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Binocular Vision Feature Issue Editorial

Linking binocular vision neuroscience with clinical practice.

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Binocularity in the human visual system poses two interesting and extremely challenging questions. The first, and perhaps most obvious stems from the singularity of perception even though the neural images we see originate as two separate images in the right and left eyes. Mechanistically we can ask how and where do we convert two images into one? The second question is more of a "why" question. By converting lateral eyes with their inherent panoramic visual field into frontal eves with overlapping binocular visual fields, primates have developed an extremely large blind region (the half of the world behind us). We generally accept that this sacrifice in visual field size was driven by the potential benefit of extracting information about the 3rd dimension from overlapping right and left eye visual fields. For some people, both of these core processes of binocularity fail: a single fused binocular image is not achieved (when diplopia or suppression is present), and the ability to accurately represent the 3rd dimension is lost (stereo-blindness). In addition to these failures in the core functions of the human binocular system, early imbalances in the quality of right and left eye neural images (e.g. due to anisometropia, monocular deprivation, and/or strabismus), can precipitate profound neurological changes at a cortical level which can lead to serious vision loss in one eye (amblyopia). Caring for patients with malfunctioning binocular visual systems is a core therapeutic responsibility of the eye care professions (optometry, ophthalmology and orthoptics) and significant advances in patient care and subsequent visual outcomes will be gained from a deeper understanding of how the human brain accomplishes full binocular integration.

This feature issue on binocular vision brings together original articles and reviews from leading groups of neuroscientists, psychophysicists and clinical scientists from around the world who embrace the multidisciplinary nature of this topic. Our authors have taken on the big issues facing the research community tasked with understanding how binocular vision is meant to work, how it fails, and how to better treat those with compromised binocularity. These studies address deep issues about how the human brain functions and how it fails, as well as how it can be altered by therapy.

Central to new clinical approaches to binocular vision therapy is the surprisingly novel and seemingly ironic notion that in order to recover binocularity one must experience binocularity. Hidden behind this deceptively simple idea is the deeper question of what binocularity is and how perceptual binocularity relates to neural binocularity, especially in those individuals with abnormal binocular visual systems? Using modern computational and psychophysical methods Georgeson and Wallis at Nottingham (cite) examine the three possible outcomes of binocular integration: fusion, diplopia and suppression. They examine the rules by which disparity affects the likelihood of single vision and the means by which it is achieved (fusion or suppression). Because stereopsis is only possible with correlated (fusible) right and left eye images, brain regions that respond selectively to correlated signals likely play a crucial in stereopsis. By varying the fusibility of random dot stimuli, Andrew Parker's group at Oxford (Ip et al, cite) search for those regions in the visually responsive cortex that preferentially respond to fusible stimuli and report that increased responses to fusible stimuli in V3 correlate best with stereopsis.

This feature issue contains two related reviews from research groups in Canada: Mitchell and Duffy (cite), provide an insightful analysis of the role of animal models in binocular vision research. They argue for, and cleverly demonstrate the value of binocular experience in the treatment of experimental deprivation amblyopia in kittens. Even short duration of binocular experience can off-set much longer periods of deprivation. Mitchell and Duffy set the stage for a more contemporary approach to vision therapy for amblyopia by reviewing some of the now classic work by Hubel and Wiesel and others. Studies of cat and monkey showed that even a seemingly complete loss of the deprived eye's ability to drive neurons in visual cortex could be reversed by depriving the once seeing eye. Mitchell and Duffy show that this approach "works" in that it converts a once blind eve to a seeing eve, but the cost is that the once seeing eve is now blind. However, recovery of vision in the originally deprived eye is fleeting and this eye eventually reverts to deep amblyopia. a regression that could only be prevented by including extensive periods of binocular exposure during the treatment period. Ironically, the preferred mix of patching and binocular exposure observed in these kitten studies may mirror the experience of children with less than perfect compliance to patching therapy. This review describes the intriguing finding that periods of darkness can recover plasticity within a developing visual system.

Whereas Mitchell and Duffy's review provides an contemporary summary of animal models of amblyopia treatment and highlights their clinical relevance to human amblyopia, Hess and colleagues (cite) summarize the key characteristics of human amblyopia and examine the clever strategies being developed to activate binocularity in human patients with amblyopia and strabismus. By degrading the visual input to the better eye, suppression of the amblyopic eye's input can be overcome and binocular interactions can be observed. This anti-suppression approach to therapy is quite different from classic patching methods that specifically prevent any binocularity, but it parallels classic penalization methods (such as atropine therapy). The review also summarizes recent literature describing the impact of direct electrical stimulation of the visual cortex and the intriguing observation that significant binocular imbalance can be produced in adults with short term monocular deprivation. Surprisingly, this deprivation (first

reported in Italy by Lunghi, Burr and Morone, <u>(cite 2012)</u> enhances eye dominance of the *deprived* eye, and this phenomenon is longer lasting when the weaker eye of amblyopes experiences short-term deprivation.

As clinicians are aware, recovering good acuity in the amblyopic eye does not necessarily result in high quality stereo-vision, a finding also observed in the animal studies of Mitchell and colleagues. However, Hess and colleagues report that antisuppression therapy can effectively treat amblyopia and lead to often dramatic improvement in stereopsis. The success of activating binocularity in amblyopic patients by reducing the contrast signal in the non-amblyopic eye is also examined in detail by Ding and Levi (cite), and the clinical benefits of this approach are examined by Raveendran et al (cite), who look at the improvements in fixational control of strabismic amblyopes when binocular balance is achieved.

The feature issue also includes a point-counterpoint discussion of the question "Should amblyopia be treated?" in which the efficacy and value of therapy is examined by Connor & Clarke and Kulp & Cotter (cite). At issue is the relative effectiveness of the treatment itself vs. the associated components of the treatment regimen (e.g. repeat acuity testing, etc.), which can only be revealed with a randomized controlled trial. Connor and Clarke point out that only three such trials have been performed and although visual improvement was reliably seen in the treatment group, it was also seen in the control group. The issue of value is emphasized in both pro and con arguments. Kulp and Cotter point to the professional restrictions faced by amblyopes, whereas Connor and Clarke highlight the limited improvements in quality of life provided by treatment of this largely asymptomatic condition. Their debate centers on a simple question: what can be gained by treatment, and at what cost?

Although we typically associate failed fusion and accompanying diplopia with duplicate images present in each binocular hemisphere, the paper by Satgunam and Peli (cite) describes the unusual case in which diplopia can appear even though the right and left visual cortices have been made monocular by a chiasmal lesion. They describe new diagnostic and therapeutic approaches to manage these cases of bilateral hemianopia with associated ocular misalignment, and their paper challenges our understanding of core ideas about diplopia and scotomata, and reminds us that diplopia is a direct consequence of the evolutionary development of overlapping monocular visual fields.

As revealed by many studies in this feature issue, our understanding of human binocularity is still developing. However, in spite of our very limited understanding of both normal and abnormal binocularity, some patients with binocular vision defects can be treated effectively. Stereopsis is the pinnacle of human binocularity (Saladin, cite) and requires both an intact motor and sensory system, and therefore stereoacuity is perhaps the most efficient diagnostic test to evaluate the health of human binocular vision. Standardized clinical stereo-acuity tests, therefore, play an important role in diagnosing binocular disability. A report by van Doorn et al (cite), found differences between new and old stereo-tests, highlighting the crucial challenge faced by the manufacturing industries that produce such diagnostic tests. In a careful examination of common therapeutic methods for treating binocular anomalies Horwood and Toor (cite) look at the potentially confounding issues of placebo, practice and effort. Whilst their data demonstrate that convergence exercises without any coincident accommodation stimulus were the most effective treatment, they highlight the crucial role played by patient effort and clinician instructions, both of which must be controlled before claims of efficacy can be substantiated.

Given the structural, physiological, and functional costs associated with the emergence of binocular vision, it is easy to rationalize its importance to the function and quality of life. Interestingly, the growing introduction of 3D display technology, in entertainment, medical and scientific imaging assumes the user has functional binocularity and stereopsis. Therefore, as these technologies become more pervasive, the need for high quality binocularity may become a key capability for success in modern society, which emphasizes the increasing value of scientific efforts to understand binocularity and clinical efforts to salvage it or prevent its loss for a significant proportion of the population. Our binocular vision feature issue provides an excellent picture of where we now stand in this process.