

Clinical Psychophysics

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Summary

New developments in clinical psychophysics allow a non-invasive assessment of visual function which may otherwise not be possible. Measurements of spatial and temporal contrast sensitivity functions, perimetric rod and cone sensitivity, colour vision testing, and newer tests such as hyperacuity thresholds may provide information about the mechanism of an abnormality, allow earlier detection of damage, determination of retinal function in the presence of ocular media disturbances, and allow more sensitive detection of the effects of treatment on visual function. Some methods are more effective in screening or monitoring patients over time while others can be used as research tools to investigate the underlying causes of visual dysfunction. Emerging technologies such as those based on video displays and computer generated graphics and advances in methodology provide potential for new applications. The selection of which aspect of visual function to test depends on the condition (e.g., retinal degeneration or glaucoma), the goals of the investigation, and the facilities available. These non-invasive methods can provide accurate information about retinal function and further improve our ability to quantify and document this most important aspect of the eye – its role in visual function.

Psychophysical measurements of visual function include conventional measurements such as Snellen acuity, visual fields, and colour vision. More recently newer types of testing such as spatial and temporal contrast sensitivities and hyperacuity thresholds have been introduced. These provide additional information about the function of the visual system beyond that provided by conventional tests. A great strength of these studies is that they are generally non-invasive, and they allow quantitative investigation of the abnormality of the visual system in patients which might not otherwise be attainable. A major difficulty of the subjective nature of the tests is that they require the co-operation of the patient and not all patients are able to provide accurate data. However, modern techniques can provide reliable data from most patients and the degree of reliability can be assessed to allow a measure of the validity of the results.

It is important to remember that these tests measure the function of the visual system as a whole (i.e., the optics, the retina, and the higher centres of the central nervous system) and before any conclusions can be drawn about the locus of a visual defect, the potential contribution of the other elements must be considered. As an example, if the sensitivity of the dark adapted periphery of the eye is measured to monochromatic light of different wavelengths, the normal eye would be expected to show a peak near 500 nm and the shape of the function should be similar to that of the rhodopsin absorption spectrum. However, we would expect a reduction of sensitivity at the shorter wavelengths due to absorption by the crystalline lens and this can be accounted for if necessary. A further reduction of sensitivity would be expected in the shorter wavelengths if the measurements are made within the macular region where macular pigment could modify the shape of the curve.

This too can be taken into account if the measurements are made in this region. Since the task of the subject is just to report the detection of a flash of light (which would typically appear colourless), without considering any aspect of the quality of the stimulus, we would expect little effect of central nervous system factors on the overall shape of the function. Higher order effects would mainly be expected to act on the reliability of the measurement at each wavelength ("noise").

The following is intended to provide an overview of some of the newer clinical tests of visual function using psychophysical methods and will discuss some of the considerations required for interpreting the results of these tests. In particular, which types of tests may be more informative in different conditions and what kinds of questions may be answered will be discussed. Psychophysical tests, for all their difficulties, remain important and cannot be entirely replaced by more objective tests. While other investigations of the eye provide important information, some require the results of psychophysical measurements to be fully useful (i.e., reflection densitometry) and some are only indirect measures. For example, in determining whether an eye is suffering from glaucomatous damage measurement of intraocular pressure does not tell us whether there is loss of vision. Further, while a treatment may be effective in reducing intraocular pressure, its efficacy in sparing visual function may not be simply related to its pressure reducing effects. The final determining factor in deciding whether damage is occurring or hindered must be in the degree to which visual function is affected. Hence accurate methods for clinical measures of visual function remain critically important.

Spatial Contrast Sensitivity

A recent excellent series of articles has appeared on the subject of the spatial contrast sensitivity function (CSF).¹⁻⁹ It has been used in ocular hypertension¹⁰ and applied to the problem of optic neuritis.¹¹ Typically, a series of gratings of differing spatial frequencies is varied in contrast to find the threshold for visibility. The resulting curve of contrast sensitivity versus spatial frequency characteristically shows a peak in the medium spatial frequency range (5-10 cpd) with a drop-off in sensitivity at both lower and higher

values. At the high frequency limit near 30 cpd a contrast approaching 100% is required and this corresponds to visual acuity measured by the Snellen chart. Recent work has suggested a discrete loss of sensitivity at some intermediate spatial frequencies,¹² a possible relation to childhood amblyopia,^{13,14} and effects of cycloplegia.¹⁵ Contrast sensitivities at lower spatial frequencies provide additional information in that in some conditions, a loss of low frequency sensitivity has been reported with normal high frequency sensitivity and visual acuity.⁴ There is an additional importance in finding a loss of lower spatial frequency contrast sensitivity in the presence of normal higher spatial frequency contrast sensitivity in that this provides evidence for non-optical factors as the basis of the loss of sensitivity.

This introduces one of the major problems of measuring the CSF; that is, the problem of controlling the contribution of the optics. Refractive error has a substantial effect on the high frequency region of the contrast sensitivity function.¹⁶ This implies that if a retinal basis for a loss of contrast sensitivity is to be inferred, any refractive errors of the eye must be well corrected. For the case of simple refractive error the correction can be made but must be done carefully, including compensation for the viewing distance of the test. This is especially important for older presbyopic individuals. However, even if refractive error is carefully corrected, there remain potential optical errors which could affect the CSF. Pupil size could reduce high frequency contrast sensitivity due to diffraction effects if the pupil is unusually small (e.g. in the older subject with a miotic pupil or in a patient treated with pilocarpine). It could have a similar effect if the pupil is unusually large because spherical and higher order optical aberrations become more important. These optical errors can often not be fully corrected. Some techniques can, in part, bypass some of the optical errors of the eye. These include the use of laser interferometry¹⁷ and otherwise projecting grating images through the pupil.¹⁸ However, these require a clear region of the lens and are not unaffected by scattering bodies or lens alterations. It is for these reasons that great care must be taken in interpreting the results of spatial contrast sensitivity measurements in clinical applications.

Temporal Contrast Sensitivity

Temporal contrast sensitivity provides the time varying analog of the spatial contrast sensitivity function. It is usually represented as the contrast sensitivity as a function of flicker frequency in cycles per second. Especially in photopic conditions, patients will often report that the decision of whether a stimulus is flickering is an easy one to make. It has proven to show early abnormalities in glaucoma and ocular hypertension¹⁹ and in light of our current understanding of magno- and parvo-cellular systems of the primate visual system holds considerable further potential. Rod and cone mediated flicker sensitivity in the dark adapted eye has shown early dysfunction in RP²⁰ and has proven useful in detecting carriers of X-linked RP.²¹ However, in the dark adapted eye, scotopic sine wave flicker can be a difficult judgement to make, particularly at the low flicker frequencies which characterise rod mediated flicker sensitivity. An interesting rod-cone interaction has recently been found^{22,23} which has been shown to be abnormal in some retinal dysfunctions and is the subject of active investigation.

Perimetry

Some tests of visual function are inherently photopic while others are scotopic so that for example, measurements of colour vision using colour matching essentially involve foveal cone function while measurements of absolute threshold perimetry generally reflect rod mediated function. However, the distinction sometimes is not so clear, so that absolute threshold sensitivity to a long wavelength, small area (i.e. 20 minutes of arc) stimulus in the fovea may be cone mediated but outside the fovea may be rod mediated. The wavelength composition, temporal properties and other characteristics of the stimulus can be selected to emphasise the relative contribution of the rods and the cones and thereby provide a measure of photopic and scotopic function.

Photopic (or mesopic) perimetry has undergone a revolution and been rejuvenated with the advent of computerised perimeters.^{24,25} Glaucomatous visual field loss has been a major source of interest in this type of perimetry. Much activity has centered around controlling potentially confounding variables in detecting scotomas. These include the effects of defocus,^{26,27}

comparing serial measurements,²⁸ and the problem of variability,²⁹ the effects of age,³⁰ the use of various stimulus sizes³¹ and various stimulus spacing,³² the effects of light scatter,³³ fluctuations using different perimeters,³⁴ factors affecting LED (light emitting diode) perimetry,³⁶ the effects of drugs which constrict the pupil,³⁶ and peripheral field testing.^{37,38} A view which has emerged is the difference in character of field loss^{39,40,41} with diffuse and localised aspects which may be related to the similar changes seen in the nerve fibre layer.

Recent work includes early effects of glaucomatous damage,⁴² effects on central vision,⁴³ the representation of data in pseudo 3 dimensional format,⁴⁴ automated kinetic perimetry,⁴⁵ acuity perimetry,⁴⁶ scotopic perimetry in glaucoma,⁴⁷ high pass resolution perimetry,⁴⁸ and peripheral displacement thresholds⁴⁹ which may be considered a form of hyperacuity motion perimetry. New types of testing have shown some potential for earlier detection of damage. The role of newer methods is still evolving and the effects of potentially confounding variables will have to be investigated as well as their appropriateness for general clinical use. Like more conventional field testing, the effects of optical error, pupil size, ocular media changes, age, and other factors require consideration and some newer tests may suffer from poor patient acceptance or excessive testing time. Nonetheless, there is a clear need for improvement in photopic perimetry and this promises to be an active area in the near future.

Colour vision

A recent book on defective colour vision⁵⁰ and the proceedings of a meeting on colour vision deficiencies⁵¹ provide evidence of the continued activity in this area. An especially good review has just appeared⁵² which covers current basic research in this area which will no doubt have an important impact on clinical questions in the near future. An excellent discussion of acquired colour vision defects in glaucoma has also recently been published.⁵³ Comparisons have been made of colour vision to retinal nerve fibre layer appearance,⁵⁴ age and perimetry,⁵⁵ and area of visual field.⁵⁶

A different type of approach is that where the blue mechanism has been investigated in terms of sensitivity changes (i.e., in glaucoma and

ocular hypertension⁵⁷⁻⁵⁹) which includes measurements made at different retinal locations in the macular region. Measurements of short wavelength cone sensitivities have been made in the ageing eye⁶⁰⁻⁶¹ and in macular oedema of the diabetic eye.⁶² In general, colour vision measurements must consider the effects of the yellowing of the crystalline lens and ageing.^{63,64} These reports of a particular susceptibility of the blue mechanism promise considerable potential.

Retina

Clinical investigations of the function and malfunction of the retinal degenerations have benefited substantially from the use of non-invasive techniques such as psychophysics and fundus reflectometry. Much can be learned about the underlying causes of the loss of vision from these new methods. It is vital to co-ordinate these different types of studies to answer questions about the underlying causes of the dysfunctions. For example, if we wish to know whether the loss of night vision in a retinal degeneration is entirely due to loss of rhodopsin in the photoreceptors or whether the defect involves a more proximal mechanism such as the neural elements of the retina, we must correlate the threshold elevation with the measured rhodopsin.

Patients with retinitis pigmentosa (RP) have been extensively studied in terms of genetic type, clinical findings, retinal function measured electrophysiologically and psychophysically, and by fundus reflectometry. Several important findings have emerged^{65,66} and a number of instruments have been developed for making perimetric measurements in scotopic conditions.⁶⁷⁻⁶⁹ It is clear that within genetic types there are fundamentally different forms of disease which are consistent among family members. One form shows diffuse loss of rod function ("D" type) throughout the retina while cone function may be nearly normal until later in the disease. In the other form there is concomitant loss of rod and cone function in retinal regions ("R" type) with areas where rod and cone function can be nearly normal early in the disease coexisting with regions of severely abnormal rod and cone function.⁷⁰⁻⁷¹ Further there are fundamental differences in the relation between rhodopsin and sensitivity.⁷²⁻⁷⁴ In the "D" type relatively substantial amounts of

rhodopsin can be measured even where retinal sensitivity is severely reduced while the "R" type the loss of rhodopsin can account entirely for the sensitivity loss. These findings suggest fundamentally different processes and the classification of RP families into pure RP type is important for understanding disease mechanisms and for interpreting the results of other studies. The relation between rhodopsin levels and scotopic sensitivity has also been investigated in humans with sector RP,⁷⁵ choroideremia⁷⁶ and vitamin A deficiency.⁷⁷

Variations in delayed rates of dark adaptation have been found in some regions of the retina of Sorsby's fundus dystrophy.⁷⁸ This was attributable to the corresponding rhodopsin regeneration rate which was also found to be delayed. Severely delayed dark adaptation has been found in some patients with RP^{79,80} with a time course of hours or even days. This similarity in time course to that of the outer segment renewal mechanism could reflect the effects of an underlying abnormality of shortened outer segments. It has been suggested that an abnormality in the balance between outer segment renewal and phagocytosis may be involved in RP⁸¹ and these non-invasive techniques may provide a means of indirectly measuring these processes in patients. Abnormal diurnal variation in visual sensitivity in patients with retinal oedema has been measured⁸² and reports of abnormalities in sensitivity with a daily variation⁸³ suggest that we may be able to relate abnormalities in RP patients to animal findings of diurnal rhythms of outer segment renewal mechanisms which could be tested by manipulating the light-dark cycle in patients. Absolute threshold measurements have shown interesting abnormalities in age related macular degeneration^{84,85} and techniques of measuring scotopic function⁸⁶ hold much promise for the near future.

Video display devices

A strong new area of technology involves the use of video display units (VDUs) for testing. These have long been used as psychophysical stimulus generators.⁸⁷⁻⁹⁴ Although a variety of psychophysical measurements⁹⁵⁻⁹⁷ have been made, perimetric threshold determinations have only recently been attempted⁹⁸⁻¹⁰³ and it is necessary further to develop and test the technology.¹⁰⁴⁻¹¹¹

Computer generated graphics and video

display units have an important appeal in that they allow the use of a great variety of stimuli of different form, spatial configuration, spectral composition, location and other factors determined simply by a mathematical expression describing their characteristics. This removes the limitations to a large extent of the hardware changes which would otherwise be needed to alter these parameters. Of course, there are some kinds of stimuli which are better formed using other techniques (e.g., narrow wavelength band stimuli). However, some measurements which would otherwise be prohibitively tedious or have been impossible to perform in the past are now possible using computer generated graphics. These include such potential tests as movement sensitivity, iso-luminant colour stimuli, flashes of "darkness", and others. These new types of tests may allow more selective and sensitive measures of the function of the visual system while the technology makes it easy to implement the new tests.

Retinal abnormalities have been further investigated on a microscopic scale using the newly developed technique of fine matrix perimetry to further characterise retinal function with higher spatial resolution.^{112,113,78} These measurements are made using video displays and computer generated graphics with methods to control the optics of retinal image formation¹¹⁴⁻¹¹⁷ and eye movements and using computer image analysis and processing of the data. These measurements are correlated with rhodopsin density measurements to allow further characterisation of the retinal abnormalities on a microscopic scale in particular at the edge of the advancing front of the degeneration and on the borders between nearly normal and severely affected retina.¹¹⁸

Statistics and screening

For all of these tests an important component which must not be overlooked is the design and interpretation using statistical methods.¹¹⁹⁻¹²³ It is also useful to consider the implications of screening tests^{124,125} for such common diseases as glaucoma.

Newer tests

Emergent techniques for the assessment of visual performance have recently been reviewed¹²⁶ and there has been considerable activity in the

development of newer types of testing which would be expected to have a greater impact in the near future. One test incorporates the stimulus into a fundus camera,¹²⁷ another uses colour matching to estimate foveal cone pigment optical density,¹²⁸ the flash-on-flash paradigm suggested that loss of foveal sensitivity in some patients with RP could not be attributed to decreased quantum catch,¹²⁹ static and kinetic perimetry have been combined into one test,¹³⁰ and hyperacuity testing^{131-134,49} has shown a new approach of measuring spatial vision with little artefactual susceptibility to optical errors. Recent advances in our understanding about the pathological changes of some abnormalities¹³⁵ combined with knowledge of the visual system¹³⁶ suggest new approaches to detect damage at an earlier stage, provide information about the mechanism of an abnormality, the determination of retinal function in the presence of ocular media disturbances, and the effects of treatment on visual function. Emerging technologies such as those based on video displays and computer generated graphics and advances in methodology provide potential for new applications. These non-invasive methods can provide accurate information about retinal function and further improve our ability to quantify and document this most important aspect of the eye – its role in visual function.

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