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A review of postoperative cognitive dysfunction: Diagnostic and rehabilitation

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Abstract:
Postoperative cognitive dysfunction is a very common event after cardiac surgery, especially in elder patients and with lower education levels. The prevention of POCD should be done using a few simple features before surgery and during surgery, such as corticosteroids before surgery to reduce inflammation of the brain, which affect cognition. When possible, the anesthetic technique must be performed using the bispectral index (BIS) for controlling the length and depth of surgical anesthesia. The use of anesthetics that cause less damage in cognition in relation to other drugs that are already established as POCD trigger can also be the best way. The use of imaging tests that facilitate the research of cognitive disorders such as the use of structural and functional MRI or EEG for the accuracy of the survey brain region affected and that affected functions are good resources for cognitive rehabilitation. The cognitive rehabilitation techniques are very diversified as the use of digital games and activities that stimulate neuropsychological functions. The use of direct electrical current stimulation (tDCS) or of other electrical stimulation techniques can help the patient on rehabilitation of cognitive functions during the postoperative period.

***Keywords**: Traumatic brain injury, cognitive rehabilitation therapy, adults, cognitive scales, well-being, functional status.*
***Trial registration:** This trial will be registered at www.clinicaltrials.gov*

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INTRODUCTION AND REVIEW OF LITERATURE

The main cognitive functions of humans are perception, attention, memory, language and executive function. All these functions are intrinsically linked and require a harmony and cerebral compass to work with balance. When these functions have some decrease resulting from apraxia and agnosia we can say that there are cognitive dysfunction. Cognitive disorders may arise in several ways; such as by a Trauma Brain Injure (TBI), stroke, and psychopathological disorders and neuropathology. Cognitive dysfunction may also be taken on some surgical procedures and anesthetic events. This specific Cognitive dysfunction is called postoperative cognitive dysfunction (POCD) (1,2). The (POCD), can occur from days to weeks after surgery and eventually remain at life. Most of these cognitive changes are temporary with resolution in between six weeks and six months after the procedure, which ultimately minimizing medical attention on the importance of transitory cognitive deficits on the quality of life of the patient. Even if transient, this perioperative adverse event can delay the patient's recovery and, when long-term, compromise the patient's return to their activities (3,4).

According to Monk et al., a significant number of elders undergoing surgery with general anesthesia have cognitive dysfunction in the postoperative period, transient and reversible manner, but in some cases, dysfunctions become chronic (5). The POCD comprises from subtle disorders in any of areas of cognition, even disabling disorders such as delirium and dementia. The etiology of POCD is multifactorial and the risk factors are not well defined (6).

The incidence of POCD is of difficult precision, however is well defined that patient age is a risk factor for worsening of the condition. It is estimated in scientific studies that patients over the age of 65 years have POCD up to 10% after 3 months of surgical event (7).

Technological and pharmacological advances of recent decades have contributed to increasing safety and reducing surgical mortality. Beside the age, several factors have been studied and related to POCD, such as, the physical condition, family history, drug use and alcohol, quality of life, education. Among the risk factors involved are the pre- operative (age, education, previous diseases), intraoperative (number of emboli, duration of procedure, blood pressure, temperature) and postoperative (temperature, procedure of recovery). One of the risk factors currently much investigated is the type of anesthesia as well as its depth. There seems to be no causative relationship between general anesthesia and long-term POCD. However, regional anesthesia may decrease mortality and the incidence of POCD early after surgery (8).

The population age is a risk factor less challenged for pre-operative cognitive decline, while still cause unwarranted. Progressive atherosclerosis linked to silent cardiovascular disease and factors intrinsically related to embolization seem to be the most acceptable explanation for the POCD associated with the elderly. Elderly are predisposed to vascular changes and the cerebral blood flow auto regulation, must also have an abnormal response to drugs and a natural reduction in the cognitive level, which, combined with a small cognitive impairment postoperatively, may result in a significant impact on quality of life (9). Understanding the factors related to the surgical treatment of the elderly is a challenge to medical staff. These patients have a decrease in functional reserves of various organs and systems and, tolerate very little requirements posed by surgical stress. Some factors are related to decreased autonomic homeostatic capacity, impaired immune function and decreased aerobic capacity (10).

Another pre-operative factor that should be mentioned in the pathogenesis of POCD is the educational level. Not fully know is how a higher level of education implies a cognitive reserve, but a hypothesis that would explain this association is based on the fact that education increases the synaptic density in the neocortex, increasing the neuronal communication and minimizing the signs of cognitive impairment (11,12). History of comorbidities such as diabetes mellitus, hypertension and chronic renal failure, are preoperative factors, are also related to impaired neurological outcomes in postoperative (13).

In addition a large number of factors may predict the risk of POCD, genetic factors contribute for occurrence of these events. The literature is insufficient in this kind of studies about this risk factor, but is well know that among the possible genetic polymorphisms with risk factors for POCD is the presence of the ε4 allele of the apolipoprotein E (Apo-ε4) (14). This polymorphism is recognized and well established as a risk factor for Alzheimer's disease and related neurodegenerative disorders, affecting mainly the areas of concentration, memory and language. Some researches, cited by Rasmussen et al., refer to a possible role of genetic factors involved in the pathogenesis of postoperative cognitive changes and the presence of the allele 4 of apolipoprotein-ε (15).

Aggravation of pre-existing injuries; cognitive dysfunction; cause of neurological impairment may be the identification of a susceptible genotype developing POCD as well as a plasma biomarker can allow early intervention preoperative preventing impairment of cognitive functions. Evaluation of plasma biomarkers of brain damage, NSE and S100β also produce studies with little significant results. NSE is generally considered a marker of cerebral injury while S100β is a glial marker (16). In studies of biomarkers and POCD, have been observed that contents of NSE and S100β increase over time post-surgery, suggesting a preoperative inflammatory response. Some studies reveal that the most appropriate time for blood collection for NSE is 36 hours after surgery, in which occurs the maximum concentration of S100β and NSE protein, showing that there is a negative correlation between the early increase in NSE and cognitive dysfunction (17).

The intraoperative risk factors, such as the formation of emboli, whose genesis would be the atheroma of the aortic wall; aggregated platelets, air bubbles originating from the oxygenator and/or heart chambers, may be the primary cause of brain injury or aggravation of pre-existing injuries. These are subdivided into micro and macro emboli, the first more relevant to emergence of POCD. The duration of the surgery is also associated with increased micro vascular obstruction pistons, which suggests a relationship between these factors and the development of cognitive dysfunction. The mean arterial pressure during the surgical procedure is also hypothesized cognitive dysfunction, intraoperative blood pressure and hence cerebral hypo perfusion a potential cause of neurological impairment. Another factor that may contribute to neurological lesions is the hyperglycemia, especially in cardiac surgery, and the effect of temperature during surgery (18).

Therefore, with the knowledge of risk factors, it is possible to predict those individuals who have a higher chance of developing POCD and thus provide protective mechanisms, reducing sequels and avoiding the installation of irreversible brain damage. The postoperative cognitive dysfunction is common after the first week or the first few months after a surgery. There is

a need for post-operative evaluation of cognitive functions, however it is very important to preoperative evaluation to the knowledge of how the patient is before the surgical event and that a comparison of cognitive functioning of this person can be made before and after surgery. POCD is more common after cardiac surgery and the risk for POCD increases with age, type of operation, and duration of anesthesia. Knowing how to prevent POCD is very important, however few studies are conducted on prevention (19). Neuroprotection therapy aims minimizing the activation of toxic processes and to increase the endogenous mechanisms of protection. Some medications that increase the risk for cognitive dysfunction are anticholinergics, benzodiazepines, sedatives, antidepressants and antiparkinsonism (20).

Studies on the possible damage after surgery in general anesthesia are necessary, especially when planning a surgery and the type of anesthesia (21). There are no claims about which would be the best anesthetics for general anesthesia and neither anesthetic, which cause less damage to brain after a surgical anesthetic event. However it is believed that the anesthetic Sevoflurane is best drug when associated with cognitive performance after surgery compared to the short- term recovery, especially when compared to the anesthetic (22). Anesthesia is not the primary factor for POCD, though few, there are ongoing studies looking for evidence on all the risk factors involved in a surgical procedure (23).

The anti-inflammatory administration before surgical procedures can attenuate postoperative pain, fatigue, nausea and vomiting, speeding patient recovery, offering the opportunity return to daily activities in a short time. In consequence of the improvement in the quality of life of patients after intake of anti-inflammatory drugs to relieve pain, vomiting and postoperative recovery period, probably anti-inflammatory drugs can also reduce cognitive dysfunction. But there is a need for studies on the correlation or association of improved quality of life of patients in the postoperative period and consequent improvement in cognitive functions because of ingestion of anti-inflammatory (24).

DISCUSSION

This review enables investigate which risk factors trigger this commitment and what higher cortical functions may be affected. Corticosteroids, acting in controlling the speed of protein synthesis, prevent anti-inflammatory and immunosuppressive action, can prevent or suppress inflammatory processes of various kinds and, if administered in the preoperative period, will cause the patient has benefits for your recovery period, easing the unpleasant symptoms during the convalescent period (25).

Studies show that anesthetic drugs affect cognition, at least temporarily. Starting from the assumption that the patient is unconscious, without a sense of what is happening to him during the surgical process and so amnesiac, the brain is a target organ for possible neurological changes and many of these changes are characterized by cognitive decline and mental confusion after anesthesia. There is - growing evidence that for long periods or even permanent neurological occur and neuronal changes resulting from the anesthetic administration (26). There are studies that raise the possibility that anesthetic drugs and also the depth of anesthesia may favor the occurrence of cognitive dysfunction post-surgery. But there are still few studies which have specifically studied these factors as potential risk for the development of POCD, but the authors of this research are an invitation to other researchers to conduct studies on anesthetic drugs and convinced anesthetic depth that anesthesia techniques and types of anesthetics specific used in surgery can contribute to the recovery of the patient in shorter time in the post-operative period (27), or studies that combined studies types of anesthetic techniques should also be performed, such as acupuncture and anesthetic drugs (28).

Monitoring of anesthesia depth might reduce cognitive impairment after non-cardiac surgery severe in older people. The literature show us that the control undergoing general anesthesia under surgery can be, although few studies have specifically investigated the effect of bispectral Index (BIS) monitoring, to reduce the incidence of POCD(29,30). The maintenance hypothesis of anesthesia depth at an optimum range can optimize neuroprotection and limit neurotoxicity (31).

Elderly patients or with low educational levels tend to have higher cognitive impairment after surgery, however there is a large difficulty in assessing these patients with conventional neuropsychological tests. Some studies suggest that different cut-off points are required for Standard tests when used with these populations (32,33). But how can we rehabilitate a patient presenting POCD? There are some methods currently used to help the reestablishment of the cognitive functions. Currently, medical treatment resources and/or psychoeducational are commonly used for the treatment of diseases that impair cognitive functions that lead executive in operating losses, attentional, motivational and emotional.

Due to the diversity and of the extensive battery of neuropsychological tests for the diagnosis Cognitive dysfunction is usually difficult to achieve. However, with

a neuropsychological postoperative evaluation it is possible to make a neuropsychological postoperative rehabilitation protocol (7,34).

A valuable resource for the evaluation of POCD is Magnetic resonance imaging (MRI), which can obtain accurate measurements on the structure and functioning of the brain that the neuropsychological tests cannot obtain. The cognitive decline after surgery is common in elderly patients who are subject to various other cognitive risks, including progressive dementia, vascular insults, and not specific impact of aging; it is also difficult to conceive an appropriate control to surgery. It is also believed that patients with cognitive reserve a smaller than expected for the age, that is to say to submit a prior cognitive decline surgery, may have a greater impairment of a patient having a better cognitive before surgery (35).

The transcranial direct current electrical stimulation (tDCS) can promote the recovery of patients in postoperative period. Studies show good results as to the intervention on depressive symptoms, bipolar disorder and stroke. The tDCS is a technique that rearranges brain structure and function through stimulation for a neuroplasticity. Neuroplasticity, which is the dynamic structural and functional reorganization of central nervous system connectivity due to environmental and internal demands, is recognized, as a major physiological basis for adaption of cognition, and behavior, and of utmost importance thus is normal brain function. Pathological Alterations of plasticity are increasingly explored the pathophysiological foundation of diverse neurological and psychiatric diseases. Non-invasive brain stimulation techniques, for instance, (NIBS), repetitive transcranial such as magnetic stimulation (rTMS) and transcranial direct current stimulation (tDCS), are able to induce and modulate neuroplasticity in humans. Therefore, they have potential to alter pathological plasticity on the one hand, and foster physiological plasticity on the other, in neuropsychiatric diseases to reduce Symptoms, and Enhance rehabilitation (36). Among these still little known therapies, but with promising findings, we find the transcranial direct current stimulation (tDCS), one capable of stimulating the human brain with some technical advantages, being painless and noninvasive (37). The tDCS neuromodulation consists of simple and less expensive technique, being capable of inducing changes in the motor cortex excitability up to one hour after the end of stimulation. These changes depend on the polarity of the electric current being applied and the stimulus duration. The anodic current polarity is responsible for increasing cortical excitability, while the cathodic polarity is liable for adverse effects suppressing cortical excitability. Lasting brain plasticity processes depend on changes taking place directly in synaptic strength and result in anatomical changes; the function of the tDCS is to change this synaptic strength (38).

The effect of tDCS has been observed in neuropsychiatric disease, promoting improvements to the motor, behavioral and emotional areas. Neuroplasticity is a physiological property of the Central Nervous System (CNS) that allows the brain to adapt to different stimuli and is intrinsically linked to learning processes. This plasticity enables the individual with a neurological or psychiatric commitment to reorganize neurologically some functional capabilities, and displays previously lost skills, for example, motor and cognitive rehabilitation for people who have been affected by Cerebral Vascular Accident (CVA) or Postoperative Cognitive Dysfunction (POCD) (39). Knowing the neuroplasticity, the beneficial effect of tDCS and possible cognitive impairment after cardiac surgery, could the stimulation by tDCS reduce the incidence of POCD in patients undergoing non-cardiac surgery under general anesthesia? The neuromodulation via tDCS is being widely used and several studies are being conducted with this technique for psychiatric disorders, pain, and depression, motor disorders. Studies on the prevention or the possibility of rehabilitating impaired cognitive functions after a surgical event is to be hypothesized (40,41). Probably the tDCS can better cognitive function, once they reach areas of the brain responsible for mood and also the functions memory, attention and executive.

Another technique widely used for the rehabilitation of cognitive functions is neurofeedback. This technique consists of training that allows normalize brain changes of a cognitive dysfunction, causing the areas of the cortex receive and transmit electrical discharges, which are the bases of communication between neurons. Patients with POCD can benefit from the stimulus and neurofeedback can rehabilitate the impaired functions such as long-term memory, working memory, attention and executive functions. The neurofeedback and biofeedback can also be used for psychiatric disorders, pain control and neurological problems and the use in the postoperative period of several surgeries (42).

The use of activities and games, which stimulate the impaired, the cognitive functions are methods that are now widely used by clinical neuropsychologists. Much is currently known about the neural plasticity and how the human brain can be changed through mental stimulation, physical and new learning and that effects received by games via the virtual world have the same effect on the human brain (43,44).

Study revealed a volumetric increase in brain areas in a group of players through the MRI technique from the effect of the video games. The increase in gray matter was noted in specific areas of the right hippocampal formation, the right dorsolateral prefrontal cortex and the cerebellum bilateral (45). These brain areas are directly linked to neuropsychological functions responsible for planning seeks strategies for solving problems, body coordination command, visuospatial and memory formation, then it is the rehabilitation possibility when using the games. On the other words, the games might be tools for treating patients with mental health problems, making changes in brain regions that are directly compromised by pathologies such as schizophrenia, Stress Disorder Post-traumatic or degenerative diseases such as Alzheimer and Parkinson (46).

There are several studies and research centers analyzing the property of video games for the stimulation of cognitive functions. Researchers at the University of California have created a game that can especially help elderly to perform several tasks simultaneously (44). Researchers suggest that such games may be offered as a complementary treatment for depression, anxiety and stress, however the implementation of this therapeutic resource can have its drawbacks and be as addictive as drugs and true drugs. So digital games such as video games bring many benefits, but we have to evaluate the conditions of use and for what purpose these tools will be used (47). The use of digital game as a tool for neuropsychological rehabilitation in patients with neurological diseases has contributed to the holistic treatment of person committed, when the video games or digital games are allied to psychotherapeutic treatment, cognitive skills can be enhanced (48).

CONCLUSION

In conclusion, the main objective of this review was to show the incidence of POCD, what possible methods to assess cognitive function before and after a surgical anesthetic event, and the importance of studying on possible resources for neuropsychological rehabilitation in addition to research on the possibility of further studies with existing techniques for rehabilitation, but not yet consecrated.

Conflict of interest and financial disclosure

The authors followed the International Committee or Journal of Medical Journals Editors (ICMJE) form for disclosure of potential conflicts of interest. All listed authors concur with the submission of the manuscript, the final version has been approved by all authors. The authors have no financial or personal conflicts of interest.

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