The objectiveFIELD® Analyzer (OFA®) in multiple sclerosis

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Summary

Following the changes to the McDonald Criteria regarding the optic nerve,[1] and the interest in the visual system at the 2025 ACTRIMS, we have drafted this summary about a novel and readily available form of rapid, non-contact, visual assessment for MS and other neurological disorders. The method exploits multifocal methods to tease out focal injuries to the optic nerves, optic radiations, and brain in approximately 90 seconds, for both eyes. The instrument, the objectiveFIELD® Analyzer (OFA®), is a form of perimetry that provides familiar outputs based upon normative data, except that these are separately reported for response sensitivities and delays. One of OFA's more interesting properties is that it detects damage due to MS as readily in eyes that have not experienced optic neuritis as those that have. This suggests OFA is reporting on progressive damage rather than the history of inflammation and so may be a good adjunct to MR scanning. We review recent papers on the device, one of which is a 10-year follow-up showing that even an older and less efficient OFA method was quite predictive of the transition to progressive MS. Being a rapid and very easy test, OFA works well in children and infirm persons.

Viewpoint

There was significant interest at the 2025 ACTRIMS meeting in using the eyes as a window into multiple sclerosis (MS). This was in part due to the 2024 revisions to the McDonald criteria for multiple sclerosis (MS) diagnosis adding the optic nerve as a fifth location for demonstrating dissemination in space.[1] Accordingly, we thought it would be

timely to highlight our group's work over the last few decades developing novel, multifocal visual stimuli along with innovative methods of analysis that provide accurate, repeatable, objective, and, importantly, non-invasive and rapid assessment of the visual function of both the eyes and the brain.

An early method that showed promise for assessing MS-related damage involved our measurement of dichoptic, sparse, multifocal visual evoked potentials (mfVEPs).[2] In this case, 'sparse' refers to timing: transient visual stimuli are presented relatively infrequently at each of multiple test locations, specifically at a frequency of about 1/second. This differs from the standard, rapid random contrast-reversal stimuli used by most other mfVEP studies, where the stimuli are presented without an intervening stimulus-free interval. We have shown that temporally sparse stimuli increase per-region response amplitudes by up to 15-times and their associated signal-to-noise ratios by about 4 times.[3] In our mfVEP studies, stimuli were presented dichoptically, with many stimuli being delivered to multiple regions of each eye. Though sparsely delivered at any individual location, stimuli were presented over a wide extent of the visual fields of both eyes many times per second. In this way multiple areas of focal damage within the optic nerves and radiations can be rapidly detected.

Some years ago, we reported that, as the mfVEP stimuli were made more and more sparse temporally, the ability to identify eyes of persons living with MS that had *not* previously been affected by optic neuritis (ON) became as accurate as the ability to identify those eyes which had been affected by a previous episode of ON.[2] This finding suggested that the technique might be measuring not just the results of inflammation, but the progressive MS-related damage associated with loss of axons and grey matter, something which might represent a useful adjunct to MR scanning, especially in secondary progressive disease.[4] Our hypothesis was that the sparse mfVEPs were actually detecting abnormalities in the post-geniculate pathways, bearing in mind that there is a large cortico-thalamic feedback loop in the optic radiations, which contains more efferent fibres from V1 layer 6 than afferents.[5-7] The larger responses to the sparse stimuli are perhaps caused by a gain control operating in the loop, possibly engaging the larger number of efferent fibres, thereby increasing the chance of observing damage.[8] Although the optic radiations make up only about 1% of total brain white matter, T2

lesions in the radiations typically represent 7 to 10% of the total T2 lesion load in MS.[9] Hence, sparse multifocal stimuli may have been detecting damage to both the afferent and the smaller efferent fibres in the post-geniculate pathways, not just damage to the optic nerves themselves.

Looking for a non-contact objective alternative to VEPs, we began to record pupil responses to sparse stimuli, or multifocal pupillographic objective perimetry (mfPOP). As in the case of mfVEPs, both response sensitivity (amplitude) and delay (latency) could be determined for each location in the visual field. It appears that the pupillary responses to these transient stimuli were actually cortically driven rather than occurring at a brain-stem level,[10, 11] which agrees with the neuroanatomy.[12] The subsequent development and refinement of this technique across successive versions has resulted in 39 peer-reviewed publications (see https://konanmedical.com/objectivefield/). Much of the work has investigated glaucoma, macular degeneration and diabetic retinal disease, but we have also published several papers on neurological disorders, including Alzheimer's, concussion, migraine and epilepsy.[13-16]

Figure 1. The objectiveFIELD analyser in use, showing a test subject and the display as seen by the operator during testing. Multifocal transient stimuli are presented independently to the two eyes, and the cortically driven pupillary responses to the stimuli are captured by video cameras.

An early version of the mfPOP method was able to repeat the findings of mfVEPs in being able to identify optic nerves without a prior history of optic neuritis in people with MS,[17] albeit at a somewhat lower sensitivity. Nevertheless, even the findings of that early mfPOP version were subsequently shown to be predictive of MS progression when the same individuals were re-examined 10 years later.[18] Two more recent versions of the mfPOP device incorporating updated analysis software have demonstrably improved its diagnostic power and efficiency, so it is now possible to test both eyes simultaneously in under 90 seconds.[19] Test subjects enjoy the test, and we have assessed children as young as 8 years[20] and persons with mild cognitive impairment.[13]

A fourth-generation mfPOP device was recently released (Figure 1). This is now available commercially in the form of the objectiveFIELD® Analyzer (OFA®). To date, regulatory clearance for the OFA has been obtained in the USA, Japan, Europe, Canada and Australia. As with other commercially available perimeters, the OFA reports per-region data as Total Deviations (TDs) and Pattern Deviations (PDs) relative to normative data for both response sensitivity and delay. Other familiar perimetric measures, such as the Mean Defect and Pattern Standard Deviations, are also provided. In addition to the standard stimulus presentation, the fourth-generation device offers both wide field and macular tests. The OFA is easy to use, its footprint is small, and no special lighting is required.

In summary, we believe the OFA represents an extremely useful clinical tool for the investigation of many different aspects of MS, including its underlying pathophysiology. By examining the vision of individuals with MS, mfPOP can provide objective measurement of disease severity, progression, and response to treatment and, as above, it may also have a role in initial diagnosis and prognostication.

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