THE PREFERRED RETINAL LOCUS IN MACULAR DISEASE

Toward A Consensus Definition

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Background: Eccentric viewing in macular disease has been described for half a century. However, a clear definition of eccentric viewing and preferred retinal locus (PRL) does not exist. Here, we determine how the PRL in macular disease is defined by researchers active in this field and, based on the responses received, propose a standardized definition of the preferred retinal locus.

Method: A literature review of articles describing the PRL or eccentric viewing was performed. The first and senior authors of all identified publications were contacted and were asked to define the preferred retinal locus. Themes of responses were identified using inductive qualitative research techniques.

Results: Frequently recurring themes related to the definition of the PRL included 1) it is a retinal area used for fixation, 2) it is task specific, 3) more than one PRL can be used, 4) it is a well-defined region of retina, and 5) the same PRL is used on repeated testing.

Conclusion: Based on the responses received, a consensus definition of the PRL is proposed. It is suggested that researchers define the PRL carefully in experimental reports and an instrument that images the retina is used to define the location of the PRL.

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If someone with advanced macular disease and bilateral central scotomas looks straight toward an object, the image will fall within the scotoma and the object will not be seen. A common adaptive strategy, known as eccentric viewing, involves directing the eye such that the image falls onto the comparatively healthy peripheral retina. The region of retina used is frequently referred to as the preferred retinal locus (PRL).

The use of nonfoveal retina to fixate a target was described for the foveal scotopic scotoma by Nagel in Helmholtz's Treatise on Physiological Optics in 1911.[1] The first report on nonfoveal fixation of visual field loss was for those with hemianopia in 1922,[2] while eccentric viewing in macular disease was described by von Noorden and Mackensen[3] in 1962 and referred to by Enoch and Johnson[4] in 1977. The fixation loci used by patients with central scotomas for words and point targets identified by direct observation of the retina was first described by Mainster et al[5] in 1982, using a scanning laser ophthalmoscope. The term ''preferreed retinal locus'' was first used by Timberlake in presentations in the 1980s (G Timberlake, PhD, written communication, 2009), while the first journal article to explicitly use the phrase ''PRL'' was by Roger Cummings in 1985.[6]

Researchers have used a wide range of methods to detect the presence of a PRL. Even in two of the earliest PRL articles, it was defined in different ways: Cummings et al[6] directed the patient to view the target ''so that it appeared to be the clearest,'' while Timberlake et al[7] assessed the habitual viewing condition by asking subjects to look at a target ''as if you were trying to look at a small, far-away object''. More recently, PRLs have been described for tasks such as reading sentences,[8,9] pursuing moving targets,[10] and performing visual search. The PRL has also been described for people with good vision and simulated scotomas.[11–13] Multiple instruments have

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been used to measure the PRL, including the scanning laser ophthalmoscope,[7,14,15] eye trackers,[6,16] fundus cameras,[17] ophthalmoscopes,[18] the visuscope,[19] microperimeters,[20] and examining entoptic phenomena.[4]

The variety of techniques and tasks used to measure the PRL raises questions about the definition of the PRL itself. For example, if a patient uses an eccentric location consistently for one laboratory fixation task, does that patient necessarily have a PRL? Or would confirmation of the PRL be required across more than one task or outside of the laboratory? To answer these and other questions, we attempt here to develop a new consensus definition of a PRL. Such a consensus will aid research by helping to establish consistency across laboratories in use of the term and possibly measurement procedures. A unified definition of the PRL will be extremely useful for 1) exploratory research, 2) evaluating animal models of central scotoma, and 3) experiments that use artificial scotomas in those with good vision to simulate the effects of vision loss.

A unified definition will be especially useful for clinical trials of fixation training in people with macular disease. To date, these outcomes have included the retinal area where a patient can ''look for and fixate a letter large enough to be clearly identified'';[21] and subjective assessments of fixation and saccade performance when using peripheral retina.[22] Furthermore, some studies report the use of a different PRL without explaining how the PRL is defined at all.[23] Clinical trials require clearly defined outcome measures,[24] and a consensus definition of PRL use will enable future clinical trials of fixation training to be compared more easily. This problem has been highlighted by Stelmack et al[25] in 2004, who stated ''it is necessary to develop and validate objective and quantitative measures . . . to evaluate [eccentric viewing] behavior, to characterize the visual capabilities of EV loci, and to evaluate both the efficacy and effectiveness of EV training.'' They add that ''without such objective measures, it will not be possible to build a consensus among providers on how patients should be evaluated for EV training, what criteria should be used to judge patient eligibility for training, and which methods are most cost-effective in producing the desired outcome.''

We performed a survey of authors who have published work on the PRL in the peer-reviewed scientific literature. We used qualitative research techniques to determine which elements form part of the definition of the PRL and the methods that are believed to be the most appropriate for finding the PRL. We suggest a new definition of the PRL based on the consensus opinion of scientific researchers in this field and invite colleagues to comment on our proposed definition.

Methods

Literature Search

To identify researchers who have published work on the PRL, searches were performed on the PubMed database (National Center for Biotechnology Information, Bethesda, MD) using the Boolean search parameters (''PRL'' OR ''preferred retinal locus'' OR ''pseudofovea'' OR ''fixation locus'' OR ''eccentric viewing'' OR "eccentric fixation) AND (''macular'' OR ''scotoma'').

The same search parameters were used for conference abstracts posted on the American Academy of Optometry (www.aaopt.org) and the Association for Vision in Research and Ophthalmology (www.arvo.org) Web sites. Nonrelevant articles (e.g., where PRL was used as an abbreviation for photoreceptor layer) were removed. First and senior authors of each article were identified.

E-mail Contact

E-mail addresses for each of these authors were collected from the manuscript, from the American Academy of Optometry or the Association for Vision in Research and Ophthalmology database, or by contacting known colleagues. Each author was e-mailed a standard message containing the questions below. If no response was received after eight weeks, a further reminder message was sent.

Open-Ended Questions

Each identified author was asked to provide a brief (1–2 sentences) answer to the following questions:

1. How would you define a preferred retinal locus?
2. How would you establish that a person is indeed using a PRL?
3. Would your definition also apply to the use of a ''PRL'' in someone observing a scene with a simulated (artificial) scotoma?

Qualitative Analysis Techniques

Responses were analyzed using an inductive process of identifying themes from the responses obtained and then determining the frequency of each theme in the response set. This ''grounded theory'' technique has been widely used in qualitative research.[26]

Results

In total, 67 relevant articles, 34 Association for Vision in Research and Ophthalmology abstracts, and 17 American Academy of Optometry abstracts were identified. Fifty-eight unique first or senior authors were identified. E-mail addresses or other contact details could not be found for 2 authors (3%).

A response was received from 38 authors (66%). Two declined to answer the question (one thought that she had been outside the field for too long to give an informed answer and one asked a colleague to respond on his behalf). Two pairs of authors gave a joint response, as did one group of three authors. This led to a total of thirty-two unique responses.

Definition of a Preferred Retinal Locus

Although the thirty-two responses each contained a unique definition of the PRL, certain recurrent themes in the definitions were found. Table 1 summarizes the themes that were identified in more than one definition.

Twenty-nine definitions (91%) used fixation as a part of the definition, such as

> "The chosen retinal location for fixation after central vision loss" (Response 12)
> "An area outside the fovea use to fixate a target . . ." (Response 10).

Nine reported that the PRL was task specific or that the task had to be specified for the PRL to be defined:

> "The PRL for fixation . . . may not be the same as the PRL for reading, face recognition, etc" (Response 8)
> "One should establish whether a constant PRL is used for different tasks" (Response 20)
> "The retinal area that a person uses as a PRL may be task dependent" (Response 9).

In seven definitions, the PRL had to be used repeatedly either within a session or between experimental sessions:

> "The same retinal location locus will be used while performing the same or similar tasks during a single study session and on subsequent days" (Response 9)
> "A discrete region of retina which is repeatably used . . ." (Response 6).

The size or circumscribed nature of the PRL was indentified as being important in seven responses, although none specified an exact maximum or minimum size for the PRL:

> "any PRL must be shown to be relatively small. A PRL the size of the posterior pole is probably not a PRL. What constitutes "relatively small" needs to be addressed" (Response 14)
> ". . . an area of the retina, with a size proportional to its eccentricity . . ." (Response 4)
> ". . .localized (approx 1-2 degrees in diameter, but dependent on scotoma size) retinal area . . ." (Response 23).

Eight respondents (25%) mentioned that there may be more than one PRL:

> "One or more areas . . ." (Response 1)
> "Patients may use multiple PRLs depending on the task . . ." (Response 23).

Method of Assessing a Preferred Retinal Locus

Table 2 summarizes the methods used to identify the PRL. There are more responses than respondents to this question because many people suggested more

Table 1. Themes and Frequency of Response Identified in Definitions of the PRL

Theme	Number of Definitions Including This Theme (%)
Region corresponding to target fixation	29 (91)
May be specific to a given task	9 (28)
Possibly more than one region	8 (25)
Discrete, circumscribed, or small region	7 (22)
Recurrently, habitually, or repeatedly used	7 (22)
Used as the oculomotor reference point	6 (19)
With attentional deployment	2 (6)

Table 2. Methods Used to Assess the PRL

Method	Number of respondents
Scanning laser ophthalmoscope	16
MP-1 microperimeter	8
Microperimetry (instrument not specified)	4
Observing eye position/corneal reflection	5
Fundus camera	3
Eye tracker	3
Self-report of missing scene features	3
From pattern of errors when reading	2
Direct ophthalmoscopy/visuscope	2
Power refractor	1
Conventional perimetry	1
Clock face	1
Grid test	1
Visual skills for reading test	1

than one technique. Several respondents differentiated between clinical and laboratory work, for example

> ''Clinically, I look at the pattern of errors on a task. If the person misses the ends of words, this indicates the PRL is right of the scotoma in retinal co-ordinates . . . Research: I would use an SLO or an eye tracker'' (Response 27).

Can a Preferred Retinal Locus Be Defined in a Subject With an Artificial Scotoma?

Twelve (37.5%) of the responses asserted that their PRL definition could apply to someone with an artificial scotoma, while 13 (41%) believed that the definition could not apply to such cases. Six responses were more guarded and could not be easily fit into either response category, for example

> ''If individuals consistently use a specific part of the retina in such a task then I would call it a PRL. However, I doubt an artificial scotoma could be induced long enough to produce a consistent area of extra-foveal fixation'' (Response 11).

Discussion

We have not attempted to systematically review the PRL literature in this publication because this has recently been performed.[27] Few of these publications included a stated definition of the PRL and hence the need to approach authors to ask the criteria they each use to define the PRL. To achieve this, we have solicited definitions of the PRL from researchers in the field of low vision rehabilitation research. Collating the responses and identifying the most common ones indicates that the definition of a PRL should include the fact that 1) it is a retinal region where fixations are made, 2) it relates to a specific task, 3) it may involve one or more areas, 4) it is a discrete well-defined region, 5) its use is repeatable within and between trials, 6) it may be used as the oculomotor center, and 7) it may be used for attentional deployment. To contract this into a single statement, we suggest the following definition of the PRL:

> ''One or more circumscribed regions of functioning retina, repeatedly aligned with a visual target for a specified task, that may also be used for attentional deployment and as the oculomotor reference.''

Although for brevity, we have not defined ''repeatedly,'' it is clear from our responses that it is required that to be defined as a PRL, the retinal area used should be the same in different experimental sessions over the course of (at least) several days. Variability in fixation position has been described for nearly a century: in Helmholtz's book, Nagel writes ''It is an interesting fact that this fixation place [referring to fixation outside the scotopic foveal scotoma] varies under certain circumstances even in the same individual.'' Attentional deployment (the ability to ''pay attention'' to a specific retinal area) is important because it is known to guide saccades[28] and is thought to be an important factor in determining PRL location.[29]

In his response to us, Dr. George Timberlake indicated that in his first use of the term PRL, he intended ''preferred'' in the sense of ''habitually used,'' not in the sense of ''more desirable'' or ''better.'' There did not appear to be a clear consensus over whether the PRL is by definition the best retinal region to use. While several respondents repeated Timberlake's original use of the term,

> ''It is important to acknowledge that the PRL does not always provide the best locus for all visual functions'' (Response 16)
> ''. . . irrespective of the efficiency of using such a strategy'' (Response 20),

others defined the PRL as being the best region for a given task:

> ''. . . which enables best possible resolution or visual function in relation to tasks like reading'' (Response 22)
> ''. . . developed in time as the most favourable fixation locus . . .'' (Response 26).

There appeared to be some debate over whether, in normal vision, the fovea itself is the PRL. Two respondents specifically mentioned that the PRL can be defined in people without scotomas:

> ''For the majority of eyes, and fixation targets, the PRL will (presumably) be the fovea'' (Response 21)
> ''This is likely debatable but even in the normal eye, I refer to the fovea as the PRL'' (Response 7).

However, 15 responses specified that the PRL must be outside the fovea or only exists in the presence of a central scotoma:

> ''An area outside the fovea use to fixate a target . . .'' (Response 10)
> ''. . . retinal area outside a central scotoma . . .'' (Response 14).

For identifying the PRL, most responses suggested using a system that simultaneously images the retina and presents stimuli, such as a microperimeter or scanning laser ophthalmoscope. This may be

a function of the fact that we canvassed the opinion of published researchers, which means that we did not survey the opinion of many expert clinicians who perform PRL training. In a clinical setting, less elaborate techniques (such as noticing the pattern of errors when reading a letter chart) are more commonly used for determining the characteristics of the PRL.

A limitation of our research method is that the relatively small size of the low vision research field means that we are known to many of the respondents. This may have introduced some bias into the responses (e.g., as one of us (M.D.C.) has published articles describing multiple PRLs, this phenomenon may have been overreported in the responses to us). Only two thirds of the authors who we contacted responded to our question. Although this may introduce some bias into our results we do not think this is likely to be systematic, rather it is a reflection of the time demands placed on academics and clinicians. While the article would be strengthened by a response rate closer to 90%, we think that two reminder e-mails are sufficient to allow all of those who wish to respond to our question to do so.

PubMed only provides comprehensive results from 1966. Although it would have been possible to search databases that cover more historical articles, such as Excerpta Medica, Zentralblatt fur die Gesamte Ophtalmologie und ihre Grenzgebiete, and Zentralblatt fuer Praktische Augenheilkunde, we feel it unlikely that authors who have not published on this subject in the past 40 years would be in a position to provide a contemporaneous opinion about the current definition of the PRL.

Our simple descriptive statistical approach assigns equal weight to each response received. This may slightly underreport suggestions, which were agreed by pairs or small groups of authors who returned a joint statement. We have not attempted to weight responses by the kudos of the researcher: equal weight is given to the response of an author who has one published conference abstract and an author who has several peer-reviewed journal articles published over several years. Neither have we attempted to weight the responses by the quality of evidence presented in the articles that we identified from our search. Our qualitative research approach was primarily designed to identify recurring themes in responses rather than to quantify the number of people in the community who believe a certain statement.

We have not solicited responses from the authors who we have contacted about our proposed definition. Rather than recanvas the opinions of this relatively small group of researchers, we would prefer to allow clinicians, rehabilitation workers, and others to respond to our definition. We hope to update our definition, in time, based on the responses from a broader range of the low vision rehabilitation community. An ideal method to improve the validity and acceptance of our definition would be roundtable discussion at international meetings and this is something that we will consider in the future.

This work has highlighted the disparate (and at times contradictory) range of definitions of the PRL used by different researchers. The most contentious question was the question over whether a PRL could, in theory, develop in an artificial scotoma paradigm. Responses to this question were nearly equally split, showing a considerable lack of consensus on this issue. That behavior with an artificial scotoma that matches the above definition would not necessarily be considered a true PRL suggests that some additional criteria may need to be added. For example, it could be that PRLs are thought to be used more automatically by patients than the PRL analog that would be used by a subject in an artificial scotoma experiment. Whether the neural specialization associated with a PRL can only develop in the absence of a functioning fovea is a question, which we think warrants further investigation.

A further area of contention was whether a healthy fovea can be referred to as the ''PRL.'' Strictly speaking, our definition would include the fovea of people with healthy eyes; however, we acknowledge that many would not refer to the fovea as a PRL.

We are reluctant to specify whether the PRL should include the fovea case or not as we did not directly ask this question in our e-mail questionnaire. Given the diversity of views expressed by our respondents on whether the fovea can indeed be defined as a PRL, it would seem appropriate that this question should be asked more explicitly in future developments of this definition. We emphasize that our definition is very much a starting point for future research.

As there is a lack of consensus on the definition of the PRL, it is important for researchers to define their interpretation of the PRL in research papers. We have attempted to create a consensus based PRL definition on the basis of most frequent responses we received to our posted questions. While we do not expect every researcher or clinician to adopt this definition of the PRL, it does reflect the most commonly used defining features of the PRL amongs currently active researchers in this field. We hope that this proposed definition will stimulate debate amongs clinicians and researchers and welcome suggestions for changes or updates to our proposal.

Key words: scotoma, macular disease, fixation, preferred retinal locus, perimetry, eccentric viewing.

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Appendix

Two of the authors (M.D.C. and G.E.L.) and the following people provided responses, which were analyzed for this study.

Harold Bedell, Isabel Cacho, Eric Castét, Sing Hang Cheung, Salomon Cohen, Roger Cummings, Chris Dickinson, Don Fletcher, Kyoko Fujita, Ester Gonzalez, Vivienne Greenstein, Krister Inde, Antonio Filipe Macedo, Sam Markowitz, Bob Massof, Andre Messias, Sven-Erik Nilsson, Ulla Nilsson, Eli Peli, Josh Pratt, Klaus Rohrschneider, Gary Rubin, Ron Schuchard, Eric Schumacher, Martin Steinbach, Janet Sunness, Luminita Tarita-Nistor, George Timberlake, Cornelis Verezen, Enzo Vingolo, Gale Watson, Stephen Whittaker, Stanley Woo, and Harry Zwick.