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Entering the new era of cognitive scoring? Eye-tracking assessment in neurodegenerative disorders

Nowa era badania zdolności poznawczych? Ocena ruchu gałek ocznych w chorobach neurodegeneracyjnych

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Abstract

Background: The incidence of dementia and cognitive deterioration is on the rise. Therefore, objective, fast and repetitive cognitive scoring methodology to screen the population and guide the diagnostic process is needed. Eye-tracking provides gaze patterns metrics based on the pupil size and the point of gaze assessment. **Methods:** The study evaluated 60 patients with medical anamnesis, Montreal Cognitive Assessment – MoCA test, Geriatric Depression Scale – GDS, and eye-tracking protocol. The novel object recognition test consisted of 30 seconds observation of the set of three images, followed by a 90-second pause, and a repeated 30-second observation of the set of three images with the change of one of them. The comparison was made between the metrics of three subgroups, which were created based on MoCA score and named as controls: ≥26, mild cognitive impairment: 21–25, and dementia: <20. **Results:** For the novel object recognition task, a control group compared to a dementia group was more interested in the new object during a free observation (repeated measure ANOVA, $p = 0.03$). Moreover, during the observation of the second set of images, the pupil dilation as a result of a memory recall is more prominent in the control group (t-test, $p = 0.009$). **Conclusion:** Eye-tracking is a potentially useful tool for objective assessment of patients' cognitive status. Further studies are needed to evaluate norms across different ages and cut-off points.

Keywords: dementia, eye-tracking, mild cognitive impairment, cognitive deterioration, screening

Streszczenie

Wprowadzenie: Częstość występowania otępienia i zaburzeń poznawczych wzrasta, co pociąga za sobą potrzebę opracowania obiektywnej, szybkiej i powtarzalnej metodologii badań przesiewowych i wsparcia procesu diagnostycznego. Okulografia (*eye-tracking*) dostarcza parametry ruchów gałek ocznych, które są wykreowane na podstawie rozmiaru źrenicy i oceny punktu skupienia wzroku. **Materiały i metody:** W badaniu wzięło udział 60 pacjentów – w ocenie wykorzystano wywiad, Montrealską Skalę Oceny Funkcji Poznawczych (Montreal Cognitive Assessment, MoCA), Geriatryczną Skalę Depresji (GDS) oraz protokół badania okulograficznego. Test rozpoznawania nowych obiektów polegał na obserwacji trzech ilustracji przez 30 sekund, po której nastąpiła 90-sekundowa pauza oraz powtórna 30-sekundowa obserwacja zestawu trzech ilustracji z jedną nową. Parametry ruchów gałek ocznych porównano pomiędzy trzema grupami wydzielonymi na podstawie wyniku MoCA: grupą kontrolną (≥26), grupą z łagodnymi zaburzeniami poznawczymi (21–25) oraz grupą z otępieniem (<20). **Wyniki:** W czasie swobodnej obserwacji w czasie testu rozpoznawania nowych obiektów grupa kontrolna była znacząco bardziej zainteresowana nowym obiektem niż grupa z otępieniem (analiza wariancji z powtarzanymi pomiarami, $p = 0{,}03$).

Ponadto w czasie obserwacji drugiego zestawu ilustracji grupa kontrolna charakteryzowała się większym poszerzeniem źrenicy w wyniku odtwarzania pamięciowego (*t*-test, $p = 0{,}009$). **Podsumowanie:** Badanie okulograficzne jest potencjalnie użyteczną metodą obiektywnej oceny funkcji poznawczych pacjentów. Istnieje potrzeba dalszych badań w celu ustalenia norm dla poszczególnych grup wiekowych i ograniczeń dla odchyleń od normy.

Słowa kluczowe: otępienie, okulografia (*eye-tracking*), łagodne zaburzenia poznawcze, zaburzenia poznawcze, badania przesiewowe

INTRODUCTION

Incidence of dementia is currently on the rise with the current occurrence of 50 million patients worldwide (WHO – Fact Sheets). Measuring cognitive status plays a pivotal role for detection, monitoring clinical progression and evaluating effects of disease-modifying therapies. Current guidelines enable diagnosis of dementia mainly based on clinical anamnesis or cognitive tests (NICE guideline, 2018). Unfortunately, both Mini-Mental State Examination (MMSE) and the Montreal Cognitive Assessment (MoCA) have their own limitations: time-consumption, the necessity of intact verbal communication, not perfect intra- and inter-rater reliability and ability to be performed only twice a year (Coen et al., 2016; Spencer et al., 2013). Consequently, the need for an improved measure that can detect clinically meaningful changes in cognitive deterioration was expressed.

Eye movements are controlled by the cortical structures and the brainstem. The network is wide and very sensitive to any disruptions in the circuit. Even slight neurodegenerative areas can result in ocular motility disturbances (Anderson and MacAskill, 2013; MacAskill and Anderson, 2016; Salimi et al., 2017). Eye-tracking is a pervasive technology which gives a possibility to distinguish gaze events (saccades, fixations) along their parameters: number, speed, acceleration, duration for saccades and number, and duration and dispersion for fixations. Raw gaze data is obtained thanks to corneal reflection of infra-red light from the illuminator (Duchowski, 2017). It is commonly used in psychology research, marketing, bioengineering (brain–computer interfaces), communication, education and entertainment (Duchowski, 2017).

Pupil dilation is modulated by the brain's locus coeruleus-norepinephrine system. It is controlled by physiological arousal and attention, and it has been widely used as a measure of subjective task difficulty and mental effort (Eckstein et al., 2017; Mitra et al., 2017). During the active phase of a memory recall, the pupil dilates as a physiological reaction (Kucewicz et al., 2018).

The growing number of studies addresses the issue of eye-tracking usage in medicine for the assessment of Alzheimer's disease, Parkinson's disease, aphasia, frontotemporal dementia, Huntington's disease, amyotrophic lateral sclerosis and many more (Anderson and MacAskill, 2013; Linse et al., 2018; Pavisic et al., 2017; Yu et al., 2016).

MATERIAL AND METHODS

Study design

This study is a double-center, observational, prospective study conducted in Łódź, Poland. The study was approved by the local Research Ethics Committee (RNN/255/17/KE from 11/07/2017) and all participants provided written informed consent according to the guidelines established by the Declaration of Helsinki.

Participants

Data were collected from 63 individuals. Three protocols were excluded from the analysis due to loss of the data. The study population was divided based on MoCA score to possible clinical groups and named as follows: a control group (≥26), a mild cognitive impairment (MCI) group (21–25) and a dementia group (≤20) (Magierski et al., 2015; Tsai et al., 2016). The groups were homogenous considering comorbidities. There were more women among participants (Tab. 1).

Inclusion criteria were: age >40 years old, intact ocular motility, the ability to obtain consent and a medical history. Exclusion criteria were: cranial nerve pathology (III, IV, VI), strabismus; diplopia; papilledema; optic neuritis; or other known disorder affecting cranial nerve II, macular edema, retinal degeneration, hydrocephalus, sarcoidosis, myasthenia gravis, multiple sclerosis or other

	Dementia	MCI	Control	*p*
Quantity	20/60 (33%)	20/60 (33%)	20/60 (33%)	
Age	76.4 ± 9.2	67.6 ± 14.5	62.4 ± 14.0	0.063
Sex (F)	14/20 (70%)	8/20 (40%)	15/20 (75%)	0.048
GDS	0.8 ± 1.05	0.4 ± 0.8	0.25 ± 1	0.34
MoCA	16.7 ± 3.8	23 ± 1.4	27.2 ± 1.3	<0.001
Arterial hypertension	15/20	10/20	8/20	0.07
Cardiac failure	7/20	6/20	4/20	0.56
Diabetes mellitus	5/20	3/20	2/20	0.43
Headaches	1/20	4/20	1/20	0.21
Hypothyroidism	0/20	3/20	1/20	0.15

Tab. 1. Baseline characteristics

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demyelinating disease, active or acute epilepsy, stroke/cerebral hemorrhage/traumatic brain injury (TBI) in last 10 years.

Materials

Materials used during the research consisted of pen and paper, MoCA examination, Geriatric Depression Scale (GDS), the anamnesis formula as well as Pupil Labs eye-tracking glasses with binocular eye cameras and a world camera (120 Hz) (Pupil Labs). The eye-tracking protocol was displayed on a 14-inch laptop's screen.

Procedures

Each patient firstly participated in the anamnesis gathering when inclusion/exclusion criteria were evaluated. After that, the same single examiner performed MoCA and GDS tests. During the last part, patient firstly underwent calibration process for eye-tracking glasses. Then, a 2:54-minute eye-tracking protocol was displayed. It consists of (a) a welcome screen not considered for further analysis, (b) novel object recognition tests: sets of 3 pictures similar in complexity and neutral in content were displayed twice with a 90-second pause in between and a change of the middle object, (c) sequence memorisation: firstly, the sequence of alternating circles and squares was displayed, and the patient was asked to stare at the sequence continuation after 66s, (d) trail making: similar to the first part of MoCA – the patient was asked to make a visual path connecting the sequence 1-A-2-…-D, (e) a smooth pursuit and saccade task: the patient was asked to follow the moving object, (f) proverb reading: "every cloud has a silver lining" (Polish: "nie ma tego złego, co by na dobre nie wyszło").

The whole examination took place in the room with similar lightning conditions (only artificial light) and took 20–55 minutes in total.

Data analysis

Each dataset was denoised – blinks were removed (Holmqvist et al., 2012). Fixations parameters were obtained due to I-DT algorithm with Pupil Player and velocity-based saccades parameters with Gaze Data Explorer® (Matulewski et al., 2018; Salvucci and Goldberg, 2000). Moreover, a pupil diameter was assessed, as well as the percentage of time spent on particular picture during the novel object recognition task (Kohonen's neural networks). Baseline characteristics were compared between groups with the χ^2 test for categorical variables, and Kruskal–Wallis ANOVA with post-hoc tests for continuous variables. Where applicable, *t*-test and ANOVA were used. An alpha level of 0.05 was used for all statistical tests. The analysis was performed using Statistica v13.1.

RESULTS

General metrics were compared, and no global differences were found (including a subanalysis for the age ~65 years old). The relevant task-specific findings include:

1. Novel object recognition – healthy people are more interested towards new object than people with dementia (repeated measure ANOVA, $p = 0.03$). In the beginning, all groups explored the three objects evenly (for the middle object: C = 35 ± 22.7%, D = 35 ± 25.7%). For the second round of object, the focus on the middle, new object has focused (C = 40.6 ± 22.9%) or dispersed (D = 29 ± 18%) (Fig. 1).

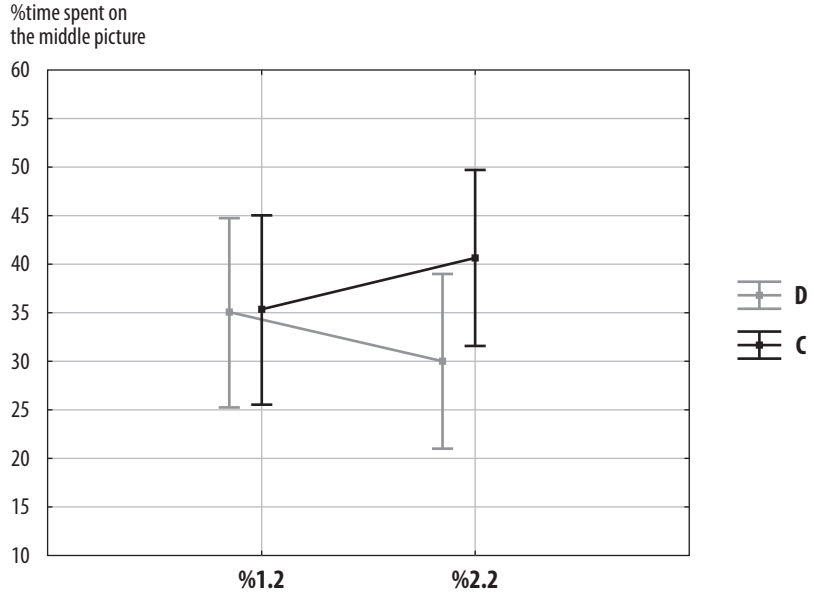

Fig. 1. Novel object recognition task output

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2. Sequence memorisation – a physiological reaction of pupil dilation caused by the memory retraction was more prominent for cognitively healthy individuals (pupil size growth D = 2.5 ± 0.46 mm; M = 3.37 ± 0.74 mm; C = 3.44 ± 0.98 mm; *t*-test, $p = 0.009$).

Beside the eye-tracking experiment, the inverse correlation between GDS score and the orientation score (part of MoCA test) was found (gamma co-efficient = –0.26, $p < 0.05$). Moreover, 60% of patients would prefer eye-tracking based examination to pen-to-paper version of MoCA.

DISCUSSION

These pilot-study findings are promising for the future of eye-tracking assisted diagnosis and quantitative staging of dementia. A longitudinal validation study to determine the specificity and sensitivity of the mobile eye tracker to clinically relevant changes over time should be performed. The possibility of free observation in patient's natural environment should be explored.

Most studies on the eye movement and dementia have been conducted under controlled laboratory settings. While researchers have identified significant differences between healthy subjects and patients with Alzheimer's disease when reading sentences, the studies are limited to the use of fixed eye trackers and the control of head movements through a chinrest (Fernández et al., 2015). Moreover, MMSE was incorporated in the vast majority of studies, despite worse sensitivity and specificity towards MCI detection than MoCA (Chau et al., 2015, 2017; Tsai et al., 2016). In our study, metrics were obtained during free observation, which provided the patient with more comfort.

Our study was limited to a small number of patients. It was performed in two centres, was observational, which could introduce selection or measurement bias. However, evaluations were performed by the same operator to minimise these effects. Moreover, the dementia group was older than the other groups, the differences did not reach statistical significance, though.

Future big cohort studies should validate the difference and correlation between gaze metrics, and fully exclude an intra-person variability of gaze patterns (Bargary et al., 2017). Additionally, the learning effect of repetitive cognitive scoring using eye-tracking should be evaluated.

CONCLUSIONS

Eye-tracking is a promising tool for cognitive assessment. Further investigations are required for the sensitivity and specificity assessment as well as defining the cut-off values.

Conflict of interest

None.

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