Central adaptation after optic neuritis: Is the whole greater than the sum of its parts?

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Readers of this journal will be familiar with the fact that visual evoked potentials (VEPs) arising from eyes that have recovered from optic neuritis show prolonged latency. They may be less aware, however, that prolonged latency is often seen in the VEPs from the unaffected fellow eyes that are not clinically involved. To date, there has been no clear explanation for this finding, which is often attributed to subclinical demyelination.

In this issue of Neurology®, Raz et al. challenge this assumption, suggesting that the prolongation of VEP from the unaffected (fellow) eye is part of a central adaptive mechanism that allows the brain to deal with input from the damaged contralateral optic nerve.

In their study, the authors looked at the VEPs of 17 patients at least a year after a reasonably good recovery from typical optic neuritis. As expected, VEP latencies from both affected and fellow eyes were prolonged compared with controls. However, detailed analysis of the VEPs arising from unaffected (fellow) eyes revealed that, while there was indeed a delay in time-to-peak, there was no delay in time-to-onset; the delay in time-to-peak was achieved by a broadening of the evoked potential itself. This broadening was not seen in affected eyes, which demonstrated delayed time-to-start as well as delayed time-to-peak, consistent with slowed conduction along the damaged optic nerves.

The authors have previously shown that apparent clinical recovery from optic neuritis is not always accompanied by a return of motion perception to normal. Indeed, the degree of abnormality of motion perception appears to be strongly correlated with prolongation of the VEP. In the current study, patients again exhibited impaired motion perception in their affected eyes consistent with VEP latency prolongation. However, motion perception was unimpaired in unaffected (fellow) eyes despite similarly prolonged latencies. With both eyes viewing, the authors found that the ability to detect retinal disparity (i.e., spatial differences that give information about depth) when stimuli were presented briefly to both eyes was inversely proportional to the difference between the time-to-peak latencies from the 2 eyes.

What do these findings mean? Because there was no impairment of motion perception, the observed delay of the VEPs from unaffected (fellow) eyes was unlikely to have been due to subclinical demyelination. Instead, the authors suggest that the broadening of the VEP represents a central adaptive mechanism whose purpose is to synchronize the arrival of information from the 2 eyes at the cortex. Simultaneity is likely to be highly important in allowing those cells in the visual cortex that receive input from both eyes to extract information such as binocular disparity. By delaying input from the unaffected (fellow) eye so that visual information from the 2 eyes reaches the cortex simultaneously, this postulated adaptive process would facilitate any binocular cortical process, such as stereopsis. This is consistent with the observation that binocular disparity detection was better if there was little or no difference between VEP latencies from the 2 eyes.

The basis for the prolongation of VEP latencies in unaffected (fellow) eyes is unclear. It could be driven by the visual cortex itself or, quite possibly, occur at the level of the lateral geniculate nucleus. If this is indeed a central adaptive mechanism to optic nerve damage, it is conceptually similar to the mechanism thought to account for clinical recovery from vestibular nerve damage (e.g., acute vestibular neuritis): in some cases there may be partial recovery of the vestibular nerve itself but the majority of the recovery occurs centrally at the level of the vestibular nuclei, which adapt to compensate for the asymmetric input from the 2 sides. As a result of this central adaptation, patients become asymptomatic even though they clearly have persistent asymmetry of peripheral input, as demonstrated by an abnormal head impulse test. In a similar manner, patients recovering from unilateral optic neuritis can become asymptomatic despite persistent peripheral asymmetry demonstrated by a relative afferent pupillary defect. Analogous central adaptation in response to focal damage could, of course, occur in other regions of the CNS.

The findings from this study may also provide insight into binocular summation (i.e., viewing with 2 eyes is better than viewing with one), a phenomenon that can be observed when assessing visual function near the threshold of detection. After recovery from unilateral optic neuritis, many patients demonstrate impaired binocular
summation and, indeed, some patients find that binocular vision is worse than monocular vision from their better eye (“binocular inhibition”). The underlying mechanisms leading to binocular summation and inhibition are not well understood, but they may be linked to the adaptive process proposed in this study.

The study by Raz et al. is just an initial observation on 17 patients but, like all good research, it generates more questions than it answers and the finding is clearly worthy of further investigation. It is still too early for this to have an immediate effect on clinical care. However, if confirmed by subsequent studies, this process of central temporal adaptation may represent a more widespread phenomenon by which the brain recovers from damage. If so, it could guide the development of new therapies or rehabilitation strategies in patients with afferent visual pathway damage, perhaps analogous to vestibular exercises. Speculating even further, because prolonged latency can be easily measured, it could prove a useful tool in monitoring central adaptation response to emerging therapies.

Raz et al. challenge us to view the afferent visual pathway as a whole when considering recovery from a discrete injury to one of its constituent parts. Our understanding of central adaptive mechanisms is evolving and we should keep our eyes open to the implications of future developments in this exciting area of research.

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**REFERENCES**


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