Journal of Health Sciences

RESEARCH ARTICLE Open Access

Cognitive function recovery rate in early postoperative period: comparison of propofol, sevoflurane and isoflurane anesthesia

Munevera Hadžimešić[1]*, Semir Imamović[1], Vasvija Uljić[1], Mirsad Hodžić[2], Fatima Iljazagić-Halilović[1], Renata Hodžić[3]

[1]Department of Anaesthesiology and Reanimatology, University Clinical Centre Tuzla, Trnovac bb, 75000 Tuzla, Bosnia and Herzegovina. [2]Department of Neurosurgery, University Clinical Centre Tuzla, Trnovac bb, 75000 Tuzla, Bosnia and Herzegovina. [3]Department of Neurology, University Clinical Centre Tuzla, Trnovac bb, 75000 Tuzla, Bosnia and Herzegovina.

ABSTRACT

Introduction: There is no simple answer to the question as to when the brain function is back to normal after anaesthesia. Research done so far has identified different factors influencing the rate of cognitive function recovery and type of anaesthetic as one of those factors.

Methods: This study encountered 90 patients hospitalized in neurosurgical department of University Clinical Centre Tuzla in period from October 2011 to may 2012 year. Aim of the study was to compare influence of three different anesthetics (propofol, isoflurane and sevoflurane) on recovery rate of cognitive performance 1, 5 and 10 minutes following extubation. Assessment of cognitive functions was preformed using the short Orientation-Memory-Concentration (OMC) Test. All patients included in the study underwent lumbar microdiscectomy surgery and were allocated to one of three groups: propofol, sevoflurane and isoflurane.

Results: Trough comparison of OMC test values there is obvious superiority in recovery of cognitive functions between propofol group and inhaled anesthetic group, after 1 minute ($p = 0.008$) and after 5 minutes ($p = 0.009$). Comparison of propofol and isoflurane anesthesia shows significantly faster recovery of cognitive performance in propofol group (after 1 minute $p = 0.002$, 5 minutes $p = 0.004$, 10 minutes $p = 0.038$). Faster recovery of cognitive function is present in sevoflurane compared to isoflurane group only 1 minute after extubation $p = 0.049$.

Conclusions: Fastest recovery of cognitive performance appears after propofol anesthesia, than follows sevoflurane based anesthesia and after that isoflurane anesthesia.

Keywords: Postoperative cognitive dysfunction, propofol, sevoflurane, isoflurane, anesthesia

INTRODUCTION

General anesthesia encompasses amnesia, hypnosis (defined as a lack of perceptive awareness to non-noxious stimuli), analgesia, immobility, and blunting of autonomic reflexes. These effects are induced by specific interactions of general anesthetics on

* Corresponding author: Munevera Hadžimešić, Department of Anaesthesiology and Reanimatology, University Clinical Centre Tuzla, Trnovac bb, 75000 Tuzla, Bosnia and Herzegovina
Phone: +3873561152300; E-mail: mhadzimesic@rotech.ba

Submitted: 9 February 2013 / Accepted 20 March 2013

UNIVERSITY OF SARAJEVO
FACULTY OF HEALTH STUDIES

discrete neuronal loci (1). For a long time it has been believed that anesthetic effects do not outlast their pharmacological action, and that the target organ is restored to its pre-anesthetic state with the elimination of anesthetic agent (2). Brain function changes during and in the immediate period after general anesthesia, which is characterized with depressed consciousness, impaired attention, memory, and prolonged reaction time (1). Cognition is defined as the mental processes of perception, memory, and information processing, which allows the individual to acquire knowledge, solve problems, and plan for the future (2). Postoperative disturbance in cognition, or as often been referred to as postoperative cognitive dysfunction (POCD) is a term used variably and it is useful to make a distinction between three types of cognitive deterioration after surgery. POCD needs to be distinguished from postoperative delirium, which is transitory and intermittent disturbance of consciousness that usually occurs shortly after surgery, and short-term cognitive disturbance that may be apparent in early postoperative course. Short-term cognitive impairment occurs relatively frequently and may be due to a combination of factors, including surgery and anesthetic agents and it lasts several days after surgery (1, 3). While POCD is deterioration of intellectual function presenting as impaired memory or concentration, long-term complication of surgery and anesthesia related with changes in cognitive performance, both are usually assessed trough various neuropsychological tests (3-5). Propofol is the most frequently used IV anesthetic today, it is short acting intravenous anesth etic used as an induction agent, for sedation and maintenance of anesthesia. Propofol hypnotic activity is mostly mediated through enhancing γ-aminobutyric acid (GABA) induced chloride current through its binding to the β-subunit of $GABA_A$ receptor (6). Propofol is rapidly metabolized mostly in the liver however since its clearance exceeds hepatic blood flow, extrahepatic metabolism is suggested, its metabolites are considered inactive (1). Half-life of propofol after initial dose is 2 to 8 minutes (7), and even after prolonged infusions, propofol provides rapid recovery (1). Volatile anesthetics are relatively inexpensive drugs, easily administered via inhalation, readily titrated, and have a high safety ratio. Depth of anesthesia can be quickly adjusted in a predictable way while monitoring tissue levels via end-tidal concentrations, in addition inhaled anesthetic cause relaxation of skeletal muscle (8). Sevoflurane (1-trifluoromethyl-2,2,2-trifluoroethyl monofluoromethyl ether) was synthesized in the 1970s, but its introduction into clinical practice was delayed, due to the occurrence of toxicity in experimental animals, it was first used in 1981 (1). Sevoflurane is relatively insoluble in blood and has a low blood–gas partition coefficient (0.65); it is slightly more soluble than nitrous oxide and desflurane. Since its tissue–blood partition coefficients are also low, induction and recovery from anaesthesia are extremely rapid, and the level of anaesthesia is easily controlled (9). Isoflurane, (1-chloro-2,2,2-trifluoroethyl difluoromethyl ether) was synthesized by R.C. Terrell during the 1960s, and is now widely used as an inhalational agent, it is a clear, non-flammable liquid at room temperature and has a high degree of pungency. There has been a period of controversy concerning the use of isoflurane in patients with coronary disease because of the possibility for coronary steel effect arising from the potent effects of isoflurane on coronary vasodilatation (8, 9). All potent inhaled anesthetic cause dose dependant decrease in cerebral metabolic rate, paralleling changes in electro encephalography (EEG). Duration of recovery of cognition after anesthesia is variable and depends on many factors such as type of surgery, type of anesthesia, duration of surgery, respiratory complications, and second operation as well as patient related factors (1).

Aim of this study is to obtain adequate insight in cognitive performance recovery rate in early postoperative period after use of different anesthetic for maintaining anesthesia.

METHODS

We conducted a prospective study with 90 patients hospitalized in neurosurgical department of University Clinical Centre Tuzla in period from October 2011 to May 2012. Aim of the study was to compare influence of three different anesthetics (propofol, isoflurane and sevoflurane) on recovery rate of postoperative cognitive disorders in early postoperative period. All patients included in the study underwent lumbar microdiscectomy surgery due to herniated lumbar disc, and were assessed as ASA I (American Society of Anesthesiologists) physical status. Written consent was obtained from all the patients included in the study. Patients were randomly allocated to one of three groups and received designated anaesthetics, each group consisting of thirty patients: Group 1 - propofol maintained anesthesia; Group 2 - sevoflurane maintained anesthesia; Group 3: isoflurane maintained anesthesia.

Balanced anesthesia was used in all three groups. Patients where premedicated using either diazepam 5 mg or midazolam 2.5 mg and fentanyl 0.10 mg. Following induction with propofol 1.5 to 2.5 mg/kg, tracheal intubation was facilitated with atracurium, which was also used in maintaining muscular relaxation in a doze 0.3-0.6 mg. Anesthesia was maintained using nitrous oxide (N_2O) and oxygen (O_2) in ratio 60:40 in all three groups and in group 1 with continuous propofol infusion 8 to 10 mg/kg/h. In group 2 to N_2 O: O_2 mixture, 1. 0 volume % of sevoflurane was added for maintaining anesthesia and in group 3, 1.0 volume % of isoflurane. In all three groups analgesia was provided with fentanyl boluses ranging form 0.05 to 0.10 mg per dose. Assessment of cognitive functions was preformed 1, 5 and 10 minutes following extubation, using the short Orientation-Memory-Concentration (OMC) Test or Short Blessed Test (Appendix 1) (10). This test addresses cognitive performance in the areas of orientation, memory, and concentration. It is been used in quick evaluation of cognitive functions, and it is sensitive and reliable in detecting early cognitive impairments. OMC test possesses good metric characteristics and it is perceptive to global as well as cognitive deficits of left-brain hemisphere. Short OMC test consists of six questions and it is a part of larger test known as Blessed Information-Memory Concentration (BIMC) test, consisting of 26 questions (10).

Statistical analysis

Results are displayed in numeric-percentual form, as well as mean value with standard deviation (SD). Significance was evaluated using Chi square test and Student test, and correlation between gender and cognitive disorder caused by specific anesthetic was estimated using Pearson's Test. Regression analysis was used to identify factors influencing recovery of cognitive functions. Statistical analysis was performed with a confidence interval of 95% and value of $p <0.05$ was considered statistically significant.

RESULTS

The study is conducted in University Clinical Centre Tuzla, it included 90 patients randomly allocated in three groups each group consisting of 30 patients. Average age of patients in all three groups was 45.47 (SD ± 8. 03 years), average age in group 1 was 45.48 years (SD ± 7.98), in group 2 it was 46.23 years (SD ± 8.63) and in group 3 patients' average age was 45.37 years (SD ± 7.94). Out of 90 patients included in the study, 58 were men (64.44%) and 32 (35.56 %) were women. In-group 1 there were 21 (70 %) men and 9 (30 %) women, in group 2 out of 30 patients 20 (66.7 %) were men and 10 (33.3 %) were women and group 3 consisted of 17 (56.7 %) men and 13 (43.3 %) women. Demographic (age, gender) characteristics, body mass index (BMI), smokers-non/smokers, duration of anesthesia is shown in (Table 1), gender distribution of patients shown in (Figure 1).

TABLE 1. Demografic and clinical characteristics of patients

	Propofol		Sevoflurane		Isoflurane		p
n	30		30		30		
Age	44.83 + 7.54		46.23 + 8.63		45.37 + 7.94		0.79
Gender	n	%	n	%	n	%	
Male	21	70.0	20	66.7	17	56.7	0.53
Female	9	30.0	10	33.3	13	43.3	
Smoking	11	36.6	9	30.0	10	33.3	0.75
BMI	24.6 + 4.66		23.06 +3.27		24.5 + 3,65		0.83
Duration of anesthesia (minutes)	96.67 + 18.68		99.00 + 21.01		96.37+ 19.79		0.85

BMI body mass index

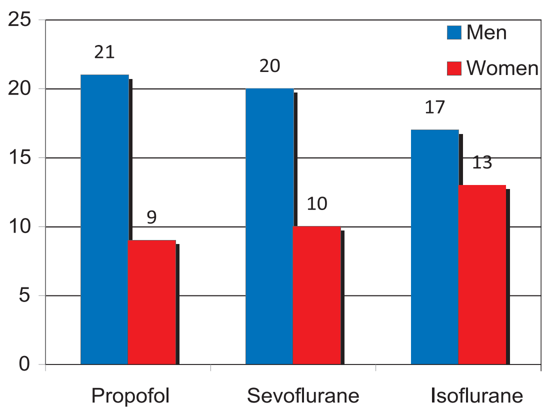

FIGURE 1. Gender distribution of the patients

TABLE 2. Cognitive performance recovery depending on type of anaesthetic

Test	Propofol	Sevoflurane	Isoflurane	p
OMC score - 1 minute	8.41±10.21	11.57±10.64	17.13±10.80	0.008*
OMC score - 5 minutes	2.41 ± 3,33	4.03 ± 5.67	7.20 ± 7.80	0.009*
OMC score - 10 minutes	0.76 ± 1,53	1.73 ± 2.36	2.97 ± 5.39	0.060

OMC Orientation-Memory-Concentration Test

TABLE 3. Cognitive performance recovery comparison of propofol and sevoflurane anesthesia

Test	Propofol	Sevoflurane	p
OMC score - 1 minute	8.41 ± 10.21	11.57 ±10.64	0.251
OMC score - 5 minutes	2.41 ± 3,33	4.03 ± 5.67	0.190
OMC score - 10 minutes	0.76 ± 1,53	1.73 ± 2.36	0.066

OMC Orientation-Memory-Concentration Test

TABLE 4. Cognitive performance recovery comparison of propofol and isoflurane anesthesia

Test	Propofol	Isoflurane	p
OMC score - 1 minute	8.41 ± 10.21	17.13 ± 10.80	0.002*
OMC score - 5 minutes	2.41 ± 3,33	7.20 ± 7.80	0.004*
OMC score - 10 minutes	0.76 ± 1,53	2.97 ± 5.39	0.038*

OMC Orientation-Memory-Concentration Test

TABLE 5. Cognitive performance recovery comparison of sevoflurane and isoflurane anesthesia

Test	Sevoflurane	Isoflurane	p
OMC score - 1 minute	11.57 ± 10.64	17.13 ± 10.80	0.049*
OMC score - 5 minutes	4.03 ± 5.67	7.20 ± 7.80	0.079
OMC score - 10 minutes	1.73 ± 2.36	2.97 ± 5.39	0.256

OMC Orientation-Memory-Concentration Test

As seen in (Table 1), there was no statistical significance in age distribution of the patients (p = 0.79), there was also no statistical significance between the groups concerning gender allocation (p = 0.53). In group 1 there was 11 (36.6%) smokers, in group 2 there was 9 (30 %) and in group 3, 10 (33.3 %) patients were smokers. No statistical significance between the observed groups in correlation to smoking was noticed (p = 0.75). BMI was in group 1 24.6 (± 4.66), in group 2 23.06 (± 3.27) and in group 3, 24.5 (± 3.65), there was also no significance concerning BMI between the groups (p = 0.83). Average duration o anesthesia in group 1 was 96.67 minutes (SD ± 18.68), in group 2 average length of anesthesia was 99 minutes (SD ± 21) and in group 3 it was 96.37 minutes (SD ± 19.79). There was no statistical significance between the groups concerning length of anesthesia (p = 0.85).

Influence of specific anesthetic on cognitive functions recuperation was evaluated based on the values obtained performing OMC test. As seen in (Table 2), trough comparison of OMC test values there is obvious correlation and statistical significance present regarding recovery of cognitive functions depending on the type of anesthetic used. This statistical significance is present in evaluation of cognitive function recovery between propofol group and inhaled anesthetic group, after 1 minute (p=0.008) and after 5 minutes (p =0.009), after 10 minutes there was no significant difference (p=0.006).

By comparing intravenous anesthesia with propofol to inhaled anesthesia with sevoflurane no statistically significant difference was found (OMC score after 1 minute p=0.251, OMC score after 5 minutes p = 0.190 and OMC score after 10 minutes p=0.066) (Table 3).

Comparison of propofol and isoflurane anesthesia shows significant difference in recovery of cognitive functions between groups. Cognitive recovery was significantly quicker in propofol group expressed by

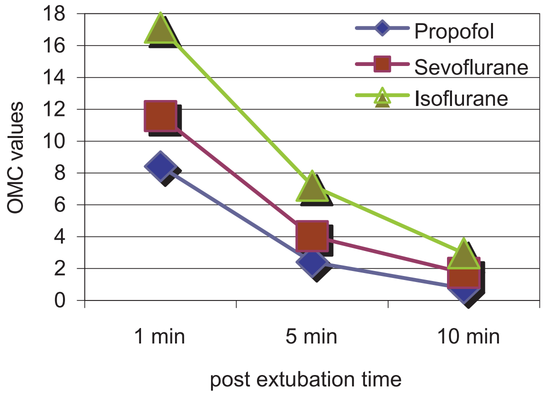

FIGURE 2. Cognitive performance recovery rate depending on type of anesthetic used

OMC score and after one minute p = 0.002, after 5 minutes p=0.004 and after 10 minutes p=0.038 as shown in (Table 4).

As seen from (Table 5) statically significant difference exists between sevoflurane and isoflurane group, indicating faster recovery of cognitive function in sevoflurane group only 1 minute after extubation p=0.049.

Based on values of OMC test preformed 1, 5 and 10 minutes after extubation it is clearly visible that the fastest recovery of cognitive function appears after propofol anesthesia, than follows sevoflurane based anesthesia and after that isoflurane anesthesia, where cognitive performance recuperation is the slowest (Figure 2).

DISCUSSION

Despite technological development in field of surgery and anesthesiology during the last decades, postoperative cognitive dysfunction is still relatively frequent complication in surgical patients. After surgery, elderly patients in particular often display evidence of a temporary state of cognitive function deterioration. Anesthetics administered as part of a surgical procedure may alter the patient's behavioural state by influencing brain activity (11). Brain is the target organ for anesthetics and their effects on brain activity are often present after ending of the surgical procedure and awakening of the patient. Available literature offers no definite conclusion on possible differences between anesthetics and their influence on cognitive functions and duration of cognitive impairment.

International study on cognitive dysfunctions examined influence of age on POCD; results of this study have shown higher incidence of POCD in patients age 60 to 81 years (average age 68 years) up to 26% compared to patients age 40 to 60 years (average age 51 years) where cognitive dysfunction was found in 19% of patients examined (10). Average age of patients included in our study was 45.47 years (SD ± 8.03) and age range in all three groups was approximately same, age did not significantly influenced recovery rate of cognitive function. Out of 90 patients included in the study, 64.44 % were men and 35.56 % were women, there was no statistically significant difference between the groups in correlation to gender.

Use of inhaled anesthesia is widespread, frequently used inhaled anesthetics are sevoflurane, isoflurane and desflurane usually in combination with N_2O, only several studies examined influence of these anesthetics on cognitive functions (13). Isoflurane is present in anaesthesiological practice for a long time and there are various studies that explored effects of isoflurane on cognitive performance in postoperative period. Study conducted by Tsai et al. in year 1992, explored influence of isoflurane and desflurane on cognitive dysfunction in patients undergoing elective orthopaedic surgery and found desflurane to be superior to isoflurane regarding cognitive recovery (14). These results were also confirmed in studies conducted by Dupont et al. and Loscar et al. in patients who underwent elective thoracic surgery (15, 16). Sevoflurane is most common inhaled anesthetic in current anaesthesiological practice. In the study conducted by Schwender et alt. cognitive and psychomotor performance recovery was quicker and more complete after sevoflurane compared to isoflurane anesthesia (17, 18). Superiority of sevoflurane compared to isoflurane anesthesia in cognitive performance recovery was proven in analysis done by El-Dawlatly (19). Our results show sevoflurane to be superior to isoflurane when cognitive performance recovery was concerned.

Recovery of cognitive functions in our study was superior in propofol group compared to inhaled anesthesia with sevoflurane and isoflurane, determined with OMC test, measured in the first and fifth minute. Larsen et alt. conducted a study on accuracy of the answers concerning orientation, short term memory and concentration. Results of this study showed that 30 minutes after anesthesia administration, patients in the remifentanil-propofol and in the desflurane groups gave significantly more correct responses in the Trieger Dot Test and Digit Substitution Test (DSST) compared with sevoflurane (18). There are other findings such as these of Magni et alt. who proved in there study that total intravenous anesthesia with propofol/remifentanil shows no patient benefit over sevoflurane/fentanyl-based anesthesia in terms of recovery and cognitive functions (20). It is generally assumed that general anesthesia is completely reversible state, but this cannot be proved, Jevtovic-Todorovic et alt. found histological changes in the brain of animals exposed to isoflurane, N2 O, ketamine and midazolam (21). All the patients included in the study were discharged form the hospital in due time, with out verified permanent cognitive disorders. There is no simple answer to the question as to when brain function is beck to normal after anesthesia, research done so far has identified different factors influencing rate of cognitive function recovery, and type of anesthetic is confirmed to be significant factor by several studies conducted so far.

CONCLUSIONS

This study confirmed faster recovery of cognitive performance following propofol anesthesia compared to anesthesia with sevoflurane and isoflurane, after first and fifth minute after extubation. Though OMC score was lower in propofol group, ten minutes post extubation, compared to inhale anesthetic group, still statistical significance was not found. When compared propofol and sevoflurane anesthesia, OMC scores were lower in propofol group, but with out statistical significance. It was established that the recovery of cognitive performance was superior after propofol anesthesia compared to isoflurane, and statistical significance was observed at all three times measured. Sevoflurane anesthesia shoved faster recovery of cognitive functions compared to isoflurane anesthesia after first and fifth minute post extubation. Fastest recovery of cognitive performance appears after propofol anesthesia, than follows sevoflurane based anesthesia and after that isoflurane anesthesia.

COMPETING INTERESTS

None to declare.

ACKNOWLEDGEMENTS

None.

REFERENCES

1. Miller RD, Eriksson LI, Fleisher LA, Wiener-Kronish JP, Young WL. Miller's Anesthesia: 7th Ed. Churchill Livingstone; 2008.567p-789p
2. Hanning CD. Postoperative cognitive dysfunction. Br J Anaesth. 2005;95:82–87.
3. American Psychiatric Association. Diagnostic and Statistical Manual of Mental Disorders, 4th edn (DSM-IV). International version. Washington DC: American Psychiatric Association, 1995.
4. Bryson GL, Wyand A. Evidence-based clinical update: General anesthesia and the risk of delirium and postoperative cognitive dysfunction. Can J Anaesth. 2006;53:669–77.
5. Fong HK, Sands LP, Leung JM: The role of postoperative analgesia in delirium and cognitive decline in elderly patients: A systematic review. Anesth Analg. 2006;102:1255–66.
6. Krasowski MD, Nishikawa K, Nikolaeva N, et al. Methionine 286 in transmembrane domain 3 of the GABAA receptor beta subunit controls a binding cavity for propofol and other alkylphenol general anesthetics. Neuropharmacology. 2001;41:952-964.
7. Simons P, Cockshott I, Douglas E. Blood concentrations, metabolism and elimination after a subanesthetic intravenous dose of (14) C-propofol (Diprivan) to male volunteers. Postgrad Med J.1985; 61-64.
8. T N Calvey, N E Williams. Principles and Practice of Pharmacology for Anaesthetists 5-th edt;2008.123p.
9. Paul G Barash, Bruce F Collen, Robert K Stoelting. Clinical Anesthesia: 5th Ed. Lippincott Williams &Wilkins Publishers;2006:156-170p.
10. Blessed G, Tomlinson BE, Roth M. The association between quantitative measures of dementia and senile change in the cerebral grey matter of elderly subjects. Br J Psychiatry.1968; 114:797-811.
11. Mandal PK, Schifilliti D, Mafrica F, Fodale V. Inhaled Anesthesia and Cognitive Performance. Drugs of Today. 2009;45(1):47-54.
12. Kanbak M, Saricaoglu F, Akinci SB, Oc B, Balci H, Celebioglu B, Aypar U. The effects of isoflurane, sevoflurane, and desflurane anesthesia on neurocognitive outcome after cardiac surgery: a pilot study. Heart Surg Forum. 2007;10(1): E36-41.
13. Tsai SK, Lee C, Kwan, WF, Chen BJ. Recovery of cognitive functions fter anaesthesia with desflurane or isoflurane and nitrous oxide. Br J Anaesth. 1992;69(3): 255-8.
14. Dupont J, Tavernier B, Ghosez Y, Durinck L, Thevenot A, Moktadir-Chalons N, Ruyffelaere-Moises L, Declerck N, Scherpereel P. Recovery after anaesthesia for pulmonary surgery: desflurane, sevoflurane and isoflurane. Br J Anaesth. 1999;82(3):355-9.
15. Loscar M, Allhoff T, Ott E, Conzen P, Peter K. Awakening from anesthesia and recovery of cognitive function after desflurane or isoflurane. Anaesthesist. 1996;45(2):140-5.
16. Schwender D, Muller A, Madler M, Faber-Zullig E, Ilmberger J. Recovery of psychomotor and cognitive functions following anesthesia Propofol/alfentanil and thiopental/isoflurane/alfentanil. Anesthetist.1993;42(9): 583-91.
17. Larsen B, Seitz A, Larsen R. Recovery of cognitive function after remifentanil-propofol anesthesia: a comparison with desflurane and sevoflurane anesthesia. Anesth Analg.2000;90:168-174.

18. El-Dawlatly AA. Sevoflurane vs. isoflurane anesthesia: A study of postoperative mental concentration and fine motor movements. Middle East J Anaesthesiol.2002;16(4):394-404.

19. Magni G, Baisi F, La Rosa I, Imperiale C, Fabbrini V, Pennacchiotti M L, Rosa G. No difference in emergence time and early cognitive function between sevoflurane-fentanyl and propofol-remifentanil in patients undergoing craniotomy for supratentorial intracranial surgery. J Neurosurg Anesthesiol. 2005;17(3): 134-8.

20. Jevtovic-Todorovic V, Hartman RE, Izumi Y, et al. Early exposure to common anesthetic agents causes widespread neurodegeneration in the developing rat brain and persistent learning deficits. J Neurosci. 2003;23:876-882.

APPENDIX 1. Orientation-Memory-Concenctration Test OMC (10)

Question	Max error 1min	Max error 5min	Max error 10min	point X	Disorder severity
What year is it now?	1	1	1	____ x 4	= ____
What month is now?	1	1	1	____ x 3	= ____
Repeat this phrase : Clinical Centre Trnovac	1	1	1	____ x 3	= ____
What time is approximately? (guessing time one hour ±)	1	1	1	____ x 3	= ____
Count reverse from 20 to 1	2	2	2	____ x 2	= ____
Recite months from december to january	2	2	2	____ x 2	= ____
Repete sentence (today is a beautiful day)	5	5	5	____ x 2	= ____
Repete sentence (today is a beautiful day)	5	5	5	____ x 2	= ____