TITLE: Update on the Preferred Retinal Locus: What we have learned about visual function and the development of this pseudofovea in the context of macular disease?

SPONSORING SECTIONS: Low Vision (LV)

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OVERVIEW:

The majority of patients in the U.S. with low vision suffer from macular disease. In cases where the foveae of eye each become non-functional, the visual system creates a new pseudo-fovea, the preferred retinal locus (PRL). The use of peripheral retina to fixate a target due to a central scotoma was described by Nagel in Helmholtz’s Treatise on Physiological Optics in 1911. The peripheral fixation loci used by patients with central scotomas was then described and first measured by Mainster et al in 1982, using a scanning laser ophthalmoscope. The term “preferred retinal locus” first appeared in the literature in 1985. It therefore has been over thirty years since the PRL was first described in the literature, and our understanding of how a PRL is developed, the visual potential of the PRL, and how to optimize a patient’s PRL has greatly expanded. In this symposium, we discuss the developments in our understanding of the PRL, and how to best utilize this knowledge to improve the visual function of the low vision patient.

OBJECTIVES:
1. To update attendees on recent developments in how the PRL develops
2. To explore current rehabilitation strategies to enhance the PRL, and examine evidence regarding their efficacy
3. To educate attendees regarding the role the PRL plays in guiding eye movements
4. To critically examine how clinicians measure the PRL and explore alternate strategies

MODERATOR:
Nicole Ross

PROGRAM (100 minutes)

Introduction: History of the preferred retinal locus (5 minutes)
Nicole Ross, OD, MSc, FAAO
New England College of Optometry

This talk will provide a brief introduction to the symposium. We will review the early literature on the preferred retinal locus, and the impact this discovery has made on how we understand visual functioning in patients with bilateral macular disease. This talk will serve to introduce the objectives of the symposia and the subsequent speakers.
The fovea is used as a locus for fixation and as the saccadic oculomotor reference. Thus, when a new object of interest is selected, a saccade is made to place the image of that object on the fovea. When the fovea has been lost, as often occurs in macular disease, most people develop a preferred retinal locus (PRL) that becomes the locus for fixation and may become the oculomotor reference. The reason that the location of the PRL varies widely between individuals is not known. We have replicated the study by Kwon, Nandy and Tjan (2013), showing that people with healthy eyes can be trained in a few hours, using a gaze-contingent (simulated) scotoma, to develop a PRL, as fixation location and oculomotor reference. As macular disease progresses, the lesion size increases, so the location of the PRL must change. We are finding that increasing the size of a simulated scotoma increases the eccentricity of the PRL while the orientation of the PRL remains stable, and that the new PRL is quickly adopted as the fixation location and oculomotor reference. Both studies used symmetric circular simulated scotomas.

To measure the location of the PRL of a person with macular lesions that have obliterated the fovea, we determine the probable location of the (former) fovea using population-average data with the optic nerve head as a reference. Then, PRL location is defined relative to the fovea. When using a Nidek MP-1 for this purpose, we found substantial measurement noise even measuring the location of the fovea of a healthy eye. This variance can be attributed in part to the position of the fixation target within the field of the MP-1, and thus the locations of the retinal components in the image, which suggests image distortion. For eyes with a macular lesion, repeatability with the MP-1 was worse as PRL eccentricity increased, as fixation stability decreased, as the time between measurements increased, and it varied with the locations of the fixation target and the optic nerve head.

Despite the PRL becoming the fixation location and oculomotor reference, which suggests neural plasticity, the benefits that could come from that reallocation of attentional resources seem to be limited in patients with real central scotomas. Studies by our group and others usually do not find a benefit to the PRL among people with a real central scotoma in task performance when compared to an equivalent retinal location (e.g. same eccentricity), except, perhaps for reading. While studies with a simulated scotoma and theoretical considerations suggest that some PRL locations are better than others, there is little convincing evidence that training a PRL provides a benefit.

**Does having a PRL influence the structure and function of visual cortex? (20 mins)**

Kristina Visscher, PhD.
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**Introduction:** In people with healthy vision, central and peripheral vision have different functions. For example, objects in central vision are regularly attended, while objects in peripheral vision are only occasionally attended. Our data show that these different functions are reflected in the structure and function of cortical areas associated with central vs. peripheral vision.

Following macular disease, the function of a part of the peripheral visual field, the preferred retinal locus (PRL), becomes more like that of central vision. I will discuss evidence about whether use of a PRL influences the structure and function of visual cortex. Specifically, I will
focus on whether having a PRL makes originally peripherally-responsive regions more similar in structure and functional connectivity patterns to centrally-responsive regions in healthy vision participants.

**Methods:** We collected structural and functional MRI data from healthy vision participants, as well as a group of patients with macular disease who had lost central vision bilaterally (some with, and some without a PRL), and their matched controls. Primary visual cortex (V1) was identified anatomically and segmented into central and peripheral portions. We tested how centrally-representing and peripherally-representing parts of V1 differed in cortical thickness and resting state functional connectivity. We also compared these measures in people with macular disease with and without PRL vs. matched controls.

**Results and Discussion:** In people with healthy vision, centrally-responsive V1 was thicker than peripherally-responsive V1. Also, the patterns of functional connectivity to frontal and parietal networks known to be involved in cognitive control were consistent with the functions of central and peripheral vision. These functional and structural patterns echo each other and are consistent with the functions of central vs. peripheral vision.

People who have lost central vision due to macular disease use peripheral vision for the types of tasks for which healthy vision participants use central vision. Mirroring this behaviorally effect, peripherally-responsive parts of visual cortex become, in some ways, more similar to centrally-responsive parts of visual cortex in controls. Most strikingly, peripheral V1 is significantly thicker in people with macular disease than controls. Also patterns of functional connectivity are different in participants with vs. without macular disease.

These results will be discussed in the context of use-dependent cortical plasticity and the development of a preferred retinal locus.

**Oculomotor Re-referencing Following Central Vision Loss (20 mins)**

Susana T.L. Chung and Girish Kumar
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**Abstract:**
For people with normal vision, eye movements usually place the object of interest close to the fovea, the presumed reference locus for oculomotor movements. When the fovea becomes dysfunctional as in the case of people with central vision loss, where is the reference locus for ocular movements? In this presentation, we will present evidence, based on functional retinal imaging, showing that people with long-standing central vision loss exhibit a shift in the reference locus for both involuntary and voluntary eye movements such that the preferred retinal locus (PRL) replaces the fovea as the reference locus.

**Brief Outline:**

1. Brief review of the preferred retinal locus (PRL) for oculomotor eye movements in people with normal vision.

2. Involuntary eye movements: fixational eye movements
   - Retinal images were recorded using a scanning laser ophthalmoscope (SLO) while participants with long standing central vision loss performed a simple fixation task.
   - Eye positions were extracted from the recordings using a cross-correlation technique and were sampled at 540 Hz; slow drifts and microsaccades were identified.
   - The mean retinal location corresponding to the image of the fixation target was defined as the fixational PRL.
   - Slow drifts and microsaccades were analyzed to determine if they were directed toward
3. Voluntary eye movements: saccadic eye movements
   • Retinal images were recorded using a high-resolution scanning laser ophthalmoscope (TSLO) while participants with long standing central vision loss performed a saccadic task.
   • Eye positions were extracted from the recordings as described above.
   • Characteristics of saccadic eye movements were analyzed.
   • The mean retinal location corresponding to the landing positions of the first saccade (catch-up saccades were not analyzed) was defined as the saccadic PRL.
   • The direction of the first saccade was analyzed to determine if the saccade was directed toward the presumed foveal location or the saccadic PRL.

Do we need to train people with central scotomas to use an eccentric PRL? (20 mins)

Gary Rubin, PhD  
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The development and effective use of a preferred retinal locus (PRL) is essential for visual rehabilitation of patients with bilateral central scotomas. It is widely assumed that patients with newly acquired scotomas will benefit from training procedures broadly known as “eccentric viewing training” At last count, we identified 45 studies of EVT over the past 30 years, most of which concluded that EVT was beneficial. Do we really need another study? EVT is widely used in Sweden, other parts of Europe, USA and the Middle East. The UK is the exception, with EVT not being covered by the National Heath Service. One reason for the lack of coverage is the weakness of the evidence. Of the 45 studies, only 1 was a randomized controlled clinical trial (RCT) and the study was small, involving only 40 patients. For more than a decade we have been arguing that additional evidence is needed and that evidence needs to meet the high standards of an RCT.

Moreover, there are reasons to question whether EVT is necessary or beneficial. Evidence from a longitudinal study of patients with newly diagnosed AMD suggests that most patients develop an effective PRL on their own, without training, and with 6 months from the loss of central vision. Other evidence suggests that the development of a single PRL is not necessary; perhaps not even desirable, as patients with multiple PRLs use them strategically to accomplish reading tasks. Finally, there is evidence that switching a patients PRL to a theoretically optimal location may impede reading performance.

With this background in mind we initiated an RCT to compare low vision rehabilitation with and without EVT. The study, funded by Fight for Sight, had a recruitment goal of 200 and will stop recruiting in June 2015. The primary outcome measure is visual ability measured by the Massof Activity Index, and secondary outcomes include reading speed and comprehension, fixation stability, and health-related quality of life. Final result won’t be available until December when the 6-month follow-up will be completed, but a preview of results from the first 150 patients will be presented.

Panel Discussion (15 minutes)