less tightly compacted around the axons thereby affecting the efficiency of axonal conduction.[144–146] In human V1, there is a progressive loss of intracortical myelin content in the stria of Gennari that begins around 30 years of age and continues to decline into the late 90s.[147] Some animal studies have also found a loss of intracortical inhibition in V1 that leads to poor orientation selectivity,[148–150] and treating V1 of old monkeys with the neurotransmitter GABA sharpens orientation selectivity of V1 neurons so they are similar to the selectivity found in young adults.[150]

Neurobiological milestones

Our studies of human V1 have found that the expression of many synaptic and non-synaptic proteins decreases in older adults (Figure 3). There are losses for GAD65, the enzyme that makes the on-demand pool of GABA,[24] Ube3A, an E3 ubiquitin ligase that is necessary for experience-dependent plasticity,[23] classic-MBP that is necessary for normal axonal myelination,[21] and GluN2A, the mature subunit of the NMDA receptor that regulates certain forms of plasticity.[22] Not all synaptic proteins change on aging; for example, expression of the $GABA_A$ receptor subunit does not decline.[24] Interestingly, most of the proteins that do change shift toward the more juvenile-like partner. For example, the age-related loss of GluN2A shifts the 2A:2B balance toward more 2B, and that may reinstate a more plastic environment.[127] Also, the loss of classic-MBP shifts the composition of MBP to favor the immature oligodendrocyte protein Golli-MBP[21] which can give rise to various developmental regulated isoforms of MBP.[151] These shifts toward more juvenile-like neural proteins raise the possibility that there is support for a more plastic environment in aging. However, not all of the changes

point to greater plasticity since there is a loss of Ube3A, a protein that is necessary for experience-dependent plasticity in the visual system.[152] Perhaps, the age-related losses of these important neural proteins reflect an internal drive to maintain stable functioning of visual cortical circuits in the face of degraded inputs due to optical changes[153,154] and neurodegenerative processes.[143]

Conclusions

We have demonstrated lifelong changes in the neurobiological mechanisms found in human V1 that support neural development, plasticity, and processing of visual information. These changes can be described in five stages: very early establishment of mechanisms for E-I transmission; a novel stage of variability in young children; maturation of low-level mechanisms in older children; continued fine-tuning through teens and young adults; and age-related losses. How far these five stages of V1 maturation will generalize across the 20 cortical areas that process visual information remains unknown. This is an important question to address, especially for developing new cortically inspired treatments for adult-acquired vision loss, since plasticity in the extrastriate area may prove to be important for supporting maintenance or recovery of vision caused by a retinal disease.

The first three figures summarize key milestones for visual system development and illustrate compelling similarities between the timing of visual, anatomical, and neurobiological milestones in human V1. Tapping into these neurobiological mechanisms is going to be key for the next generation of treatments for visual disorders. For example, a wide range of potential new therapies has been developed in animal models for amblyopia. The treatments include everything from fine-tuning of traditional patching therapy[155,156] to drug treatments,[157] to novel visual stimulation paradigms[158] and visual environments.[159–161] Also, it is likely that normal age-related changes in human V1 interact with the spreading neurodegeneration caused by diseases like glaucoma. In contrast to the excitement from preclinical models, no new plasticity-based treatments have crossed the chasm into clinical practice. One of the impediments has been the lack of information about neurobiological mechanisms in the human visual cortex, but our studies are beginning to fill that gap. Although our approach to studying neurobiology in human V1 does not provide information about circuitry, synaptic function, cellular type, or laminar localization, these data are valuable as the first steps for identifying neurobiological mechanisms that underlie visual perception and plasticity in humans. In addition, these data will help to guide future human and animal studies by making it easier to make more direct links between the neurobiological developments of V1 in humans and animal models, that can pave the way for the translation of biologically inspired vision treatments.

Acknowledgments

We thank Kyle Hornby and Drs Kate Williams, Joshua Pinto, and Simon Beshara for technical help and Justin Balsor for comments on the manuscript. An NSERC grant RGPIN-2015-06215 was awarded to KMM, and Woodburn Heron OGS awarded to CRS.

Disclosure

The authors report no conflicts of interest in this work.

References

1. Hubel DH, Wiesel TN. Receptive fields of single neurones in the cat's striate cortex. *J Physiol*. 1959;148(3):574–591.
2. Hubel DH, Wiesel TN. The period of susceptibility to the physiological effects of unilateral eye closure in kittens. *J Physiol*. 1970;206(2):419–436.
3. Levelt CN, Hübener M. Critical-period plasticity in the visual cortex. *Annu Rev Neurosci*. 2012;35(1):309–330.
4. Sengpiel F. Plasticity of the visual cortex and treatment of amblyopia. *Curr Biol*. 2014;24(18):R936–R940.
5. Hensch TK. Critical period regulation. *Annu Rev Neurosci*. 2004;27(1):549–579.
6. Turrigiano GG. The dialectic of Hebb and homeostasis. *Philos Trans R Soc Lond B Biol Sci*. 2017;372(1715):20160258.
7. Smith GB, Heynen AJ, Bear MF. Bidirectional synaptic mechanisms of ocular dominance plasticity in visual cortex. *Philos Trans R Soc Lond B Biol Sci*. 2009;364(1515):357–367.
8. Cooke SF, Bear MF. How the mechanisms of long-term synaptic potentiation and depression serve experience-dependent plasticity in primary visual cortex. *Philos Trans R Soc Lond B Biol Sci*. 2014;369(1633):20130284.
9. Kiorpes L. Visual development in primates: neural mechanisms and critical periods. *Dev Neurobiol*. 2015;75(10):1080–1090.
10. Mavroudis IA, Manani MG, Petrides F, et al. Age-related dendritic and spinal alterations of pyramidal cells of the human visual cortex. *Folia Neuropathol*. 2015;53(2):100–110.
11. Eickhoff SB, Rottschy C, Kujovic M, Palomero-Gallagher N, Zilles K. Organizational principles of human visual cortex revealed by receptor mapping. *Cereb Cortex*. 2008;18(11):2637–2645.
12. Huttenlocher PR. Morphometric study of human cerebral-cortex development. *Neuropsychologia*. 1990;28(6):517–527.
13. Huttenlocher PR, de Courten C, Garey LJ, Van der Loos H. Synaptogenesis in human visual cortex – evidence for synapse elimination during normal development. *Neurosci Lett*. 1982;33(3):247–252.
14. Burkhalter A. Development of forward and feedback connections between areas V1 and V2 of human visual cortex. *Cereb Cortex*. 1993;3(5):476–487.
15. Burkhalter A, Bernardo KL, Charles V. Development of local circuits in human visual cortex. *J Neurosci*. 1993;13(5):1916–1931.
16. Takashima S, Chan F, Becker LE, Armstrong DL. Morphology of the developing visual-cortex of the human infant – a quantitative and qualitative Golgi-study. *J Neuropathol Exp Neurol*. 1980;39(4):487–501.
17. Leuba G, Garey LJ. Evolution of neuronal numerical density in the developing and aging human visual cortex. *Hum Neurobiol*. 1987;6(1):11–18.

18. Burkhalter A, Bernardo KL. Organization of corticocortical connections in human visual cortex. *Proc Natl Acad Sci U S A*. 1989;86(3):1071–1075.
19. Wong-Riley MT, Hevner RF, Cutlan R, et al. Cytochrome oxidase in the human visual cortex: distribution in the developing and the adult brain. *Vis Neurosci*. 1993;10(1):41–58.
20. Pinto JGA, Jones DG, Williams CK, Murphy KM. Characterizing synaptic protein development in human visual cortex enables alignment of synaptic age with rat visual cortex. *Front Neural Circuits*. 2015;9:3.
21. Siu CR, Balsor JL, Jones DG, Murphy KM. Classic and Golli myelin basic protein have distinct developmental trajectories in human visual cortex. *Front Neurosci*. 2015;9:138.
22. Siu CR, Beshara SP, Jones DG, Murphy KM. Development of glutamatergic proteins in human visual cortex across the lifespan. *J Neurosci*. 2017;37(25):6031–6042.
23. Williams K, Irwin DA, Jones DG, Murphy KM. Dramatic loss of Ube3A expression during aging of the mammalian cortex. *Front Aging Neurosci*. 2010;2:18.
24. Pinto JGA, Hornby KR, Jones DG, Murphy KM. Developmental changes in GABAergic mechanisms in human visual cortex across the lifespan. *Front Cell Neurosci*. 2010;4:16.
25. Gilmore JH, Knickmeyer RC, Gao W. Imaging structural and functional brain development in early childhood. *Nat Rev Neurosci*. 2018;19(3):123–137.
26. Ellemberg D, Lewis TL, Liu CH, Maurer D. Development of spatial and temporal vision during childhood. *Vision Res*. 1999;39(14):2325–2333.
27. Kovacs I, Kozma P, Fehér A, Benedek G. Late maturation of visual spatial integration in humans. *Proc Natl Acad Sci U S A*. 1999;96(21):12204–12209.
28. Owsley C. Aging and vision. *Vision Res*. 2011;51(13):1610–1622.
29. Hartshorne JK, Germine LT. When does cognitive functioning peak? The asynchronous rise and fall of different cognitive abilities across the life span. *Psychol Sci*. 2015;26(4):433–443.
30. Hamer RD, Norcia AM, Tyler CW, Hsu-Winges C. The development of monocular and binocular VEP acuity. *Vision Res*. 1989;29(4):397–408.
31. Norcia AM, Tyler CW. Spatial frequency sweep VEP: visual acuity during the first year of life. *Vision Res*. 1985;25(10):1399–1408.
32. Pirchio M, Spinelli D, Fiorentini A, Maffei L. Infant contrast sensitivity evaluated by evoked potentials. *Brain Res*. 1978;141(1):179–184.
33. Morrone MC, Burr DC. Evidence for the existence and development of visual inhibition in humans. *Nature*. 1986;321(6067):235–237.
34. Hadad B, Schwartz S, Maurer D, Lewis TL. Motion perception: a review of developmental changes and the role of early visual experience. *Front Integr Neurosci*. 2015;9(583):5532.
35. Birch E, Petrig B. FPL and VEP measures of fusion, stereopsis and stereoacuity in normal infants. *Vision Res*. 1996;36(9):1321–1327.
36. Teller DY, Peeples DR, Sekel M. Discrimination of chromatic from white light by two-month-old human infants. *Vision Res*. 1978;18(1):41–48.
37. Bornstein MH. Infants are trichromats. *J Exp Child Psychol*. 1976;21(3):425–445.
38. Boothe RG, Dobson V, Teller DY. Postnatal development of vision in human and nonhuman primates. *Annu Rev Neurosci*. 1985;8(1):495–545.
39. Wilcox T. Object individuation: infants' use of shape, size, pattern, and color. *Cognition*. 1999;72(2):125–166.
40. Baker TJ, Tse J, Gerhardstein P, Adler SA. Contour integration by 6-month-old infants: discrimination of distinct contour shapes. *Vision Res*. 2008;48(1):136–148.
41. Taylor G, Hipp D, Moser A, Dickerson K, Gerhardstein P. The development of contour processing: evidence from physiology and psychophysics. *Front Psychol*. 2014;5:719.
42. Lai Y-H, Wang H-Z, Hsu H-T. Development of visual acuity in preschool children as measured with Landolt C and Tumbling E charts. *J AAPOS*. 2011;15(3):251–255.
43. Birch EE. Amblyopia and binocular vision. *Prog Retin Eye Res*. 2013;33:67–84.
44. Jando G, Miko-Barath E, Marko K, Hollody K, Toeroek B, Kovacs I. Early-onset binocularity in preterm infants reveals experience-dependent visual development in humans. *Proc Natl Acad Sci U S A*. 2012;109(27):11049–11052.
45. Birch EE, Holmes JM. The clinical profile of amblyopia in children younger than 3 years of age. *J AAPOS*. 2010;14(6):494–497.
46. Maurer D, Lewis TL, Brent HP, Levin AV. Rapid improvement in the acuity of infants after visual input. *Science*. 1999;286(5437):108–110.
47. Birch EE, Swanson WH, Stager DR, Woody M, Everett M. Outcome after very early treatment of dense congenital unilateral cataract. *Invest Ophthalmol Vis Sci*. 1993;34(13):3687–3699.
48. Rakic P. Neuroscience. No more cortical neurons for you. *Science*. 2006;313(5789):928–929.
49. Clowry G, Molnár Z, Rakic P. Renewed focus on the developing human neocortex. *J Anat*. 2010;217(4):276–288.
50. Bhardwaj RD, Curtis MA, Spalding KL, et al. Neocortical neurogenesis in humans is restricted to development. *Proc Natl Acad Sci U S A*. 2006;103(33):12564–12568.
51. Flower MJ. Neuromaturation of the human fetus. *J Med Philos*. 1985;10(3):237–251.
52. Kostovic I, Rakic P. Development of prestriate visual projections in the monkey and human fetal cerebrum revealed by transient cholinesterase staining. *J Neurosci*. 1984;4(1):25–42.
53. Sauer B. Quantitative analysis of the laminae of the striate area in man. An application of automatic image analysis. *J Hirnforsch*. 1983;24(1):89–97.
54. Michel AE, Garey LJ. The development of dendritic spines in the human visual cortex. *Hum Neurobiol*. 1984;3(4):223–227.
55. Fagiolini M, Fritschy J-M, Löw K, Möhler H, Rudolph U, Hensch TK. Specific GABAA circuits for visual cortical plasticity. *Science*. 2004;303(5664):1681–1683.
56. Chen L, Yang C, Mower GD. Developmental changes in the expression of GABA(A) receptor subunits (alpha(1), alpha(2), alpha(3)) in the cat visual cortex and the effects of dark rearing. *Brain Res Mol Brain Res*. 2001;88(1–2):135–143.
57. Liao D, Scannevin RH, Huganir R. Activation of silent synapses by rapid activity-dependent synaptic recruitment of AMPA receptors. *J Neurosci*. 2001;21(16):6008–6017.
58. Huang X, Stodieck SK, Goetze B, et al. Progressive maturation of silent synapses governs the duration of a critical period. *Proc Natl Acad Sci U S A*. 2015;112(24):E3131–E3140.
59. Sweeny TD, Wurnitsch N, Gopnik A, Whitney D. Sensitive perception of a person's direction of walking by 4-year-old children. *Dev Psychol*. 2013;49(11):2120–2124.
60. Richman JE, Lyons S. A forced choice procedure for evaluation of contrast sensitivity function in preschool children. *J Am Optom Assoc*. 1994;65(12):859–864.
61. Scharre JE, Cotter SA, Block SS, Kelly SA. Normative contrast sensitivity data for young children. *Optom Vis Sci*. 1990;67(11):826–832.
62. Yu T-Y, Jacobs RJ, Anstice NS, et al. Global motion perception in 2-year-old children: a method for psychophysical assessment and relationships with clinical measures of visual function. *Invest Ophthalmol Vis Sci*. 2013;54(13):8408–8419.
63. Banks MS, Aslin RN, Letson RD. Sensitive period for the development of human binocular vision. *Science*. 1975;190(4215):675–677.
64. US Preventive Services Task Force; Grossman DC, Curry SJ, Owens DK, et al. Vision screening in children aged 6 months to 5 years: US Preventive Services Task Force recommendation statement. *JAMA*. 2017;318(9):836–844.
65. Lewis TL, Maurer D. Multiple sensitive periods in human visual development: evidence from visually deprived children. *Dev Psychobiol*. 2005;46(3):163–183.
66. Birch EE, Li SL, Jost RM, et al. Binocular iPad treatment for amblyopia in preschool children. *J AAPOS*. 2015;19(1):6–11.

67. Lyall AE, Shi F, Geng X, et al. Dynamic development of regional cortical thickness and surface area in early childhood. *Cereb Cortex*. 2015;25(8):2204–2212.
68. Garrett DD, Kovacevic N, McIntosh AR, Grady CL. The modulation of BOLD variability between cognitive states varies by age and processing speed. *Cereb Cortex*. 2013;23(3):684–693.
69. Shew WL, Yang H, Petermann T, Roy R, Plenz D. Neuronal avalanches imply maximum dynamic range in cortical networks at criticality. *J Neurosci*. 2009;29(49):15595–15600.
70. Gordus A, Pokala N, Levy S, Flavell SW, Bargmann CI. Feedback from network states generates variability in a probabilistic olfactory circuit. *Cell*. 2015;161(2):215–227.
71. Lewis TL, Maurer D. Effects of early pattern deprivation on visual development. *Optom Vis Sci*. 2009;86(6):640–646.
72. Almoqbel FM, Irving EL, Leat SJ. Visual acuity and contrast sensitivity development in children: sweep visually evoked potential and psychophysics. *Optom Vis Sci*. 2017;94(8):830–837.
73. Narasimhan S, Giaschi D. The effect of dot speed and density on the development of global motion perception. *Vision Res*. 2012;62:102–107.
74. Ellemberg D, Lewis TL, Maurer D, et al. The effect of displacement on sensitivity to first- and second-order global motion in 5-year-olds and adults. *Seeing Perceiving*. 2010;23(5–6):517–532.
75. Ellemberg D, Lewis TL, Maurer D, Brar S, Brent HP. Better perception of global motion after monocular than after binocular deprivation. *Vision Res*. 2002;42(2):169–179.
76. Gunn A, Cory E, Atkinson J, et al. Dorsal and ventral stream sensitivity in normal development and hemiplegia. *Neuroreport*. 2002;13(6):843–847.
77. Bogfjellmo LG, Bex PJ, Falkenberg HK. The development of global motion discrimination in school aged children. *J Vis*. 2014;14(2):19.
78. Hadad B-S, Maurer D, Lewis TL. Long trajectory for the development of sensitivity to global and biological motion. *Dev Sci*. 2011;14(6):1330–1339.
79. Joshi MR, Falkenberg HK. Development of radial optic flow pattern sensitivity at different speeds. *Vision Res*. 2015;110(Pt A):68–75.
80. Epelbaum M, Milleret C, Buisseret P, Dufier JL. The sensitive period for strabismic amblyopia in humans. *Ophthalmology*. 1993;100(3):323–327.
81. Keech RV, Kutschke PJ. Upper age limit for the development of amblyopia. *J Pediatr Ophthalmol Strabismus*. 1995;32(2):89–93.
82. Li RW, Young KG, Hoenig P, Levi DM. Perceptual learning improves visual performance in juvenile amblyopia. *Invest Ophthalmol Vis Sci*. 2005;46(9):3161–3168.
83. Liao M, Zhao H, Liu L, et al. Training to improve contrast sensitivity in amblyopia: correction of high-order aberrations. *Sci Rep*. 2016;6:35702.
84. Mintz-Hittner HA, Fernandez KM. Successful amblyopia therapy initiated after age 7 years: compliance cures. *Arch Ophthalmol*. 2000;118(11):1535–1541.
85. Morishita H, Hensch TK. Critical period revisited: impact on vision. *Curr Opin Neurobiol*. 2008;18(1):101–107.
86. Bavelier D, Levi DM, Li RW, Dan Y, Hensch TK. Removing brakes on adult brain plasticity: from molecular to behavioral interventions. *J Neurosci*. 2010;30(45):14964–14971.
87. Chen X, Levy JM, Hou A, et al. PSD-95 family MAGUKs are essential for anchoring AMPA and NMDA receptor complexes at the postsynaptic density. *Proc Natl Acad Sci U S A*. 2015;112(50):E6983–E6992.
88. Liu S, Cull-Candy SG. Synaptic activity at calcium-permeable AMPA receptors induces a switch in receptor subtype. *Nature*. 2000;405(6785):454–458.
89. Gainey MA, Hurvitz-Wolff JR, Lambo ME, Turrigiano GG. Synaptic scaling requires the GluR2 subunit of the AMPA receptor. *J Neurosci*. 2009;29(20):6479–6489.
90. Desai NS, Cudmore RH, Nelson SB, Turrigiano GG. Critical periods for experience-dependent synaptic scaling in visual cortex. *Nat Neurosci*. 2002;5(8):783–789.
91. Mrsic-Flogel TD, Hofer SB, Ohki K, Reid RC, Bonhoeffer T, Hübener M. Homeostatic regulation of eye-specific responses in visual cortex during ocular dominance plasticity. *Neuron*. 2007;54(6):961–972.
92. Turrigiano GG, Nelson SB. Homeostatic plasticity in the developing nervous system. *Nat Rev Neurosci*. 2004;5(2):97–107.
93. Tyagarajan SK, Fritschy J-M. Gephyrin: a master regulator of neuronal function? *Nature*. 2014;15(3):141–156.
94. Kooijmans RN, Self MW, Wouterlood FG, Belien JAM, Roelfsema PR. Inhibitory interneuron classes express complementary AMPA-receptor patterns in macaque primary visual cortex. *J Neurosci*. 2014;34(18):6303–6315.
95. Donato F, Rompani SB, Caroni P. Parvalbumin-expressing basket-cell network plasticity induced by experience regulates adult learning. *Nature*. 2013;504(7479):272–276.
96. Bucher K, Dietrich T, Marcar VL, et al. Maturation of luminance- and motion-defined form perception beyond adolescence: a combined ERP and fMRI study. *Neuroimage*. 2006;31(4):1625–1636.
97. Meier K, Giaschi D. Effect of spatial and temporal stimulus parameters on the maturation of global motion perception. *Vision Res*. 2017;135:1–9.
98. Schrauf M, Wist ER, Ehrenstein WH. Development of dynamic vision based on motion contrast. *Exp Brain Res*. 1999;124(4):469–473.
99. Germine LT, Duchaine B, Nakayama K. Where cognitive development and aging meet: face learning ability peaks after age 30. *Cognition*. 2011;118(2):201–210.
100. Mondloch CJ, Le Grand R, Maurer D. Configural face processing develops more slowly than featural face processing. *Perception*. 2002;31(5):553–566.
101. Grady CL, Mondloch CJ, Lewis TL, Maurer D. Early visual deprivation from congenital cataracts disrupts activity and functional connectivity in the face network. *Neuropsychologia*. 2014;57:122–139.
102. Mondloch CJ, Segalowitz SJ, Lewis TL, Dywan J, Le Grand R, Maurer D. The effect of early visual deprivation on the development of face detection. *Dev Sci*. 2013;16(5):728–742.
103. Maurer D, Mondloch CJ, Lewis TL. Sleeper effects. *Dev Sci*. 2007;10(1):40–47.
104. Holmes JM. Effect of age on response to amblyopia treatment in children. *Arch Ophthalmol*. 2011;129(11):1451–1457.
105. Karni A, Bertini G. Learning perceptual skills: behavioral probes into adult cortical plasticity. *Curr Opin Neurobiol*. 1997;7(4):530–535.
106. Levi DM, Li RW. Perceptual learning as a potential treatment for amblyopia: a mini-review. *Vision Res*. 2009;49(21):2535–2549.
107. Sasaki Y, Nanez JE, Watanabe T. Advances in visual perceptual learning and plasticity. *Nat Rev Neurosci*. 2010;11(1):53–60.
108. Polat U, Ma-Naim T, Belkin M, Sagi D. Improving vision in adult amblyopia by perceptual learning. *Proc Natl Acad Sci U S A*. 2004;101(17):6692–6697.
109. Sklar JC, Goltz HC, Gane L, Wong AMF. Adaptation to laterally displacing prisms in anisometropic amblyopia. *Invest Ophthalmol Vis Sci*. 2015;56(6):3699–3708.
110. Levi DM, Polat U. Neural plasticity in adults with amblyopia. *Proc Natl Acad Sci U S A*. 1996;93(13):6830–6834.
111. Levi DM. Perceptual learning in adults with amblyopia: a reevaluation of critical periods in human vision. *Dev Psychobiol*. 2005;46(3):222–232.
112. Jehee JFM, Ling S, Swisher JD, van Bergen RS, Tong F. Perceptual learning selectively refines orientation representations in early visual cortex. *J Neurosci*. 2012;32(47):16747–16753.
113. Ding J, Levi DM. Recovery of stereopsis through perceptual learning in human adults with abnormal binocular vision. *Proc Natl Acad Sci U S A*. 2011;108(37):E733–E741.
114. Li RW, Levi DM. Characterizing the mechanisms of improvement for position discrimination in adult amblyopia. *J Vis*. 2004;4(6):7.
115. McMahon DBT, Leopold DA. Stimulus timing-dependent plasticity in high-level vision. *Curr Biol*. 2012;22(4):332–337.
116. Du Y, Zhang F, Wang Y, Bi T, Qiu J. Perceptual learning of facial expressions. *Vision Res*. 2016;128:19–29.

117. Rowley CD, Sehmbi M, Bazin PL, et al. Age-related mapping of intracortical myelin from late adolescence to middle adulthood using T1-weighted MRI. *Hum Brain Mapp*. Epub 2017 Apr 30.
118. Miller DJ, Duka T, Stimpson CD, et al. Prolonged myelination in human neocortical evolution. *Proc Natl Acad Sci U S A*. 2012;109(41): 16480–16485.
119. Sowell ER, Peterson BS, Thompson PM, Welcome SE, Henkenius AL, Toga AW. Mapping cortical change across the human life span. *Nat Neurosci*. 2003;6(3):309–315.
120. Sowell ER, Thompson PM, Toga AW. Mapping changes in the human cortex throughout the span of life. *Neuroscientist*. 2004;10(4):372–392.
121. Gogtay N, Giedd JN, Lusk L, et al. Dynamic mapping of human cortical development during childhood through early adulthood. *Proc Natl Acad Sci U S A*. 2004;101(21):8174–8179.
122. McGee AW, Yang Y, Fischer QS, Daw NW, Strittmatter SM. Experience-driven plasticity of visual cortex limited by myelin and Nogo receptor. *Science*. 2005;309(5744):2222–2226.
123. Abraham WC, Bear MF. Metaplasticity: the plasticity of synaptic plasticity. *Trends Neurosci*. 1996;19(4):126–130.
124. Philpot BD, Sekhar AK, Shouval HZ, Bear MF. Visual experience and deprivation bidirectionally modify the composition and function of NMDA receptors in visual cortex. *Neuron*. 2001;29(1):157–169.
125. Philpot BD, Espinosa JS, Bear MF. Evidence for altered NMDA receptor function as a basis for metaplasticity in visual cortex. *J Neurosci*. 2003;23(13):5583–5588.
126. Philpot BD, Cho KKA, Bear MF. Obligatory role of NR2A for metaplasticity in visual cortex. *Neuron*. 2007;53(4):495–502.
127. Yashiro K, Philpot BD. Regulation of NMDA receptor subunit expression and its implications for LTD, LTP, and metaplasticity. *Neuropharmacology*. 2008;55(7):1081–1094.
128. Brewer AA, Barton B. Visual cortex in aging and Alzheimer's disease: changes in visual field maps and population receptive fields. *Front Psychol*. 2014;5:74.
129. Sekuler R, Hutman LP, Owsley CJ. Human aging and spatial vision. *Science*. 1980;209(4462):1255–1256.
130. Allard R, Renaud J, Molinatti S, Faubert J. Contrast sensitivity, healthy aging and noise. *Vision Res*. 2013;92:47–52.
131. Betts LR, Sekuler AB, Bennett PJ. The effects of aging on orientation discrimination. *Vision Res*. 2007;47(13):1769–1780.
132. Habak C, Faubert J. Larger effect of aging on the perception of higher-order stimuli. *Vision Res*. 2000;40(8):943–950.
133. Konar Y, Bennett PJ, Sekuler AB. Effects of aging on face identification and holistic face processing. *Vision Res*. 2013;88:38–46.
134. Rousselet GA, Gaspar CM, Pernet CR, Husk JS, Bennett PJ, Sekuler AB. Healthy aging delays scalp EEG sensitivity to noise in a face discrimination task. *Front Psychol*. 2010;1:19.
135. Wilson HR, Mei M, Habak C, Wilkinson F. Visual bandwidths for face orientation increase during healthy aging. *Vision Res*. 2011;51(1):160–164.
136. Allard R, Lagacé-Nadon S, Faubert J. Feature tracking and aging. *Front Psychol*. 2013;4:427.
137. Bennett PJ, Sekuler R, Sekuler AB. The effects of aging on motion detection and direction identification. *Vision Res*. 2007;47(6):799–809.
138. Betts LR, Taylor CP, Sekuler AB, Bennett PJ. Aging reduces center-surround antagonism in visual motion processing. *Neuron*. 2005;45(3):361–366.
139. Fernandez R, Monacelli A, Duffy CJ. Visual motion event related potentials distinguish aging and Alzheimer's disease. *J Alzheimers Dis*. 2013;36(1):177–183.
140. Kavcic V, Martin T, Zalar B. Aging effects on visual evoked potentials (VEPs) for motion direction discrimination. *Int J Psychophysiol*. 2013;89(1):78–87.
141. Bourne RRA, Stevens GA, White RA, et al. Causes of vision loss worldwide, 1990–2010: a systematic analysis. *Lancet Glob Health*. 2013;1(6):e339–e349.
142. Yücel YH, Gupta N. A framework to explore the visual brain in glaucoma with lessons from models and man. *Exp Eye Res*. 2015;141: 171–178.
143. Gupta N, Yücel YH. Glaucoma as a neurodegenerative disease. *Curr Opin Ophthalmol*. 2007;18(2):110–114.
144. Peters A, Sethares C. Is there remyelination during aging of the primate central nervous system? *J Comp Neurol*. 2003;460(2):238–254.
145. Peters A, Moss MB, Sethares C. Effects of aging on myelinated nerve fibers in monkey primary visual cortex. *J Comp Neurol*. 2000;419(3):364–376.
146. Peters A, Verderosa A, Sethares C. The neuroglial population in the primary visual cortex of the aging rhesus monkey. *Glia*. 2008;56(11): 1151–1161.
147. Lintl P, Braak H. Loss of intracortical myelinated fibers: a distinctive age-related alteration in the human striate area. *Acta Neuropathol*. 1983;61(3–4):178–182.
148. Miyamoto A, Hasegawa J, Hoshino O. Dynamic modulation of an orientation preference map by GABA responsible for age-related cognitive performance. *Cogn Process*. 2012;13(4): 349–359.
149. Hua T, Kao C, Sun Q, Li X, Zhou Y. Decreased proportion of GABA neurons accompanies age-related degradation of neuronal function in cat striate cortex. *Brain Res Bull*. 2008;75(1):119–125.
150. Leventhal AG. GABA and its agonists improved visual cortical function in senescent monkeys. *Science*. 2003;300(5620):812–815.
151. Harauz G, Ladizhansky V, Boggs JM. Structural polymorphism and multifunctionality of myelin basic protein. *Biochemistry*. 2009;48(34):8094–8104.
152. Yashiro K, Riday TT, Condon KH, et al. Ube3a is required for experience-dependent maturation of the neocortex. *Nat Neurosci*. 2009;12(6):777–783.
153. Artal P, Guirao A, Berrio E, Piers P, Norrby S. Optical aberrations and the aging eye. *Int Ophthalmol Clin*. 2003;43(2):63–77.
154. Glasser A, Campbell MC. Biometric, optical and physical changes in the isolated human crystalline lens with age in relation to presbyopia. *Vision Res*. 1999;39(11):1991–2015.
155. Mitchell DE, Kind PC, Sengpiel F, Murphy K. Brief daily periods of binocular vision prevent deprivation-induced acuity loss. *Curr Biol*. 2003;13(19):1704–1708.
156. Mitchell DE, Kind PC, Sengpiel F, Murphy K. Short periods of concordant binocular vision prevent the development of deprivation amblyopia. *Eur J Neurosci*. 2006;23(9):2458–2466.
157. Maya-Vetencourt JF, Sale A, Viegi A, et al. The antidepressant fluoxetine restores plasticity in the adult visual cortex. *Science*. 2008;320(5874):385–388.
158. Cooke SF, Bear MF. Visual experience induces long-term potentiation in the primary visual cortex. *J Neurosci*. 2010;30(48):16304–16313.
159. Eaton NC, Sheehan HM, Quinlan EM. Optimization of visual training for full recovery from severe amblyopia in adults. *Learn Mem*. 2016;23(2):99–103.
160. Montey KL, Eaton NC, Quinlan EM. Repetitive visual stimulation enhances recovery from severe amblyopia. *Learn Mem*. 2013;20(6): 311–317.
161. Montey KL, Quinlan EM. Recovery from chronic monocular deprivation following reactivation of thalamocortical plasticity by dark exposure. *Nat Commun*. 2011;2:317.
162. Lewis TL, Kingdon A, Ellemberg D, Maurer D. Orientation discrimination in 5-year-olds and adults tested with luminance-modulated and contrast-modulated gratings. *J Vis*. 2007;7(4):9.
163. Jeon ST, Maurer D, Lewis TL. Developmental mechanisms underlying improved contrast thresholds for discriminations of orientation signals embedded in noise. *Front Psychol*. 2014;5:977.
164. Ling BY, Dain SJ. Color vision in children and the Lanthony New Color Test. *Vis Neurosci*. 2008;25(3):441–444.