MEDICAL SCIENCE MONITOR

CLINICAL RESEARCH

e-ISSN 1643-3750
© Med Sci Monit, 2014; 20: 173-181
DOI: 10.12659/MSM.889776

Received: 2013.09.12
Accepted: 2013.11.13
Published: 2014.02.03

Evaluation of the Trail Making Test and interval timing as measures of cognition in healthy adults: Comparisons by age, education, and gender

Authors' Contribution:
Study Design A
Data Collection B
Statistical Analysis C
Data Interpretation D
Manuscript Preparation E
Literature Search F
Funds Collection G

ABCDEFG 1 **Włodzimierz Płotek**
ABCDEFG 2 **Wojciech Łyskawa**
ABCDEFG 3 **Anna Kluzik**
ABCDEFG 1 **Małgorzata Grześkowiak**
ABCDEFG 1 **Roland Podlewski**
ABCDEFG 1 **Zbigniew Żaba**
ABCDEFG 3 **Leon Drobnik**

1 Department of Teaching Anaesthesiology and Intensive Therapy, Poznań University of Medical Sciences, Poznań, Poland
2 Department of Anesthesiology and Intensive Therapy, Medical Center in Pleszewo, Pleszew, Poland
3 Department of Anaesthesiology, Intensive Therapy and Pain Treatment, Poznań University of Medical Sciences, Poznań, Poland

Corresponding Author: Włodzimierz Płotek, e-mail: plotekw@poczta.onet.pl
Source of support: Departmental sources

Background: Human cognitive functioning can be assessed using different methods of testing. Age, level of education, and gender may influence the results of cognitive tests.

Material/Methods: The well-known Trail Making Test (TMT), which is often used to measure the frontal lobe function, and the experimental test of Interval Timing (IT) were compared. The methods used in IT included reproduction of auditory and visual stimuli, with the subsequent production of the time intervals of 1-, 2-, 5-, and 7-seconds durations with no pattern. Subjects included 64 healthy adult volunteers aged 18–63 (33 women, 31 men). Comparisons were made based on age, education, and gender.

Results: TMT was performed quickly and was influenced by age, education, and gender. All reproduced visual and produced intervals were shortened and the reproduction of auditory stimuli was more complex. Age, education, and gender have more pronounced impact on the cognitive test than on the interval timing test. The reproduction of the short auditory stimuli was more accurate in comparison to other modalities used in the IT test.

Conclusions: The interval timing, when compared to the TMT, offers an interesting possibility of testing. Further studies are necessary to confirm the initial observation.

MeSH Keywords: Frontal Lobe • Interval Timing • Trail Making Test • Cognition • Education – methods

Full-text PDF: http://www.medscimonit.com/download/index/idArt/889776

4579 4 — 39

Indexed in: [Current Contents/Clinical Medicine] [SCI Expanded] [ISI Alerting System] [ISI Journals Master List] [Index Medicus/MEDLINE] [EMBASE/Excerpta Medica] [Chemical Abstracts/CAS] [Index Copernicus]

Background

Cognitive evaluation has become increasingly popular in psychology, psychiatry, internal medicine, and anesthesiology [1–3]. The assessment of human cognition uses different types of measure (e.g. Wechsler intelligence test, Raven test, Stroop test, and trail making test), and all of them contain a certain component of timing (the tested subject has a limited time to perform a test). Psychometric tests are used in psychiatry and internal medicine, but the possibility of cognitive evaluation in anesthesiology remains underdeveloped.

However, when studying the literature, there are several examples of the professional application of psychometric testing. In one of the most spectacular international surveys – the International Study of Post-Operative Cognitive Dysfunction (ISPOCD-1), in which 1218 patients from 13 hospitals from Europe and USA were tested – the prevalence of the postoperative cognitive impairment reached 25.8% after 1 weak, with 9.9% of patients with cognitive dysfunction after 3 months. When thorough analysis of the possible risk factors was undertaken, age, duration of the anesthesia, low education, the second operation, infections, and respiratory disorders were recognized. At the late stage only age was a risk factor for postoperative cognitive impairment [1].

In contrast, every-day functioning is strongly affected by the passing of time. The human timing can be discussed in terms of various perspectives: very quick ones (reflexes ranged in milliseconds), interval timing (IT) (every-day activities ranged in seconds, like driving the car), and even longer (hours, days, circadian rhythms) [2]. There are studies evaluating the timing disturbances in some neurological and psychiatric disorders: focal hemisphere lesions, major depression and mania, or drug abuse [3–5]. The perception of time was also a subject of very intense studies in which anxiety and unpleasant experiences were used as factors affecting time estimation, but the results are not consistent [6,7]. The methods used in the IT studies are various and include different time scopes and use of prospective or retrospective paradigms of testing, and thus are difficult to compare.

Scientists tried to explain estimation of the time intervals up to 20 s by using 2 different theories: the attentional counter and the internal clock theory. Proposed by Hick et al., the attentional counter (1977) is based on the existence of a cognitive timer requiring attention that counts subjective time events. That is why when additional cognitive tasks are being performed (thus competing for attention) the time estimation is less accurate when compared with the results achieved by the subjects concentrated only on the time estimation. The internal clock theory presented by Matell and Meck (1984) is based on the assumption that particular patterns of neuron activity can become a starting sign for the internal clock, and the following intervals are connected with the unique pattern of activation of the cortex neurons, which later can be read by other regions of the brain (e.g. basal ganglia) [8]. This might suggest the existence of many internal clocks measuring the time. Conversely, in 2008 van Rijn and Taatgen provided evidence suggesting the existence of a single clock with an underlying nonlinear timescale [9].

Anesthesiology provides the reversible suppression of consciousness and is interested in a complete mental recovery. That is a reason for growing interest among anesthesiologists in the subject of postoperative cognitive performance, because the psychometric testing brings important information about patient's general condition after anesthesia and surgical procedures. Perioperative psychological and metabolic stress may negatively affect the patient's level of consciousness. We were particularly interested on the possible influence of the following factors: age, level of education, and gender on the selected cognitive test and IT. All these factors may influence performance on psychometric tests, but their potential role in IT is not well elucidated in the literature. To our knowledge, this is the first study comparing TMT and IT in terms of age, education, and gender in the same evaluation. The test, which is free from the above-mentioned confounding factors, may be easier to use when comparing different groups of tested patients.

The aims of the study were to check:
1. TMT and IT performance in healthy people,
2. Possible influence of age, education, and gender on TMT and IT,
3. Accuracy of perception of the selected time intervals,
4. Usefulness of IT in terms of cognitive testing.

Material and Methods

The study was approved by the Bioethics Committee of Poznan University of Medical Sciences and was conducted in accordance with the Declaration of Helsinki. The study was conducted among 64 healthy adult volunteers, aged 18–63 (33 women, 31 men), who were willing to participate in the study. The participants were recruited from volunteers willing to participate in the study after reading a special announcement at the university and hospitals. After completing tests, each participant received a small gift. None of the participants were treated with psychoactive drugs, and none had a history of neurologic or psychiatric disease, alcoholism, or narcotic abuse (exclusion criteria). Before the psychometric evaluation, all participants were clinically tested by a physician to find the symptoms of diseases that could influence cognitive fitness (with special attention to anemia, dehydration, and thyroid gland pathology).

Indexed in: [Current Contents/Clinical Medicine] [SCI Expanded] [ISI Alerting System]
[ISI Journals Master List] [Index Medicus/MEDLINE] [EMBASE/Excerpta Medica]
[Chemical Abstracts/CAS] [Index Copernicus]

The study consisted of 3 steps of testing using the same sequence for each participant:
1. screening tests,
2. trail making test (TMT): A, B, B-A,
3. tests of interval timing (IT).

Screening tests

Healthy adult volunteers of both sexes were tested initially for the presence of pre-existing cognitive disturbances and depression: mini-mental state examination (MMSE), clock drawing test (CDT), and Beck depression inventory (BDI). The Polish version of MMSE was used [10]. The average score was above 24 points. CDT was used in a version presented by Shulmann in 1986. We asked the subjects to draw the face of the clock on a sheet of paper with a pre-drawn (10 cm diameter) circle and to draw the hands of the clock to denote 3: 00. There was no time limit for completing the test. The errors were categorized on 5 levels and only the first level of error was considered physiological [11]. BDI is a 21-item self-report instrument developed to assess symptoms of depression. It consists of 21 questions, each scored 0–3 points. A score of 9 or greater suggests the subject has symptoms of depression [12].

The trail making test (TMT) measured the frontal lobe function. In Part A, participants are asked to link numbered points randomly distributed on a sheet of paper in ascending order according to numbers. In Part B, the participants are asked to link numbers and letters alternately. The researcher measures the time of test performance, counts the number of errors, and calculates the difference in times: B-A.

Test of interval timing (IT)

IT was assessed by using a special electronic device constructed by the Poznan University of Technology (supervised by Dr Jacek Jelonek, Poland) producing auditory and visual impulses of different duration (1, 2, 5, and 7 s). The first series of impulses was the set of auditory impulses presented in the headphones, and the next one was of visual modality presented on the screen as an emotionally irrelevant picture. Each modality (auditory or visual) was repeated 3 times, but the duration of each signal was presented in a random alternating order (e.g. 1-5-2-7 s, 5-7-2-1 s) to prevent learning the length of impulse. The participants were not aware of the duration of the signal. The sequence was the same for each participant. When the signal ended, the subject was asked to press a special button for as long as the duration of the earlier presented signal, without any additional auditory or visual feedback. Two s after copying the signal, the next impulse occurred, which was subsequently repeated by the subject. The test of time interval production was performed without previous patterns, and the participants were asked to press the button for a given interval (1, 2, 5, 7 s) 3 times in a random order with no feedback information. The test was performed in a quiet dimmed room without clocks. All the volunteers were tested in the afternoon (the same period of human activity, thus avoiding the possibility of chronobiological fluctuation in level of attention stemming from different times of day).

The group of tested participants was divided as follows:
1. Age: subgroups: 18–25, 26–37, 38–49, and ≥50 years old.
2. Education was divided according to the Polish system of schooling: primary and vocational, secondary, and higher.
3. Gender.

Statistical analysis

Statistical analysis was performed using STATISTICA 10.0 StatSoft, Inc. (2011). The basic demographic data and the results of the screening tests are presented as minimal and maximal values, mean, and standard deviation. Additionally, the TMT results, median with 95% CI were calculated and are presented in tables. The distribution of demographic data, and TMT and IT results was tested with the Kolmogorov-Smirnov test. The relationship between gender and the level of education, TMT, and age, as well as TMT and level of education was checked using Pearson's chi-square test. To find a relationship among parts of TMT and gender, the t test for TMT-A, and Mann-Whitney test for TMT-B and TMT B-A were applied.

The relation of the achieved results in IT in comparison to the patterns of real durations 1, 2, 5, and 7 s, the t test was used. The IT and age was analyzed using ANOVA with post hoc Scheffe method. To investigate possible relationships between level of IT and education, ANOVA analysis with post hoc Tamhane test were performed. The post hoc test was used to perform a multiple comparison analysis. For an equal variance, Scheffe method was used, and for a non-homogeneous variance, Tamhane test was used. For the assessment of IT and gender, the t test was used. To assess the accuracy of interval timing, we compared the reproduced/produced intervals to real durations by using the t test. The statistical comparison between TMT and all trials of IT was performed with the application of Pearson's chi-square test. In all statistical tests, $p<0.05$ was considered statistically significant.

Results

We chose a group of healthy individuals who were willing to participate in the study. Demographic data and the results of screening tests are presented in Table 1.

One participant was qualified with BDI result of 23 pts, suggesting pre-existing symptoms of depression and was consulted by

Indexed in: [Current Contents/Clinical Medicine] [SCI Expanded] [ISI Alerting System]
[ISI Journals Master List] [Index Medicus/MEDLINE] [EMBASE/Excerpta Medica]
[Chemical Abstracts/CAS] [Index Copernicus]

Table 1. Demographic data of the participants and the results of screening tests (n=64).

	Min.	Max.	Mean	SD
Age (years)	18.00	63.00	37.50	11.51
BMI	18.07	34.05	24.49	4.11
BDI (pts)	0.00	23.00	3.19	3.60
MMSE (pts)	25.00	30.00	29.27	1.19
CDT (level of errors)	0.00	1.00	0.08	0.27
Education	Women (n=33)		Men (n=31)	
higher (n=28) total: 43.7%	14		14	
secondary (n=27) total: 42.2%	15		12	
primary/vocational (n=9) total: 14.1%	4		5	

BMI – Body Mass Index; BDI – Beck Depression Inventory; MMSE – Mini Mental State Examination; CDT – Clock Drawing Test.

Table 2. Trail Making Test results in the tested group of volunteers (n=64).

	Min.	Max.	Mean	SD	Median	95% CI
TMT-A seconds	12.00	40.00	24.19	5.93	23.5	22.7;25.7
TMT-A errors	0.00	3.00	0.30	0.61		
TMT-B seconds	28.00	172.00	63.19	28.64	54.5	56.0;70.3
TMT-B errors	0.00	2.00	0.47	0.69		
TMT B-A seconds	13.00	132.00	38.61	26.09	28.0	32.1;45.1

TMT – Trail Making Test; A, B – parts of TMT; TMT B-A – differences between times B and A.

psychologist, who excluded the existence of depression. The results of the other tests (MMSE and CDT) were within norms, and the participant was included in the study.

The t test results revealed no statistical differences between the sexes in terms of age, MMSE, CDT, and BDI (p>0.05). Women had significantly higher BMI (women: 22.99, SD 3.91; men 26.10, SD 3.73, p=0.002); the distribution of this attribute was normal, confirmed by Kolmogorov-Smirnov test. The data on gender differences in education are presented in Table 1, but no significant differences were noted in the statistical analysis.

Trail Making Test (TMT)

TMT was performed easily and with a few errors (Table 2).

Kolmogorov-Smirnov test results revealed normal distribution of TMT-A results (Z=0.814, p=0.522). TMT-B and TMT B-A results did not have normal distribution (Z=1.825, p=0.003; Z=1.785, 0.003, respectively).

Older participants required a longer time to perform the test (Table 3).

Statistical analysis with Pearson's chi-square test revealed the mutual relationships between TMT performance and age. For TMT-A: P=0.39, p=0.001; TMT-B: P=0.42, p=0.001; TMT B-A: P=0.31, p=0.014.

Higher level of education was associated with a shorter time of TMT performance (Table 3). Pearson's chi-square test revealed a correlation between level of education and the TMT-B (P=0.35, p=0.005), and B-A (P=0.38, p=0.002).

Women performed TMT better than men, when analyzed B-A (Table 3).

Indexed in: [Current Contents/Clinical Medicine] [SCI Expanded] [ISI Alerting System] [ISI Journals Master List] [Index Medicus/MEDLINE] [EMBASE/Excerpta Medica] [Chemical Abstracts/CAS] [Index Copernicus]

Table 3. Trail Making Test results; comparison by age, education, and gender.

	Parameter	TMT-A: mean (SD) seconds	TMT-B: mean (SD) seconds	TMT B-A: mean (SD) seconds
Age in years (n)	18–25 (14)	21.21 (5.37)	54.35 (18.85)	32.43 (17.28)
	26–37 (20)	22.65 (5.25)	54.25 (23.21)	31.70 (22.44)
	38–49 (20)	26.05 (5.55)	65.10 (30.93)	38.55 (28.50)
	≥50 (10)	27.70 (6.36)	89.60 (31.44)	61.20(28.65)
Education (n)	Higher (28)	23.25 (5.95)	52.36 (15.88)	29.11 (15.16)
	Secondary (27)	24.52 (5.21)	67.81 (33.53)	42.30 (30.97)
	Primary/vocational (9)	26.11 (7.82)	83.00 (32.10)	57.11 (26.79)
Gender (n)	Women (33)	24.30 (4.23)	54.55 (14.70)	30.24 (14.42)
	Men (31)	24.06 (7.39)	72.39 (36.36)	47.52 (32.38)

TMT – Trail Making Test; A, B – parts of TMT; SD – Standard Deviation; n – number of participants.

This was confirmed by Mann-Whitney test (Z=2.02, p=0.044).

Interval timing (IT)

All results of IT presented a normal distribution on the basis of Kolmogorov-Smirnov test. Statistical analysis with t test revealed that the 2nd (shorter than the pattern), 3rd (longer than the pattern) trial of auditory; the 1st, 2nd (both shortened) visual 1-s intervals, as well as all 2-s auditory intervals (the 1st was longer, the 2nd and 3rd were longer than the pattern) did not reach statistical significance when compared to the pattern. All mean reproduced 2-, 5-, and 7-s visual stimuli were significantly shortened in comparison with the presented pattern. All mean produced time intervals were also significantly shortened (Table 4).

Statistical analysis using ANOVA and post hoc Scheffe test among the age groups revealed that only single relationships between age and IT for 2 trials of visual 1-s intervals could be detected (ANOVA: the 1st trial: F=3.67, p=0.017, the 2nd trial F=3.76, p=0.015; Scheffe test – the 1st trial: ≥50 years old *vs.* 18–25 years old, p=0.027, the 2nd trial ≥50 years old *vs.* 38–49 years old, p=0.044).

For the relationships between level of education and IT, ANOVA analysis with post hoc Tamhane test was performed. Only 7-s production with no previous pattern for the 2nd and 3rd trials were statistically significant (ANOVA: the 2nd trial F=4.63, p=0.013, the 3rd trial F=3.52, p=0.036; Tamhane test: the 2nd trial vocational-higher p=0.017, the 3rd trial vocational-higher p=0.05).

To evaluate the influence of gender on IT, the t test was used, and only 1 relationship (very likely accidental) during the 3rd trial of 1-s production was detected (p=0.041) – women had shorter intervals compared with men.

To assess the accuracy of IT, the reproduced/produced intervals were compared to real durations with the use of the t test (decreasing p was considered as the degree of inaccuracy). The most accurate were 2-s auditory stimuli (p=0.845, 0.410, 0.567 in the 3 consecutive trials), less accurate were auditory 1-s stimuli (p=0.040, 0.507, 0.279 in the 3 consecutive trials), then visual 1-s intervals (p=0.069, 0.063, 0.031 in the 3 consecutive trials). Interval production was the least accurate (p<0.002 in all trials).

The statistical comparison between the results of TMT and IT found only 2 correlations between TMT-A, and single trial with auditory stimuli A-1s-3 (P=0.313; p=0.012), as well as TMT errors and A-7s-1 (P=0.246; p=0.05), when analyzed with Pearson's chi-square test. No other correlation was noted.

Discussion

The study evaluated 2 methods of cognitive testing in healthy adult volunteers: the well-known TMT and the experimental IT, in terms of age, level of education, and gender.

In the tested group, the subgroup of women was equal in terms of age (women mean 37.33 years, men 37.68 years), but slightly more numerous: 33 (51.56%) *vs.* 31 men (48.44%). According to official 2011 Polish demographic data from the Central Statistical Office (CSO), women constituted 52.11%, and men 47.89% of the whole population. Hence, the distribution of this attribute in the participants of the study is comparable to the general population. The higher level of education among tested women was not confirmed by the statistical evaluation, although it is in accordance with the demographic distribution provided by CSO [13].

TMT was chosen as a simple cognitive test assessing visual attention, task switching, speed of processing, and executive

Indexed in: [Current Contents/Clinical Medicine] [SCI Expanded] [ISI Alerting System] [ISI Journals Master List] [Index Medicus/MEDLINE] [EMBASE/Excerpta Medica] [Chemical Abstracts/CAS] [Index Copernicus]

Table 4. Interval timing test results. The reproduction of auditory (A), visual stimuli (V), and time production without pattern (P) in milliseconds (n=64).

	Min.	Max.	Mean	SD
A-1s-1	436.00	1974.00	1088.84	339.08
A-1s-2*	400.00	1775.00	973.17	321.42
A-1s-3*	454.00	1787.00	1042.85	313.82
A-2s-1*	843.00	3778.00	2015.47	631.06
A-2s-2*	667.00	4914.00	1930.67	668.56
A-2s-3*	826.00	4254.00	1961.77	531.18
A-5s-1	2005.00	6858.00	4557.47	1044.52
A-5s-2	2596.00	7454.00	4505.00	1051.32
A-5s-3	2669.00	6350.00	4544.41	872.01
A-7s-1	3146.00	9354.00	6155.52	1337.83
A-7s-2	3757.00	9164.00	6371.80	1070.61
A-7s-3	3776.00	8461.00	6398.31	1108.94
V-1s-1*	400.00	2582.00	911.20	383.29
V-1s-2*	400.00	1674.00	927.27	307.83
V-1s-3	400.00	1880.00	908.48	332.77
V-2s-1	548.00	2993.00	1723.38	447.21
V-2s-2	687.00	2641.00	1691.34	435.49
V-2s-3	764.00	3179.00	1808.11	509.05
V-5s-1	1798.00	6249.00	4277.77	847.71
V-5s-2	2234.00	5849.00	4376.63	686.97
V-5s-3	1841.00	6230.00	4451.08	827.77
V-7s-1	3487.00	8347.00	6251.11	867.24
V-7s-2	2504.00	8205.00	6189.34	1027.68
V-7s-3	2400.00	8377.00	6114.04	1380.81
P-1s-1	244.00	1444.00	755.14	281.27
P-1s-2	121.00	1675.00	872.34	314.89
P-1s-3	219.00	1799.00	859.77	327.19
P-2s-1	407.00	3358.00	1390.88	502.74
P-2s-2	359.00	2792.00	1572.14	493.31
P-2s-3	358.00	2967.00	1634.95	584.89
P-5s-1	584.00	6144.00	3805.08	1101.07
P-5s-2	632.00	7288.00	4167.52	1269.39
P-5s-3	651.00	6336.00	4307.28	1243.15
P-7s-1	667.00	8606.00	5792.25	1633.53
P-7s-2	722.00	9264.00	5997.91	1899.48
P-7s-3	818.00	9592.00	6031.17	1860.65

A – auditory; V – visual; P – time production without pattern; 1s,2s,5s,7s – intervals in seconds; 1,2,3: consecutive trials.
* t-test; $p>0.05$, the rest of trials: $p\leq0.05$.

Indexed in: [Current Contents/Clinical Medicine] [SCI Expanded] [ISI Alerting System]
[ISI Journals Master List] [Index Medicus/MEDLINE] [EMBASE/Excerpta Medica]
[Chemical Abstracts/CAS] [Index Copernicus]

functioning. We did not want to confront the participant with the excessive cognitive load characteristic for solving numerous tasks, thus leading to the accelerated loss of attention. IT is a method used in cognitive studies in healthy subjects and those with pathological changes, yet it has not been widely used in psychometric evaluation [3,14]. IT is connected with attention, memory, and decision making. There are some data indicating the possibility of IT performance application in some practical areas, such as by Baldauf et al., who found the time production to be a valid indicator of cognitive involvement in a simulated driving test, and Płotek et al., who used it for cognitive assessment after intravenous anesthesia for endoscopic procedures [15,16].

Functional MRI performed during TMT showed the activity of frontal regions in the left hemisphere, as well as left middle and superior temporal gyrus activity. TMT activates left-sided dorsolateral and medial frontal regions; left middle and superior temporal gyri were also activated [17].

Cook and Pack collected information on the neural basis of IT, and concluded that the interval timing is supported by different brain areas: thalamus, striatum, posterior parietal, and prefrontal areas of cortex, basal ganglia, cortico-striatal loops, cerebellum, and prefrontal cortex. The neurons use synaptic plasticity, adaptation, and neural circuit dynamics to support the interval timing [18]. Kumral et al. reported cases of thalamic insult that resulted in isolated time disorientation and loss of time sense. The patients could not state the actual date, did not know the exact time of the day, and were unable to estimate time intervals. This report proves the role of the thalamus in interval timing and circadian time assessment [19]. People with frontal cortex lesions as well as Korsakoff syndrome estimated time intervals less accurately then normal control subjects; this is connected with the depletions in working and episodic memory that contribute to correct estimation of short (<30 s) and long (>30 s) intervals of time [20]. There is a certain overlap of TMT and IT in terms of supporting frontal lobes, thus providing a basis for mutual comparisons. However, imaging studies also pointed out the role of the thalamus, cerebellum, and basal nuclei in the IT, so the neural representation of IT seems to be more robust and complex than TMT [21].

The 5s and 7 s auditory and visual stimuli, as well as interval production with no previous pattern, were shortened in comparison with the tested intervals, which is consistent with the trend towards overestimation of short (up to 5 s) intervals and underestimation of longer intervals [22]. The repetition of 1s and 2 s auditory and visual was more complex. It was difficult to reach a conclusion about the strict pattern of reproduction, as many results did not reach statistical significance. Studies with greater number of trials implementing this range of seconds could be planned to explain this observation.

The impact of age, education, and gender on cognitive functioning is presented in the literature. The group selected for the study can be considered young (mean age 37.50 years) in comparison with the results of other authors evaluating the influence of age on different aspects of human biology. Boledovičová selected groups of men and women with mean age 46.1 and 45.4 years, respectively, for evaluation of relationships among age, body composition, and blood pressure, which is more than selected in the present study [23]. However, the calculated mean age stands in the middle of young and old populations, as proposed by Petrofsky et al. The authors divided the studied group into young (mean age 25.0 years) and old (mean age 58.6 years) participants for analysis of the impact of diabetes, age, and BMI on vascular endothelial function [24].

A group of Italian scientists guided by Amodio showed a strong relationship between age, level of education, and type of job in relation to TMT performed by 300 healthy volunteers originating from northern Italy. Job, interaction age, and education level influenced the difference TMT-B minus TMT-A in the Amodio study [25]. Tombaugh tested TMT in a population of 911 community-dwelling individuals aged 18–89 years and observed the influence of age and education on TMT performance [26]. The mean results obtained by Polish participants are similar to Tombaugh's results. The mean age of our group was 37.5 years, and for this age in the Amodio study (range 35–44, n=39), the mean value of TMT-A was 28.54 s, SD 10.09 s (in our study the mean was 24.19 s; SD 5.93 s), and for TMT-B was 58.46 s, SD 16.41 s (in our study, 63.19 s, SD 28.64 s). According to Giovanolli, gender influenced Part A of TMT, but not Part B [27]. Takeda et al. used near-infrared spectroscopy (NIRS) while testing participants with TMT in terms of previous knowledge of the TMT, the order of TMT, and gender. The increase in oxy-Hb was higher in participants who had no knowledge of the TMT (with no influence on the performance time). TMT-A results were not affected by gender, but males had higher oxy-Hb [28]. Summarizing, our results on TMT seem to be in accordance with other studies. The fact that the test results depend on various factors makes difficulties in interpretations.

During our study, a trial of IT consisting of 36 consecutive attempts covering the range of 1–7 seconds was applied, and only 3 statistically significant relationships between age and IT were noted, which supports the initial conclusion about the lack of the mutual relationship between age and IT in the chosen paradigm of testing. This observation is partly supported by the results of Desai et al., although they used only visual stimuli, in contrast to our paradigm involving auditory stimuli and interval timing assessment with no previous pattern.

In addition, the authors chose older participants for their study. There are also some common features with our study: the

Indexed in: [Current Contents/Clinical Medicine] [SCI Expanded] [ISI Alerting System] [ISI Journals Master List] [Index Medicus/MEDLINE] [EMBASE/Excerpta Medica] [Chemical Abstracts/CAS] [Index Copernicus]

duration of the time intervals and number of trials. The main conclusion drawn from the study was that age did not influence the interval timing [29]. An age-related increase in the underproduction of the intervals with statistically significant changes occurring in the subjects aged 51–60 years was presented in the literature. Interestingly, a greater underproduction was achieved by women when longer intervals (1 and 5 min) were implemented in the test [30].

Surnina assessed the time production of intervals of 1, 3, 5, 7, and 10 s duration by using a stopwatch. The authors found overestimation of 1-s intervals and underestimation of the other intervals, independent of gender. The results are partly consistent with our findings, because overestimation was detected in case of the reproduction of 1-s intervals for auditory stimuli, but could not be found in longer intervals, the reproduction of visual stimuli or production with no pattern did not repeat the results achieved by Surnina et al. In discussion, on the basis of the analyzed literature, Surnina et al. concluded that overestimation is characteristic for the older population, because this phenomenon could not be observed in subjects 17–25 years old [31]. In our study the population was quite young, so probably we could not observe the phenomenon of overestimation.

We know from previous studies that education is associated with neuropsychological performance. Adjusted years of education were associated with fluency and higher cognitive processes, while the ratio between the adjusted years of education and age was associated with tasks implicating working memory, according to Lam et al. [32]. The similar simple comparison cannot be drawn if IT is discussed. While analyzing the influence of education on IT, only 3 out of 36 possible significant results were noted. It is difficult to state the strict pattern of mutual relationship. To our knowledge, there is no literature on this subject and it is impossible to compare our findings to results of other studies. In the future, more attention should be paid to this subject. Nevertheless, if this trend is confirmed in subsequent studies, IT may be very useful in psychometric testing, as the level of education will not affect the general performance and it allows for easy comparisons between groups of individuals with various levels of education.

Only 1 statistically significant relationship between gender and IT performance was found. Hence, in our study, gender did not influence time perception. Data from the literature have contradictory results. Some researchers, such as Rammsayer et al. and Hancock et al., showed that females overestimate time intervals relative to males when using verbal estimation, and underestimate when using production techniques [33,34]. Block, Hancock, and Zakay searched a database containing more than 10 000 references on the psychology of duration judgments and found studies on 4794 females and 4688 males, and concluded that although overall sex difference in duration judgment magnitude was small but statistically significant. Females sustain attention to time more in the prospective paradigm and have better episodic memory in the retrospective paradigm [35]. The lack of such a result in our study may arise from the number of tested participants.

When analyzing the accuracy of IT performance, the most accurate reproduction was performed when 2-s and 1-s auditory stimuli were analyzed. Visual stimuli were less accurate, and the least precise were tests of IT without the previous pattern. The results relating to the superiority of auditory stimuli over visual stimuli were also discussed in the available literature. On the sub-second scale, the time perception is amodal and free from the cognitive processing, as was suggested by Zhang et al. on the basis of the sophisticated psychological paradigm of the study [36]. In the studies on different ways of learning artificial grammar, Conway and Christiansen discovered qualitative learning biases among the senses. Audition afforded better learning of input sequences [37]. Modality differences in memory testing were also presented by other researchers, such as Collier and Logan, who found a temporal advantage of auditory modality in short-term memory (2000) [38]. Freides stated that audition is better for the accuracy of temporal patterns, and vision is better for spatial tasks [39]. Our results, although very different from the type of testing used in the cited studies, seem to be consistent with the results of other researchers in various fields of psychological assessment. The time production is based on the abstract idea of time and requires retrieval of information stored in the memory; it seems to be much more difficult and demanding, so it has the highest error.

Finally, a comparison of TMT and IT results was performed, and only 2 correlations were observed, suggesting that the tests are not correlated with each other, and the neurobiological similarity does not easily translate to results achieved by the participants of the study. Future fMRI neuroimaging studies evaluating subsequent TMT and IT performance by the same subjects could yield more information about the nature of the problem. The other interesting comparison would be to choose a cognitive test, which represents neurobiological basis more similar to IT in comparison to the TMT.

The performed study has some advantages, such as comparing a well-known cognitive test with an experimental way of testing. The tests were performed by healthy individuals in the same external conditions, according to the same scheme of evaluation. The results are interesting and worth further exploration. The IT test in a portable computerized form may become a useful tool in perioperative assessment, yielding information about patients' cognitive functioning. The early postoperative period is especially associated with various cognitive disturbances that may accompany serious clinical complications. If future studies confirm this initial observation, the IT test may

Indexed in: [Current Contents/Clinical Medicine] [SCI Expanded] [ISI Alerting System] [ISI Journals Master List] [Index Medicus/MEDLINE] [EMBASE/Excerpta Medica] [Chemical Abstracts/CAS] [Index Copernicus]

be free from interpretational limitations such as the influence of age, education, and gender. The obvious limitation of the study is the small number of participants. According to a consulted statistician, to establish statistically reliable physiological norms, more than 200 subjects should be tested.

Summarizing the results of the study, adult healthy volunteers performed TMT easily, with few errors. Repetition of the longer 5- and 7-s intervals, as well as production of all intervals without pattern, was shortened. The reproduction of the shorter 1- and 2-s auditory and visual stimuli was more complex. Age, education, and gender have a more pronounced impact on the trail making test than on the interval timing test. The reproduction of the short auditory stimuli was the most accurate.

Conclusions

The trail making test and interval timing test allow measuring cognition in healthy adults. The evaluation of interval timing test appears to be most useful as a cognitive assessment tool. The interval timing test is resistant to confounding factors such as age, education, and gender. Further studies are needed to confirm initial observations.

Statement

All the authors have approved the final manuscript.

The authors declare no conflict of interests.

References:

1. Moller JT, Cluitmans P, Rasmussen LS et al: Long-term postoperative cognitive dysfunction in the elderly: ISPOCD 1 study. Lancet, 1998; 351: 857–61
2. Buhusi CV, Meck WH: What makes us tick? Functional and neural mechanisms of interval timing. Nat Rev Neurosci, 2005; 6: 755–65
3. Bshor T, Ising M, Bauer M et al: Time experience and time judgment in major depression, mania and healthy subjects. A controlled study of 93 subjects. Acta Psychiat Scand, 2004; 109: 222–29
4. Coslett HB, Shenton J, Dyer T, Wiener M: Cognitive timing: neuropsychology and anatomic basis. Brain Res, 2009; 1254: 38–48
5. Wittman M, Carter O, Hasler F et al: Effects of psilocybin on time perception and temporal control of behavior in humans. J Psychopharmacol, 2007; 21: 50–64
6. Lam M, Eng GK, Rapisarda A, Subramaniam M et al: Formulation of the age-education index: measuring age and education effects in neuropsychological performance. Psychol Assessment, 2013; 25: 1: 61–70
7. Westman AS: Development of time concepts: differentiating clock and calendar from apparent durations. J Genet Psychol, 1987; 148: 259–70
8. Taatgen NA, Anderson JR, Dicksion D, van Rijn H: Time interval estimation: internal clock or attentional mechanism? Proceedings of the twenty-seventh annual meeting of the cognitive science society, 2005; 2122–27
9. Van Rijn H, Taatgen NA: Timing of multiple overlapping intervals: How many clocks do we have? Acta Psychol (Amst), 2008; 129(3): 365-75
10. Folstein MF, Folstein SE, Fajiang G: MMSE Krótka Skala Oceny Stanu Umysłowego. Przewodnik Kliniczny. Pracownia Testów Psychologicznych, 2009 [in Polish]
11. Krzymiński S: Test rysowania zegara. Postępy Psychiatrii i Neurologii, 1995; 1: 21–30 [in Polish]
12. Beck AT, Ward CH, Mendelson M: An inventory for measuring depression. Arch Gen Psychiat, 1961; 4: 561–71
13. Central Statistical Office. *http://www.stat.gov.pl/gus/index_ENG_HTML.htm*
14. Wittman M. Carter O, Hasler F et al: Effects of psilocybin on time perception and temporal control of behavior in humans. J Psychopharmacol, 2007; 21: 50–64
15. Baldauf D, Burgard E, Wittmann M: Time perception as a workload measure in simulated car driving. Appl Ergon, 2009; 40(5): 929–35
16. Płotek W, Cybulski M, Kluzik A et al: Psychomotor function and interval timing in patients receiving intravenous anesthesia for endoscopic procedures. Sci World J, 2012; 2012: 317897
17. Zaksanis KK, Mraz R, Graham SJ: An fMRI study of the Trail Making Test. Neuropsychologia, 2005; 43: 1878–86
18. Cook EP, Pack CC: Parietal cortex signals come unstuck in time. PLoS Biol, 2012; 10(10): e1001414
19. Kumral E, Gulluoglu H, Dramali B: Thalamic chronotaraxis: isolated time disorientation. J Neurol Neurosur Ps, 2007; 78: 880–82
20. Mitura M, Kinsbourne M, O'Connor M: Time estimation by patients with frontal lesions and by Korsakoff amnesics. J Int Neuropsych Soc, 2000; 6: 517–28
21. Dreher JC, Grafman J: The roles of the cerebellum and the basal ganglia in timing and error prediction. Eur J Neurosci, 2002; 16: 1609–19
22. Zakay D: The evasive art of subjective time measurement: Some methodological dilemmas. In: Block RA (ed.), Cognitive models of psychological time. Hillsdale, NJ: Erlbaum, 1990; 59–84
23. Boledovičová M, Hendl J, Lišková L et al: Blood pressure relation to body composition and age: analysis of a nurse-led investigation and consultation program. Med Sci Monit, 2014; 20: 612–17
24. Petrofsky JS, Alshammari F, Singh Bains G et al: What is more damaging to vascular endothelial function: diabetes, age, high BMI, or all of the above? Med Sci Monit, 2014; 20: 257–63
25. Amodio P, Wenin H, Del Piccolo F et al: Variability of trail making test, symbol digit test and line trait test in normal people. A normative study taking into account age-dependent decline and sociobiological variables. Aging Clin Exp Res, 2002; 14: 117–31
26. Tombaugh TN: Trail Making Test A and B: normative data stratified by age and education. Arch Clin Neuropsychol, 2004; 19: 203–14
27. Giovagnoli AR, Del Pesce M, Mascheroni S et al: Trail Making Test: normative values from 287 normal adult controls. Ital J Neurol Sci, 1996; 17: 305–9
28. Takeda C, Notoya M, Sunahara N, Inoue K: Identification of three factors influencing trail making test performance using multichannel near-infrared spectroscopy. Tohoku J Exp Med, 2011; 223: 103–12
29. Desai VR: The effects of aging and brain damage on time perception. CUREJ, 2007; 1–13
30. Espinosa-Fernandez L, Miro E, Cano M, Buela-Casal G: Age-related changes and gender differences in time estimation. Acta Psychol, 2003; 112: 221–32
31. Surnina OE, Antonova NV, Kapusnyak ON: Production of time intervals by aged subjects. Hum Physiol, 2003; 29: 1: 76–79
32. Lam M, Eng GK, Rapisarda A et al: Formulation of the age-education index: measuring age and education effects in neuropsychological performance. Psychol Assessment, 2013; 25(1): 61–70
33. Hancock PA, Rausch R: The effects of sex, age, and interval duration on the perception of time. Acta Psychol, 2010; 133: 170–79
34. Rammsayer T, Lustnauer S: Sex differences in time perception. Percept Motor Skill, 1989; 68: 195–98
35. Block RA, Hancock PA, Zakay D: Sex differences in duration judgments: a meta-analytic review. Mem Cognition, 2000; 28: 1333–46
36. Zhang H, Chen L, Zhou X: Adaptation to visual or auditory time intervals modulates the perception of visual apparent motion. Front Integr Neurosci, 2012; 6: 100
37. Conway CM, Christiansen MH: Modality-constrained statistical learning of tactile, visual, and auditory sequences. J Exp Psychol, 2005; 31: 24–39
38. Collier GL, Logan G: Modality differences in short-term memory for rhythms. Mem Cognition, 2000; 28: 529–38
39. Freides D: Human information processing and sensory modality: cross-modal functions, information complexity, memory and deficit. Psychol Bull, 1974; 81: 284–310

Indexed in: [Current Contents/Clinical Medicine] [SCI Expanded] [ISI Alerting System] [ISI Journals Master List] [Index Medicus/MEDLINE] [EMBASE/Excerpta Medica] [Chemical Abstracts/CAS] [Index Copernicus]