VR-based assessment and intervention of cognitive functioning after stroke

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Summary:

Worldwide, stroke affects one out of every six individuals, being associated with physical and cognitive impairments, and leaving a striking footprint on individuals, their families and society. Assessment of acquired deficits and rehabilitation of lost and compromised functions is based typically on exercises that may not replicate the demands of everyday life activities lacking ecological validity. These tests fail at predicting daily functioning and their similarity with daily life activities is far from being sound. Assessing and training cognitive functions under an ecologically oriented approach, i.e. using exercises that replicate instrumental activities of daily living (IADL) seems to be the suitable strategy to follow. Virtual Reality (VR) worlds have been used to simulate IADL for assessment and rehabilitation of acquired cognitive deficits since the late 1990's. This chapter reports and debates existing studies that

support the use of VR in this context. When it comes down to veridicality and verisimilitude, evidences illustrate the opportunity of adopting this strategy that outperforms traditional paper and pencil exercises. A glance through the perspective of a therapist, that has adopted VR for cognitive rehabilitation in patients with stroke is also debated.

Keywords: stroke, Cognitive assessment, Cognitive rehabilitation, Instrumental Activities of Daily Living; Virtual Reality

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Section 1: Cognitive function after stroke.

Stroke is an epidemic disease: one in six people will experience stroke during their lifetime (World Stroke Organization 2020). This health condition is the second leading cause of death for individuals over 60, the fifth's for individuals aged 15 to 59 years (Caprio & Sorond, 2018; Johnson et al. 2016; WSO, 2020), and the third reason of disability worldwide (Caprio & Sorond 2018; Johnson et al. 2016). According to Johnson and colleagues (2016), 70% of stroke and 87% of deaths related to stroke or disability occur in low- and medium-income countries, afflicting individuals at the peak of their productive life.

Stroke leads to sudden death of brain cells due to a lack of oxygen resulting from an interruption of blood flow to the brain. This disruption is caused by obstruction or rupture of a brain artery (Johnson et al. 2016). The updated definition of stroke proposed by the Stroke Council of the American Heart Association/American Stroke Association defines stroke as a result of an acute focal injury to the central nervous system of vascular cause, namely cerebral infarction, intracerebral haemorrhage and subarachnoid haemorrhage. This event, even in asymptomatic patients, is potentially associated with serious consequences, such as cognitive and functional decline (Sacco et al. 2013).

Deficits in cognitive abilities such as attention, memory and executive functioning are among the most frequent problems (Tang 2018), conflicting with quality of life and treatment adherence (Cumming et al. 2013). Executive functions comprise a set of integrated skills that include problem solving, planning, shifting, updating, inhibition, self-monitoring, cognitive flexibility and working memory (De Luca et al. 2016), being crucial for the everyday functioning through the performance of instrumental activities of daily living (IADL) (Sadek et al. 2011). For example, finances, shopping, choosing

clothes to wear, or preparing a meal, etc., are aspects that require proper executive functioning due to its cognitive complexity (Lezak et al. 2012). This means that stroke patients may show compromised ability in participating in meaningful activities and social relationships, affecting daily life activities. Therefore, assessing stroke's impact on cognitive functioning, but also on daily life activities, is essential to define a rehabilitation plan that seeks to improve the functional domains affected and to promote the returning to routines and the autonomy in everyday life activities (Bogdanova et al. 2016).

Compromised performance of IADL (Reppermund et al. 2013) can strongly affect the quality of life of both patients (Stites et al. 2018) and family caregivers (Karg et al. 2018), who are the cornerstone of patients' support, representing increased costs for the health care delivery system (Prince et al. 2015). Hence, solutions designed to assess cognitive functioning and the performance of IADL may have beneficial effects not only for stroke patients, but also for families and society.

Section 2: VR-based neuropsychological assessment

Neuropsychological assessment, while sampling multiple cognitive domains (e.g., attention, memory, and executive functioning), provides countless insight into the neurocognitive, behavioural and emotional functioning (Parsons 2011).

Traditionally, neuropsychological assessment uses paper-and-pencil tests to examine cognitive functions. For example, cancellation tests are typically used to assess attention abilities, whilst the Wechsler Memory Scale is among the most widely used tests for memory assessment (Camara et al. 2000). Executive functioning, in turn, is typically assessed using the Frontal Assessment Battery (Lima et al. 2008). However, research

has provided evidence on the lack of ecological validity of these standard neuropsychological measures (Spooner et al. 2006). In other words, these tests may fail to adequately predict how a person perform IADL, once they do not accurately replicate the complexity and diversity of tasks individuals experience in their real environments (Parsons 2011).

Advanced technology offers a potential solution to the traditional simple and static stimuli presentation, that does not capture the features of the real-world context (Parsons 2015). Virtual reality (VR) is a special case of a technology that can be adopted for computer-based neuropsychological assessment and has been increasingly considered as providing more ecologically valid assessments (Parsons 2011). Virtual environments are easily designed to reproduce aspects of the real world, namely IADL (i.e., shopping, dressing or preparing meals) (Gamito et al. 2016). As such, when compared to traditional tests, VR-based assessment may closely resemble real-life performance, while maintaining rigorous experimental control (Rizzo et al. 2014). Furthermore, computer-based approaches offer a unique set of advantages, including: increased standardization and ease of test administration; increased precision of timing presentation and response latency measurement (Parsons 2011; Cernich et al. 2007); greater ease in scoring and accessing data (Cernich et al. 2007); minimization of floor and ceiling effects; and quantification of a wider range of abilities (Tarnanas et al. 2014).

VR applications that track and monitor behavioural responses while individuals perform IADL have been developed in recent years (Parsons 2015). Research has generally suggested that these VR tools allow for the assessment of cognitive functioning, particularly IADL, in people with different conditions. For example, previous studies have found that the performance in VR tasks predicts the scores in traditional

neuropsychological tests from patients with epilepsy (Grewe et al. 2014), acquired brain injuries (Jovanovski et al. 2012) and even from normative samples (Oliveira et al. 2017). Furthermore, VR IADL tasks seem to be able to discriminate cognitive deficits. One example is the Virtual Kitchen Test, which is a VR IADL test that reflects a real-life activity of food preparation. The results from a sample of patients with cognitive deficits have shown that scores (errors and task execution times) were positively correlated with the performance on traditional neuropsychological tests, being able to differentiate patients from healthy controls (Gamito et al. 2015).

Regarding stroke patients, two studies were found assessing difficulties related to neglect, a common disorder after stroke. Broeren and colleagues (2007) report that using a virtual environment depicting a cancellation task may be useful to assess visual search deficits associated with neglect of stroke patients. These results were aligned with a previous study for neglect (Kim, Kim, Ku et al., 2004). Another study with stroke patients explored the usability and performance in a supermarket test, suggesting differences in patients' performance comparing to healthy controls (Kang, Ku, Han et al., 2008). In addition, performance on a virtual shopping task (VMall) was also poor in post-stroke patients when compared to different healthy groups (Rand, Katz & Weiss, 2007). Taken together these results highlight the potential usability of VR IADL tasks for cognitive assessment in stroke patients. Neuropsychological assessment not only plays a central role in assisting diagnosis but also in providing the guidelines for appropriate therapeutic and personalised rehabilitation plans for patients with cognitive deficits (Parsons 2011).

Section 3: Stroke rehabilitation

Addressing stroke's sequelae requires an interdisciplinary approach with key implications to patients' success considering the medical, surgical, and psychological effects of this diagnosis (Capizzi et al. 2020). Furthermore, the focus should be placed on the individual's functioning level (i.e., ability to perform IADL) rather than on the disease (diagnosis).

WHO defines rehabilitation as a set of interventions designed to optimize functioning and reduce disability in individuals with health conditions in interaction with their environment (WHO 2019). After conducting a scoping review on rehabilitation services, WHO authored 'The rehabilitation in health systems: Guide for action'. This guide set the emphasis of rehabilitation on the impact of health condition on the person's life by primarily focusing on the improving of functioning and on reducing of the experience of disability (WHO, 2019).

Aiming at offering options for rehabilitation that replace traditional paper-and-pencil approach, new interventions, which some are still on an embryony stage, are commonly framed within the following categories (Bogdanova et al. 2016; Dang et al. 2017; Storm & Utesch 2019):

- Hyperbaric Oxygen Therapy (HBOT): This type of treatment describes the inhalation of 100% oxygen under the pressure greater than atmosphere absolute, currently used for neurological diseases due to its therapeutic benefits (inhibition of apoptosis, suppression of inflammation, protection of the integrity of blood-brain barrier, and promotion of angiogenesis and neurogenesis);
- Non-invasive Brain Stimulation: Repetitive transcranial magnetic stimulation characterises a painless, non-invasive, easily operated treatment with few adverse reactions and relevant positive effects in rehabilitation of stroke patients. Modification

of neuronal excitability, by generating excitatory or inhibitory activity according to the frequency used, providing potential benefits in memory deficits, attention impairments and depression symptoms;

- **Limb or Organ Function Reconstruction:** This approach is based on low-frequency pulse current to stimulate limb or organ dysfunction that favours replacement or correction of lost function in limbs and organs, promoting functional reconstruction by adjusting the advanced nerve centre;
- **Behavioral and Emotional Therapies:** Behavioral changes post stroke often include mood disorders (e.g., anger, depression, anxiety) but also physical or verbal aggression. Emotional instability of stroke patients needs to be addressed, otherwise, it may hamper rehabilitation outcomes. Psychological intervention (individual or group modalities) may promote coping skills training with a benefit in emotional regulation, namely in anger/rage management;
- **Mental Practice Interventions:** Frequently used with stroke survivors to improve motor function. Mental practice is supported by the imaginary representation of a motor action or skill – motor imagery by mentally performing an action instead of physically – sparing repetition/training as well as supervision or the resort to equipment.

Although, some of these alternatives to paper-and-pencil assessment are still controversial and under debate (Ding et al. 2014, Smadar et al. 2019, Cramer 2018), the use of computers and VR are being increasingly used in stroke rehabilitation. VR Cognitive Training (VRCT) allows an intuitive training, supported by combined auditive and visual stimulations, that can engage different components of the cognitive apparatus, namely memory, attention and executive functioning. And because VR provides a three-dimensional experience, training IADL in virtual contexts that

resembles real day to day activities is possible. These properties of VR caught the attention of therapists and researchers alike and is going to be further discussed in the next section.

Section 4: VRCT rehabilitation after stroke

All the above-mentioned interventions rest on the underlying assumption of neuroplasticity, meaning that cognitive stimulation can potentially modify brain structure and function in reaction to environmental diversity, an adaptive potential that may promote the ability to learn new skills and behaviours. In fact, studies have provided evidence of neuroplasticity following cognitive interventions with mild cognitive impairment (Belleville et al. 2011). Systematic reviews suggested significant gains in cognitive function through cognitive training, an empirical evidence that has supported the growing interest and development of cognitive-based interventions (Martin et al. 2011).

Within this scope, VRCT has emerged as an alternative to paper-and-pencil exercises. VRCT seems to be a valuable approach offering the following advantages: the adaptation of exercises to specific needs and cognitive status offering personalization of treatment (Coyle et al. 2014); the use of serious games, which can promote individuals' motivation (Kueider et al. 2012) and positively impact mental and physical health (Gamito et al. 2011); the provision of behavioural feedback to the therapist (Gamito et al. 2017); cost-effective, less labor-intensive and easily disseminated solution (Kueider et al. 2012); and ecological validity, once the exercises in virtual environment can be similar to activities of daily living, promoting transfer of learned skills to everyday living (Garcia-Betances et al. 2015; Doniger et al. 2018; Gamito et al. 2019).

Accordingly, VRCT seems to be the only available option when it comes to simulate IADL. The adoption of IADL-based VRCT for cognitive rehabilitation appears to promote the inclusion of functional aspects of cognition while improving generalization of the desired effects via training in these activities. Also, the ability to create standardized treatment plans where repetition and task-specific learning may be easily implemented. Another advantage is related to personalisation of exercises to meet the patients' needs that are specific of each phase of stroke recovery (Ferreira-Brito et al. 2019).

There are diverse virtual reality environments targeting cognitive improvement, but few have adopted a multidomain approach. One example of the former is the Systemic Lisbon Battery (SLB) (Gamito et al. 2016). SLB has been used by these authors for cognitive assessment and rehabilitation in different populations with cognitive deficits (Gamito et al. 2014; Gamito et al. 2014; Oliveira et al. 2017). This battery comprises IADL exercises, such as: a) morning hygiene task (basic cognitive functioning), using the brush teeth and shower; b) wardrobe task (executive functions), to choose clothes; c) shoe rack test (attention), for pairing shoes; d) virtual kitchen task (attention and executive functions), to prepare a cake; e) supermarket and pharmacy tasks (memory and executive functions), for purchases of articles; f) virtual gallery task (attention and executive functions), for observation and identification of details in virtual paintings (for further insights on SLB, please see:

<https://www.youtube.com/watch?v=hW8cqrp3CMs>). Studies with SLB have been suggesting that VR may be an efficient tool to improve cognitive functions in the context of different conditions, namely substance use disorders (Gamito et al. 2014), aging (Gamito et al. 2019; Gamito et al. 2020) and following acquired brain injuries as

traumatic brain injury (Gamito et al. 2011) or stroke (Gamito et al. 2015; Oliveira et al. 2020).

In stroke patients, SLB was the cradle for two studies. In a controlled study on VR vs treatment-as-usual, the results showed significant improvements in memory and attention abilities (Gamito et al. 2015). However, in a recent study, consisting in a brief intervention (approximately of 240 h), improvements on global cognitive functioning were found but not in executive functions or specific cognitive abilities (Oliveira et al. 2020). These results suggest that the use of functional behaviours on activities of daily living, involving different cognitive abilities and demands, are useful to promote cognitive functioning of stroke patients. However, longer rehabilitation plans may be needed in order to provide more consistent enhancements in cognitive and executive functioning.

Complementary contributions of the Systemic Lisbon Battery are discussed in the next section, where the reader can find the testimony of a therapist that has been using SLB for several years in the largest rehabilitation centre in Portugal.

The effectiveness of VRCT among stroke patients was also supported in a recent meta-analysis. Aminov and colleagues (2018), reveal significant small to moderate effect sizes of virtual rehabilitation on patients' cognition. Another recent study (Rogers et al. 2018), comparing computer-based rehabilitation with classical interventions suggested a small overall effect on cognition but did not reveal specific effects related to cognitive rehabilitation approach (i.e., computer-based rehabilitation did not produce higher effects when compared to classical interventions).

A randomized controlled trial (RCT) comparing VR with classical intervention in acute stroke patients suggested similar effects both at the level of attention and memory, but

superior effects of VR for improving daily living performance were found, supporting far transfer effects of this kind of training to overall functionality (Cho & Lee 2019). Overall, these findings suggest that VR may be more effective at producing global improvements in cognition.

However, a further challenge besides demonstrating the efficacy of cognitive rehabilitation approaches is to determine the optimal timing to implement such interventions (Bernhardt et al. 2017). Also, no standardized treatment protocols or clinical guidelines are yet established (Bognadova et al. 2016), which is a significant barrier to the implementation of this approach directed at improving patients' cognition and psychological functioning. Despite the promising results, consistent evidence based on multidomain interventions (Ballesteros et al. 2015) with larger samples (Kueider et al. 2012; Ballesteros et al. 2015) are required to provide more robust empirical support for the efficacy and the mechanisms underlying VRCT interventions.

Section 5: VRCT: a testimony from a therapist

VRCT exercises started at the Alcoitão Rehabilitation Medicine Center (CMRA, <http://cmra.pt/>) in 2009 through the “Casa” program, in the adult stroke and traumatic brain injury of the inpatient population, to provide cognitive stimulation, namely memory and attention. In 2016, SLB was introduced, and the exercises extended to the adult population on an outpatient basis and to adolescents attending the Center's Pediatric Rehabilitation and Development Service. The consultation is carried out frequently by psychologists and, in the outpatient clinic, by physicians. There has been a higher frequency of the adult population, especially those who are hospitalized.

As inclusion criteria, patients need to have a good verbal comprehension and good vision ability. Patients with a significant state of cognitive deterioration, that prevents the normal prosecution of sessions, continue with the traditional rehabilitation approach.

In the inpatient adults there is a previously established protocol of 10 sessions with an increasing level of difficulty. Intervention with the adult population of the outpatient clinic and with adolescents is longer and flexible, with the possibility of having about 20 sessions, while respecting the “base standard” of the first 10. In the case of adolescents, sometimes activities are adapted to the age group, for example, going to the pharmacy can be replaced by another activity where the patients try to remember the brands and colours of the cars and, sometimes, by the execution of memory and attention exercises on the virtual computer that is in the bedroom of the SLB scenario.

To illustrate the sessions, we briefly exemplify the activities of two patients that have used SLB, during their hospitalization following ischemic stroke (see Table 1 and 2).

Table 1: Mr. A., 58 years old, hospitalized, suffered an Ischemic Stroke, 10 sessions.

Cognitive status	SLB performance	Therapeutic intervention
- Slight Anosognosia.	- In the description of the activities, he showed lack of inhibitory control, while being careless with the activities, along with memory difficulties.	- Awareness of the difficulties and alternatives to deal with them (revealed little critical judgement).

- Impairment of executive functions. Lack of cognitive flexibility. Perseveration.	- The patient forgot about shopping at the supermarket and pharmacy but remembered with the use of cues.	- The team talked about the need for supervision in the personal management of Mr. J's treatments.
- Lack of attention, attention dispersion and tendency to error without correction.	- Revealed difficulties in learning less familiar and more complex information.	- The team spoke with the wife about the need to help managing Mr. J.'s personal life, reinforcing the good initiative and availability shown by Mr. J.
- Difficulties in spontaneous information retrieval.	- In replying to specific questions related to the tasks (for instance, what is the door number of the apartment)	- The promotion of tasks related to memory difficulties, while using cues related to the target information for helping memory retrieval.

Table 2: Mr. B., 58 years old, hospitalized, suffered an Ischemic Stroke, 10 sessions.

Cognitive status	SLB performance	Therapeutic intervention
- Expressive aphasia.	- Difficulty in remembering the door number, street name, brand of grocery and	- The new tasks were introduced gradually.

pharmacy products (he remembered better with visual stimuli).		
- Generalized cognitive impairment.	- Slowness in carrying out activities, especially those that involved alternating attention.	- The use of non-verbal communication was reinforced.
- Slight difficulties in spontaneous information retrieval, especially verbal information.	- Anxious and worried about not doing the activities properly.	- These difficulties and Mr. B.'s awareness about these difficulties were discussed with the team.
- Low self-esteem and self-confidence.		
- Lack of cognitive flexibility.	- Difficulties in set shifting between tasks, for instance by having difficulties in choosing clothes from the wardrobe according to different criteria.	- Providing exercises based on set shifting ability of increasing difficulty.

In these sessions it was observed positive aspects associated with SLB and some negative that may give rise to some reflection in order to improve the program and the

hardware. These aspects are common to many other sessions that we have had with other patients.

A first positive aspect is the fact that this scenario is closer to reality, allowing one to try to relate the tasks performed in SLB with the day to day. For example, we found that Mr. A. is a rash person and little care for managing his money, while Mr. B. is more careful and has a good sense of prices, being also methodical with regard to the ingredients needed for cooking and careful when choosing the drugs at the pharmacy.

Another positive aspect of the program relates to its non-verbal characteristics, allowing the patient to put into practice non-verbal thinking, more concrete and effective for carrying out daily activities. This is an important aspect of SLB in the sense that it allowed creating, throughout the sessions, a parallelism with real life, by talking to the participants, watching them during hospitalization and talking to family members and the rehabilitation team.

When comparing SLB with the most traditional assessment and cognitive stimulation tests, namely Montreal Cognitive Assessment and Weschler Memory Scale, we found that this battery, being closer to reality and less verbal, is quite suitable for people with aphasia, making it possible to show more clearly the real abilities and difficulties of these people. This was particularly evident with Mr. B., who showed difficulties in participating in these more verbal and abstract tests.

SLB also proved to be both a playful and therapeutic tool, reinforcing the motivation and the ability to fantasize (they were often enthusiastic about good cars) and allowing, unlike other tests, to have an immediate answer about performance.

The difficulties were mainly related to hardware interaction, because due to neurological injuries, hemiparesis in Mr. A. and Mr. B., they revealed motor difficulties

in the use of the mouse, especially Mr. B. who was not familiar to technologies. It should be noted that these motor limitations and respective difficulties in the practical use of the program have been a constant in the population of CMRA, which were overcome with motivation and with the help from therapists in using the mouse.

Finally, it is important to emphasize that SLB has been an important instrument of mediation of the therapeutic relationship, which makes it possible to play and be more comfortable with people and at the same time to access their psychological characteristics.

VRCT with SLB allows the therapist to have an immediate feedback about the abilities and difficulties encountered, permitting to find compensatory strategies, together with the patient, with the people close to him/her and with the rehabilitation team.

As previously mentioned, VR has a good ecological validity, as it is close to the reality of everyday life and uses many non-verbal tasks, being an important aspect in the cognitive rehabilitation of people with aphasia. Some authors (Gamito et al. 2014; Larson et al. 2014; Oliveira et al. 2014; Oliveira et al. 2017; Rosa et al. 2017) had made reference to these important characteristics, an aspect that has been frequently demonstrated in clinical practice at CMRA.

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