Principles and Practice of Clinical Electrophysiology of Vision

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A Year Book Medical Publishers imprint of Mosby-Year Book, Inc.

Mosby-Year Book, Inc.
11830 Westline Industrial Drive
St. Louis, MO 63146

1 2 3 4 5 6 7 8 9 0 CL CL MV 95 94 93 92 91

Library of Congress Cataloging-in-Publication Data
Principles and practice of visual electrophysiology / [edited by] John R. Heckenlively, Geoffrey B. Arden.
p. cm.
Includes bibliographical references.
Includes index.
ISBN 0-8151-4290-0
1. Electroretinography. 2. Electrooculography. 3. Visual evoked response. I. Heckenlively, John R. II. Arden, Geoffrey B. (Geoffrey Bernard)
[DNLM: 1. Electrooculography. 2. Electrophysiology. 3. Electroretinography. 4. Evoked Potentials, Visual. 5. Vision Disorders—physiopathology. WW 270 P957]
RE79.E4P75 1991 91-13378
617.7 1547—dc20 CIP
DNLM/DLC
for Library of Congress

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Electroretinography and Visual Evoked Cortical Potential in Developmental Delay

Scott R. Lambert
Anthony Kriss

CLINICAL DESCRIPTION

In 1961, Illingsworth[7] reported two young infants who were visually inattentive. Their vision gradually improved, and by the time they were 6 months of age, it seemed to be normal. Aside from one child walking late, their development was otherwise normal, and no organic cause could be identified for their poor visual performance during early infancy.

Delayed visual maturation is a retrospective diagnosis that can only be made confidently after an infant develops normal vision and other disease processes have been excluded. In most cases, parents note visual inattention when their infant is 2 to 3 months of age. Visually directed behavior usually develops in children with delayed visual maturation before they are 6 months of age.[9] Children with a variety of ocular diseases and structural abnormalities of the central nervous system have also been described as having "delayed visual maturation"[3]; however, the diagnosis of delayed visual maturation is probably best reserved for the idiopathic condition as originally described by Illingsworth.[7] Impaired vision during infancy secondary to injuries of the central nervous system (e.g., perinatal asphyxia, hydrocephalus, encephalitis, intraventricular hemorrhages, or structural abnormalities of the posterior visual pathway) is more appropriately referred to as cortical visual impairment.[13] While visual improvement occurs in many children with cortical visual impairment, the visual recovery is seldom complete.[8] In contradistinction, children with idiopathic delayed visual maturation have normal visual acuities when tested later in childhood.[2]

Infants with delayed visual maturation are frequently delayed in other spheres of development as well.[2,9] A few children with "idiopathic" delayed visual maturation have developed seizure disorders.[2] In these cases, neuroimaging studies need to be performed, and the diagnosis of "delayed visual maturation" should be reassessed. A high percentage of children with delayed visual maturation also develop strabismus.[2,9] Although delayed visual maturation occasionally occurs in infants delivered preterm,[6] most have been delivered full term and have had normal birth weights.[2,7,9]

ELECTROPHYSIOLOGICAL FINDINGS

Historical

The electrophysiological findings associated with delayed visual maturation were initially described by Mellor and Fielder in 1980.[11] They reported that the electroretinogram (ERG) was normal but the flash visual evoked potential (VEP) was absent or "imma-

ture" (e.g., lacking the negative peak preceding the main positive component). However, when these children were retested after they had become visually attentive, the flash VEP was found to be normal. Other reports have described flash VEPs as being delayed[5] or as having an "abnormal configuration."[2] Pattern–onset-offset (40 ms on, 70 ms off) VEPs were recorded in eight infants with delayed visual maturation.[6] In one case, the VEPs were absent, while in the others the VEPs were "significantly attenuated"; however, no information concerning the normal responses for this age group or its variability was given. Another report found varied findings in 12 patients with delayed visual maturation.[3] Two children had normal flash VEPs, 7 were found to have "immature" waveforms, and 3 had reduced amplitudes. While most children with delayed visual maturation have been reported to eventually develop normal VEPs,[5, 6] a few patients have been reported to have persistent VEP abnormalities.[2, 3]

The VEP is known to undergo marked maturational changes during the first 6 months of life (Fig 74–1).[12] While a reduction in the latency of the main positivity is the best characterized of these changes in the VEP, changes also occur in the waveform and amplitude. None of the previous reports of VEPs recorded from infants with delayed visual maturation compared their results with age-matched controls.

The Hospital for Sick Children Study

We recently conducted a prospective study comparing the ERGs and VEPs of children diagnosed as having delayed visual maturation with age-matched controls. Ten children with a presumptive diagnosis of delayed visual maturation were included in our study. All were delivered full term, had normal Apgar scores, and had a birth weight of 6 lb or more. When initially examined, none of the children manifested visually directed behavior (even to a bright light). Each had a complete ophthalmological assessment to exclude other ocular disorders. All of the children were examined by a pediatrician or a pediatric neurologist to exclude systemic or neurological disorders as well. Four of the patients had computed tomographic (CT) scans of the head. One of these patients had generalized cerebral atrophy on a CT scan and because of this was excluded from our study.

The remaining nine patients with delayed visual

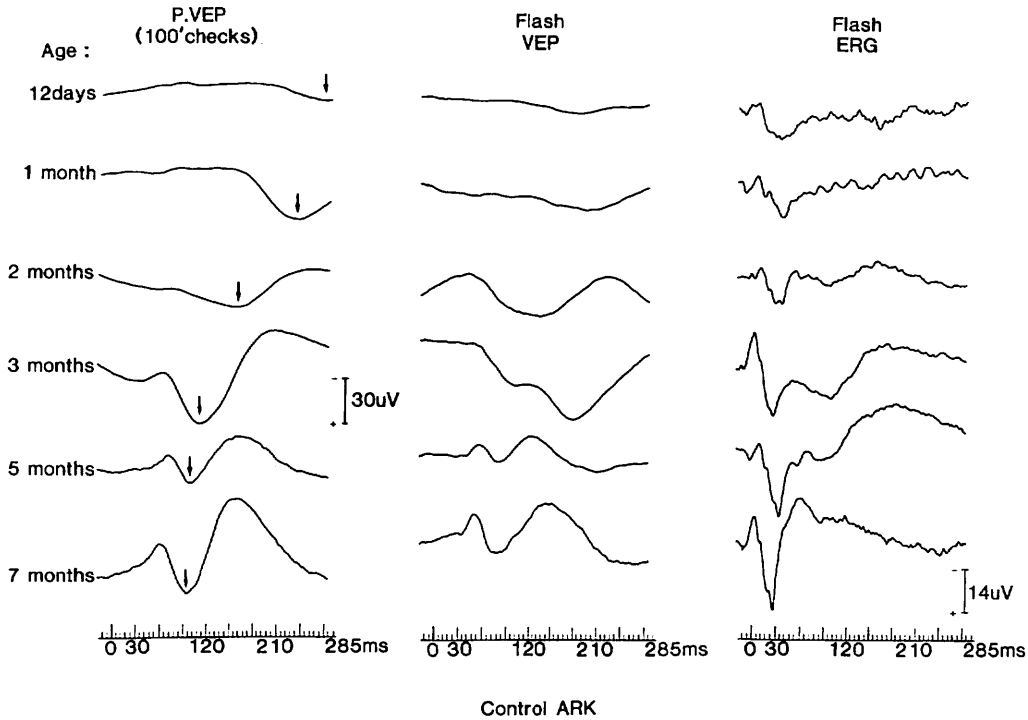

FIG 74–1.
Pattern-reversal VEPs *(P.VEP)* to 100-minute checks, flash VEPs *(F.VEP)*, and flash ERGs *(F.ERG)* from the same healthy infant were recorded during the first 7 months of life. Note the marked changes in VEP latencies and ERG amplitudes during the first 3 months.

maturation had serial recordings of both flash and pattern-reversal VEPs (to 100-minute checks). In addition, computer-averaged skin ERGs to flash stimulation were recorded in a darkened room. VEPs and ERGs were also recorded from 31 control infants in the same age group as the patients with delayed visual maturation. Eleven of these infants had serial recordings. All had visual behavior appropriate for their age. Each child was examined to exclude other ocular or neurological disorders.

Infants with delayed visual maturation were initially examined at a mean age of 3.4 months (range, 1 to 6 months). Behavioral responses to visual stimuli developed at a mean age of 5.5 months (range, 3 to 8 months). The mean follow-up period was 10 months. All of these patients had an improvement in their vision that occurred gradually over a period of several weeks or months. At the end of the study, seven of the nine patients had vision appropriate for their age. Two children had had a marked improvement in their visual acuity but still had subnormal visual acuity for their age at the conclusion of our study.[9]

Five of the patients were delayed in achieving other developmental milestones. One child had a pyridoxine-responsive seizure disorder that was well controlled by daily administration of pyridoxine. Neurological abnormalities were not detected in any of the other patients.

The amplitudes and latencies of a- and b-wave components of the ERGs from patients with delayed visual maturation were not significantly different from those of age-matched controls (Fig 74–2).[9] The latency of the main positivity of both flash and pattern VEPs from infants less than 3 months of age

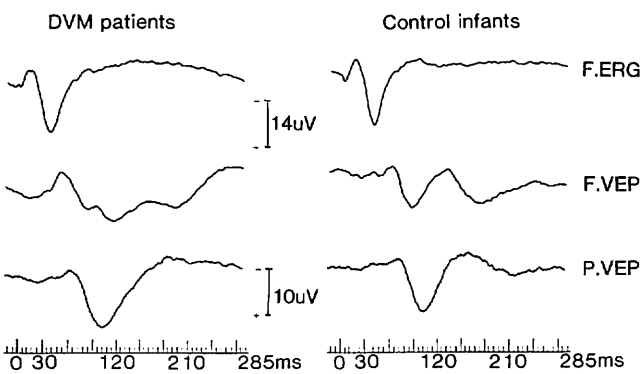

FIG 74–2.
Comparison of group average ERG and VEP waveforms for patients with delayed visual maturation *(DVM)* and age-matched controls. No conspicuous differences were apparent for either ERGs or VEPs.

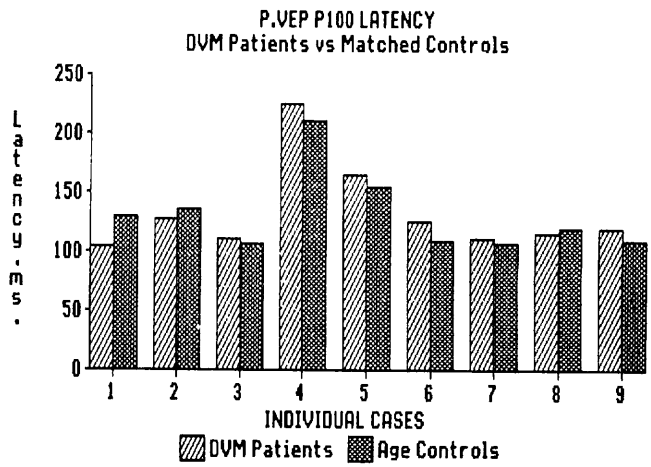

FIG 74–3.
Latency of P100 for patients with delayed visual maturation *(DVM)* and age-matched controls. There were no statistically significant differences when comparing the two groups.

were increased when compared with adult levels; however, no consistent difference was noted in the latency of flash or pattern-reversal VEPs when comparing patients with delayed visual maturation with age-matched controls (Fig 74–3). The latency of the pattern-reversal VEP was significantly delayed in one of the subjects after 9 months of follow-up. One patient also had an unusual "w" waveform with two positivities between 80 and 120 ms. This morphology was not seen in any of our controls. The significance of this finding is not known; however, this patient had a visual acuity of 6/6 when examined at 3 years of age and appeared to be developing normally.

PATHOPHYSIOLOGY

The pathophysiology of delayed visual maturation is not known. Although there are reports that foveal cones are not fully mature until several months after birth,[1] the presence of a well-preserved ERG and VEP in patients with delayed visual maturation indicates that much of the visual pathway is functional. The amount of myelin surrounding the anterior visual pathway fibers also increases during the first 2 years of life.[10] A delay in this process should affect the speed of transmission along the visual pathway. Two findings suggest that a delay in myelination is not likely to be the cause of delayed visual maturation. First, pupillary responses are normal in these patients, and second, VEP latencies are not significantly delayed when compared with age-matched controls.

Dendritic and synaptic proliferation continues to occur during the first few months of life.[4] A delay in this process is the most likely cause of delayed visual maturation. This lag may involve interconnections between the primary visual cortex and other regions of the brain concerned with visual attentiveness.

Delays in other spheres of development suggest that other parts of the brain may be immature as well. While CT scanning failed to reveal abnormalities in our patients with delayed visual maturation, it is possible that magnetic resonance or positron-emission scanning might have helped to elucidate the basis for this disorder.

DIFFERENTIAL DIAGNOSIS

Delayed visual maturation should be diagnosed after excluding other ocular and neurological disorders associated with impaired vision during infancy. Normal age-appropriate VEPs and ERGs are helpful in establishing this diagnosis and can help to reassure anxious parents. If electrophysiological test results are abnormal, alternative diagnoses should be investigated. Magnetic resonance imaging of the brain is a useful adjunctive study if the diagnosis is in doubt. The condition most commonly confused with delayed visual maturation is cortical visual impairment. In contradistinction to children with delayed visual maturation, many infants with cortical visual impairment have had a hypoxic insult or have widespread neurological disease. Abnormalities suggestive of anterior visual pathway dysfunction such as optic atrophy or nystagmus also make the diagnosis of delayed visual maturation untenable. The visual prognosis of idiopathic delayed visual maturation is good in most cases, and one can reassure parents that the infant's vision is likely to improve by the age of 6 months.

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