Role of Electrophysiologic techniques in diagnosis &follow up of pediatric amblyopia

ESSAY

Submitted for partial fulfillment of Master degree in ophthalmology

BY

Mariam Abd El-Rahman Mohammad El-Said

M.B.B, ch.

Supervisors

Prof. Dr. Mohammad Ahmed El-Sada

Professor of Ophthalmology

Faculty of Medicine

Cairo University

Prof. Dr. Rawya Aly El-Abyad

Professor of Ophthalmology

Research Institute of Ophthalmology

Faculty of Medicine

Cairo University

2010

ACKNOWLEDGMENT

Praise is to GOD, the Cherisher and Sustainer of the worlds.

I would like to express my profound gratitude and respect to ***Prof. Dr. Mohammad Ahmed El-Sada,*** *professor of ophthalmology, Cairo University and thank him for his outstanding encouragement, advice and his sincere endless support throughout this work.*

I feel greatly indebted to ***Prof. Dr. Rawya Aly El-Abyad,*** *professor of ophthalmology, Research Institute of ophthalmology, for her great care and patience, sincere guidance, tremendous effort and continuous valuable advice throughout this work.*

Whatever I say will never express my sincere gratitude and appreciation to my family who is always behind my success.

Abstract

Amblyopia is a major public health problem that needs early diagnosis in infants &young children to increase their chances for proper treatment & management. Amblyopia in this group of population is susceptible to be missed & hence the need for screening.

Subjective methods of estimation of pediatric visual acuity are liable to observation bias. Electrophysiologic techniques –on the other hand- allow objective diagnosis, screening & following up of infants or children with amblyopia.

Among the three electrophysiologic techniques (EOG, ERG &VEP) used in clinical practice, VEP proved to play the most important role in diagnosis, screening & following up of pediatric amblyopia. EOG has a minimal role while pattern ERG role solely lies in its ability to differentiate amblyopia from cases of reduced central vision of unexplained aetiology as that occurring in cases of occult macular degeneration.

Key Word:

Role of Electrophysiologic techniques in diagnosis & follow up of pediatric amblyopia

List of figures:

List of abbreviations:

EOG	Electrooculography
ERG	Electroretinography
EUA	Examination Under Anesthesia
fMRI	functional Magnetic Resonance Imaging
LGN	Lateral Geniculate Nucleus
(M)	Magnocellular pathway
mfERG	Multifocal electroretinography
mfVEP	Multifocal visually evoked potential
μv	Microvolt
ms	Millisecond
OKN	Optokinetic nystgmus
OPs	Oscillatory Potentials
(P)	Parvocellular pathway
PERG	Pattern electroretinography
PET	Positron Emission Tomography
PL	Preferential looking
PVEP	Pattern visually evoked potential
RNFL	Retinal nerve fiber layer
RPE	Retinal pigment epithelium
SVEP	Sweep Visually Evoked Potential
SSVEP	Steady state Visually Evoked Potential
V1	Primary visual cortical area
VEP	Visually Evoked Potential

Contents:

Amblyopia

Definition

Amblyopia is etymologically derived from the greek word *amblyos*, meaning dull, and *opia* meaning vision.

The most widely accepted clinical definition of amblyopia is that condition in which there is deficiency of form or spatial vision sense resulting in the reduction of visual acuity of greater than 2 lines between the eyes, or an absolute reduction in acuity below 6/9 in either eye in Snellens vision chart which can't be corrected by refraction &can't be attributed directly to the effect of any structural abnormality of the eye or the posterior visual pathway defects ***(Karki, 2006)***.

"Lazy eye" is a common non-medical term used to describe amblyopia because the eye with poorer vision doesn't seem to be doing its job of seeing.

Pathophysiology

Studies on the pathologic changes occurring with amblyopia include three levels:

1- The retina.

2-The lateral geniculate nucleus (LGN).

3-The primary visual cortical area (V1).

1- The retina:

To study the effect of amblyopia on retinal layers, the optical coherence tomography was used to obtain macular and peripapillary retinal nerve fiber layer (RNFL) thickness in children aged predominantly 6 and 12 years.

Central macular thickness may be increased in eyes with amblyopia, although it is uncertain if this precedes or follows the development of amblyopia. No differences in peripapillary RNFL thickness were found when compared with normal eyes ***(Huynh et al, 2009 &Repka et al, 2009)***.

2-The lateral geniculate nucleus (LGN):

In amblyopia the histologic study of the LGNs from a patient with ophthalmologically confirmed anisometropic amblyopia shows a decrease of cell sizes in the parvocellular layers innervated by the amblyopic eye. This decrease was more pronounced in laminae receiving crossed fibers. Changes in the LGN sizes can be explained on the basis of an afferent or retrograde effect of defocused retinal image on geniculate cell size ***(Von Noorden et al, 1983).***

3- The primary visual cortex (V1) is included by the amblyopic deficit, where monocular inputs are first combined ***(Hess, 2001).***

Through the use of the positron emission tomography (PET), ***Demer et al (1997)*** demonstrated a reduction in the neuronal activity in V1 as shown by the reduced cortical blood flow and glucose metabolism. They suggested that the visual cortex is the primary site of amblyopia& that decrease in LGN cell sizes may be caused by retrograde inhibition originating in the striate cortex in strabismic and anisometropic amblyopia. In pattern vision deprivation amblyopia, on the other hand, lack of afferent stimulation may reduce metabolic activity and thus cause the cell shrinkage.

The interruption of normal visual experience during critical developmental periods leads to alterations in subsequent organization and function of visual cortex ***(Daw, 1998)***.

In 2007, ***Conner et al*** used the functional magnetic resonance imaging (fMRI) study to compare strabismic and anisometropic amblyopes with matched control subjects. They get the following conclusions:
(1) Amblyopic eyes would produce reduced signal magnitude compared to sound and normal eyes, especially in foveal representations.
(2) Ocular dominance would shift toward the sound eye, and binocularity would be reduced in amblyopes, in all cortical regions.
(3) Nasal retina would produce weaker fMRI signal than temporal retina in strabismic amblyopes, especially in extrafoveal regions but these effects were variable, only of moderate strength, and did not distinguish strabismic and anisometropic subtypes.

Research suggests that the maximum critical period in humans is from just after birth to 2 years of age. Any disruption of binocular vision from 6 mos. to approximately 4 years will result in strabismus and/or amblyopia. Thus, every infant without an apparent problem should have their first examination between 9 mos. to one year of age ***(Cooper, 2000)*.**

As the brain of infants exhibits robust plasticity shortly after birth, the developing functional connections in visual cortex are unstable and readily disrupted by experiencing binocularly abnormal vision ***(Kiorpes, 2006)*.**

Psychophysical investigations of human amblyopia have found impaired visual acuity and contrast sensitivity in amblyopic eyes, particularly for the central visual field ***(Sireteanu & Fronius, 1990)*.**

Furthermore, asymmetric visual field deficits have been reported in strabismic with inward eye deviation; nasal retina input is impaired more than temporal retina input. This asymmetry could possibly result from biased competition between the nasal retina of the deviated eye and the fovea of the

sound eye, leading to suppression of amblyopic eye input ***(Hess & Pointer, 1985).***

However, despite many interesting theories of amblyopia and numerous neurophysiologic investigations with animal models, it is still not clearly understood how and where in the visual brain the functional connections are altered, resulting in amblyopia ***(Kiorpes, 2006).***

Prevalence

Prevalence estimates range from 2% to 3% depending on the population studied. In general, approximately 50% of patients with convergent strabismus had amblyopia at the time of initial diagnosis but evoked cortical potential studies in infants indicate a higher prevalence ***(Williams et al, 2001)***.

Classification of amblyopia

Amblyopia is classified according to many categories:

I-Organic or functional:

This is according to the presence of structural abnormalities of the retina or the optic nerve. The term functional amblyopia is often used to describe amblyopia which is potentially reversible by occlusion therapy while organic amblyopia refers to irreversible amblyopia. Functional amblyopia may be superimposed on the organic visual loss ***(Kushner, 1981)***.

II - According to the cause:

It has traditionally been subdivided in terms of the disorder that may be responsible for its occurrence:

1-Strabismic Amblyopia:

Constant, nonalternating tropias (typically esodeviations) are most likely to cause amblyopia. Differences between strabismic amblyopia & other forms of amblyopia are the following:

a- In strabismic amblyopia, grating acuity (the ability to detect patterns composed of uniformly spaced strips) is often better than Snellen acuity (the ability to discriminate high contrast shapes, as a rows of letters each smaller than the one above). This discrepancy must be considered when the results of tests based on grating detection, such as Teller card preferential looking (a method of estimating acuity in infants and toddlers), are interpreted.

b- When illumination is reduced, the acuity of an eye with strabismic amblyopia tends to decline less sharply than that of an organically diseased eye. This phenomenon is sometimes called the neutral density filter effect, after this device was used to demonstrate it.

c- Minor degrees of eccentric fixation are seen in many patients with strabismic amblyopia and relatively mild acuity loss. Eccentric fixation refers to the consistent use of a nonfoveal region of the retina for monocular viewing by an amblyopic eye ***(Kriss & Thompson, 2006)***.

2-Anisometropic Amblyopia:

Anisometropic amblyopia develops when the unequal refractive error between the two eyes cause the image to be chronically defocused in the less seeing eye. It is secondary in frequency to strabismic amblyopia. It is divided into the following subtypes:

a- Hypermetropic anisometropia, where +1.50 diopters or greater is a long-term risk factor for deterioration of visual acuity after occlusion therapy ***(Ciuffreda et al, 1991)***.

b- Myopic anisometropia, where less than –3.0 D, usually does not cause amblyopia, but unilateral high myopia (–6.0 D or greater) often results in severe amblyopic visual loss ***(Abrahamsson & Sjostrand , 1996)*** .

Unless strabismus is present, the eyes of a child with anisometropic amblyopia look normal to the family/caregiver and primary care physician, typically causing a delay in detection and treatment.

3- Isometropic or ametropic amblyopia:

This is a form of refractive amblyopia attributed to bilateral reduction in acuity resulting from large, approximately equal, uncorrected refractive errors in both eyes of a young child. Bilateral hypermetropia exceeding about +5.0 D and bilateral myopia in excess of -10.0 D carry a risk of inducing bilateral amblyopia ***(Abrahamsson &Sjostrand, 1996)***.

4- Meridional amblyopia:

Uncorrected astigmatism in early childhood may result in loss of resolving ability limited to the chronically blurred meridians.

The degree of cylindrical ametropia necessary to produce meridional amblyopia is not known, but most ophthalmologists recommend cylindrical correction of greater than 2.0 D ***(Gwiazda, 1984)***.

5-Visual Deprivation Amblyopia

Also called amblyopia exanopsia or disuse amblyopia.This is caused by any obstruction in the visual axis as in congenital cataract, corneal opacities, and ptosis. Deprivation amblyopia is the least common form of amblyopia but the most damaging and the most difficult to treat. Amblyopic visual loss resulting from a unilateral occlusion of the visual axis is worse than that produced by bilateral deprivation of similar degree because interocular

effects add to the direct developmental impact of severe image degradation ***(Birch et al, 1998)***.

6-Strabismic anisometropia: These patients have strabismus associated with anisometropia.

Diagnoses of pediatric amblyopia: (prepared by ***the American academy of ophthalmology pediatric ophthalmology/strabismus panel, 2007)***

The initial amblyopia evaluation (history and physical examination) includes all components of the comprehensive pediatric ophthalmic evaluation, with special stress upon the potential risk factors for amblyopia.

History:

- Ocular history, including prior eye problems, diseases, diagnoses, and treatments.
- Systemic history, birth weight, prenatal and perinatal history that may be pertinent (e.g., alcohol, tobacco, and drug use during pregnancy); past hospitalizations and operations; general health and development.
- Family history of eye conditions and relevant systemic diseases.

Examination:

1- Assessment of Visual Acuity and Fixation Pattern:

The method of evaluating visual acuity varies according to the child's age and level of cooperation. Diagnosis is not an issue in children old enough to read or with use of the tumbling E.