MYOPIA PRODUCED IN YOUNG CHICKS BY INTERMITTENT MINIMAL FORM VISUAL DEPRIVATION - CAN SPECTACLES CAUSE MYOPIA?

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ABSTRACT

Spectacle use has been postulated to aggravate or cause human myopia. Form visual deprivation, by complete full-time occlusion or refractive lenses, has been demonstrated to cause axial myopia in animals. We raised young chicks in conditions which closely approximate plano spectacle wear in humans. In addition, we sought to achieve more physiological conditions of form deprivation.

Nine newborn chicks were raised with intermittent monocular visual deprivation and their eye growth and refraction monitored by retinoscopy, ultrasonic A-scan biometry and with a travelling microscope. After hatching, the nictitating membranes were sutured for 3-4 days. This was followed by a transparent plano plastic cover over the same eye for 3-4 days per week. After 3 weeks, the manipulated eyes were more myopic (mean refraction -0.72 D, axial length 13.11 mm) than fellow eyes (+0.83 D, 11.99 mm) ($p<0.05$ and $p<0.01$ respectively).

These results suggest that the chick eye is exquisitely sensitive to disturbances in the visual environment; intermittent minimal manipulation by conditions simulating spectacle wear in man was myopiagenic. It is postulated that spectacles can cause form visual deprivation of foveal and nonfoveal neurons (and hence myopia) by reducing luminance and contrast, chromatic and spherical aberration (in nonfoveal neurons) and restriction and distorsion from the frame.

Keywords: Myopia, Spectacles, Eye, Development, Astigmatism.

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INTRODUCTION

In most animals, the optical power of the eyes is well matched to their length, so that images of distant objects are in focus on the retina (emmetropia). In humans, however, this matching of optical power and eye size is frequently lacking. This results in significant degrees of myopia (nearsightedness) if the eye is too long compared with its optical power, or hyperopia (farsightedness) if the eye is too short.

At birth, the eyes of several species are hyperopic and extremely variable in refractive status but quickly grow toward emmetropia[1]. This raises the possibility that myopia and hyperopia may reflect disorders of the emmetropization process.

Various hypotheses, some rather curious, involving dietary, hormonal, occupational, and psychological causes of myopia have enjoyed periods of popularity, as have a variety of mechanisms of myopia involving, for example, eyestrain, accommodation, convergence, inflammation, traction on the optic nerve, and pressure on the veins leaving the eye[2].

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Within the last decade, it has become clear that alterations in visual experience can provoke myopia: monkeys, tree shrews, and cats become myopic when deprived of form vision early in life[3-5]. In these cases, as in typical human myopia[6] the myopia involves an increase in the length of the eye. Children have also been found to become myopic when deprived of form vision because of a variety of disorders that have in common an obstruction of vision, such as ptosis, haemangiomas, or congenital cataracts[4,7,8].

These demonstrations that disturbed visual experience could influence myopia have been seen as consistent with the view that typical human myopia is due to excessive ocular accommodation (the focusing of the eye for near distances) caused by long periods of near viewing, as in reading. The principal support for this hypothesis has come historically from observations that professions requiring much reading or other close work tend to be occupied by myopes, and that there is a consistent correlation between education level and myopia[6]. In addition, one study in an Inuit community suggested that the advent of compulsory schooling, along with other accoutrements of Western civilization, was associated with an increased incidence of myopia. A long history of observations such as these has entrenched the idea that near work is a primary factor in the aetiology of myopia.

Animal research also supports an association of increased accommodation and myopia. A small amount of myopia can be produced by restricting the vision of monkeys to white drapes 18 inches away[3]. Evidence of an effect of near vision was also suggested, but not proven, by studies showing that cage-reared cats and monkeys are myopic compared with wild conspecifics. Of course, many differences other than the amount of near vision distinguish wild from captive animals. Chimpanzees raised in cages show a progression toward greater myopia as they get older, presumably as a result of captivity[2].

The results of experimental tests of the accommodation hypothesis are equivocal. There are some positive results showing reduced progression of myopia when children or animals are given daily doses of atropine, a drug that paralyzes the muscles of accommodation[1]. On the other hand, an equally

careful study, in which the need for accommodation was reduced by having chickens wear bifocals, produced no change in myopic progression. Denervation of the ciliary muscles in chicks reduced, but did not eliminate, myopia caused by visual deprivation[9]. Recently, Raviola and Wiesel have mentioned in a review that neither atropine nor optic nerve section prevent visual deprivation from producing myopia in rhesus monkeys, although either procedure is effective in the stumptail macaque[1].

As such, we should redirect our attention to studies which demonstrate the influence of visual deprivation on refraction and local eye development. In particular we should focus our efforts on exploring and characterizing the specific visual experiences which may do so.

The various hypotheses of the aetiology of myopia that have attracted serious attention have been based on work where complete and full-time form deprivation was performed on the eye[1,10-13]. This is obviously very unphysiological. It is our goal to approximate in the laboratory, the visual environment of the child who experiences excessive nearwork. In addition, we seek to propose a new hypothesis that spectacles, in itself, can lead to significant form deprivation, thereby inducing further myopic progression.

To this end, the experiment was conducted for the following goals:

1. Emulate the form-deprivation chick model of myopia
2. Simulate occasional nearwork by altering vision only intermittently to test the hypothesis that the altered visual environment of the child who reads excessively is as myopizing as one who suffers a congenital cataract or disease.
3. Simulate spectacle wear and minimising the extent of form deprivation by using clear and transparent eye occluders to investigate the proposed hypothesis that spectacle wear increases myopic progression .

Minimal visual form deprivation was performed by:

(a) Suturing the nictitating membrane soon after birth. When the sutures degraded after 34 days, surgery was not repeated. The nictitating membrane is more transparent than even the eyelid, which is itself translucent. To my knowledge, this is the first attempt to create myopia using this natural occluder.

(b) Subsequently, transparent plastic covers were attached over the eye, which the chick removed in 3-4 days. This was repeated at weekly intervals. This produced minimal or no visual distorsion and simulates the wearing of plano (or clear) spectacles at regular intervals.

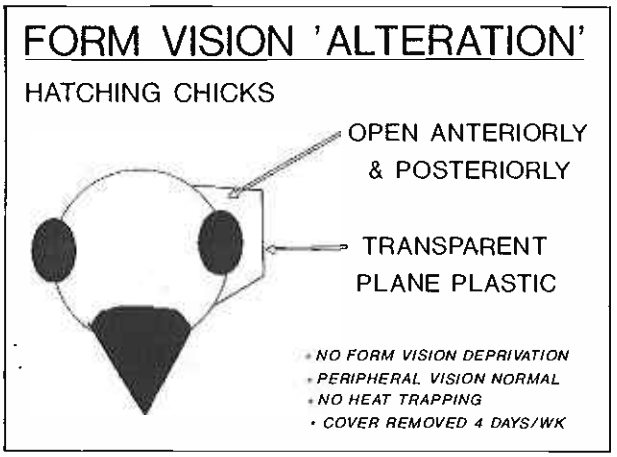
MATERIALS AND METHODS

Axial length measurements and retinoscopic refractions were made in both eyes of 9 newborn chicks. This was repeated at 3 and 4 weeks after hatching.

All manipulated eyes were right eyes, the left eyes serving as controls. On the first and second day after hatching, nictitating membrane suture was performed. The membrane was sutured to the inferior fornix of the lower lid with 8/0 polypropylene. In this way, the chicks experienced minimal form deprivation in their first few days of life, with minimal change to blinking and eye movement. All sutures were found to have degraded by 4-5 days, with the eyes fully open.

At the end of the first week, clear plastic transparent covers were then attached over the right eyes (Fig 1). The 1 cm-square covers were placed 1 mm from the eyelids to simulate the apical distance of spectacles. They served to produce minimal form vision deprivation. The covers stayed in place for 3-4 days, after which they were dislodged by the chick. Replacements were made on the first day of the subsequent week. Thus, a 3-4 day period of binocular clear vision was permitted for every 3-4 days of "spectacle wear".

Fig 1 - Chick with transparent "spectacle" over the right eye.



The ocular axial length measurements were obtained by A-scan ultrasonography with an Ophthalmic A-scan A-1000 unit (Sonomed Technology, Inc). The chicks were examined under topical anaesthesia (proparacaine hydrochloride 0.5%). Ultrasound measurements were taken with the eye open to avoid error due to lid thickness or unequal pressure of the probe on the closed lid. As the speed of sound through the chick's eye is slower than in the human (1,550 m/s), a correction factor was needed after measurements were obtained. This is mainly due to the size of the chick's crystalline lens, which is much larger than its human counterpart. For this purpose, one chick was sacrificed at 4 weeks, and its axial length measured with a travelling microscope, accurate to 0.01 mm. The results reported in the following tables have been appropriately adjusted by the constant derived.

RESULTS & OBSERVATIONS

Table I and II detail the refraction and ocular axial length measurements obtained at birth and at various intervals after hatching. Myopia developed almost consistently in the manipulated eye, which also acquired a greater length. The differences between the two eyes were shown to be statistically significant, using the Student's t test.

DISCUSSION

Chickens are used widely to explore the postnatal development of the visual system under normal and deprivation conditions. In particular, the process of myopization is being actively investigated in this species. Therefore, they serve as a

Table I - Refraction of the chicks at birth, 3 weeks and 4 weeks. In all cases, the right eye was the manipulated eye, the left serving as the control.

Refraction (Diopters)	Mean	Standard deviation	Minimum	Maximum
Newborn: Right	+1.22	0.79	+0.50	+2.50
Newborn: Left	+1.11	0.96	+0.50	+2.50
Newborn: Right-Left	+0.11+	0.33	-0.50	+0.50
3 week: Right	-0.72	1.99	-5.50	+1.00
3 week: Left	+0.83	0.83	-0.50	+2.00
3 week: Right-Left	-1.56#	2.28	-7.00	+0.50
4 week: Right	-0.50	1.56	-3.50	+1.00
4 week: Left	+0.83	0.71	+0.00	+2.00
4 week: Right-Left	-1.33@	1.66	-5.00	+0.00

\+ Not statistically significant
\# Significance level < 0.05 t = 2.17
@ Significance level < 0.05 t = 2.33

Table II - Ultrasonic axial globe length at birth and after 4 weeks

Axial length (mm)	Mean	Standard deviation	Minimum	Maximum
Newborn: Right	8.67	0.64	7.38	9.42
Newborn: Left	8.53	0.39	7.69	9.14
4 week: Right	13.11	0.51	12.46	13.86
4 week: Left	11.99	0.47	11.23	12.46
4 week: Right - Left	1.12#	0.48	0.41	1.96

Significance level < 0.01 t = 4.85

valuable animal model to study normal visual system development as well as causes underlying human visual system disorders, especially myopia.

Emmetropization is vision dependent

A variety of mechanisms have been proposed to account for the achievement of proper eye size during postnatal eye growth. The results of numerous studies with different animal species point to visual image quality as an important factor because loss of a focused image on the plane of the retina during development perturbs coordinated eye growth (causing elongation):

1. In chicks, eyes deprived of normal vision either by eyelid suture or by translucent occluders elongated excessively[10,14].
2. In monkeys, poor retinal image quality early in life due to eyelid suture or opacification of the cornea caused excessive eye elongation[12].
3. In humans, after monocular deprivation due to congenital lens opacity and to neonatal eye-lid closure[4,8] the deprived eyes were longer than the undeprived fellow eyes and normal eyes. Furthermore, a high incidence of myopia was reported in human patients suffering from a variety of ocular anomalies that caused disruption of pattern vision during early development. These findings support the idea that emmetropization is a vision-dependent phenomenon in humans also.

There is a consensus in the literature that eyelid suture prevents form or pattern vision without depriving the eye of sight[15]. This lack of form vision, as well as total visual deprivation, lead to excessive postnatal eye elongation. In this study, we have demonstrated that much less radical manipulations of vision also have the same effect.

Local retinal factors respond to visual deprivation

Neurochemical changes in the retina have been reported after occlusion or eyelid suture. For example, immunoreactivity for vasoactive intestinal peptide (VIP) increases in amacrine cells in eyelid sutured monkeys[16]. The effects of occlusion on VIP have not been investigated. In chicks[13], changes occur in the retinal dopamine (DA) system as a result of deprivation[17]. Additional support for the involvement of DA in eye growth control comes from the recent finding that apomorphine, an agent that interacts with DA receptors, prevents excessive axial elongation of eyes of visually deprived chicks. Since deprivation apparently causes neurochemical alterations in the retina itself, retinal neurotransmitter/neuromodulator substances may play a role in eye size regulation.

Although form deprivation explicitly produces eye growth in chicks and may account for the association of reading and myopia in humans, the retinal cells involved need not be form-sensitive. Any cell with transient responses would be more active in a varied environment because eye movement would continually change the level of stimulation. Thus even non-neuronal cells, such as Mueller cells or retinal pigment epithelium cells, might be less active if the eye wore an occluder or if the scene viewed were uniform. If production of a growth affecting substance depended on activity, myopia might result.

In chicks and in monkeys, form deprived eyes continue to elongate abnormally after sectioning of the optic nerve. Also, in tree shrews, lid-sutured eyes become longer after blockage of retinal ganglion cell action potentials by intravitreal injections of tetradotoxin. Since excessive axial eye elongation proceeds in the absence of retinal ganglion cell activity and of centrally arriving action potentials, retinal cells other than ganglion cells may be a source of growth regulating and coordinating factors.

These results and our study support the hypothesis that the two experimental conditions strongly linked to myopia in humans and animals - large amounts of reading and deprivation of form vision - both cause myopia by visual deprivation. Although the printed page may provide adequate stimulation for the foveal retina, it could provide an impoverished stimulus environment for other regions of the retina, resulting in myopia.

Reading and myopia

It has been argued that the activity of nonfoveal retinal neurons is lower during reading. Most retinal neurons have transient responses, but normally the movements of the eyes provide these neurons with continually changing stimuli, which renew their responses. If a neuron received exactly the same stimulus pattern before and after the eye movement, its activity would decay to zero. Thus, the activity of retinal neurons averaged over a period of time would depend on the differences between successive stimuli received as the eye's movements present the neuron with different pieces of the scene being viewed.

Three peculiarities of the printed page act to reduce the variation in stimulation that retinal neurons receive as a result of eye movements:

1. While most scenes are made up of features that vary widely in size (that is, containing a broad range of spatial frequencies), printed text contains mainly small features (that is, high spatial frequencies). Nonfoveal neurons, because they have large receptive fields, cannot resolve the features of individual letters; rather, they respond to the local luminance averaged over several letters. Thus, during reading the activity of nonfoveal neurons changes little with changes in eye position. Only in the fovea, where the neuronal receptive fields are comparable in size to the elements of the letters, will the responses change greatly. In contrast, because the heterogeneous stimuli of most scenes in the natural world include stimuli appropriate in size for neurons at different distances from the fovea, each eye movement would generally present most neurons with a substantially changed level of stimulation. If we consider the output of retinal ganglion cells viewing text, the center contains "neurons" with smaller receptive fields, which resolve smaller elements than those in the periphery. If one imagines the eye moving slightly, the activity of the "neurons" in the center would change greatly regardless of the material viewed, whereas those in the periphery would hardly change when viewing text.
2. The range of luminances present on the printed page is much smaller than is typical in outdoor scenes. White paper reflects only about ten times the light of black ink, whereas sunny surfaces may be many orders of magnitude brighter than deep shadows. This smaller range of luminance means that the response of neurons changes less from one eye position to the next; this also would lead to lower average neural activity.
3. Text is achromatic, whereas most scenes contain a variety

of colours. This may exacerbate the temporal effects, because the most numerous retinal ganglion cells (the inputs to parvocellular lateral geniculate neurons) show transient responses with a rapid time course to noncoloured stimuli, in contrast to a much slower decay to chromatic stimuli. Thus, during reading, the cell's response would fade very rapidly after each eye movement, whereas in viewing typical coloured stimuli the response would be more enduring.

This is not the first suggestion that visual deprivation of the nonfoveal retina leads to myopia. Low vision patients with disorders affecting the entire retina becomes myopic, whereas those with conditions principally affecting the foveal region remain hyperopic. In these cases, reducing the high spatial frequency content, thereby affecting primarily the fovea, did not cause myopia whereas elimination of all form vision did. This suggestion could lend credibility to the popular belief that reading in poor light is particularly bad for one's eyes because retinal neurons exhibit lower signal-to-noise ratios in dim light, even well into the photopic range.

Conceivably, the differences in ocular refraction among people with similar visual habits may be caused by a large variation in the efficacy of the mechanism of visual modulation of eye growth. Those at the low end of the range would tend to remain hyperopic, as they were at birth. These individuals would also tend to be unaffected by visual environments that lead to myopia; this would account for the fact that hyperopes tend not to become myopic after childhood. In contrast, those with more effective mechanisms of visual modulation of eye growth would become emmetropic at an early age and for the same reason would be particularly susceptible to visual environments that might lead toward myopia.

Can spectacles worsen myopia ?

Anecdotal reports abound of the more rapid increase in myopia which accompanies the start of spectacle wear for myopia. While this cannot be distinguished from the natural pattern of myopia progression (which has been inadequately documented and studied), the observation has been attributed to over-correction and the increased accommodation during nearwork with concave spectacles. In view of the current hypothesis of form deprivation being the precipitating event for myopia (rather than excessive accommodation), it is timely that this view be revised and experimental support adduced.

Our study demonstrated that minimal and intermittent form deprivation was sufficient to induce myopia. This supports our contention that spectacle wear is, in itself, myopiogenic and is independent of the optical correction achieved by lens wear. It is likely to be due to form deprivation through the following mechanisms:

1. Reduced luminance and contrast at the level of the retina. Lens multicoating, tints and reflectivity may also contribute to this effect.
2. Chromatic and spherical lens aberrations. This is of special relevance in the light of the above arguments that reading induces myopia by impairing luminance, resolution and chromaticity of nonfoveal vision.
3. Restriction and distorsion of peripheral vision due to the spectacle frame.

Although further studies are needed to further this suggestion, it supports clinical advice to minimise spectacle wear in an effort to stem the rapid progression of myopia arising from excessive reading in childhood. It is also prudent for children to look away from their reading material periodically to reduce the visual deprivation of the nonfoveal retina.

CONCLUSIONS

In this study, we have demonstrated that subtle visual deprivation presented early in life can cause myopia in the chick. Strong support is provided for the reading (nearwork) hypothesis of human myopia. In addition, we propose that spectacle wear, by impairing the nonfoveal retina's illuminance, resolution and colour sense can contribute to the disordered ocular development.

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