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Parkinson Disease, Mild Cognitive Impairment, Alzheimer Disease: Three Different Manifestations of Color Vision Impairment Pathway

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Abstract

Color Vision showed to be a useful biological marker to identify the different brain pathways implied in the different neurological diseases we investigated.

Keywords: Parkinson Disease; Mild Cognitive Impairment; Alzheimer Disease; Different Phenotypes; Color Vision Impairment Different Manifestations

Abbreviations: PD: Parkinson' s Disease; AD: Alzheimer's Disease; MCI: Mild Cognitive Impairment

Introduction

The study of color vision is an interdisciplinary subject which embraces aspects of Physics, Biochemistry, Neuro-Physiology and Psychology. Light is absorbed by pigments in the photoreceptor layer of the eye's retina initiating a photochemical reaction. By a transducer process, the various attributes of light energy are coded for transmission to the brain by neural signals; here the signals are later interpreted. The perception of color is a psychophysical experience which is dependent on the physiological coding and processing that take place in the eye and brain. The fault which gives rise to defective color vision, lies in the retina and/or visual pathway [1].

Light travers the neural layers of the retina to the photoreceptors which are in the innermost region (posterior) and is absorbed by the photo-pigments contained within the receptors; subsequently a neural discharge is initiated by which the signal is transferred to the brain. The retina has been shown to play a major role in separating out the colored elements of the stimulus from brightness characteristics and coding these two attributes. The mechanisms converting the photochemical change in the sensory receptors to an electrical potential involve complex internal chemical reaction in which changes in the potassium and sodium balance play a major part. Pharmacological agents known as neurotransmitters act to carry the coded signal from one neuron to the next as they are released from neurons at the synaptic junction. One important and novel characteristic of photoreceptors is their hyperpolarizing action (production of a negative potential in the cell membrane) as a consequence of light absorption [2].

Normally, dopaminergic neurons act in the outer and inner retina at multiple levels, producing alterations to the flow of

visual information in a complex fashion. Dopamine is a chemical messenger for light adaptation, promoting the flow of information through cone circuits while diminishing that through rod circuits [3].

Nerve impulses signaling color information are relayed from the lateral geniculate nucleus via the visual radiations, to the main visual areas of the brain, the striate cortex. The principal zones were designated Area 17 by Brodman in his classic division and then onwards to Area 18 (the occipital or para-striate cortex) and area 19 (the pre-occipital cortex) [4]. Some not-color fibers concerned with eye movements project to the superior colliculus and pre-tecta regions. The visual areas maintain strong foveal representation having specific locations within the region for each part of the visual field. Retinal organization or spatial mapping is thus preserved and fibers conveying signals from corresponding points of the two retinae remain close. Foveal regions are spatially magnified in the lateral geniculate nucleus and striate cortex to ensure maximum resolution in this region [5-7].

Acquired Color Vision Impairment

There exist a wide group of color vision disturbances which are acquired during life predominantly the results of ocular or general disease, the consequence of exposure to a chemical, toxin or medication, or resulting from physical injury to the head. The incidence of such disturbances is uncertain [8] although the estimate by Smith [9] that at least 5% of the population have an acquired defect as severe as the 8% with a congenital defect, is a valuable guideline. It is now realized that color vision changes provide a valuable means of monitoring the progress of a disease, or the toxic effects of a chemical substance, whether exposure is deliberate for therapeutic purposes or unintentional in the case of an industrial hazard.

The effectiveness of treatment can occasionally be assessed by the continued monitoring of recovery of an acquired color vision disturbance. Acquired disturbances of color vision are a highly varied group of defects with frequent departures from established patterns. They can progress from normal trichromatism to anomalous trichromatism on to a dichromatic stage and even to monochromatism where most color vision is lost, or they may be relatively stable. On recovery or withdrawal of the cause, color vision may typically revert to normality through these phases if the color loss had been considerable. A variety of related visual disturbances may accompany the color vision change, principally visual acuity and field losses [1]. Cerebral lesions can induce complete color loss [10]. When the integrity of any part of the visual pathway is threatened, by whatever cause, color vision may be impaired, and the presence of multiple perceptual abnormalities can make difficult color vision examination [11].

Patients

Fixed sampling of males allowed us to avoid the genetic Lyon phenomenon [12], which is present only in the heterozygous females for X-linked diseases such as colorblindness (the inherited red-green color vision deficiency). Therefore, the exclusion of females in our sample allowed us to avoid those heterozygous colorblind females who would be false positive for the acquired red-green color vision deficiency caused by multiple sclerosis thus altering the results analysis. The relatively high frequency of the inherited red-green colorblind females united Lyon genetic phenomenon presence by the heterozygous females for the inherited colorblindness should be the real cause to mistake discriminating between the red-green inherited colorblindness and that acquired due to multiple sclerosis. We should not comprehend if homozygous female status is really inherited or acquired; and in heterozygous status we miss all those females miming the normal color vision. The acquired color vision deficiency is real in the male cohort because they have not the compensation presence by second X chromosome and the anomaly has not hidden.

Method

Clinical Pseudoisochromatic Tests

McLaren [13] estimated that nearly 200 methods have been devised over the years, but today only about 20 are commonly encountered. An "ideal" color vision test, suitable for all purposes, and providing an unequivocal diagnosis is probably an impossibility; so, the use of two or three independent means of assessing color function is preferable, though not always practicable. Early color vision tests involved the naming of colored ribbons, wools, beads, cloth, paper or glass. Huddart [14] examined the Harris brothers with colored ribbons, probably the first color vision test.

The patient requires an indication of any appreciable color vision defect which will affect daily life and occupation; this may be important for the teenager planning a future career. Diagnosis of type and severity of a defect and advice based on interpretation of results for the individual is seldom easy, but enquiries into past confusions and difficulties with colors may assist; experience plays a major factor. A definition of normal color vision is difficult and although defects are usually classified into convenient groups, a whole spectrum of anomalies is met in practice. Many do not fall unambiguously into and one class. The difficulty is marked in relation to severity of defects, since there is no agreed defining the type or severity of inherited colorblindness and the clinical tests available frequently vary slightly in their diagnosis. Tests are designed on different principles and each type of test measures a different ability. Murray [15] says that no individual should be diagnosed as color anomalous on a single test; three different tests are requisite.

Pseudoisochromatic Test in the Present Research

After informed consent, all patients and controls had an examination by an ophthalmologist in order to rule a diabetic retinopathy, or a cataract, or an optic neuritis, or a senile

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maculopathy, or ocular fundus' anomalies that could influence the color vision analysis. Any patient who made more than 5 mistakes reading Ishihara test was diagnosed as colorblind, and was excluded from the results analysis.

Ishihara Test

The test is remarkably efficient as a screening test [16] for red and green defects, but does not test the blue anomalies. It uses one or two numbers, designed on the confusion principle. It contains four plates constructed so that normal subject sees no number but the inherited colorblind subjects see one. Some tracing paths are included for use among illiterates and young children. "Diagnostic plates" are included to separate deutan from protan. The numbers are displayed, one a pure red, the other a purple red, both on a neural background; strong protan fail to see the red number and deutan miss the purple figure [17].

The City University Test

The subject chooses the spot most closely matching the color of the central spot, using "top", "bottom", "left", and "right" for location. He does not touch the plates. One color is a natural choice for a normal subject, another is more likely to be chosen by a person who is "significantly" protan, a third is a good "deutan match" and the fourth is designed for a tritan confusion. Sometimes more than one may be chosen, perhaps a deutan as well as the normal spot. Results entered on a record sheet suggest both type and severity of any defect [18].

Farnsworth Dichotomous D-15 Test

It involves a color circle made from a blue "pilot" and 15 other colored numbered discs of effective diameter about 12 mm. The caps 1-15 are randomly arranged on the tray formed by the lid of their box and the pilot is placed at one end of the box base. The subject chooses the color appearing to match the pilot color most nearly and places it next to the pilot; he completes the sequence always matching the one he placed last. He is not pressed for time and may change the order. A normal trichromat correctly makes a sequence 1 to 15. deutan, protan, Tritan makes characteristic errors along their own axes, as a specific diagram illustrates [19].

Results

The results of the present research regard 70 patients, in total: 49 Parkinson' s Disease (PD) patients, 9 Alzheimer's Disease (AD) patients, 12 Mild Cognitive Impairment (MCI) patients.

- **Parkinson's Disease:** We examined 49 PD Calabrian all male patients (age range, 50-85 years; mean age, 67 years). All patients underwent the L-DOPA doses subdivided into two different groups: 125-300 mg/day, low daily dose; 400-1000 mg/day, high daily dose. 25/49 PD patients showed a defect of blue/yellow axis reading the three tests. 3/49 PD patients showed a defect of red/green axis reading the three tests. 4/49 PD patients were colorblind; 9/49 were excluded because showed acquired ophthalmological diseases; 8/49 patients showed normal color vision.

- **Alzheimer's Disease:** We examined 11 AD Calabrian all male patients (age range, 50-85 years; mean age, 67 years). 8/11 AD patients showed a normal color vision reading the three tests. 1/11 AD patients showed a defect of red/green axis reading the three tests, and 1/11 AD patients showed a defect of blue/yellow axis reading the three tests; 1/11 AD patients showed a black/white vision.

- **Mild Cognitive Impairment Disease:** We examined 16 MCI Calabrian all male patients (age range, 50-85 years; mean age, 67 years). 6/16 MCI patients showed a normal color vision reading the three tests. 1/16 MCI patients showed a defect of blue/yellow axis reading the three tests; 8/11 MCI patients showed a double red/green and blue/yellow defect; 1/15 MCI patients was affected by inherited impair color vision, and was excluded by the results' analysis.

Discussion and Conclusion

The analysis of the above results allowed us to precise some comments subdivided for the three neurological disorders, as below:

According with Haug [20], we affirm that the influence of Parkinson's Disease is most noticeable in signals by the short waves cone pathway which are widely separated. In the retina, the small bistratified ganglion cells which are the morphological substrate of the short-wave cone pathway have much larger receptive fields than the midget ganglion cells, and may be more dependent upon long range spatial interactions mediated dopaminergic inter-plexiform or amacrine cells. Presence of the defect of red/green axis in Parkinson's Disease confirms Silva's [21] data probing chromatic and achromatic contrast sensitivity changes in Parkinson's Disease using complex psychophysical measures designed to isolate parvocellular, koniocellular and magnocellular pathways. Significant impairment in all three pathways was found, more marked along the protan/deutan axis than the tritan. This pattern contrasts with that typically seen in aging, predominant tritan axis deficiency, or in retinal disease states such as glaucoma in which all color axes are involved with particular emphasis on the tritan axis or best macular dystrophy where color axis involvement itself [22].

Such comparisons suggest a disease specific pattern of retinal impairment in Parkinson's Disease distinct from normal ageing or the commoner ophthalmological disease which are age related.

Functional studies performed on Alzheimer's Disease showed how visual acuity, contrast sensitivity, color vision and visual integration vary with the progression of neurodegeneration. At the stage of Alzheimer's Disease where plaque deposition occurs, neurons that employ glutamate or acetylcholine are particularly damaged, as are neurons that produce serotonin and

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norepinephrine. At a stage where no plaque deposition, hyperphosphorylated tau tangles or sign of neuronal loss in cortical and hippocampal regions involved in memory deficits has occurred, a specific apoptotic process takes place in the ventral tegmental area, causing progressive degeneration of the dopaminergic neuronal population, so alterations in the dopaminergic system include reduced levels of dopamine and alterations in the dopamine receptors. Dopamine is a modulator of hippocampal synaptic plasticity and its binding to dopaminergic receptors in the dorsal hippocampus is a major determinant of memory encoding. Ventral tegmental area dopaminergic neurons also target nucleus accumbens and the cerebral cortex, mediating the control of incentive motivation and reward processing. Degeneration is selective for the ventral tegmental area as dopaminergic neurons in the adjacent substantia nigra pars compacta were intact. Moreover, basal outflow of dopamine in the hippocampus and nucleus accumbens shell is reduced, likely contributing to deficits in mesolimbic cognitive and non-cognitive symptoms.

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