

Towards customized amblyopia treatment: occlusion therapy and axial growth in anisometropic amblyopia

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Dear Editor,

Anisometropic amblyopia is characterized by unequal refractive error between the two eyes, leading to visual impairment in the more ametropic eye. Occlusion therapy, a widely used treatment, involves patching the dominant eye to stimulate neural plasticity in the weaker eye, thereby improving visual acuity. However, the refractive consequences of unilateral patching remain insufficiently documented.

A strong correlation between anisometropia and interocular axial length differences in anisometropic amblyopia has been documented^[1]. Additionally, previous studies in both animal models and clinical settings have demonstrated that deprivation of form vision disrupts emmetropization, resulting in abnormal axial growth^[2-3]. Additionally, some research has raised concerns about the unintended effects of occlusion therapy on axial elongation, particularly in anisometropic patients. Unilateral visual deprivation, such as that induced by occlusion therapy, has been shown to promote axial elongation in the patched eye^[4-5]. This phenomenon is particularly significant in anisometropic amblyopia, where preexisting interocular refractive differences are already a major concern.

We hypothesize that the effect of occlusion therapy on axial elongation varies depending on the type of anisometropia. Specifically: 1) Anisohyperopic amblyopia: In patients with anisohyperopia, occlusion therapy may induce axial

elongation in the less hyperopic (non-amblyopic) eye. This could lead to an increase in aniso-axial length, potentially decreasing hyperopia in the non-amblyopic eye and increasing anisohyperopia; 2) Anisomyopic amblyopia: In patients with anisomyopia, occlusion therapy may also promote axial elongation in the non-amblyopic (less myopic) eye. However, this could decrease aniso-axial length, further reducing anisomyopia due to more non-amblyopic eye growth; 3) Treatment implications: Given the same difference in corrected distance visual acuity (CDVA) between eyes, anisohyperopic amblyopic patients may potentially benefit from penalization methods rather than patching; however, this suggestion is based on indirect evidence and should be interpreted with caution. Additionally, based on our hypothesis and the findings of Wallace *et al*^[6], future controlled studies should evaluate whether initiating patching in anisohyperopic cases at a reduced dosage (*e.g.*, 2h per day) could optimize the balance between visual efficacy and axial safety. Also, because the non-amblyopic eye is often emmetropic or only minimally hyperopic in anisohyperopic amblyopia, penalization may be of limited feasibility or effectiveness in many patients; therefore, treatment selection (penalization versus occlusion and dosage) should be individualized based on the refractive status of the fellow eye and other patient-specific factors. Conversely, anisomyopic amblyopic patients are more likely to respond favorably to a longer duration of patching, as axial elongation in the non-amblyopic eye may help reduce anisomyopia and improve treatment outcomes.

The preferential axial elongation observed in the occluded (non-amblyopic) eye may involve mechanisms beyond simple form deprivation. Occlusion alters normal binocular experience and induces prolonged monocular viewing with the unpatched eye, which may change accommodative behavior and visual feedback signals during daily activities^[7-8]. In addition, form deprivation of the patched eye itself is a known stimulus for abnormal axial growth in experimental models, and some authors have proposed that disruption of binocularly driven coordination of emmetropization could contribute to interocular growth asymmetry^[9]. Accordingly, axial elongation in the patched eye could reflect a combination of deprivation-related growth signaling and altered binocular/oculomotor

conditions during treatment. Recent studies also suggest that binocular factors are unlikely to be major causal factors in myopia progression^[10].

The severity of amblyopia is a critical factor in determining appropriate treatment strategies^[11]. More severe cases may necessitate longer patching durations to promote visual recovery. However, balancing extended patching with the potential risk of undesirable axial elongation is crucial, particularly in anisohyperopic patients. Customizing the patching duration based on the severity of anisometropia and the specific type of refractive error may help optimize treatment outcomes while minimizing adverse effects.

To address this issue, we propose that future research investigate the hypothesis that the duration and intensity of occlusion therapy should be tailored according to the type of anisometropia, rather than relying solely on the difference in CDVA between the eyes. Furthermore, the type of anisometropia should be considered when choosing the most suitable amblyopia treatment method, such as penalization versus occlusion. A personalized approach to amblyopia therapy may potentially improve visual outcomes; however, prospective longitudinal studies are required to confirm this hypothesis before clinical implementation. We have highlighted the importance of utilizing optical biometry and conducting regular assessments to monitor interocular balance throughout treatment.

While some studies have explored the relationship between occlusion therapy and axial elongation, many suffer from methodological limitations, including small sample sizes, short follow-up periods, and lack of stratification by anisometropia type. To address these gaps, future prospective longitudinal studies—ideally larger, multicenter trials with extended follow-up—should use standardized patching regimens with baseline and serial ocular biometry (optical biometry and/or A-scan ultrasound) to define dose-response relationships (h/day), identify the minimum daily occlusion dose that may induce measurable axial length change, and determine the earliest timepoint at which elongation becomes detectable, while controlling for age and refractive profile. By deepening our understanding of the interaction between occlusion therapy and axial growth, this letter emphasizes the importance of a more personalized approach to amblyopia therapy that accounts for refractive characteristics and the potential risk of excessive axial elongation from occlusion or other intensive visual therapies; however, these hypotheses should be tested in well-designed longitudinal clinical trials before being incorporated into routine clinical practice.

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