Perception of Fechner Illusory Colors in Alzheimer Disease Patients

Background: Alzheimer disease (AD) primarily affects cognition. A variety of visual disorders was established in AD. Fechner illusory colors are produced by a rotating disk with a black and white pattern. The purpose of our research was to explore the perception of illusory colors in AD.

Material/Methods: We recruited 40 AD patients (MMSE ≥14) and 40 normal controls (CG group) matched by age, education, gender in this prospective, cross-sectional, case-control study. An achromatic Benham’s disk attached to a device to control the speed and direction of rotation was used to produce illusory colors. Primary, secondary, and tertiary RGB system colors were used for matching of illusory and physical colors.

Results: Subjects in the AD group perceived less illusory colors in 5 arcs (p<0.05) of the 8 arcs assessed. The biggest difference was found between AD and CG groups for pure blue ($\chi^2=26.87$, p<0.001 clockwise, $\chi^2=22.75$, p<0.001 counter-clockwise). Groups did not differ in perception of pure yellow opponent colors (p>0.05). Mixed colors of the blue-yellow axis were perceived less often in AD, but more frequently than pure blue (#0000FF). The sequence of colors on Benham’s disk followed a complex pattern, different from the order of physical spectral colors and opponent processes-based colors.

Conclusions: AD patients retained reduced perception of illusory colors. The perception of pure blue illusory color is almost absent in AD. The asymmetrical shift to the yellow opponent is observed in AD with red prevailing over green constituent. This may indicate cortical rather than retinal impairment.

MeSH Keywords: Alzheimer Disease • Color Perception Tests • Retinal Ganglion Cells • Sensation Disorders • Vision Disorders • Visual Cortex

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**Background**

Alzheimer disease (AD) is a progressive central nervous system degeneration, which is characterized by a gradual decline in cognitive abilities and activities of daily living [1,2]. AD is the cause of 60% to 70% of all cases of dementia [1,2]. The most common symptoms of AD are an expanding variety of cognitive disorders, which usually starts with dysfunction of memory, and, as the AD progresses, involves language, orientation, praxis, attention, and perception functions [3]. The proteinopathy, cholinergic deficit, and neurodegeneration in early AD involves brain areas responsible for noncognitive functions, including structures and pathways of vision [4–8]. Visual changes occur early in the course of AD and have a potential role as noninvasive biomarkers of AD-related neurodegeneration [9]. AD is associated with a wide variety of pathological changes in the retina and brain visual system [9]. Some of the disorders of visual function may become noninvasive markers for the diagnosis of AD, and also may provide a better understanding of the mechanisms of visual perception per se [9–17]. One of the most promising and potentially insightful provisional biomarker is color vision [10–18].

The extent and nature of vision disorders in AD patients remain controversial [9]. Some researchers have reported dysfunctional color vision and color memory in AD patients [18–20]. Some research reports indicate deficits of color perception at specific color axes according to the RGB (Red-Green-Blue) system, corresponding to the maximum sensitivity to different light wavelengths of 3 types of retinal cone photoreceptors, while others did not identify selective color vision deficits [9]. Most research reports have found abnormalities in the Tritan axis in AD patients [14,18–20], while reports from other research groups suggest that the Deutan axis may be dysfunctional [13].

Cholinergic neurons of the nucleus basalis of Meynert have a number of important functions in modulation of visual perception [21]. In AD patients, the nucleus basalis is one of the brain structures involved, degenerating at the earliest stages of the disease and leading to the cholinergic deficit in the cerebral cortex. In addition, according to the 2-streams (dorsal and ventral) hypothesis of the neural processing of visual perception, the ventral stream is associated with form and color representation; it goes to areas of the inferior temporal lobe and has strong connections to the medial temporal lobe, which encodes long-term memories [22]. This indicates that research on disorders of color perception may be a promising strategy in search of functional markers of early AD.

Among the provisional visual markers of AD, one very interesting and still poorly understood phenomenon – Fechner illusory colors – has received no attention in AD research. Our search of databases of published research articles found no scientific reports dealing with the investigation of Fechner illusory colors in AD.

Fechner illusory colors are also called subjective colors, Fechner-Behnam subjective colors, and pattern-induced flicker colors (PIFC) [23]. Fechner colors are the illusory colors that are perceived from the repeated flashing of black and white patterns. Benham's disk (also known as Benham's top) is a spinning disk with an alternating black and white pattern developed to create the experience of PIFC [23]. The Fechner illusory colors are experienced when the flicker rate of black and white stimuli is neither too slow nor too fast [23]. Usually PIFCs are seen when the speed of rotation (frequency) is going from 120 revolutions per minute (rpm) or 2 Hz up to 360 rpm or 6 Hz [23]. The most common method for measuring Fechner illusory colors is some form of color matching to determine the color experienced by the participant [23]. While PIFCs have some individual variation, there is a remarkable degree of agreement across observers [23]. Many different types of explanations have been provided to explain the experience of PIFCs. Initially, the most popular explanation of how the monochromatic or neutral flickering stimuli produce the perception of color was based on the difference in information processing speed by different types of retinal cones, especially by the relative slowness of the blue or short-wavelength cone (S cone) compared to the speed of the other 2 cones – the green or medium-wavelength cone (M cone) and the red or long-wavelength cone (L-cone).

Differences in responsivity spectra of S, M, and L type cone cells could not be an explanation, because the stimulus was monochromatic (neutral) black and white and despite that, they produced several concentric bands of different colors on the spinning disk. There were no “real” physical colors corresponding to different wavelengths of light on the disk. Also, there were no differing compositions of red, green, and blue components, which are able to imitate the real physical colors (which is the case for computer monitors and TV screens). If illusory colors are experienced due to the slowness of the S cones, then the most probable neuroanatomical substrate of PIFCs are the retinal ganglion cells, responsible for the blue-yellow opponent process [23,24]. Despite the seeming plausibility of this explanation, there are some facts that cannot be explained by the difference of information processing speed in different types of cones [23]. Until now there has been no generally accepted explanation for PIFCs. Some more recent fMRI investigations showed that Fechner illusory colors may be a cortical phenomenon associated with a ventral stream of visual information (ie, with the interaction between visual areas V1, V2, and V4), which anatomically is ongoing at the inferior temporal cortex [25]. The inferior temporal cortex has numerous connections with the medial temporal lobe and is affected by the neurodegeneration early in the course of AD.

The purpose of the study was to explore and compare perception of Fechner illusory colors in AD patients and normal controls.
Material and Methods

Study participants

The present prospective, cross-sectional, case-control study was carried out at the Alzheimer Disease and Dementia Subunit of the Department of Neurology, VUH Santariskiu Clinics. We recruited 80 participants into the study. We enrolled 40 AD patients (the AD group) and 40 control participants (the control group, CG), who were matched by age, sex, and education.

Informed consent forms (ICF), which were approved by the VU Hospital Santariskiu Clinics Biomedical Ethics Commission, were signed by all participants.

The research Protocol and ICF were approved by the VU Hospital Santariskiu Clinics Biomedical Ethics Commission (approval No. EK-42).

Inclusion/exclusion criteria

Inclusion criteria for AD group participants were: 1) AD diagnosis established based on NINCDS-ADRDA criteria; 2) mild or moderate dementia based on MMSE score 14 or more; 3) at least 65 years old; 4) education at least 8 years; 5) Hachinski Index equal to or less than 4; 6) Yesavage GDS depression score equal to or less than 19; 7) no significant vascular signs or other neurodegenerative pathology results of the head-on CT or MRI.

Exclusion criteria for AD group participants were: 1) diagnosis or any signs of any other than AD neurodegenerative disease; 2) diagnosis of any significant psychiatric disorder, such as schizophrenia, delirium, psychosis, or other; 3) diagnosis or any symptoms of significant cardiovascular, hepatic, or metabolic disorders; 4) history or evidence of past or current drug or alcohol abuse.

Inclusion criteria for control group participants were: 1) normal cognition based on MMSE score 27 or more; 2) at least 65 years old; 3) Hachinski Index equal to or less than 4; 4) education at least 8 years; 5) Yesavage GDS depression score equal to or less than 19; 6) education at least 8 years.

For the CG group, the same exclusion criteria were used as for the AD group.

Investigation tools

Mini-Mental State Examination (MMSE) score was used as a measure of overall cognitive status.

We used a Benham’s disk attached to a device of original construction to control the speed and direction of rotation. The device could rotate the Benham disk at speeds of 90 rpm, 120 rpm, 150 rpm, 180 rpm, and 210 rpm clockwise and counter-clockwise. The device was constructed and calibrated at the Gediminas Technical University, Vilnius, Lithuania. The rotation speed of 210 rpm was chosen for the main study after initial proof-of-concept investigation because it had less flicker and greater stability and saturation of observed colors.

We used a variant of the Benham disk with one half of the disk colored solid black and the other half containing 4 perfectly concentric arcs consisting of 4 black lines. The thickness of lines was equal to the white spaces between the black lines. The diameter of the disk was 120 millimeters. The distance from the observing participant to the rotating disk was 60 centimeters. The observation angle was 11.5°. Letters from A to D were assigned to the bands of stripes for the clockwise rotating disk and letters E to H were assigned for the bands of the counter-clockwise rotating disk for the purposes of further analysis (Figure 1).

We analyzed Fechner illusory colors appearing when black and white stripes were rotating fast. We used a 210 rpm (revolutions per minute) speed of rotation, or 3.5 Hz, for the reasons mentioned above. The Benham disk was covered and not visible to the participants until the disk achieved a stable angular speed. The PC monitor used to the evaluate the color template was switched off before the participant provided answers regarding the colors of the bands of stripes on the rotating disk, and only after that the monitor was switched on and the participant was asked to indicate the most resembling color on the screen. The names of the colors were not used for further analysis due to heavy influence of the color categorization in the language and a wide variety of color vocabulary used to describe the illusory Fechner colors, but the naming was needed to be sure that the participants are actually seeing some kind of color. RGB primary, secondary, and tertiary colors with the addition of 4 neutral colors were used to...
standardize the participants’ responses. The participants were asked to choose the color from the template on the monitor that most resembles the illusory color they had seen. The template for color matching was constructed from vertical bands of RGB primary, secondary, and tertiary colors with the addition of 4 neutral colors. A forced-choice paradigm was used, which was necessary to standardize the responses of participants. Codes and order of color bands used in the template for matching Fechner illusory colors with RGB colors are provided in Table 1. Numbers of colors were used for the purposes of further evaluation, but were not visible on the screen.

### Table 1. The color stripes of the template used for matching of Fechner illusory colors observed by the participants and physical primary, secondary, and tertiary colors of RGB system.

| Matching band number | Color name                  | Color HEX code | Color RGB code |
|----------------------|-----------------------------|----------------|----------------|
| 1                    | Light grey (neutral)        | #969696        | R: 150; G: 150; B: 150 |
| 2                    | White (neutral)             | #FFFFFF        | R: 255; G: 255; B: 255 |
| 3                    | Red                         | #FF0000        | R: 255; G: 0; B: 0 |
| 4                    | Orange                      | #FF7F00        | R: 255; G: 127; B: 0 |
| 5                    | Yellow                      | #FFFF00        | R: 255; G: 255; B: 0 |
| 6                    | Chartreuse green            | #7FFF00        | R: 127; G: 255; B: 0 |
| 7                    | Green                       | #00FF00        | R: 0; G: 255; B: 0 |
| 8                    | Spring green                | #00FF7F        | R: 0; G: 255; B: 127 |
| 9                    | Cyan                        | #00FFFF        | R: 0; G: 0; B: 255 |
| 10                   | Azure                       | #007FFF        | R: 0; G: 127; B: 255 |
| 11                   | Blue                        | #0000FF        | R: 0; G: 0; B: 255 |
| 12                   | Violet                      | #7F00FF        | R: 127; G: 0; B: 255 |
| 13                   | Magenta                     | #FF00FF        | R: 255; G: 0; B: 255 |
| 14                   | Rose                        | #FF007F        | R: 255; G: 0; B: 127 |
| 15                   | Black (neutral)             | #0000000       | R: 0; G: 0; B: 0 |
| 16                   | Dark grey (neutral)         | #555555        | R: 085; G: 085; B: 085 |

### Table 2. Demographic and clinical characteristics in participant groups.

|                          | AD group | CG group | p    |
|--------------------------|----------|----------|------|
| Number of subjects, N    | 40       | 40       | –    |
| Age (years), Mean ±SD    | 76.2±15  | 74.1±6.78| 0.91* ns |
| Education (years), Mean ±SD | 14.1±2.50 | 13.4±3.07 | 0.21* ns |
| Gender, Women/Men, N     | 26/14    | 25/15    | 0.82** ns |
| MMSE score, Mean ±SD     | 18.9±2.43| 29.0±0.82| <0.001* |

* t-test; ** Chi square test; ns – not significant.

**Statistical analysis**

We used the Shapiro-Wilk test for the verification of normality of data distribution. Homogeneity of variances was evaluated by means of the Levene test. Skewness and kurtosis were calculated for all distributions and used for further inferences. The t test was employed to compare continuous variables in participant groups. Comparisons between groups were performed using parametric analysis. For comparison of the groups on the basis of categorical variables, the chi-square test was used. The value of statistical significance was set at p<0.05.
The age (p=0.91), education (p=0.21), and sex (p=0.82) of AD and CG groups did not differ. Demographic characteristics and MMSE scores in AD and CG groups are presented in Table 2.

The number of AD and CG participants reporting the perception of Fechner illusory color on each arc when the Benham’s disk is rotating clockwise and counter-clockwise are provided in Table 3, based on the matching template color indicated by the participant.

### Table 3. The number of AD and CG participants reporting Fechner illusory colors matched to 16-color template (12 RGB and 4 Neutral colors included) in indicated arcs when Benham disk is rotating clockwise and counter-clockwise.

| Arc of lines | Clockwise | Counter-clockwise |
|--------------|-----------|-------------------|
| 1st arc A (outer) | 2nd arc B | 3rd arc C | 4th arc D (inner) | 1st arc E (outer) | 2nd arc F | 3rd arc G | 4th arc H (inner) |
| Participant group | AD | CG | AD | CG | AD | CG | AD | CG | AD | CG | AD | CG | AD | CG |
| Color name HEX code | | | | | | | | | | | | | | |
| 1. Light grey (neutral) #969696 | 0 | 0 | 0 | 1 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| 2. White (neutral) #FFFFFF | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| 3. Red #FF0000 | 0 | 0 | 0 | 0 | 0 | 8 | 8 | 8 | 12 | 0 | 0 | 0 | 0 | 0 |
| 4. Orange #FF7F00 | 0 | 0 | 0 | 0 | 0 | 18 | 19 | 19 | 16 | 0 | 0 | 0 | 0 | 0 |
| 5. Yellow #FFFF00 | 0 | 0 | 0 | 0 | 7 | 1 | 6 | 7 | 6 | 7 | 9 | 0 | 0 | 0 | 0 |
| 6. Chartreuse green #7FFF00 | 0 | 0 | 0 | 0 | 16 | 6 | 0 | 0 | 0 | 15 | 6 | 0 | 1 | 0 | 0 |
| 7. Green #00FF00 | 0 | 0 | 0 | 0 | 5 | 16 | 0 | 0 | 0 | 4 | 19 | 0 | 0 | 0 | 0 |
| 8. Spring green #00FF7F | 0 | 0 | 0 | 0 | 8 | 0 | 0 | 0 | 0 | 1 | 6 | 0 | 0 | 0 | 0 |
| 9. Cyan #00FFFF | 0 | 0 | 0 | 0 | 4 | 0 | 0 | 0 | 0 | 0 | 5 | 0 | 2 | 0 | 0 |
| 10. Azure #007FFF | 2 | 3 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 2 | 4 |
| 11. Blue #0000FF | 2 | 25 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 2 | 24 |
| 12. Violet #7F00FF | 3 | 3 | 0 | 3 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 4 | 3 | 4 | 4 |
| 13. Magenta #FF00FF | 2 | 2 | 5 | 20 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 5 | 17 | 4 | 1 |
| 14. Rose #FF007F | 2 | 0 | 10 | 5 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 13 | 4 | 2 | 1 |
| 15. Black (neutral) #000000 | 26 | 6 | 8 | 3 | 2 | 2 | 3 | 2 | 3 | 1 | 2 | 0 | 6 | 2 | 24 | 6 |
| 16. Dark grey (neutral) #555555 | 3 | 1 | 17 | 8 | 10 | 3 | 5 | 4 | 4 | 4 | 4 | 9 | 4 | 16 | 10 | 3 | 0 |

### Results

#### Demographic characteristics and MMSE scores

The age (p=0.91), education (p=0.21), and sex (p=0.82) of AD and CG groups did not differ. Demographic characteristics and MMSE results in AD and CG groups are presented in Table 2.
Reversing of the colors when the direction of rotation reverses is evident in Table 3. This reversal of color order, which is typical for healthy controls, remains intact in the AD group.

The numbers of AD and CG participants perceiving spectral versus neutral color on each arc of lines when the Benham’s disk is rotating clockwise (arcs A to D) and counter-clockwise (arcs E to H) is provided in Table 4.

For further analysis, the grouping of Fechner illusory colors according to blue-yellow opponent process theory was performed. Based on data provided in Table 1, pure blue color without any constituent parts of red or green (hexadecimal html code #0000FF) was assigned to group 1. The mixed colors containing both blue and yellow (red plus green, only red, or only green by RGB system) components were assigned to group 2. The colors lacking any amount of blue constituent and composed only from components of the yellow part of the blue-yellow opponent axis (ie, colors containing red plus green, or only red, or only green based on RGB system) were assigned to group 3. The scheme of assigning the matching template colors to the groups based on the blue-yellow opponent process theory is provided in Table 5.

Table 4. The perception of RGB colors versus Neutral colors in AD and CG groups.

| Arc of lines | RGB color vs. neutral | Participant group | Chi-square (df=1) | p     |
|--------------|----------------------|-------------------|-----------------|-------|
|              |                      | AD                |                 |       |
| A            | RGB color            | 11                | 34              | 26.87 | p<0.001 |
|              | Neutral              | 29                | 6               |       |
| B            | RGB color            | 15                | 28              | 8.50  | p=0.0036 |
|              | Neutral              | 25                | 12              |       |
| C            | RGB color            | 28                | 35              | 3.66  | p=0.0557 |
|              | Neutral              | 12                | 5               | ns    |
| D            | RGB color            | 32                | 34              | 0.35  | p=0.5562 |
|              | Neutral              | 8                 | 6               | ns    |
| E            | RGB color            | 33                | 35              | 0.39  | p=0.5312 |
|              | Neutral              | 7                 | 5               | ns    |
| F            | RGB color            | 29                | 36              | 4.02  | p=0.045 |
|              | Neutral              | 11                | 4               |       |
| G            | RGB color            | 18                | 28              | 5.12  | p=0.0237 |
|              | Neutral              | 22                | 12              |       |
| H            | RGB color            | 13                | 34              | 22.75 | <0.001  |
|              | Neutral              | 27                | 6               |       |

ns – not significant.

Reversing of the colors when the direction of rotation reverses is evident in Table 3. This reversal of color order, which is typical for healthy controls, remains intact in the AD group.

The numbers of AD and CG participants perceiving spectral versus neutral color on each arc of lines when the Benham’s disk is rotating clockwise (arcs A to D) and counter-clockwise (arcs E to H) is provided in Table 4.

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The differences in perception of Fechner illusory colors were grouped according to the blue-yellow opponent process constituent parts in AD and CG (Figure 2).

Discussion

AD patients retain the ability to see Fechner illusory colors, but they significantly more frequently report neutral colors (e.g., shades of gray, black, white) than participants from the control group (Table 4).

At 210 rpm, clockwise, the outermost (1st) arc appears dark saturated blue, the second set of lines pale magenta, the third arc of lines green, and the innermost (4th) arc of lines looks clear or luminescent yellow, orange, or red. When the direction of Benham disk rotation is changed to counter-clockwise, the colors reverse order. This reversal of color order when changing the direction of disk rotation remains intact in AD subjects.

The phenomenon of Fechner illusory colors is not entirely understood. A possible explanation of why the study participants see colors when looking at the rotating achromatic stimulus disk may be that the cone receptors in the human retina...
respond at different rates to red, green, and blue. Even more importantly, the latencies at the center and the surroundings differ for the different types of color-specific retinal ganglion cells. Substantial evidence exists that PIFCs appear due to neural activity in a wide range of nervous system structures, from the retina to the visual cortex, and there are some indications that the blue-yellow opponent process may explain subjects’ experience of all the different Fechner colors [24].

The color opponent process is a color theory that indicates that the human visual system interprets information about color by processing signals from cones and rods in an antagonistic manner [26]. The 3 types of cones (L for long, M for medium, and S for short wavelengths of light) have significant overlap in the wavelengths of light to which they respond; therefore, it is more efficient for the human visual system to record differences between the responses of cone cells, rather than to analyze and compare individual responses from each type of cone [26]. The opponent process theory posits the existence of 3 different opponent channels: red vs. green, blue vs. yellow, and black vs. white (achromatic) [26]. The opponent process theory accounts for neural mechanisms that receive information from the 3 types of cones and process it in a more efficient way, finally producing the various phenomena of color experience [26]. According to the opponent process theory, 2 other types of cells are involved in response to color stimuli: bipolar cells and ganglion cells [26]. The parvocellular layer

Table 5. The grouping scheme of Fechner illusory colors according to the constituent parts of the blue-yellow opponent process (the order of colors is based on composition of constituents, not on the numerical order).

| Color            | Group by RGB | Group by Blue–Yellow Opponent process | Group number in Blue–Yellow Opponent process analysis |
|------------------|--------------|--------------------------------------|------------------------------------------------------|
| 11. Blue 00      | B            | Blue+ Yellow+ (Red– Green–)          | 1                                                    |
| #0000FF          |              | (Pure blue opponent)                 |                                                      |
| 12. Violet       | B+R          | Blue+ Yellow+ (Red+ Green–)          | 2                                                    |
| #7F00FF          |              | (Mixed blue and yellow opponents)    |                                                      |
| 13. Magenta      | B+R          | Blue+ Yellow+ (Red+ Green–)          | 2                                                    |
| #FF00FF          |              | (Mixed blue and yellow opponents)    |                                                      |
| 14. Rose         | B+R          | Blue+ Yellow+ (Red– Green+–)         | 2                                                    |
| #FF007F          |              | (Mixed blue and yellow opponents)    |                                                      |
| 10. Azure        | B+G          | Blue+ Yellow+ (Red– Green+)          | 2                                                    |
| #007FFF          |              | (Mixed blue and yellow opponents)    |                                                      |
| 9. Cyan          | B+G          | Blue+ Yellow+ (Red– Green+)          | 2                                                    |
| #00FFFF          |              | (Mixed blue and yellow opponents)    |                                                      |
| 8. Spring green  | B+G          | Blue+ Yellow+ (Red– Green+)          | 2                                                    |
| #00FF7E          |              | (Mixed blue and yellow opponents)    |                                                      |
| 3. Red           | R            | Blue– Yellow+ (Red+ Green–)          | 3                                                    |
| #FF0000          |              | (Pure yellow opponent)               |                                                      |
| 4. Orange        | R+G          | Blue– Yellow+ (Red+Green+)           | 3                                                    |
| #FF7F00          |              | (Pure yellow opponent)               |                                                      |
| 5. Yellow        | R+G          | Blue– Yellow+ (Red+Green+)           | 3                                                    |
| #FFFF00          |              | (Pure yellow opponent)               |                                                      |
| 6. Chartreuse green | R+G     | Blue– Yellow+ (Red+Green+)           | 3                                                    |
| #7FFF00          |              | (Pure yellow opponent)               |                                                      |
| 7. Green         | G            | Blue– Yellow+ (Red –Green+)          | 3                                                    |
| #00FF00          |              | (Pure yellow opponent)               |                                                      |

Figure 2. The differences in perception of Fechner illusory colors grouped according to the blue-yellow opponent process axis in AD and CG groups.
cells process the color-related information and may be assigned to 2 groups: one of these groups processes the information about the difference of activity of L and M cones, while the other group processes the difference between S cones and a combined activity of both L and M cones [26]. The first type of cell is responsible for red-green opponent process axis and the second type is responsible for blue-yellow opponent process axis [26]; specifically, the latencies of processes at the center and the surrounding differ among the different types of color-specific ganglion cells [23].

Our results show that a significant difference in reporting various colors between AD and CG groups. Very few AD patients reported pure blue color (#0000FF) when viewing the outermost arc of lines on a Benham disk rotating clockwise and the innermost arc of lines on a disk rotating counter-clockwise; whereas control group participants most frequently reported clear and saturated pure blue in these arcs on the disk rotated in the same direction (Table 3). When colors seen by the study participants moved to the yellow part of the blue-yellow opponent axis, the difference between colors reported by AD and CG groups gradually vanished.

Importantly, the 4 colors visible on the disk by the healthy control group participants do not follow the RGB-derived sequence, usually provided in the published literature as “blue – green – yellow – red”. Our CG group reported the sequence “blue – magenta (or rose) – green – yellow (or orange, or red). This clearly is not the sequence expected if a unidimensional wavelength-dependent process is underlying the illusory Fechner colors. The sequence of colors reported by participants in our study is explained much more reasonably by the opponent process theory. Even more unexpected is that if all phenomenal properties of Fechner illusory colors are explained exclusively by the blue-yellow opponent axis, as is contended by Schramme et al. [24,27], the arc next to the one that appears as blue should be seen as greenish. In our study, the second arc after blue most frequently was seen as magenta or rose by the participants of both groups, and only the third one was green. When the disk was rotating clockwise, there was much more scattered reporting of colors by AD group subjects, clearly skewed to the red but not to the green (Table 3). It may be hypothesized that the colors observed on the outer and inner arcs of lines, and which are at the greatest distance from each other, are reasonably explained by the blue-yellow opponent process. The 2 middle arcs (the 2nd and 3rd clockwise and counter-clockwise) exhibit signs of intrusion of the red-green opponent process, which significantly affects visible colors only in a small range located inside of a much wider interval, which is under the influence of the blue-yellow opponent process. If this explanation of “2 opponent processes involved” is feasible, there still remains the difference between blue-yellow opponent process, responsible for “coloring” of distant arcs and red-green opponent process, which is responsible for colors of the 2 middle arcs, located near each other: when the disk is rotated clockwise, colors of the outermost and innermost arcs follow the direction from shorter (blue) to longer (yellow, or a sum of red and green) wavelengths; in contrast to this, the colors of 2 middle arcs follow the direction from longer (red) to shorter (green) wavelengths. Furthermore, red and green seem unequal in this “double-opponent process” explanation because the AD group tended to shift reported colors from green to red in both extremities of the wide blue-yellow opponent process activity range (Table 3). This cannot be explained just by the action of the 2 opponent processes at different ranges. Consequently, there is good reason to suppose that the processes ongoing at the retinal ganglion cells level are not sufficient to explain the illusory color sequence in its entirety. Thus, the phenomenon of Fechner illusory colors originates from neural activity in the retina and the more central structures of the visual system. The fMRI research findings reported by Tanabe et al suggest that the visual cortex, which processes pattern recognition, may be involved in the generation of illusory colors [25]. The results from this fMRI study indicate that modulation from V4 to V2 to V1 plays a significant role in the perception of Fechner illusory colors [25].

PIFCs may become useful in medical diagnosis [27]. The utilization of PIFCs in medical diagnosis and the biological interpretation of the neural network involved would also benefit from research on Fechner illusory colors in AD [27]. The decline in blue opponent perception, if properly standardized, may be used as a cheap and noninvasive diagnostic marker in early diagnosis of AD as an addition to other cognitive, electrophysiologic, behavioral, and emotional regulation methods [28–31]. On the other hand, the pattern of decline in perception of Fechner illusory colors in people with AD can be helpful for further research in order to understand the nature of visual perception of color, and may have even broader implications for the fundamental mind-body relationship. This kind of empirical research may lead to reconsideration of some basic premises of such renowned thought experiment as “Mary’s room” or “Mary the super-scientist” proposed by Frank Jackson and intended to argue for the existence of qualia and against physicalism. Bearing in mind the results of research using Fechner illusory colors, the initial basic premise of this thought experiment about the possibility of existence of an entirely black and white room, where Mary the super-scientist is working without any possibility to see spectral colors, seems quite problematic due to the established fact that movement of black and white patterns may produce the experience of illusory colors, indistinguishable from real physical spectral colors. This means that isolation of Mary the super-scientist in the black and white room does not provide a possibility to deprive her of subjectively experiencing colors.
Conclusions

AD patients retain the ability to see Fechner illusory colors. The reversal of color order when changing the direction of disk rotation remains intact in AD patients. The visibility of spectral illusory colors is significantly less frequent in AD patients compared with normal controls. The perception of pure blue Fechner color was markedly lower in the AD group than in the control group. The illusory colors reported by AD patients when observing the blue-producing arcs of lines are much more scattered around the pure blue color than in the control group. While a clear shift to the yellow opponent is observed among AD patients, this shift is asymmetric for red and green constituent parts of the yellow opponent. A larger shift to the red constituent is found instead of green, which makes it harder to explain all the phenomena of Fechner illusory colors solely on the basis of blue-yellow opponent process, and definitely does not correspond to the sequence of physical spectral colors. The decreased perception of blue opponent was very large, but we did not observe any impairment in perception of yellow opponent colors that do not contain blue subcomponent according to the RGB system. There is impaired perception of intermediary colors containing the blue subcomponent, but less pronounced than for pure blue. This impaired pattern of visibility of illusory colors in AD patients could be explained by the prevailing disorder in the blue-yellow opponent axis, with some noticeable effect of disorder in the red-green opponent axis only in the middle part of the much broader blue-yellow axis, which may indicate the cortical, but not the retinal, origin of the disorder in perception of Fechner illusory colors in people with AD.

Conflicts of interests

The authors have no conflicts of interest to declare.

References:

1. Alzheimer’s Association: 2016 Alzheimer’s disease facts and figures. Alzheimers Dement, 2016; 12(4): 459–509
2. Dementia Fact Sheet No.362. World Health Organization. http://www.who.int/mediacentre/factsheets/fs362/en/ Accessed on 19 October 2016
3. Lopez OL, DeKosky ST: Clinical symptoms in Alzheimer’s disease. In: Dementias. Duyckaerts C, Utian I (eds.), Handbook of Clinical Neurology. Vol. 89. Elsevier; 1st ed. 2008; 207–16
4. Berisha F, Feke GT, Trempe CL et al: Retinal abnormalities in early Alzheimer’s disease. Invest Ophthalmol Vis Sci, 2007; 48: 2285–89
5. Danesh-Meyer HV, Birch H, Ku JY et al: Reduction of optic nerve fibers in patients with Alzheimer disease identified by laser imaging. Neurology, 2006; 67: 1852–54
6. Gasparini L, Croteworthy RA, Martin KR et al: Tau inclusions in retinal ganglion cells of human P301S tau transgenic mice: effects on axonal viability. Neurobiol Aging, 2011; 32: 419–33
7. Paquet C, Boissonnot M, Roger F et al: Abnormal retinal thickness in patients with Alzheimer disease identified by OCT. Invest Ophthalmol Vis Sci, 2010; 51: 3579–86
8. Nobili L, Samnita WC: Cholinergic modulation, visual function and Alzheimer’s dementia. Vision Res, 1997; 37: 3559–71
9. Chang LY, Lowe J, Ardiles A et al: Alzheimer’s disease in the human eye. Clinical tests that identify ocular and visual information processing deficit as biomarkers. Alzheimers Dement, 2014; 10(2): 251–61
10. Iseni PM, Altinas O, Tokay T, Yuksel N: Relationship between cognitive impairment and retinal morphological and visual functional abnormalities in Alzheimer disease. J Neuroophthalmol, 2006; 26: 18–24
11. Sadun AA, Borchert M, Devita E et al: Assessment of visual impairment in patients with Alzheimer’s disease. Am J Ophthalmol, 1987; 104: 113–20
12. Cormack FK, Tovee M, Ballard C: Contrast sensitivity and visual acuity in patients with Alzheimer’s disease. Int J Geriatr Psychiatry, 2000; 15: 614–19
13. Wijk H, Berg S, Sivik L, Steen B: Colour discrimination, colour naming and colour preferences among individuals with Alzheimer’s disease. Int J Geriatr Psychiatry, 1999; 14: 1000–5
14. Pache M, Smeets CHW, Gasio P et al: Colour vision deficiencies in Alzheimer’s disease. Age Ageing, 2003; 32: 422–26
15. Hof PR, Morrison JH: Quantitative analysis of a vulnerable subset of pyramidal neurons in Alzheimer’s disease: I. Primary and secondary visual cortex. J Comp Neurol, 1990; 301(1): 55–64
16. Scinto LF, Daffner KR, Castro L et al: Impairment of spatially directed attention in patients with probable Alzheimer’s disease as measured by eye movements. Arch Neurol, 1994; 51: 682–88
17. Thiagagesh S, Farrow TF, Parks RW et al: The neural basis of visuospatial perception in Alzheimer’s disease and healthy elderly comparison subjects: An fMRI study. Psychiatry Res, 2009; 172: 109–16
18. Cronin-Golomb A, Corkin S, Rizzo JF et al: Visual dysfunction in Alzheimer’s disease: Relation to normal aging. Ann Neurol, 1991; 29: 41–52
19. Kurilo DD, Corkin S, Dolan RP et al: Broad-band visual capacities are not selectively impaired in Alzheimers disease. Neurobiol Aging, 1994; 15: 305–11
20. Rizzo M, Anderson SW, Dawson J, Nawrot M: Vision and cognition in Alzheimer’s disease. Neuropsychologia, 2000; 38: 1157–69
21. Grod M, Dan Y: Basal forebrain activation enhances cortical coding of natural scenes. Nat Neurosci, 2009; 12(11): 1444–49
22. Goodale MA, Milner AD: Separate visual pathways for perception and action. Trends Neurosci, 1992; 15(1): 20–25
23. Luo R (Ed.): Fechner’s Colors and Beham’s Top. Encyclopedia of Color Science and Technology. 1st ed., Springer, 2016
24. Schramme J: Changes in pattern induced flicker colors are mediated by the blue/yellow opponent process. Vision Res, 1992; 32(11): 2129–34
25. Tanabe HC, Sakai T, Morito Y et al: Neural correlates and effective connectivity of subjective colors during the Benham’s top illusion: A functional MRI study. Cereb Cortex, 2011; 21(1): 124–33
26. Griggs RA: Sensation and Perception. Psychology: A Concise Introduction, 4th ed. Worth Publishers, 2014
27. von Campenhausen C, Schramme J: 100 years of Benham’s top in colour science. Perception, 1995; 24(6): 695–717
28. Kuzmickienė J, Kaubrys G: Selective ability of some CANTAB battery tests to detect cognitive response to a single dose of donepezil in Alzheimer’s disease. Med Sci Monit, 2015; 21: 2572–82
29. Vahtkevičius A, Kaubrys G, Audronytė E: Distinctive effect of donepezil treatment on P300 and N200 subcomponents of auditory event-related evoked potentials in Alzheimer disease patients. Med Sci Monit, 2015; 21: 1920–27
30. Kuzmickienė J, Kaubrys G: Cognitive results of CANTAB tests and their change due to the first dose of donepezil may predict treatment efficacy in Alzheimer disease. Med Sci Monit, 2015; 21: 3887–99
31. Stefano GB: Cognition regulated by emotional decision making. Med Sci Monit, 2015; 21: 3887–99
32. Jackson F: Epithenominal qua. Philosophical Quarterly, 1982; 32: 127–36
33. Jackson F: What Mary didn’t know. Journal of Philosophy, 1986; 83: 291–95