Immersing Patients in a Virtual Reality Environment for Brain Mapping During Awake Surgery: Safety Study

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IMMERSING PATIENTS IN A VIRTUAL REALITY ENVIRONMENT FOR BRAIN MAPPING DURING AWAKE SURGERY. SAFETY STUDY

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ABSTRACT

Objective: Brain mapping by direct electrical stimulation (DES) during awake craniotomy is now a standard procedure which reduces the risk of permanent neurologic deficits. Virtual reality technology (VR) immerses the patient in a virtually controlled, interactive world, offering a unique opportunity to develop innovative tasks for peroperative mapping of complex cognitive functions. The objective of this prospective monocentric study was to evaluate the tolerance and safety of a virtual reality headset (VRH) and immersive virtual experiences in patients undergoing awake craniotomy and brain mapping by DES.

Methods: Thirty patients with a brain tumour near the language area were included. Language mapping was performed with a naming task, DO 80, presented on a digital tablet then in 2D and 3D through a VRH. During the wound closure, different VR experiences were proposed to the patient, offering different types of virtual motion or interaction with an avatar piloted by a neuropsychologist.

Results: Two patients could not use the VRH due to technical issues. No procedure was aborted, no patient experienced “VR sickness”, and all would ultimately repeat the procedure. Despite a high rate of intraoperative focal seizures, there is no argument for attributing it to VRH use.

Conclusions: We showed that it is possible, during awake brain surgery, to immerse the patient in a virtual environment and to interact with the patient, opening the field of new brain mapping procedures for complex cognitive functions.

INTRODUCTION

Brain mapping by direct electrical stimulation (DES) during awake craniotomy is now a standard procedure in adults and children, reducing the risk of permanent neurologic deficits and increasing the extent of resection of tumours [1] or the success of epilepsy surgery.

The procedure has been well documented. Briefly, it is possible to temporarily inactivate regions of the brain using DES, while patients perform neuropsychological tasks. If a patient shows decreased performance in a given task, the neurosurgeon will not remove these regions, so as to maintain brain function. Language networks are currently mapped in the dominant hemisphere [2].

Compared to language mapping, few attempts have been published concerning other cognitive functions, such as frontal executive function [3], or right hemisphere cognitive functions [4,5], such as visuo-spatial and social cognition [4–13]. This is due to the difficulties involved in adapting classic bedside neuropsychological tasks to awake surgery conditions.

Taking these limitations into account, we started to explore the use of virtual reality (VR) during awake craniotomy with the patient wearing a virtual reality headset (VRH). VR is a domain with growing applications in the field of neuroscience. This computer technology generates realistic images, sounds and other sensations that simulate a user's physical presence in a virtual or imaginary environment. A person using VRH is able to "look around" the artificial world, to move around in it and interact with virtual features or items. As such, VRH offers a unique opportunity to develop innovative tasks for perioperative mapping of complex cognitive functions. Since 2014, we have developed different approaches with different types of headsets and software. The first application developed was for avoiding postoperative hemianopsia and unilateral neglect [9].

After this pilot study, at the request of the regulation authorities [Agence nationale de sécurité du médicament et des produits de santé (ANSM)], we performed a safety study on the use of a VRH during awake craniotomy and DES of the brain. Indeed, VR can induce motion sickness (known as cybersickness or virtual reality sickness) [14,15] and the hazard of induced seizure, as for all screen video games, is an issue to explore [16,17].

Here, we present the results of a study that evaluated the tolerance and safety of a VRH and immersive experiences in patients undergoing awake craniotomy and brain mapping by DES. Advantages, limitations, and future applications of a VRH for perioperative mapping of visuo-spatial and social cognitions are discussed.

PATIENTS AND METHODS

Study design

This is a single centre, prospective, open label study. The study protocol was evaluated and approved by the ANSM, the ethics committee of the institution and the CNIL. All patients signed a written informed consent form before inclusion in the study. This study is registered in the ClinicalTrials.gov base: NCT03010943.

The inclusion criteria were: patients > 18 years old, hospitalized for a brain tumour near the language area (determined by a neuropsychological evaluation and a resting state functional MRI), in the left or right hemisphere, who gave written informed consent.

Exclusion criteria were all contraindications to awake surgery (cognitive impairment related or not related to the surgical lesion, aphasia, morbid anxiety).

Materials

This study was performed using a Samsung Gear VHR combined with a Samsung S7 smartphone (android platform), and headphones. This equipment is wireless (smartphone battery). The VRH has a visual field of 96°, an interpupillary distance of 55 ~ 71 mm, the latency is < 20 ms, a refresh rate of 60 Hz and the focus is adjustable. The VRH has a presence sensor and allows the tracking of the head orientation by accelerometer, gyroscope and geomagnetic sensor.

For this study, two applications have been developed. The first one is based on a 3D motor (Unity 3D software), to present 2D or 3D objects in stereoscopy. The second one is an interface allowing the VRH to communicate with a PC through a Bluetooth connection, from which the tasks can be selected.

The picture-naming task, DO 80, was duplicated in the VRH in two versions. The first one, in two dimensions, includes the same images as the classical naming task DO 80 presented with a digital tablet (an image with the sentence in French “this is…”), in a virtual empty open space. The second version includes the same items, but in stereoscopy (three dimensions), rotating in a virtual empty space (Fig.1). The images are always orientated in function according to the head position.

Other VR play experiences with headphones were proposed at the end of the tumour resection, during the closure time (Fig.2):

Zen parade (designed by Kevin Mack, http://www.shapespacevr.com/zen-parade.html), a three dimensional animated world of moving living sculptures; *Fractal fantasy* (designed by Julius Horsthuis, http://www.julius-horsthuis.com/vr-projects#), a virtual fractal world with visually induced illusions of self-motion; *Ocean Rift* (Picselica Ltd, https://www.oculus.com/experiences/rift/1253785157981619/), a virtual safari allowing the user to explore an underwater world full of life including dolphins, sharks, turtles; a social VR application vTime® (https://vtime.net/), allowing interactions in a virtual location with an avatar piloted by the neuropsychologist who also wore a VRH, under the control of a physician who participated in the meeting and controlled the scene on a smartphone connected to the app. These VR experiences are available in the Oculus store, although the authors provided us with improved versions. All these experiences offer a different type of virtual motion (motion around the virtual environment, passive motion of the patient himself/herself, active motion of the patient piloted by a game controller, motion of an avatar piloted by a game controller).

Operative procedure

A preoperative neuropsychological evaluation and an imagery (including anatomical MRI, diffusion tensor imaging and resting state functional MRI) were performed. After patients had signed the informed consent form, they were trained with the VRH in the surgical position. They performed the DO 80 image test in VR conditions, and were asked to choose or classify their favourite VR play experiences.

During awake craniotomy, sedation was performed using target-controlled infusion of remifentanil and propofol, and ventilation was controlled using a laryngeal mask airway (LMA). Patients were positioned in a supine or lateral position, according to the location of the tumour, with a rigid pin fixation of the head in a Mayfield frame. The scalp incision and the pin sites of the Mayfield head holder were infiltrated with diluted ropivacaine. Local anaesthetic blocks were also performed on the supraorbital, temporal, retroauricular and occipital nerves. Once the craniotomy, guided by neuronavigation (Brain Lab), was completed and the dura was opened, all sedative drugs were stopped, and the patient progressively awakened. The LMA was removed when the patient was awake. Electroencephalography signals were recorded using a 4-plot subdural electrode (4-channel Eclipse neurovascular workstation, Medtronic XOMED, INC.), placed directly adjacent but not over the area being mapped.

The first language mapping was performed by the neuropsychologist, with a naming task DO 80 presented on a digital tablet. The mapping was completed as previously described [18]. DES was applied with a bipolar electrode (tip-to-tip distance: 5 mm) delivering a biphasic current (parameters: 60 Hz, 1 ms pulse width, current amplitude from 1 to 10 mA). We conducted DES on the exposed cortical area, stimulating 1 cm^2 at each site. To be recognized as a language site, sites at which interference was identified were meticulously tested at least three times (not consecutively). Eloquent areas were defined by speech arrest, anomia, dysarthria or semantic or phonemic paraphasia and were tagged on the cortex. Then, a second set of mapping was performed, using the VRH, with the two dimensional DO 80 and then with the three dimensional DO 80 (Fig.3). The differences in response were carefully noted and the position of the eloquent area was located on the neuronavigation system.

If necessary, other tasks were used (spontaneous speech production, counting, reading, complex word repetition, pyramid and palm tree tests on a digital tablet, etc.).

If the functional cortex was identified, a minimum margin of 1 cm was respected during the resection. After tumour debulking, the resection was continued during spontaneous speech, as necessary, with subcortical electro-stimulation. At the end of resection, another mapping was completed when necessary, using the DO 80 on the digital tablet, the 2D DO 80 and the 3D DO 80 with the VRH in succession.

At the end of the resection during the closure time, the patient was invited to visualize VR play experiences (Fig. 3). At this time, antalgic titration with oxycodone was performed if necessary.

Heart rate, blood pressure, and the EEG signal were continuously recorded during the procedure. Any drug administration different to the predefined protocol was noted. Tolerance was also assessed using a questionnaire filled out by the patient, the anaesthetist, the neuropsychologist and the neurosurgeon.

Postoperative management included 4 h of observation in the post-anaesthetic care unit. Questionnaires about their feelings when wearing a VRH and watching VR images had to be completed by patients after the first VRH sessions and 48 h after surgery.

RESULTS

Thirty patients were included, 18 men and 12 women, with a median age of 45 (from 23 to 75). Among them, two patients were included twice, having a second surgery for recurrence. Patients were initially hospitalized for seizures (n=16, including 4 with status epilepticus), motor or speech deficits (n=4), cognitive deficits (n=2), headaches (n=2). For six patients, the tumor was discovered through the monitoring of their primary cancer.

Twenty-seven patients were right-handed, three were left-handed. The tumours were in the left hemisphere for 25 patients, in the right for five patients (two right-handed and three left-handed).

The mean tumour diameter was 47 mm. Tumour localization was in the frontal lobe (n=15), parietal lobe (n=9), temporo-parietal junction (n=3), insula (n=2) and temporal lobe (n=1). The lesions were glioblastoma [n=12, including primary glioblastoma (n=9), secondary glioblastoma (n=1) and recurrent glioblastoma (n=2)], anaplastic astrocytoma (n=9, including one recurrent anaplastic astrocytoma), grade 2 oligodendroglioma (n=1), or metastasis (n=8).

Eleven patients had a previous VR experience. During preoperative VR training, four patients declared visual discomfort (three with blurred vision, one with lateral hemianopia). The most chosen VR play experiences were *Ocean Rift* and *Zen Parade.*

During the surgery, the use of the headset was not possible for two patients, one due to a Bluetooth malfunction and one due to the proximity of the head holder. In total, 28 surgical procedures were performed with the VRH.

The mean duration of surgery was 4 h 12 min, the mean duration of the awake phase was 2 h 21 min. The mean intensity used for DES was 3 mA (1 to 8 mA). The mean number of sessions with the VRH was four, with a mean total duration of VRH use per patient at 24 min (from 10 to 37 min). The VR tests were performed at the beginning and at the end of the procedure for 18 patients.

The same eloquent areas were identified regardless of which DO 80 presentation was used (digital tablet, 2D VR or 3D VR). However, we observed for 3 patients that some areas for which the result was not clear using the DO 80 on the digital tablet (hesitation or delay in denomination) were clearly not eloquent when using the VRH. This result is of particular relevance and another study is needed to validate the power of the DO 80 with the VRH relative to the DO 80 on the digital tablet to undoubtedly identify the language eloquent areas.

EEG modifications (after-discharge or spike-and-wave) were observed for 13 patients during the standard brain mapping procedure (without VRH). The same abnormalities persisted during brain mapping + VRH for three of these patients.

Intraoperative seizures (IOSs) occurred for nine of these patients. All were focal seizures, disappearing rapidly after cortical irrigation with iced saline. IOSs occurred in three cases before any DES or VRH use, in five cases during DES of the motor area before VRH use, and in one case during

DES with and without VRH use. IOSs were not associated with a worse outcome. There were no postoperative seizures following the surgeries.

One patient reported a sensation of dry eyes that was known before the surgery and one reported mild nausea (related to the analgesic treatment). On the questionnaire, patients reported grade 1 side effects: anxiety (n=4), tiredness (n=4), discomfort (n=2), and pain (n=1). Despite the discomfort associated with the awake surgery procedure, no patient experienced vertigo or any vegetative signs of “VR sickness”. One patient judged the VR experience as unpleasant, but agreed to repeat it for a second surgery.

VR play sequences were proposed to patients at the end of surgery. Twenty patients agreed to look at the VR play sequences while the wound was being closed. For 12 of these patients, no further analgesia was necessary.

According to the questionnaire completed immediately after the surgery by the neurosurgeon, the anaesthetist, and the neuropsychologist, the use of the VRH was not an issue during the surgery, and all agreed to continue this study.

DISCUSSION

VR is widely explored for neurosurgery, as in all the medical fields, especially for surgical training, or to help the neurosurgeon in the operating room, as an augmented reality [19–22]. Our project, which started in 2014, was to use VR, and especially a VRH, for patients undergoing awake surgery. The goal was to develop new tasks based on a virtual environment, with the aim of exploring complex cognitive functions, such as visuo-spatial and social cognition. The first application developed was for detecting hemianopia and unilateral neglect during DES [9].

Before developing other VR tasks, we needed to confirm the feasibility, tolerance and security of this approach. In order to avoid interfering with the routine procedure of awake craniotomy and language brain mapping, we decided to duplicate the object naming task (DO 80). After a standard task using a digital tablet, the DO 80 was repeated using the VRH, in 2D then in 3D. The object-naming task is simple, allowing us to capture a variety of errors, and is the most commonly used task for language mapping [23].

At the beginning of our experience with VR in the operating room, we used the Oculus VRHs DK1 and DK2 (Oculus, Menlo Park, California), but for our study, we chose the Samsung VR. This VRH is wireless. It is a low-cost, high-quality, customizable device, with a pad control on the side of the headset and, if necessary, a game controller. Its weaknesses is to heat up after a long period of use, and to have an autonomy limited by the phone battery. However, neither of these was an issue or stopped the VRH from being used in the operating room. It was not possible to use the VRH for one patient due to a Bluetooth malfunction, leading us to consider a wired VRH for future developments.

Before the surgery, all the patients were trained easily and the acceptability was good, although 19 of them did not have previous experience with a VRH. Although previous studies have shown that younger hospitalized patients were more willing to participate in an immersive VR experience, the relatively high age (median age of 45) in our study was not a limitation [24]. Focus can be adapted for patients wearing glasses, but this can be an issue, especially with a high correction. Patients suffering from dry eyes could experience some discomfort during extended VR sessions.

In the operating room, it was not possible to position the headset in one case, due to the head holder, and some difficulties arose in five cases. These difficulties were then avoided by taking care of carefully positioning the VRH before the head holder, and before drawing the incision line.

There was no difference for number or localization of eloquent areas, between the digital tablet and the VRH. However, we observed that some areas for which the result was not clear using the digital tablet (hesitation or delay in denomination) were clearly not eloquent areas when using the VRH. The explanation would be a better visualization of the images and isolation from all the disruptive events occurring in the operating room.

“VR sickness”, which is a kind of motion sickness, was a concern before our study, especially in the conditions of an awake surgery (stress, discomfort of the position, emetic medication, etc.). Virtual reality sickness is now well known and has several physiological explanations. The first one is latency [25]. Virtual reality headsets have significantly higher requirements for latency (the time it takes for a change in input to have a visual effect) than ordinary video games. If the system is too slow to react to head movement, it can cause the user to experience virtual reality sickness. In fact, this aspect was minimized as the patient could not move the head, which was held immobilized in a head holder. Another important cause for “VR sickness” is a visual-vestibular-somatosensory conflict [25,26]. This could have been the case for our patients in a lying position viewing a differently orientated virtual world [26]. It could also have been the case with the perception of visually induced illusions of self-motion during the VR play experiences, despite the VR experience with the most impressive self-motion being chosen less frequently by the patients. Nevertheless, no patients experienced “VR sickness" and we did not observe any of the sympathetic nervous activity reported for this syndrome [27–30]. We are convinced that the good tolerance could be due to patient preparation and training.

IOS was an important concern since the convulsion hazard is a classic concern with the use of television, video games and VR experiences. The Samsung VRH manual advises consulting a physician before using the VRH if there is a history of seizures.

EEG modification (after-discharge or spike-and-wave) was observed during the standard brain mapping procedure for 13 patients. After-discharges are defined as two consecutive spikes or sharp waves, distinct from background activity, spontaneous, or within 5 sec of DES termination. They are observed frequently (71% in the literature [31]) and can sometimes result in convulsive seizures. We did not observe a significant modification of the after-discharge threshold or frequency during the procedure.

IOSs were observed in nine patients (30%) during surgery. These were focal seizures, easily stopped by irrigation of the cortex with iced physiological serum. IOSs can interfere with the patient's ability to cooperate throughout the procedure and may affect their outcome. Nevertheless, none of the procedures were aborted, and IOSs were not associated with a worse outcome. IOSs induced by DES of the cortex are not uncommon during awake surgery with a described rate from 3.4% to 31% in the literature [31–35]. It is worth noting that among these nine patients, five had a history of epilepsy and one of status epilepticus. Preoperative seizures or a history of epilepsy were correlated with IOSs, with patients who have preoperative seizures considered to have an increased susceptibility to intraoperative or postoperative seizures. Our perioperative seizure rate is in the upper range but this cannot be explained by the VRH as the seizures occurred for all the patients before its use. Moreover, the mean time period between the preoperative training with the VRH and the surgery was 23 days. The explanation of our IOS rate would be our brain mapping procedure, which always starts with a positive motor stimulation to calibrate the DES intensity. It is well known that the search for a positive motor mapping may increase the likelihood of IOSs. It is worth noting that in our study, none of the patients had a postoperative seizure during hospitalization.

The 20 patients who watched the VR experience described them as pleasant and capable of reducing pain and anxiety. It is now well demonstrated that VR could be effective for control and/or treatment of pain and anxiety [36,37].

Finally, we showed that it is possible, during awake brain surgery, to immerse the patient in a virtual environment and for the patient to interact with it. In particular, we showed that it is possible to interact with an avatar piloted by a neuropsychologist. The description of this VR experience and interactions with an avatar using the social VR platform vTime® has been published elsewhere [38]. There is consistent evidence that avatars are perceived in a similar manner to real human beings and can be used to explore the complex processes of nonverbal language, empathy, and theory of mind [39]. Social cognition, including nonverbal language, empathy, and theory of mind, is explored at the bedside through sets of complex neuropsychological tasks, including story movies, comic strips, or interactive games that depict a short story [12,13]. These tasks take time to be performed, meaning they are not compatible with the brain mapping conditions (DES length less than four seconds, fast response, and no ambiguity in the answer). Progress in VR development is currently promising, and some VRHs even allow facial expressions to be captured and transferred to a virtual avatar in real time, opening a new level of virtual human interaction. VR has the potential to combine the naturalness of everyday interactions with experimental controls required during brain mapping procedures, opening the field of new brain mapping procedures for complex cognitive functions.

CONCLUSIONS

It is possible to immerse a patient in VR using a VRH during awake brain surgery with brain mapping using DES. We did not observe VRH-induced IOSs, or VR sickness. The rapid progress in VR technology and the almost infinite possibilities to develop innovative neuropsychological tasks motivate us to continue this research work. Work is currently underway on virtual experiences dedicated to testing social cognition during awake surgery.

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DISCLOSURES

The authors report no conflict of interest concerning the materials and methods used in this study or the findings specified in this paper.

ABBREVIATION LIST

ANSM, Agence nationale de sécurité du médicament et des produits de santé; DES, direct electrical stimulation; IOS, intraoperative seizure; LMA, laryngeal mask airway; VR, virtual reality; VRH, virtual reality headset.

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FIGURE LEGENDS

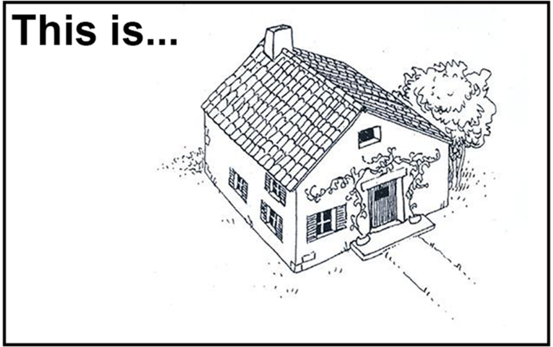
Figure 1: Example of the item « house » on a classical naming task DO 80 presented with a digital tablet, and in 3D presented with the VRH.

Figure 2: VR play experiences : A) Zen parade and Fractal fantasy with the patient wearing the VRH, B) Ocean Rift with the patient using the game controller, C) vTime® with the patient interacting with the neuropsychologist through the avatar in a virtual world.

Figure 3: Cortical mapping using the VRH.

SUPPLEMENTARY MATERIAL

French language questionnaires used to collect the impressions of patients and staff involved in the surgical and VR procedures.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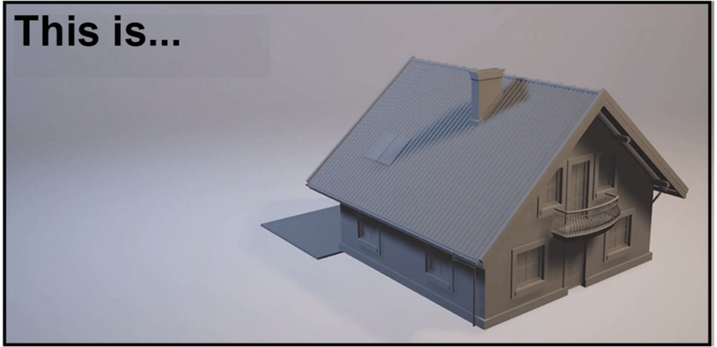
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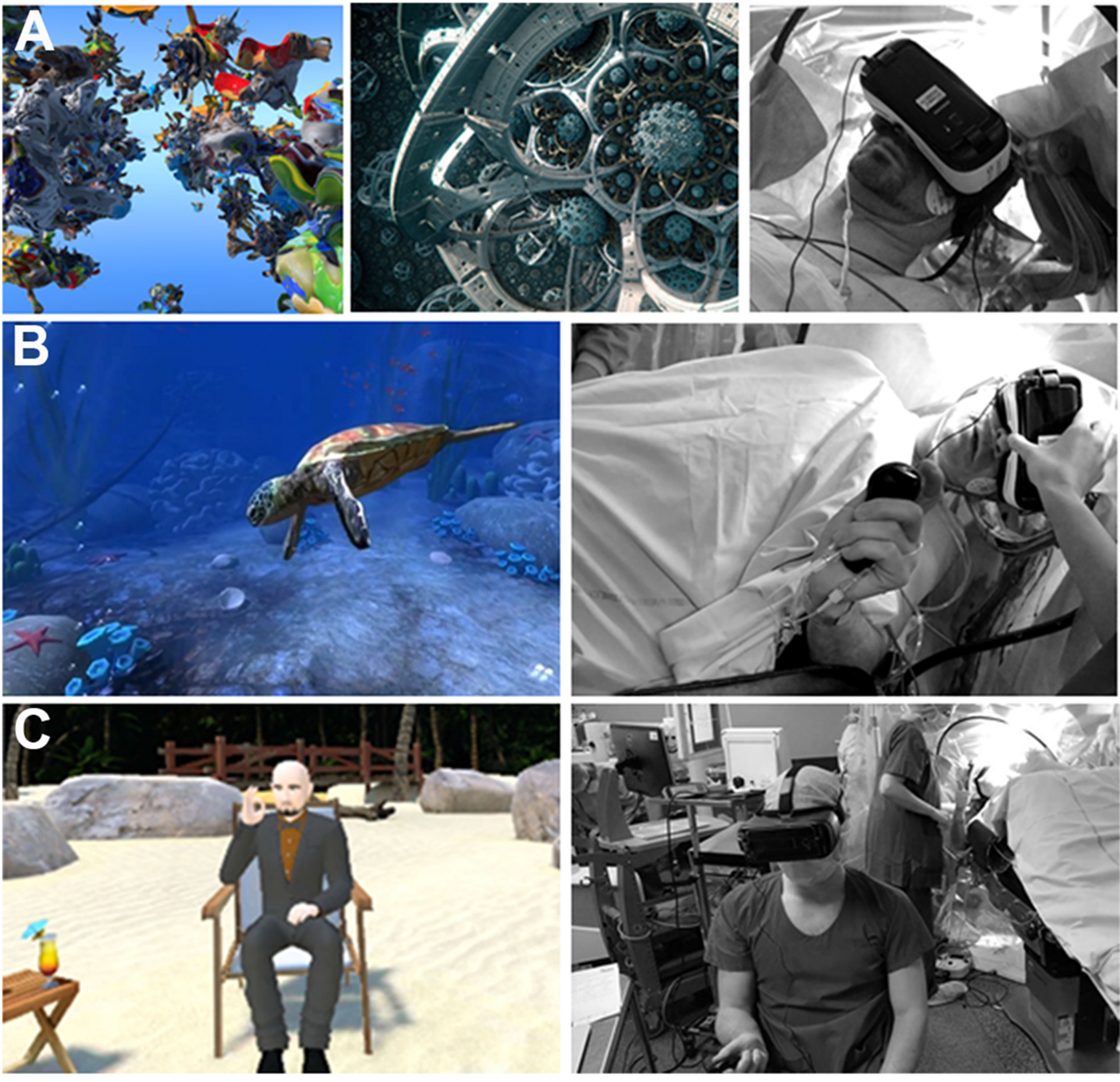

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