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**Publication Date**

2023-02-11

Peer reviewed

# Amblyopia and Non-human Animal Research<sup>1</sup>

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## Summary

This paper discusses the claim that the use of non-human animals in amblyopia research has led to our understanding and treatment of this condition. It is shown that such use was not important, that our understanding was based on human experience and that the non-human animal research confused some aspects of the situation.

Keywords: amblyopia, cataract, lazy eye, non-human animal, ocular media opacification, research, species differences, squint, strabismus

Amblyopia is defined generally as a unilateral or bilateral decrease in visual acuity caused by form vision deprivation, abnormal binocular interaction, or both, for which no organic cause can be detected by the physical examination of the eye and which, in some cases, is reversible by therapeutic measures<sup>3</sup>. It often occurs as the result of congenital conditions that do not permit both eyes to focus simultaneously. For example, if there is congenital strabismus (squint), and the child utilises one eye only, the unused eye will become amblyopic. The same holds true for congenital opacification of the ocular media as in cataract or anisometropia (unequal refraction between eyes of the same individual). The reason for reduction in vision appears to be due to a lack of proper connections from the retinal ganglion cells to other neurons in the central nervous system during postnatal development.

Since around the 1960s, there has been considerable experimental work aimed at trying to understand the processes which lead to amblyopia by using non-human animals (animals<sup>4</sup>). Cats and non-human primates have been the most studied, but chickens and tree shrews also have been used. Experimental manipulations have included perturbations such as: suturing the eyelids closed; removing an eye; causing artificial strabismus, either surgically or through the use of prisms; or, rendering the ocular media opaque. There have been numerous assertions by those presently doing this sort of work that these manipulations have led to significantly greater understanding of amblyopia and that the results have been used to develop treatment methods for affected humans. Nevertheless, in reviews of treatment regimens in 2016, authors did not mention any animal studies<sup>5</sup>. Authors promoted continued clinical research involving human patients and did not mention any reliance on or need for animal research<sup>6</sup>. Another author of a review only mentioned that animal research reached the same conclusions as that done in clinical trials with patients<sup>7</sup>.

There are, however, major differences in the development and structure of the visual systems of humans and other animals<sup>8</sup>. The cat, who is widely used, does not have a macula or fovea, two regions of the retina of primary importance for human vision. These areas account for essentially

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1 The intent of this review is to demonstrate that reliance on animal research is unnecessary to understand or treat amblyopia in people. Although some of the references may be considered 'dated', this only serves to show just how much understanding and management has remained unchanged over the decades despite thousands of animals being subjected to some of the worst privation imaginable. In addition to the lack of scientific credibility or necessity, there are strong moral arguments against subjecting non-consenting beings to harm and death; this subject is addressed in another manuscript ([Buyukmihci 2022-12-01](#)).

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3 [von Noorden 1978](#)

4 Purely for the sake of convenience, I may refer to animals other than humans as "animals", recognising that all are animals of one kind or another; there is no intention to imply that any, even a human being, is morally superior or intrinsically more valuable than another.

5 [Koo et al 2017](#); [Tailor et al 2016](#)

6 [Kraker 2016](#); [Tailor et al 2016](#)

7 [Vagge & Nelson 2016](#)

8 [Packwood & Gordon 1975](#); [Palmer & King 1982](#); [Rodieck 1979](#); [Van Essen 1979](#)

all useful vision occurring in the human being and it is the development, or lack thereof, of their connections in the brain that are of the utmost importance in amblyopia<sup>9</sup>. Although there are some general similarities between humans and cats with respect to neuroanatomy, the differences are so great that the results obtained in this work do not appear to have had any meaning for the human situation based upon a lack of references to this work in reports on human clinical conditions. The cat 'model' cannot predict what changes may occur in humans when vision is deprived either monocularly or binocularly. Furthermore, the experimental situation in the cat and other animals is entirely artificial, a perturbation of an otherwise normal animal. Spontaneously occurring visual deprivation in human children, however, often is associated with other developmental defects which tend to modify and confound the situation.

Although there are many structural and physiological similarities between certain non-human primates and human primates, there are still problems in extrapolating the information to the human situation. In some cases, for example with myopia, there is considerable difference between similar non-human primate species with respect to the results following similar experimental manipulations<sup>10</sup>. The complex behaviour and cognition of most non-human primate species, however, means that these animals likely suffer more profoundly than other species under laboratory conditions, particularly when used in invasive research<sup>11</sup>. Although one could argue this is "speciesist", this should raise great ethical concerns which should proscribe the use of these animals.

There has been considerable concern expressed by vision scientists other than just myself that the experimental work is either not relevant or may be misleading with respect to the human condition and its treatment<sup>12, 13</sup>.

When evaluating the claims for the importance of animal work, one also must bear in mind that this work largely is neurophysiological dealing with single cell recordings. This work does not measure vision, which has a large psychological component in people, and has little to

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9 [von Noorden 1978](#)

10 [Raviola & Wiesel 1985](#) (When atropine was used in one eye of either rhesus or stump-tailed macaques, different results were obtained with respect to the production of myopia. There also was a difference in the effects of artificially closing one eye between these otherwise similar primates.)

11 [Padrell et al 2021](#)

12 [Hoyt 1980](#); [Marg 1982](#); [Metz 1985](#); [Vaegan & Taylor 1979](#); von Noorden [1978, 1988](#); [von Noorden & Maumenee 1968](#); [Wick et al 1992](#)

13 Hoyt reported that animal work had suggested that binocular patching, as done in phototherapy of jaundiced children, might be harmful ([Hoyt 1980](#)). The data from children, however, suggested that binocular patching was not harmful. Marg pointed out that the results of examination of amblyopic children were at odds with some of the experimental work and that, along with the conflicting findings between animal species, this seemed to demonstrate that one could not extrapolate animal results to children with confidence ([Marg 1982](#)). He stated that the animal "models" were not entirely valid for children. Metz noted that the type of occlusion done in experimental work was different from that used therapeutically in children with amblyopia ([Metz 1985](#)). He was concerned because the experimental work done on cats could be interpreted to suggest that amblyopic children should not be patched. Such an interpretation, based on animal studies, would be most unfortunate for amblyopic children. von Noorden and Maumenee were critical of the classical work of Wiesel and Hubel because of the substantial difference in neuroanatomy and neurophysiology between cats and humans ([von Noorden & Maumenee 1968](#)). von Noorden later commented on how data from animals could not be applied directly to humans, and that there were differences between monkeys and cats in the various studies done ([von Noorden 1978](#)). In his Jackson Memorial Lecture ([von Noorden 1988](#)), he again was critical of animal experiments with regard to infantile esotropia (convergent strabismus). He pointed out that the monkey work was not analogous. He concluded that there is no animal "model" for infantile esotropia, despite all the work which had been done making infant monkeys strabismic.

do with vision in terms of behaviour and function. This is even alluded to by some investigators in their own publications<sup>14</sup>. One cannot adequately study vision in non-human animals because there is no meaningful and relevant communication with them, and cellular recordings do not tell you whether and how these animals see.

In addition, some of this work has involved substantial suffering on the part of the animals. For example, in one study, monkeys were deprived of sight in one eye for periods up to five years<sup>15</sup>. In at least one case, one monkey was deprived of her or his sight in *both* eyes for a period of one year<sup>16</sup>. In many cases, the eyes themselves had been removed in these and other sentient creatures<sup>17</sup>.

Animals also have been subjected to neuromuscular blocking agents such as gallamine triethiodide, sometimes with what appeared to be inadequate attention to anaesthesia. These agents paralyse most of the muscles in the body, but leave the animal conscious and able to feel pain and experience anxiety even though they cannot respond by moving. In some cases, the experimenters did not appear to be aware that these agents *do not* provide any anaesthesia or analgesia<sup>18</sup>.

Blakemore, who was one of the leading defenders of experimental work involving animals, had made the claim that amblyopia “...*was poorly understood until about 25 years ago when experimental research involving animals began to tackle the question of its origin...in the absence of any real knowledge of the cause of the disease there was no single agreed method of treatment.*”<sup>19</sup> This statement was contrary to available facts. Treatment for, or prevention of, amblyopia had been successfully accomplished many years before the experimental work was even considered<sup>20, 21</sup>.

There is no evidence that there has been any improvement in the treatment or prevention of amblyopia since the early part of the 1900s. Abraham<sup>22</sup> made the following comments concerning Claud Worth, who retired from practice almost 50 years before experimental work began:

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14 [Blakemore & Vital-Durand 1979](#)

15 [Swindale et al 1981](#)

16 [Blakemore & Vital-Durand 1986](#)

17 [Insausti et al 1984](#)

18 In a letter to Richard Whitehead, dated 8 June 1987, Colin Blakemore, who used gallamine triethiodide extensively in his work, made the following statement: “...there is the possibility that muscle relaxants themselves may have some anaesthetic or analgesic action...” This is preposterous in that it has long been known that these agents have no anaesthetic or analgesic properties ([Goodman & Gilman 1970](#)).

19 This is from a document entitled, “A reply to criticism of experiments involving visual deprivation,” dated September 1987, and written and distributed by Blakemore.

20 [Abraham 1972](#); [Brændstrup 1944](#); [Cibis 1975](#); [Peter et al 1932](#); [von Noorden & Maumenee 1968](#)

21 Cibis recounted that Paulos of Aegina, in the seventh century, was the first to attempt what now is considered rational treatment of strabismus and amblyopia by using masks in an attempt to force the deviated eye to look straight ahead ([Cibis 1975](#)). She also pointed out that this concept was improved upon by von Graefe, Donders and other influential ophthalmologists in the nineteenth century because they correctly believed that strabismus caused amblyopia. Abraham noted that Claud Worth, a nineteenth century ophthalmologist, was recommending early treatment of anisometropia because he knew this condition could lead to strabismus and amblyopia ([Abraham 1972](#)). In a symposium on the subject, Peter and others recommended early treatment of strabismus or anisometropia, and early patching of the problem eye to prevent amblyopia ([Peter et al 1932](#)). They also cautioned that the good eye cannot be continuously patched or else the amblyopia would transfer to it. They, therefore, recommended alternate patching of the normal and abnormal eyes, which still is being done today.

22 [Abraham 1972](#)

*“It is surprising how little...has been added to the major store of knowledge as he presented it, at least from the practical viewpoint...Worth’s emphasis on early treatment of the error of refraction and the amblyopia is still the keynote of the most rational approach to the treatment of the strabismic child...”*

Blakemore also had claimed that “...before the animal research began it was not known whether squint could cause amblyopia or whether the existence of poor vision in one eye causes the squint.”<sup>23</sup> This was categorically untrue. For example, Claud Worth had made the proper association in the nineteenth century<sup>24</sup>. Even as early as the 18th century, George Louis Leclerc Comte de Buffon pointed out that amblyopia leads to strabismus<sup>25</sup>.

Blakemore also had stated that there was “...no clear view about the time of onset or duration of the period of sensitivity to the disease,”<sup>26</sup> the implication being that the animal work had provided the answer. This sensitive period is, however, species-specific and is very different in non-human primates, cats and humans, both qualitatively and quantitatively<sup>27</sup>; experimental work on animals could not shed light on the human situation. Furthermore, the fact that earlier ophthalmologists had been recommending early correction of strabismus, and early diagnosis and correction of anisometropia, indicates that they had known and understood the concept of a sensitive period long before the experimental work using animals. Nevertheless, although studies in animals also suggested that changes were permanent some time after the critical period, this has not always been the case with human patients<sup>28</sup>.

When the situation surrounding amblyopia is reviewed, it is found that all the work which has been done on animals has been on the basis of information derived from human observations or which could have been done on human patients<sup>29</sup>. All the hypotheses so far examined by experimental work were known by physicians in this field years before the experimental work was done. The available history also seems to indicate that there has been essentially no change in concepts or in treatment methodologies since the 1800s at least. Modern day experimental work, therefore, appears to have had no significant effect on how amblyopia is managed today. Patching of the dominant eye, which started before animal experimentation, is still the most common treatment despite decades of animal experiments<sup>30</sup>.

There is no question that we can continue to learn more about amblyopia without resorting to experimentation on other animals. Keep in mind that any information we obtain from experimental work must still be confirmed in humans. Moreover, there are many ways to humanely study humans to get the answers we need with respect to understanding brain function as it may relate to amblyopia or treating amblyopia<sup>31</sup>. By carefully studying the

23 “A reply to criticism of experiments involving visual deprivation,” September 1987.

24 [Abraham 1972](#)

25 [Marg 1982](#)

26 “A reply to criticism of experiments involving visual deprivation,” September 1987.

27 [Brændstrup 1944](#); [Daw 1998](#); [El Mallah et al 2000](#); [Headon et al 1985](#); [Marg 1982](#); [Murphy & Mitchell 1987](#); [Peter et al 1932](#); [Vaegan & Taylor 1979](#); [von Noorden 1978](#); for a review, see [Mitchell & Maurer 2022](#)

28 [Daw 1998](#); [El Mallah et al 2000](#); [Wick et al 1992](#)

29 [Abraham 1972](#); [Brændstrup 1944](#); [Campbell 1979](#); [Cibis 1975](#); [Freeman 1979](#); [Mitchell et al 2009,2011](#); [Peter et al 1932](#); [Schwarzkopf et al 2007](#); [Smith 1981](#); [von Noorden & Maumenee 1968](#)

30 [Lunghi et al 2016](#)

31 [Alexander et al 2010](#); [Arden & Barnard 1979](#); [Birch et al 1990](#); [Cowey et al 2011](#); [Curran & Lynn 2009](#); [Demer et al 1988](#); [Enoch et al 1979](#); [Hoyt et al 1981](#); [Hudak et al 2011](#); [Johnson et al 1988](#); [Kiyosawa et al 1989](#); [Klein et al 2010](#); [Larsson et al 2010](#); [Lawwill 1978](#); [Liang et al 2016](#); ...5

human situation in the first place, we not only derive information that is more meaningful in caring for human patients, we also save the resources that would have been expended upon animal studies and we prevent suffering and loss of life of the animals who would have been used.

Many of the hypotheses based upon observation of spontaneous cases of amblyopia or other similar vision disturbance in people have since been confirmed or supported in contemporary studies of human patients<sup>32</sup>. Situations such as those seen in these human studies are what I consider to be 'nature's experiments'. By taking advantage of these, it is not unreasonable to predict that we will continue to improve our understanding of amblyopia and similar conditions. By studying people who have lost an eye early in life, who have had untreatable or untreated opacification of the ocular media early in life, or who have had other perturbations of their developing visual system for reasons unrelated to the eye, we can learn a tremendous amount<sup>33</sup>. These situations are not uncommon and they provide the necessary conditions to understand how vision develops in the human being. These, not the experimental studies in other animals, have led, and will continue to lead, to the most important information on how to manage vision disorders in people.

Harming or killing animals in the name of science does not make it noble or right. We do to these individuals what we do because we are capable of doing so, operating under the morally reprehensible 'principle' of "might makes right". Our own sense of morality demands that our treatment of them be fair and just.

Cited information<sup>34</sup>:

1. Abraham, Samuel V. 1972-03-01 "A tribute to Claud Worth" *Annals of Ophthalmology* 4(3):171-175 <https://www.ncbi.nlm.nih.gov/pubmed/4552003>  
*"Here, almost 80 years later, we are given a chance to evaluate his work. It is surprising how little change seems indicated, how little has been added to the major store of knowledge as he presented it, at least from the practical viewpoint."*  
*"Worth's definition of convergent strabismus includes six essential points, still relevant... [one being] acquired amblyopia."*  
*"Worth accepted 'disuse of convergence' as a factor in the production of divergence. He notes that this is usually accompanied by marked amblyopia."*  
*"Worth knew and expressed his belief that central scotomas were variable, not constant. Von Noorden's excellent work on amblyopia follows this thought. [Worth] was cognizant of the danger of producing amblyopia of the better eye by treatment in those under 6 years."*  
*"Worth's emphasis on early treatment of the error of refraction and the amblyopia is still the keynote of the most rational approach to the treatment of the strabismic child, with early surgery where indicated."*
2. Alexander, Daniel C.; Hubbard, Penny L.; Hall, Matt G.; Moore, Elizabeth A.; Ptito, Maurice; Parker, Geoff J.M. and Dyrby, Tim B. 2010-10-01 "Orientationally invariant indices of axon diameter and density from diffusion MRI" *NeuroImage* 52(4):1374-1389  
<https://dx.doi.org/10.1016/j.neuroimage.2010.05.043>

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- [...4 Lunghi et al 2016; Lynn & Curran 2010; Mitchell et al 1983; Oster et al 1990; Prins et al 2016; Sireteanu et al 1990; von Noorden et al 1983](#)
- 32 [Awaya et al 1973; Bradley & Freeman 1981; Cerny 1987; El Mallah et al 2000; Hoyt et al 1981; Ingram et al 1990; Johnson et al 1982; Moran & Gordon 1982; O'Leary & Millodot 1979; Singh & Schulz 1984; von Noorden 1981; von Noorden & Maumenee 1968; von Noorden et al 1983; Weiss & Ross 1992; Wright et al 1987](#)
  - 33 In addition to the references on human studies already cited, there have been other studies utilising contemporary technology to further our understanding of naturally occurring amblyopia in people ([Demer et al 1988](#)) or vision in normal volunteers ([Enoch et al 1979; Kiyosawa et al 1989](#)).
  - 34 The list of references is not intended to be exhaustive on any particular subject. Rather, I have provided just a few examples to emphasise certain points.

*They used diffusion magnetic resonance imaging in human volunteers.*

3. Arden, G.B. and Barnard, W.M. 1979-01-01 "Effect of occlusion on the visual evoked response in amblyopia" Transactions of the Ophthalmological Societies of the United Kingdom 99(3):419-426 <https://www.ncbi.nlm.nih.gov/pubmed/298825>
4. Awaya, Shinobu; Miyake, Yozo; Imaizumi, Yukiko; Shiose, Yoshihiko; Kanda, Takako and Komuro, Kuniko 1973-01-01 "Amblyopia in man, suggestive of stimulus deprivation amblyopia" Japanese Journal of Ophthalmology 17:69-82  
*"Nineteen cases of unilateral amblyopia, 10 males and 9 females, were examined: their age ranged from 4 to 16 years. All of them had a history of unilateral occlusion of the eye, in 16 cases within 13 months and in 3 cases within 36 months after birth. Fifteen cases underwent occlusion of about one week due to lid surgery for entropion and 4 cases had a longer occlusion period due to hemangioma, eczema and burns of the lid. The role of unilateral occlusion in the development of amblyopia was discussed and the term 'stimulus deprivation amblyopia' was thought to apply to the cases."*
5. Birch, E.E.; Stager, D.R.; Berry, P. and Everett, M.E. 1990-04-01 "Prospective assessment of acuity and stereopsis in amblyopic infantile esotropes following early surgery" Investigative Ophthalmology & Visual Science 31(4):758-765  
<https://www.ncbi.nlm.nih.gov/pubmed/2335443>
6. Blakemore, Colin and Vital-Durand, François 1979-01-01 "Development of the neural basis of visual acuity in monkeys: Speculation on the origin of deprivation amblyopia" Transactions of the Ophthalmological Societies of the United Kingdom 99(3):363-368  
<https://www.ncbi.nlm.nih.gov/pubmed/298814>  
*"It is surely the performance of visual neurones, not their mere number, that determines an animal's acuity."  
"...the loss of acuity which characterizes occlusion amblyopia has no correlate in degraded performance of LGN cells. This result seems to suggest that monkeys differ in this respect from kittens, in which uniocular deprivation...and even convergent squint...have been found to cause a deficiency in the spatial resolution of LGN cells."*
7. Blakemore, C. and Vital-Durand, F. 1986-11-01 "Effects of visual deprivation on the development of the monkey's lateral geniculate nucleus" The Journal of Physiology 380(1):493-511 <https://www.ncbi.nlm.nih.gov/pmc/articles/PMC1182950/>  
*"One monkey...was binocularly deprived from birth until recording at 358 days of age, and a further animal...was reared normally until 44 days and then had the lids of both eyes closed until recording at 195 days."*
8. Bradley, A. and Freeman, R.D. 1981-09-01 "Contrast sensitivity in anisometric amblyopia" Investigative Ophthalmology & Visual Science 21(3):467-476
9. Brændstrup, Poul 1944-03-01 "Amblyopia ex anopsia in infantile cataract" Acta Ophthalmologica 22(1):52-71 <https://dx.doi.org/10.1111/j.1755-3768.1944.tb07449.x>  
*"...the child's eye shows pronounced lability which gradually decreases and, about the 7th year of life, ceases entirely. If the cataract appears after the 8th year of life, functional amblyopia will be of rare occurrence."  
Refers to papers published in the 1800's on "...reports of bilateral reversible massive functional weak sight after blepharospasm of long standing in infants..."*
10. Buyukmihci, Nedim C 2022-12-01 "Serious Moral Concern Is Not Species-limited" <https://escholarship.org/uc/item/6604b7qj>
11. Campbell, F.W. 1979-01-01 "Recent attempts to link psychophysics with neurophysiology in vision research" Transactions of the Ophthalmological Societies of the United Kingdom 99(3):326-332 <https://www.ncbi.nlm.nih.gov/pubmed/298808>  
*"In 1743, Count de Buffon introduced the now well-established amblyopia therapy of occluding the good eye in order to encourage the 'lazy' eye to function better..."*
12. Cerny, Mary E. 1987-04-01 "Detection and treatment of congenital cataracts and amblyopia" Research Resources Reporter 11(4):1-7  
*"[A] study of 7 [human] infants with complete cataracts...revealed that children who had been operated on before 8 weeks of age and then fitted with extended wear contact lenses appeared to develop normally in visual, behavioral, and mental skills. Infants who underwent cataract surgery more than 2 months after birth lagged significantly behind all the others, despite adequate correction."  
With respect to VEPs being recorded by Sokol, "In adults and verbal children, there is*

- good correlation between what the patient says he sees, in terms of his own acuity or resolution, and what the brain puts out in terms of electrical stimulus."*
13. Cibis, Lisa 1975-01-01 "Fifth Annual Richard G. Scobee Memorial Lecture: History of amblyopia and its treatment" *The American Orthoptic Journal* 25:54-61  
<https://doi.org/10.1080/0065955X.1975.11982368>  
*"Paulos of Aegina (Alexandria, 7th century AD) was the first known to attempt rational treatment of strabismus and, in my opinion, treatment of amblyopia. Using masks made of nut shells with small perforations in the center, he intended to force the strabismic eye to 'look straight ahead'..."*  
*"Strabismus masks, as suggested by Paulos of Aegina, were depicted in the works of the French ophthalmologist Ambroise Paré in 1564. These masks came into disrepute in the 18th century when Charles St. Yves...realized that in strabismic persons the covered eye remained deviated." and stated that "it is necessary in many cases to cover the good eye completely in order for the deviating eye to straighten out...We...owe to him the introduction of passive as well as active amblyopia treatment."*  
*"Albrecht von Graefe (1828-1870), Donders (1818-1889), and other influential ophthalmologists of that time postulated that amblyopia was caused by strabismus, which prevents the deviating eye from being used, and the term 'amblyopia ex anopsia' was coined...the most plausible treatment for this condition was to force the amblyopic eye to take over the task of seeing at least part of the time and thus occlusion therapy as suggested 100 years earlier came into vogue."*
  14. Cowey, Alan; Alexander, Iona and Stoerig, Petra 2011-07-01 "Transneuronal retrograde degeneration of retinal ganglion cells and optic tract in hemianopic monkeys and humans" *Brain* 134(7):2149-2157 <https://dx.doi.org/10.1093/brain/awr125>  
*Humans with lesions similar to those experimentally caused in the monkeys were also used and compared. It was found that the degeneration of certain cells in the retina after damage to similar parts of the brain was similar and could be determined easily in the humans.*
  15. Curran, William and Lynn, Catherine 2009-12-23 "Monkey and humans exhibit similar motion-processing mechanisms" *Biology Letters* 5(6):743-745  
<https://www.ncbi.nlm.nih.gov/pmc/articles/PMC2827983/>
  16. Daw, Nigel W. 1998-04-01 "Critical Periods and Amblyopia" *Archives of Ophthalmology* 116(4):502-505 <https://doi.org/10.1001/archoph.116.4.502>
  17. Demer, Joseph L.; von Noorden, Gunter K.; Volkow, Nora D. and Gould, K. Lance 1988-04-15 "Imaging of cerebral blood flow and metabolism in amblyopia by positron emission tomography" *American Journal of Ophthalmology* 105(4):337-347  
[https://doi.org/10.1016/0002-9394\(88\)90294-2](https://doi.org/10.1016/0002-9394(88)90294-2)  
*"Imaging of relative cerebral blood flow...showed reduced activation of primary visual cortex by the amblyopic as compared with the sound eye...[and for glucose metabolism]...reduced activation of primary and accessory visual cortex by the amblyopic as compared with the sound eye in two amblyopic subjects."*  
*"These studies have indicated that positron emission tomography is feasible for the investigation of brain function in human amblyopia. ...the greatest value of this technique probably lies in its use in locating and characterizing the poorly understood extrastriate regions involved in vision. This technique has great potential for further research."*
  18. El Mallah, Mai K.; Chakravarthy, Usha and Hart, Patricia M. 2000-09-01 "Amblyopia: is visual loss permanent?" *The British Journal of Ophthalmology* 84(9):952-956  
<http://www.ncbi.nlm.nih.gov/pmc/articles/pmc1723664/>  
*"Older people with a history of amblyopia who develop visual loss in the previously normal eye can experience recovery of visual function in the amblyopic eye over a period of time. This recovery in visual function occurs in the wake of visual loss in the fellow eye and the improvement appears to be sustained."*
  19. Enoch, Jay M.; Birch, David G. and Birch, Eileen E. 1979-11-09 "Monocular light exclusion for a period of days reduces directional sensitivity of the human retina" *Science* 206(4419):705-707 <https://dx.doi.org/10.1126/science.493976>  
*"Single eyes of young adult observers were occluded for as long as 10 days. Directional sensitivity of the retina ... under photopic conditions was dramatically reduced at every retinal location tested in all subjects. The maximum effect was observed within 3 to 5*



- days, and recovery took place at approximately the same rate after termination of patching."*
20. Freeman, R.D. 1979-01-01 "Rotating grating treatment for amblyopia" Transactions of the Ophthalmological Societies of the United Kingdom 99(3):460-462  
<https://www.ncbi.nlm.nih.gov/pubmed/399813>  
*"Arneson described this treatment rationale in the context of what is now referred to as competition between afferent pathways from both eyes for synaptic sites in visual cortex (Arneson, 1938)."*
  21. Goodman, Louis S. and Gilman, Alfred (eds) 1970-01-01 "The Pharmacological Basis of Therapeutics, 4th ed." London: Macmillan Company
  22. Headon, M.P.; Sloper, J.J.; Hiorns, R.W. and Powell, T.P.S. 1985-02-01 "Sizes of neurons in the primate lateral geniculate nucleus during normal development" Developmental Brain Research 18(1-2):51-56 [https://dx.doi.org/10.1016/0165-3806\(85\)90249-4](https://dx.doi.org/10.1016/0165-3806(85)90249-4)  
*"In the primate, unlike the cat, the period of maximum sensitivity to visual deprivation does not correspond to a period of rapid cell growth in the LGN."*
  23. Hoyt, Creig S. 1980-11-01 "The long-term visual effects of short-term binocular occlusion of at-risk neonates" Archives of Ophthalmology 98(11):1967-1970  
<https://doi.org/10.1001/archoph.1980.01020040819004>  
*"...occlusion of the eyes of infants undergoing [phototherapy] is now standard practice in most neonatal units." The experimental observations of non-human animal work  
"...prompted us to challenge the safety of binocular patching in our nursery. Yet, the data from children observed suggest that binocular patching is not harmful to interocular alignment or the development of stereoacuity."*
  24. Hoyt, Creig S.; Stone, Robert D.; Fromer, Carl and Billson, Frank A. 1981-02-01 "Monocular axial myopia associated with neonatal eyelid closure in human infants" American Journal of Ophthalmology 91(2):197-200 [https://doi.org/10.1016/0002-9394\(81\)90173-2](https://doi.org/10.1016/0002-9394(81)90173-2)  
*"These experimental studies suggest that early attenuation of pattern vision may be a relevant factor in the genesis of axial myopia. However, this thesis has been challenged by the work of von Noorden and Crawford...who were unable to demonstrate a consistent relationship between neonatal eyelid closure and axial myopia in monkeys studied in their laboratory. We report clinical and ultrasonic data for eight infants who developed monocular axial myopia associated with prolonged eyelid closure in early infancy."  
The eyelids of the children in this report had been closed for various medical reasons.*
  25. Hudak, Mariann; Gervan, Patricia; Friedrich, Björn; Pastukhov, Alexander; Braun, Jochen and Kovacs, Ilona 2011-11-04 "Increased readiness for adaptation and faster alternation rates under binocular rivalry in children" Frontiers in Human Neuroscience 5:128  
<https://www.ncbi.nlm.nih.gov/pmc/articles/PMC3208241/>
  26. Ingram, R.M.; Arnold, P.E.; Dally, S. and Lucas, J. 1990-03-01 "Results of a randomised trial of treating abnormal hypermetropia from the age of 6 months" The British Journal of Ophthalmology 74(3):158-159 <https://www.ncbi.nlm.nih.gov/pmc/articles/PMC1042038/>
  27. Insausti, R.; Blakemore, Colin and Cowan, W.M. 1984-03-22 "Ganglion cell death during development of ipsilateral retino-collicular projection in golden hamster" Nature 308(5957):362-365 <https://doi.org/10.1038/308362a0>
  28. Johnson, Chris A.; Post, Robert B.; Chalupa, Leo M. and Lee, Timothy J. 1982-07-01 "Monocular deprivation in humans: a study of identical twins" Investigative Ophthalmology & Visual Science 23(1):135-138 <https://iovs.arvojournals.org/article.aspx?articleid=2159356>  
*One of the twins had been monocularly deprived since birth with a congenital lens opacity (cataract). The deprived eye was 2mm longer than the normal eyes, and the acuity of all normal eyes was similar, and reduced in the deprived eye.*
  29. Johnson, Lenworth N.; Yee, Robert D.; Weissman, Barry A.; Helper, Robert S. and Martin, Deidre A. 1988-03-01 "Contact-lens correction of aphakic infants and children: Early behavioral and VER results" Annals of Ophthalmology 20(3):89-91  
<https://www.ncbi.nlm.nih.gov/pubmed/3400956>
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[https://doi.org/10.1016/0002-9394\(89\)90009-3](https://doi.org/10.1016/0002-9394(89)90009-3)

- Volunteers and patients were examined with PET and the investigators were able to show reductions in regional cerebral glucose metabolism, more profound in the patients with optic neuropathy.*
31. Klein, Johannes C.; Rushworth, Matthew F.S.; Behrens, Timothy E.J.; Mackay, Clare E.; de Crespigny, Alex J.; D'Arceuil, Helen and Johansen-Berg, Heidi 2010-06-01 "Topography of connections between human prefrontal cortex and mediodorsal thalamus studied with diffusion tractography" *NeuroImage* 51(2):555-564 <https://www.ncbi.nlm.nih.gov/pmc/articles/PMC2877805/>
  32. Koo, Euna B.; Gilbert, Aubrey L. and VanderVeen, Deborah K. 2017-01-01 "Treatment of amblyopia and amblyopia risk factors based on current evidence" *Seminars in Ophthalmology* 31(1):1-7 <https://dx.doi.org/10.1080/08820538.2016.1228408>
  33. Kraker, Raymond 2016-12-01 "Future research using amblyopia treatment dose monitors" *JAMA Ophthalmology* 134(12):1354 <https://dx.doi.org/10.1001/jamaophthalmol.2016.3791>
  34. Larsson, Jonas; Heeger, David J. and Landy, Michael S. 2010-12-01 "Orientation selectivity of motion-boundary responses in human visual cortex" *Journal of Neurophysiology* 104(6):2940-2950 <https://www.ncbi.nlm.nih.gov/pmc/articles/PMC3007646/>  
*Used functional magnetic resonance imaging (fMRI).*
  35. Lawwill, Theodore 1978-05-01 "Electrophysiologic aspects of amblyopia" *Ophthalmology* 85(5):451-464 [https://dx.doi.org/10.1016/S0161-6420\(78\)35650-5](https://dx.doi.org/10.1016/S0161-6420(78)35650-5)  
*"Ingenious investigators have discovered a great deal about amblyopia in the intact human being by using psychophysical and electrophysiologic techniques. ... By supplying unique stimuli separated in time or space to the visual field of one or both eyes, it is possible to determine which neural interactions in visual processing occur at different levels of the visual system, from the retina to the cortex, and to discover which specific steps in processing are abnormal in amblyopia."*
  36. Liang, Minglong; Xie, Bing; Yang, Hong; Yu, Longhua; Yin, Xuntao; Wei, Luqing and Wang, Jian 2016-03-01 "Distinct patterns of spontaneous brain activity between children and adults with anisometropic amblyopia: a resting-state fMRI study" *Graefes Archive for Clinical and Experimental Ophthalmology* 254(3):569-576 <https://dx.doi.org/10.1007/s00417-015-3117-9>
  37. Lunghi, Claudia; Morrone, Maria Concetta; Secci, Jacopo and Caputo, Roberto 2016-04-01 "Binocular rivalry measured 2 hours after occlusion therapy predicts the recovery rate of the amblyopic eye in anisometropic children" *Investigative Ophthalmology & Visual Science* 57(4):1537-1546 <https://www.ncbi.nlm.nih.gov/pmc/articles/PMC4909145/>  
*The most used treatment for anisometropic amblyopia during childhood is occlusion therapy, which consists of patching the nonamblyopic eye for extended periods of time.*
  38. Lynn, Catherine and Curran, William 2010-10-12 "A comparison of monkey and human motion processing mechanisms" *Vision Research* 50(21):2137-2141 <https://dx.doi.org/10.1016/j.visres.2010.08.007>  
*Human volunteers were used to do sophisticated tests on motion processing.*
  39. Marg, Elwin 1982-06-01 "Prentice Memorial Lecture: Is the animal model for stimulus deprivation amblyopia in children valid or useful?" *American Journal of Optometry and Physiological Optics* 59(6):451-464 <https://doi.org/10.1097/00006324-198206000-00001>  
*One method of measuring visual acuity in infants is the preferential looking technique as modified and used by Held and his group, who originally discovered the phenomenon in infants.*  
*"This finding in babies came as a surprise because of tacit assumptions in the application of the animal findings to the clinical situation..."*  
*"It is also time to question whether our understanding of the prevention and treatment of amblyopia can be more efficiently and effectively learned in the clinic than in the laboratory."*  
*"While measuring amblyopia objectively in children, we have found an amazing modifiability or sensitivity of the neurovisual system. It does not seem to be directly comparable to experiments performed on cats and monkeys...Of special concern is the method of determining function in these animal experiments. Activity of single neural units was measured rather than functional visual acuity."*  
*"It is clear that the critical period for different functions is not exactly the same even in the same species...The sensitive period for monocular deprivation...may well be different from that for binocular vision deprivation...Environmental factors can modify the period as*

*pointed out in a thorough review by Mitchell...*

*"...cross-suturing is not necessary [in the cat] to obtain almost complete recovery of visual acuity in the originally deprived eye...In the monkey, however, reverse suturing is essential... These experiments demonstrate that there is at least one important species difference between cat and monkey other than the obvious ones of hue discrimination and resolution. They also demonstrate that extrapolation of these conflicting models to children cannot be done with confidence."*

*"Thus by keeping cats in the dark except during monocular deprivation, the modelers have been asking a question that has no counterpart in the clinically important monocular deprivation of infants. The monkey data have been similarly misleading in this regard."*

*"There is new evidence from man that the optic nerve may be involved in some human stimulus deprivation amblyopias... contrary to the classical model originated by Wiesel and Hubel..."*

40. Metz, Henry S. 1985-02-01 "Permanence of the visual recovery that follows reverse occlusion of monocular deprived kittens" *Investigative Ophthalmology & Visual Science* 26(2):249 <https://iovs.arvojournals.org/article.aspx?articleid=2159767>  
*The type of occlusion in the cat study to which this letter referred was different than usually used in amblyopic humans. "Lid occlusion eliminates form but considerable light can still reach the eye and might have a different effect upon the eye behind the lid closure than would be produced by a patch. The concern about acuity in the formerly nondeprived eye not reaching normal levels after lid occlusion was removed may therefore be due to a different type of deprivation than is usually produced by clinical patching therapy. I...would hope that their results, based on the experimental technique described, were not interpreted to suggest that patching may do more harm than good, and would not influence clinicians to be less vigorous with their patching therapy. ...I think work will be necessary to more closely simulate the human clinical situation before further conclusions can be reached."*
41. Mitchell, D.E.; Howell, E.R. and Keith, C.G. 1983-06-01 "The effect of minimal occlusion therapy on binocular visual functions in amblyopia" *Investigative Ophthalmology & Visual Science* 24(6):778-781 <https://iovs.arvojournals.org/article.aspx?articleid=2176841>
42. Mitchell, Donald E.; Kennie, Jan; Schwarzkopf, D. Samuel and Sengpiel, Frank 2009-05-21 "Daily mixed visual experience that prevents amblyopia in cats does not always allow the development of good binocular depth perception" *Journal of Vision* 9(5):22.1-7 <https://doi.org/10.1167/9.5.22>  
*Because the experimental conditions imposed on the kittens are essentially those that can occur naturally due to certain eye diseases, the information could easily have been derived from studies on humans.*
43. Mitchell, Donald E.; Sengpiel, Frank; Hamilton, David C.; Schwarzkopf, D. Samuel and Kennie, Jan 2011-06-16 "Protection against deprivation amblyopia depends on relative not absolute daily binocular exposure" *Journal of Vision* 11(7):13 <https://doi.org/10.1167/11.7.13>  
*There are naturally occurring situations in humans that mimic the experimental manipulations and which can be exploited (and have been) to study this sort of amblyopia in people.*
44. Mitchell, Donald E. and Maurer, Daphne 2022-04-06 "Critical Periods in Vision Revisited" *Annual Review of Vision Science* (): <https://doi.org/10.1146/annurev-vision-090721-110411>
45. Moran, Jeffrey and Gordon, Barbara 1982-01-01 "Long term visual deprivation in a human" *Vision Research* 22(1):27-36 [https://dx.doi.org/10.1016/0042-6989\(82\)90163-8](https://dx.doi.org/10.1016/0042-6989(82)90163-8)  
*This patient had a congenital unilateral cataract removed at 19yr of age. His visual acuity improved, but only somewhat.*  
*"Thresholds of the deprived binocular portions of the nasal retina were greatly elevated by light falling on the non-deprived eye. Visual function in the non-deprived eye was normal."*
46. Murphy, K.M. and Mitchell, D.E. 1987-05-01 "Reduced visual acuity in both eyes of monocularly deprived kittens following a short or long period of reverse occlusion" *The Journal of Neuroscience* 7(5):1526-1536 <http://www.ncbi.nlm.nih.gov/pmc/articles/pmc6568822/>
47. O'Leary, D.J. and Millodot, M. 1979-11-15 "Eyelid closure causes myopia in humans" *Experientia* 35(11):1478-1479 <https://dx.doi.org/10.1007/BF01962795>  
*"Humans with unilateral ptosis are more myopic in the closed eye than in the normal eye. The effect seems unrelated to visual loss. In pairs of humans ranked for sleep and*

- myopia, the more myopic tends to sleep the more. We conclude that eyelid closure causes myopia.*"
48. Oster, John G.; Simon, John W. and Jenkins, Paul 1990-12-01 "When is it safe to stop patching?" *The British Journal of Ophthalmology* 74(12):709-711 <https://www.ncbi.nlm.nih.gov/pmc/articles/PMC1042272/>
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*"The feline limits of fusion and qualitative stereopsis reported here are quite different from those reported from human psychophysical experiments."  
The cat's visual acuity is "...about one-sixth that of..." the human.  
The experiment also was repeated, in essence, on human subjects to determine if the difference between the results in the cats and those previously reported for humans was due to species differences. Those results argued that it was due to species differences.  
"[W]e attempted to measure the limits of fusion and qualitative stereopsis on human subjects, using the same procedures we used in the cat experiments."*
50. Padrell, Maria; Llorente, Miquel and Amici, Federica 2021-10-01 "Invasive Research on Non-Human Primates—Time to Turn the Page" *Animals* 11(10):2999 <https://www.ncbi.nlm.nih.gov/pmc/articles/PMC8532895/>
51. Palmer, A.R. and King, A.J. 1982-09-16 "The representation of auditory space in the mammalian superior colliculus" *Nature* 299(5880):248-249 <https://doi.org/10.1038/299248a0>
52. Peter, L.C.; Chavasse, B.; Ormond, A.; Alabaster; Williamson-Noble; Barrie, S.; Hepburn, M.; Stewart, S.; Maddox and van der Hoeve 1932-01-01 "Symposium on the treatment of non-paralytic squint" *Transactions of the Ophthalmological Societies of the United Kingdom* 52:325-380  
*"The treatment of squint should begin when the diagnosis is made."  
"...central amblyopia which is found in the squinting eye...all phases of treatment yield the best results before the sixth year of life...it is disastrous to delay treatment until the child is of school age...the fight against amblyopia may be begun even in a child six months of age."  
"The deprivation and the central scotoma can be transferred from one eye to the other by forced occlusion of the fixing eye in children up to 5 or 6 years of age. The younger the child, the easier it is to transfer the squint and the lowered vision. The time required in young children, about the age of three, for amblyopia to develop after squint becomes fixed, is brief. It is probable that it develops even more rapidly in infants."  
"...methods of preventing and of correcting amblyopia...either atropine can be used in the fixing eye, or the fixing eye can be occluded for a time each day. Atropine is least satisfactory... it is partly through this method, which in instances was carried on indefinitely without consulting the physician, that squint was shown to be transferable from one eye to the other."  
With respect to occlusion therapy, "If amblyopia has not developed, a two-hour session each day usually is sufficient to prevent deterioration of vision."  
"Amblyopia rarely if ever develops after the seventh year in any form of squint. For the same reason (perfectly formed and developed maculae), amblyopia and squint cannot be transferred from one eye to the other after the seventh year."  
"Our attack upon the problem of squint is made on the same principles as it was thirty years ago."  
"Then again an evolutionary theory of squint brings with it more than ever the conviction that prevention is better than cure... there is...a whole group of causes -- the refractive errors -- the correction of which, before the time when the infant's visual reactions assume primate characteristics, would prevent the development of squint. Wholesale refraction of every child reaching the age of, say, 12 months, might in this regard be a reasonable and powerful preventative of squint...or simply if there is a squint in the family, it should be refracted under complete mydriasis at a very early age..."  
"...in order to appreciate correctly the appearance of objects in space...the centres of the other sensory organs must be developed, and the transcortical fibres connecting these with the visual centres must be also developed. Probably a period of some two or three years is passed during childhood before the centres and their communications one with*

*another are fully matured."*

*"If then we are correct in assuming that the eyes are not anatomically or functionally complete at birth, and that the stimulus of light, form, movement, etc., is necessary to normal development of full visual capacity, any interference with the clarity of the media in one eye will produce a definite delay in the completion of the development, and the retardation may be such that improvement is delayed beyond the time when development is possible."*

53. Prins, Doety; Hanekamp, Sandra and Cornelissen, Frans W. 2016-03-01 "Structural brain MRI studies in eye diseases: are they clinically relevant? A review of current findings" *Acta Ophthalmologica* 94(2):113-121 <https://dx.doi.org/10.1111/aos.12825>  
*"Future structural MRI studies can contribute to (i) further establish relationships between ocular and neurological neurodegenerative disorders, (ii) investigate whether brain degeneration in eye diseases is reversible, (iii) evaluate the use of neuroprotective medication in ocular disease, (iv) determine optimal timing for retinal implant insertion and (v) establish structural MRI examination as a diagnostic tool in ophthalmology."*
54. Raviola, Elio and Wiesel, Torsten N. 1985-06-20 "An animal model of myopia" *The New England Journal of Medicine* 312(25):1609-1615  
<https://dx.doi.org/10.1056/NEJM198506203122505>  
*"Thus, myopia in monkeys seems to be induced by the alteration of the visual input rather than by a physical effect of the closed lids. A similar phenomenon has been observed in human beings: Myopia develops when the transparency of the dioptric mediums of the eye is impaired early in life, as in cases of opacities of the cornea...lens...and vitreous body...There is even a human equivalent of monkey lid-fusion myopia, for it has been reported that hemangiomas of the lids, ptosis, and lid suture in children are associated with a myopic refractive error..."*  
*"...the experiments with atropine administration suggest that the mechanism of eye elongation is different in rhesus and stump-tailed macaques: accommodation seems to have a role in *M. arctoides* but not in *M. mulatta*."*  
*"...studying the effect of lid fusion after section of the optic nerve. Again, we obtained different results in *M. mulatta* and *M. arctoides*."*
55. Rodieck, R.W. 1979-03-01 "Visual pathways" *Annual Review of Neuroscience* 2:193-225  
<https://dx.doi.org/10.1146/annurev.ne.02.030179.001205>
56. Schwarzkopf, D. Samuel; Vorobyov, Vasily; Mitchell, Donald E. and Sengpiel, Frank 2007-01-01 "Brief daily binocular vision prevents monocular deprivation effects in visual cortex" *The European Journal of Neuroscience* 25(1):270-280 <https://doi.org/10.1111/j.1460-9568.2006.05273.x>  
*There are established methods of obtaining essentially the same information from people.*
57. Singh, Gurinder and Schulz, Elisabeth 1984-01-01 "Bilateral deprivation amblyopia" *Annals of Ophthalmology* 16(1):86-88 <https://www.ncbi.nlm.nih.gov/pubmed/6703579>  
*"Two children had toxic bilateral cataracts at the ages of 36 months and 41 months and were deprived of treatment for the next 15 and eight years, respectively. After successful surgery the visual results were about 20/40 in both eyes. This visual recovery suggests that the susceptibility to bilateral stimulus deprivation at this age is slight but not absent, and...longtime deprivation beyond the sensitive period does not effect [sic] greatly the ultimate outcome of the treatment."*
58. Sireteanu, Ruxandra; Fronius, Maria and Katz, Birgit 1990-01-01 "A perspective on psychophysical testing in children" *Eye* 4(6):794-801 <https://dx.doi.org/10.1038/eye.1990.125>
59. Smith, Douglas C. 1981-09-04 "Functional restoration of vision in the cat after long-term monocular deprivation" *Science* 213(4512):1137-1139  
<https://dx.doi.org/10.1126/science.7268422>  
*"These results are in agreement with the known electrophysiological effects of these recovery conditions and are also similar to the effects of reverse occlusion or loss of the nonamblyopic eye in human amblyopes."*
60. Swindale, N.V.; Vital-Durand, F. and Blakemore, C. 1981-11-24 "Recovery from monocular deprivation in the monkey. III. Reversal of anatomical effects in the visual cortex" *Proceedings of the Royal Society of London. Series B, Containing Papers of a Biological Character* 213(1193):435-450 <https://dx.doi.org/10.1098/rspb.1981.0074>
61. Tailor, Vijay; Bossi, Manuela; Greenwood, John A. and Dahlmann-Noor, Annegret 2016-09-01

- "Childhood amblyopia: current management and new trends" British Medical Bulletin 119(1):75-86 <https://www.ncbi.nlm.nih.gov/pmc/articles/PMC5862311/>  
*"Areas timely for developing research Impact of amblyopia on education and quality of life; optimal screening timing and tests; optimal administration of conventional treatments; development of child-friendly, effective and safe binocular treatments."*
62. Vaegan and Taylor, David 1979-01-01 "Critical period for deprivation amblyopia in children" Transactions of the Ophthalmological Societies of the United Kingdom 99(3):432-439 <https://www.ncbi.nlm.nih.gov/pubmed/298827>  
*"However, the critical period for the effects of strabismus may not be the same as that for visual deprivation, which is how the animal critical period has been defined."  
"Burian (1966) found, as we have done, that occlusion amblyopia is most likely before age 3."  
"Thus the effect of deprivation occurs more slowly and remains possible for a longer period in children than in animals."  
"In unilateral congenital cataract, surgery [sic] and optical correction, if indicated, should be completed within the first 4 months of life. Our experience indicates that, at all ages before adolescence, optical correction after the onset of cataract should be treated as a matter of urgency and combined with vigorous occlusion treatment."*
63. Vagge, Aldo and Nelson, Leonard B. 2016-09-01 "Amblyopia update: new treatments" Current Opinion in Ophthalmology 27(5):380-386 <https://dx.doi.org/10.1097/ICU.0000000000000293>
64. Van Essen, D.C. 1979-03-01 "Visual areas of the mammalian cerebral cortex" Annual Review of Neuroscience 2:227-263 <https://dx.doi.org/10.1146/annurev.ne.02.030179.001303>
65. von Noorden, Gunter K. 1978-05-01 "Application of basic research data to clinical amblyopia" Ophthalmology 85(5):496-504 [https://dx.doi.org/10.1016/S0161-6420\(78\)35652-9](https://dx.doi.org/10.1016/S0161-6420(78)35652-9)  
*"Amblyopia has now been produced successfully in models of various species, but data from cats, squirrels, and dogs cannot be applied automatically to man. There are differences in the anatomic and functional organization of the visual system of cats and primates. Human amblyopia involves primarily foveal vision rather than peripheral vision..."  
"Moreover, in spite of many similarities of the visual deprivation syndrome in the different species, results from our studies in monkeys are different in some respects from those obtained in cats. For instance, unlike in the cat, unilateral lid closure in the monkey affects not only the binocularly innervated portion of the lateral geniculate nucleus but also the monocular portion...In addition, we have been unable thus far to show that the morphology of different classes of neurons in the lateral geniculate nucleus of the monkey is selectively affected by visual deprivation as it is in cats..."  
"Amblyopia is now defined as a unilateral or bilateral decrease of visual acuity caused by form vision deprivation, abnormal binocular interaction, or both, for which no organic cause can be detected by the physical examination of the eye and which, in appropriate cases, is reversible by therapeutic measures."  
"Research in amblyopic animal models has confirmed many older concepts regarding human amblyopia based solely on clinical observation and psychophysical experimentation."*
66. von Noorden, Gunter K. 1981-02-01 "Amblyopia caused by unilateral atropinization" Ophthalmology 88(2):131-133 [https://dx.doi.org/10.1016/S0161-6420\(81\)35063-5](https://dx.doi.org/10.1016/S0161-6420(81)35063-5)  
*"...unilateral atropinization during visual immaturity may actually cause amblyopia. Three reported cases demonstrate this point."*
67. von Noorden, G.K. 1988-01-01 "A reassessment of infantile esotropia: XLIV Edward Jackson Memorial Lecture" American Journal of Ophthalmology 105(1):1-10 [https://doi.org/10.1016/0002-9394\(88\)90113-4](https://doi.org/10.1016/0002-9394(88)90113-4)  
*"...advances in our knowledge can be expected from the rapidly emerging discipline of infant psychophysics."  
"Finally, we must ask whether animal experiments have helped us to better understand the pathophysiology of essential infantile esotropia. It is true that the so-called binocular cells in the striate cortex are permanently lost in infant monkeys after artificial strabismus... However, these cells also disappear in nonstrabismic monkeys after eyelid suture...or after experimentally induced anisometropia... Thus far the loss of binocularly innervated striate neurons has only been linked to an absence of stereopsis... There is no*

- evidence from animal research that binocular functions other than stereopsis, such as sensory and motor fusion, are similarly affected by abnormal visual experience early in life. There is currently no animal model for essential infantile esotropia."*
68. von Noorden, G.K. and Maumenee, A.E. 1968-02-01 "Clinical observations on stimulus-deprivation amblyopia (amblyopia ex anopsia)" *American Journal of Ophthalmology* 65(2):220-224 [https://doi.org/10.1016/0002-9394\(68\)93590-3](https://doi.org/10.1016/0002-9394(68)93590-3)  
*One patient in this report had corneal scarring of the right eye at two years of age. Penetrating keratoplasty was done at 26 years of age, but visual acuity did not improve and convergent strabismus was present when left eye was occluded. The other patients had similar types of histories.*  
*"Juler [1921] emphasized the close relation between the functional result and the age at occurrence of cataract. Similar observations have been reported by Broendstrup [1944]..."*  
*"It has been known for a long time that normal development of the visual system depends to a certain extent on adequate stimulation of the retina during early infancy and childhood."*  
*Concerning the experiments of Wiesel and Hubel, "...it is not appropriate to transfer these data uncritically, to similar situations in humans, since the morphologic and functional organization of the visual system in cats is substantially different from that in man."*
69. von Noorden, G.K.; Crawford, M.L.J. and Levacy, R.A. 1983-06-01 "The lateral geniculate nucleus in human anisometric amblyopia" *Investigative Ophthalmology & Visual Science* 24(6):788-790 <http://iovs.arvojournals.org/article.aspx?articleid=2176853>  
*"Histologic study of the LGNs from a patient with ophthalmologically confirmed anisometric amblyopia shows a decrease of cell sizes in the parvocellular layers innervated by the amblyopic eye. This decrease was more pronounced in laminae receiving crossed fibers."*
70. Weiss, Avery H. and Ross, Eric A. 1992-07-01 "Axial myopia in eyes with optic nerve hypoplasia" *Graefe's Archive for Clinical and Experimental Ophthalmology* 230(4):372-377 <https://doi.org/10.1007/bf00165948>
71. Wick, Bruce; Wingard, Michael; Cotter, Susan and Scheiman, Mitchell 1992-11-01 "Anisometric amblyopia: Is the patient ever too old to treat?" *Optometry and Vision Science : Official Publication of the American Academy of Optometry* 69(11):866-878 <https://doi.org/10.1097/00006324-199211000-00006>  
*"From these results we conclude that following a sequential management plan for treatment of anisometric amblyopia can yield substantial long-lasting improvement in visual acuity and binocular function for patients of any age."*
72. Wright, Kenneth W.; Wehrle, Malcolm J. and Urrea, Paul T. 1987-03-01 "Bilateral total occlusion during the critical period of visual development" *Archives of Ophthalmology* 105(3):321 <https://dx.doi.org/10.1001/archopht.1987.01060030035012>  
*Bilateral occlusion during critical period extends the critical period and does not lead to loss of visual acuity. Unilateral occlusion results in amblyopia.*