A novel virtual reality approach for functional lateralization in healthy adults

Beata Sokolowska *

Bioinformatics Laboratory, Mossakowski Medical Research Centre Polish Academy of Sciences, Warsaw, Poland

A R T I C L E   I N F O

Keywords:
Functional lateralization
Virtual reality
Handedness
Footedness
Posturography

A B S T R A C T

Functional lateralization relates to a natural asymmetry in the dominance right or left body side, and is a fundamental principle of the brain. The hemispheres of the brain control the contralateral body side, and show subtle, yet striking, anatomical asymmetries and functional lateralization. Innovative technologies, including Virtual Reality (VR), are entering the areas of experimental research, modeling and simulation related to the study of lateralization, with new perspectives of different applications in modern medical practice. Researchers/clinicians note that there are fewer VR studies with healthy participants, and which are important in evaluating/interpreting clinical outcomes, and testing the usefulness, limitations, and sensitivity of VR. The presented influence of the domination of upper/lower limbs on the performance of VR exercises was studied in healthy right-handed adults. Virtual testing sessions were performed independently with both/dominant/non-dominant hands, and the similar VR sessions were conducted on a Wii Balance Board (WBB) with the choice of body side, at different levels of the difficulty. The obtained results are consistent with other studies which show that cognitive-motor training in VR with the WBB platform is a very sensitive and promising tool for recognizing/assessing functional asymmetries of the right-left body side not only in disturbed lateralization, but also in the test training of healthy subjects.

1. Introduction

Functional lateralization relates to a natural asymmetry in the dominance right or left body side (Serrien and Sovijarvi-Sap, 2015; Cochet, 2016; Alqadah et al., 2018; Afonso et al., 2020) in terms of brain lateralization such as its structure, function or behavior (Toga and Thompson, 2003; Westerhausen et al., 2014; Allen et al., 2021), for instance as handedness and footedness, or other sensory laterality preferences such as eyedness, earedness (Alqadah et al., 2018; Germann et al., 2019; Harrison et al., 2021).

Functional lateralization is a fundamental principle of the human brain (Gazzaniga and Sperry, 1967; Geschwind and Levitsky, 1968; Harrison, 2015). The human brain is divided into left and right hemispheres, connected by a large bundle of nerve fibers called the corpus callosum, and after surgical complete transection of it the separation of the hemispheres is observed in split-brain studies (Gazzaniga, 1995; de Haan et al., 2020). The hemispheres of the brain control the contralateral side of the body, and show subtle, yet striking, anatomical asymmetries and functional lateralization. Nevertheless, the comprehensive taxonomy of structural/functional laterality and its organization in the brain, as well as the mechanisms that underlie the establishment of these hemispheric specializations, and their physiological/behavioral implications, remain largely unknown (Duboc et al., 2015). Lots of evidences suggesting that a similar pattern of brain lateralization occurs in all vertebrates, humans included, have allowed the emergence of different model systems (e.g. model organisms as rodents, mice, chickens, Zebrafish, Caenorhabditis elegans or Drosophila) to investigate the development/function of brain asymmetries and their impact on behavior (Rogers, 2017, 2019; Alqadah et al., 2018). Handedness is a better, faster, and more precise performance or individual preference for using the hand, known as the dominant hand (Cashmore et al., 2008; Ocklenburg et al., 2013) that can be partially explained by molecular mechanisms establishing the right–left asymmetry early during embryological development (Brandler et al., 2013). Footedness is a natural preference of one’s left or right foot for various purposes, and is also with regard to handedness (Barut et al., 2007; Muraleedharan et al., 2020). Noticeable the ubiquitous presence of neuronal, sensory, motor, and postural asymmetries across several different species strongly...
suggested that asymmetry represents an evolutionary advantage (Corballis, 2009; Stancher et al., 2018). Some studies have found that functional asymmetry can influence training effects and sport performance (Davids and Araújo, 2010; Radzak et al., 2017; Bishop et al., 2018). The different models of lateralization have been proposed (Porac and Coren, 1981; Sainburg, 2014; Rogers, 2019). The basic, considered as the norm in human, are two unilateral models: (a) a right-sided laterality model (prevailing in the human population); and (b) a left-sided model (Bartolomeo and Thiebaut de Schotten, 2016) or after amputation of one (Bogdanowicz, 1992; Annett, 2009; Papadatou-Pastou et al., 2020).

Homogeneous right-sided lateralization indicates the dominance of the right hand, right leg and right eye on the left body side; and (d) an unsteady/undefined model (in general for hand, leg or eye). In addition, other functional lateralization models have been defined, that are less advantageous/favorable than one-sided dominance, such as: (c) a crossed model (denotes the domination of the hand, leg and eye on different body sides); and (d) an unsteady/undefined model (in general the dominance cannot be determined for hand, leg or eye).

In approximately 75–90% of the human population across many cultures prefers to use the right hand to achieve a wide number of tasks involving various levels of dexterity, and about 80% is right footed, at least in the adult population (Corbetta et al., 2006; Muraliedharan et al., 2020). Control of hands is contralateral, such that the right hand is under left hemisphere control and the left hand is under right hemisphere control. In particular, language is lateralized in the left hemisphere in 87–96% of the human population; however, not all people are right-handed, as one might assume (Khedr et al., 2002). It is important to know however, that no function is 100% lateralized, and instead are characterized by greater involvement of one hemisphere but also involving participation of the other. Lateralization is a progressive process that develops gradually with age (Duboc et al., 2015) to include neuromotor development (Derakhshan, 2009; Coddard Blythe, 2017). In some diseases the lateralization can be disturbed (Kathiriya and Sri, 2012) or after brain damage (Oertel-Knochel et al., 2012; Ocklenburg, 2012), in mental diseases, such as schizophrenia (Oertel-Knochel et al., 2012; Ocklenburg et al., 2015), in depressive disorders (Bruder et al., 2017), in children with autism (Floris et al., 2016), in split-brain patients (D’Alberto et al., 2017), in stroke (Buchmann and Randerath, 2017), in tumors (Tozaki et al., 2019), in pain (Allen et al., 2021), and after brain damage (Bartolomeo and Thiebaut de Schotten, 2016) or after amputation of limb(s) (Taylor et al., 2007).

Various methods are used to assess lateralization both in health (Hebbal and Mysorekar, 2006; Utesch et al., 2016; Yang et al., 2020) and in disease (Buchmann and Randerath, 2017; Cameron et al., 2017; Paquet et al., 2017). Note that new innovative medical technologies of the 21st century (Sandri et al., 2018; Scataglini and Paul, 2019; Gogia, 2019), especially those using of virtual reality methods (Li et al., 2017; Stanica et al., 2020; Wittkopf et al., 2020; Rathinam, 2021; Trost et al., 2021) are entering the areas of experimental research, modeling and simulation related to the study of lateralization, with new perspectives of various applications in diagnostics, therapy, (neuro)rehabilitation, and (home) healthcare (Baheux et al., 2007; Buxbaum et al., 2012; Dieguez and Lopez, 2016; Floegel and Kell, 2017; Triandafilou et al., 2018; Arlati et al., 2019; Manuweera et al., 2019; Pawlowski, 2019; Schaffer and Sainburg, 2021). These studies proposed novel and creative solutions and clinical or experimental approaches using VR. Nevertheless, researchers and clinicians note that there are fewer virtual reality studies with healthy participants, and which are important in evaluating and interpreting clinical outcomes, and testing the usefulness, limitations, or sensitivity of various VR systems, procedures and protocols.

The aim of the research was to assess and analyze functional motor laterization with the use of virtual reality methods and algorithms offered by the innovative computer system of (neuro)rehabilitation of NEUROFORMA in twenty-five right-handed healthy adults (as illustrated in Fig. 1). The proposed virtual test training sessions were performed with both hands, dominant and non-dominant one, independently, and similar VR sessions were conducted on a Wii Balance Board (WBB, posturographic platform) with a choice of body side, at different levels of difficulty such as easy, medium and high difficulty.

2. Results

Table 1 presents the results of virtual sessions during which the BALLS and BUTTERFLY exercises were performed with both hands, the dominant and non-dominant one, independently. Table 2 shows the results of same sessions carried out on the WBB platform for the full range of motion and right or left swings of the exercising persons, reacting to the appearing objects in virtual reality environment of the NEUROFORMA system. The training program was conducted for these exercises first at easy level, and then at subsequent levels of increasing difficulty.

2.1. VR exercises for hands

The virtual BALLS exercises for upper limbs, i.e. pointing the proper
Table 1. The results of VR exercises for hands and different levels of difficulty.

| Hands   | Easy level       | Medium level | Difficult level | P<sup>Δ</sup> |
|---------|------------------|--------------|-----------------|--------------|
| **BALLS exercises** |                  |              |                 |              |
| Both    | 100.0 ± 0.0      | 99.86 ± 0.36 | 98.43 ± 1.55    | NS           |
| Dominant| 100.0 ± 0.0      | 98.93 ± 1.49 | 96.79 ± 1.87<sup>★</sup> | <0.003<sup>★★</sup> MD |
| Non-dominant | 100.0 ± 0.0    | 98.36 ± 2.34 | 93.21 ± 3.53<sup>★</sup> | <0.003<sup>★★</sup> MD |
| **BUTTERFLY exercises** |                  |              |                 |              |
| Both    | 99.67 ± 0.58     | 99.52 ± 1.08 | 95.81 ± 2.36    | <0.001       |
| Dominant| 99.24 ± 1.00<sup>★</sup> | 97.29 ± 4.40<sup>★</sup> | 93.43 ± 2.26<sup>★</sup> | <0.001       |
| Non-dominant | 98.29 ± 1.71    | 95.43 ± 2.52<sup>★</sup> | 90.14 ± 4.63<sup>★</sup> | <0.001       |

Notes: *P < 0.003, **P < 0.001, ***P < 0.0001 dominant or non-dominant versus both hands; *P < 0.003, **P < 0.001, ***P < 0.0001, dominant versus non-dominant hands; symbol of A denotes P for comparison among the different levels: easy versus medium (EM), easy versus difficult (ED) and medium versus difficult (MD). The symbol of NS denotes not statistically significant.

Table 2. The results of VR exercises on the posturographic platform for different ranges of motion and difficulty levels.

| Motion range | Easy level       | Medium level | Difficult level | P<sup>Δ</sup> |
|--------------|------------------|--------------|-----------------|--------------|
| **BALLS exercises on the platform** |                  |              |                 |              |
| Full        | 100.0 ± 0.0      | 98.43 ± 2.10 | 93.71 ± 4.07<sup>★</sup> | <0.001<sup>★★</sup> MD |
| Right       | 99.71 ± 0.73     | 97.00 ± 2.04<sup>★</sup> | 90.07 ± 6.45<sup>★★★★</sup> | <0.003        |
| Left        | 99.57 ± 1.09     | 95.57 ± 2.01<sup>★</sup> | 87.50 ± 7.25<sup>★★★★</sup> | <0.003        |
| **BUTTERFLY exercises on the platform** |                  |              |                 |              |
| Full        | 99.52 ± 0.60     | 97.29 ± 1.65 | 93.76 ± 2.62<sup>★</sup> | <0.001       |
| Right       | 98.38 ± 1.47<sup>★</sup> | 95.33 ± 2.01<sup>★</sup> | 90.71 ± 1.87<sup>★</sup> | <0.001       |
| Left        | 97.14 ± 2.31<sup>★</sup> | 93.05 ± 2.16<sup>★</sup> | 87.19 ± 5.30<sup>★★★★</sup> | <0.001       |

Notes: *P < 0.003, **P < 0.001, ***P < 0.0001 right or left versus full ranges; *P < 0.003, **P < 0.001, ***P < 0.0001 right versus left sides; symbol of A denotes P for comparison among the different levels: easy versus medium (EM), easy versus difficult (ED) and medium versus difficult (MD).

Overall, the VR results, as expected, were better when exercising with both hands and were lower for one hand. Significantly lower scores were observed in the case of exercises performed with the non-dominant hand at the medium and difficult levels. Furthermore, following the butterfly’s trajectory was a more sensitive exercise in recognizing the dominant hand.

2.2. VR exercises on posturographic platform

Participants also performed the same BALLS and BUTTERFLY sessions on the WBB platform by controlling their posture to move a crosshair on the monitor screen (Table 2). The BALLS exercises had more higher scores than BUTTERFLY ones. At the easy level, the results did not depend on the range of movement. Nevertheless, a tendency to get lower scores were observed for the left range of motion. The lowest average score was obtained for the BALLS at the high advanced level in the left range, i.e. 87.5 ± 7.2, and was statistically significant compared to the easy level of difficulty, i.e. 99.6 ± 1.1 (P = 0.001). The BUTTERFLY exercises required constantly following the butterfly on the screen through body swings while standing on the WBB platform, which was quit a challenge compared to the exercises using hands. The differences in scores between the right and left side were greater and statistically significance both at the easy (98.4 ± 1.5 versus 97.1 ± 2.3, P = 0.000098), medium (95.3 ± 2.0 versus 93.0 ± 2.2, P = 0.000099) and difficult level (90.7 ± 4.4 versus 87.2 ± 5.3, P = 0.00006).

Overall, as expected, better results were achieved for the full motion range to control the crosshair’s movement, and lower scores were obtained for the one-sided ranges. Significantly lower results were observed for left-sided deflections and they were statistically significantly in comparison with the right-side ones. The impact of emerging distractors was minimal as the task was relatively simple for a healthy person. At the difficulty level, right-side tasks were more effective/correct than left ones. Similar to manual sessions, the results suggest that following the butterfly’s trajectory is a more sensitive exercise in identifying the dominant body side, and revealing functional asymmetries of postural control.

2.3. Scoring distributions of VR exercises

The obtained results showed that VR exercises enable the assessment of differences of functional lateralization regarding the body side. The tested exercises resemble an interactive computer game. Achieving good results in the training program allows to advance to a higher level in the next round of the exercise. According to a computer algorithm of performance, an each task which was performed perfectly without any errors gave maximum score of 100 (100%), and scores in range of 95–100 were defined as a very good execution and always allow to move to the next level of the exercise. Similar, subsequent scores in 90–95 range testify to good performance and also allowed for promotion in the next round. But scores below 90 usually did not allow to advance to the next exercise level. This situation was often motivated to achieve better results for progress during the training sessions. The distributions of scores of the BALL and BUTTERFLY exercises taking into account the promotion/progress factor are shown in Figs. 2 and 3, respectively.

Note that the virtual BALLS are interesting cognitive tasks that engage the participant emotionally, and also do not require the same physical effort as constantly following the BUTTERFLY during the training sessions. This was reflected in the BALLS scoring, so significant differences between hands were only seen at the difficulty level of the exercise (Fig. 2A). In addition, the posturographic sessions were more difficult than hand (manual) ones. Thus, the posturographic BALLS showed not only lower left-field scores (mean 87.5 ± 7.2), but also 50% of the tasks did not promoted at the difficult level (Fig. 2B). The results indicated that the BUTTERFLY is an excellent exercise for comparing the functional asymmetries of body side (Fig. 3). It was observed that in exercises by the non-dominant upper limb, the promotion decreased faster (33.3% of exercises) than in the case of the dominant one (only 14.3%). This situation was even more pronounced of the lower limbs (47.6% versus 28.6% of the left and right range, respectively). These
differences between the left and right side of the body were statistically significant.

In summary, this two-step VR testing analysis is an interesting and motivating factor that also influences on participant performance. The final grade concerns the result from the exercise rounds and the possibility of advancement to the next level in the next round, when multi-round sessions of selected exercises are implemented in testing/examination program. In this study, three-round sessions were conducted at three different levels of difficulty for the each test exercise of the training program.

3. Discussion

As mentioned in the introduction, the implementation of new innovative technologies is a dynamically developing direction in the field of neuroscience (e.g. neurobiology, neuropsychology or neuro(bio)informatics) research and (bio)medical and health applications, but the attention of scientists and clinicians is primarily focused on understanding and comparing the clinical effects between classical and novel approaches (Worthen-Chaudhari, 2015; Pourmand et al., 2017; Juras et al., 2019; Riva et al., 2019; Zajac-Lamparska et al., 2019; Santos et al., 2020; Fallon et al., 2021), much less research have been devoted to studying the influence of these technologies on healthy people, which can also help create new directions for the development and applications of VR (Virk and McConville, 2006; Llorens et al., 2016; Sokołowska and Sokołowska, 2019). An important research premise is the need to determine the feasibility of VR-based protocols and associated user training for both patient groups and healthy controls (not only for comparison purposes, but also to define safe health limits of proposed VR applications). Likewise, a systematic review of 20 studies by Juras and colleagues (Juras et al., 2019) outlines various standards used in balance training programs in neurological practice, and comparing VR interventions between conventional rehabilitation and no intervention exhibited the better results. For instance, in clinical study using VR technology, Stryla and Banas (Stryla and Banas, 2016) reported that over 69% of cerebrovascular incidents resulted in limiting of motor functions of the upper limb on the side opposite to the cerebral hemisphere in which the damage occurred. Paresis of the upper limb

Fig. 2. The scoring distributions of very good (95–100), good (90–95) and no-sufficient (<90) performance to promotion on an higher level of exercises. Left panel shows the results of both, dominant and non-dominant hands of the virtual BALLS for easy, medium and difficult tasks; and right panel shows the results of full, right and left ranges of the virtual posturographic BALLS for easy, medium and difficult tasks (and P level of statistically significance of the observed differences in the selected ranges).
especially dominant side) greatly impedes or prevents performing the activities of daily living, and significantly reduces the quality of life. Hence, the main tasks in rehabilitation of the patients is to maximize the restoration of functional efficiency of the paretic upper limb. In the study, a 6-week rehabilitation program was carried out in a medical centre, containing kinesiotherapy, physical therapy, therapeutic massage and 10 h of exercises in the VR NEUROFORMA environment, divided into therapy sessions. The non-paretic hand was treated as a basis for comparison in relation to the paretic one. The NEUROFORMA is an innovative hybrid VR tele-platform with serious games and interactive workout for exercising as well as motor and cognitive functions, and balance control. The authors presented positive effects of physiotherapy in the virtual environment on motor re-education and improvement of upper limb function and reported that VR sessions were attractive and motivating for participants. Additionally, it should be noted that the innovative modern technology can be support for qualitative assessments as test methods. For example, this approach is presented by Buxbaum’s team (Buxbaum et al., 2012). The authors reported that hemispatial neglect is a disabling disease of arousal, perception and action which is recognized in approximately 40–50% of right-hemisphere stroke patients and a lower proportion of left-hemisphere stroke ones. Patients with neglect are impaired in the detection of objects, individuals, and events on the contralesional side of space. The researchers also pointed out the neglect is often diagnosed on a basis of pencil-and-paper tasks requiring the cancellation or bisection of lines or other stimuli, but this classic test, may not be sensitive enough to detect subtle deficits. Accordingly, the investigators proposed a new Virtual Reality Lateralized Attention Test (VRLAT), as travelling along a virtual, non-branched path in six task levels, either by using a joystick for a participant-driven option, or by passively observing the environment while an examiner navigates the path for an examiner-driven option. Participants were asked to identify virtual objects on both sides of the path and to avoid colliding with the objects. The collisions were signaled by auditory feedback and corresponding to obstructed progress. The VRLAT has three array forms: simple, complex and enhanced. Results of the study demonstrated that the Virtual Reality Lateralized Attention Fig. 3. The scoring distribution of very good (95–100), good (90–95) and no-sufficient (<90) performance to advance on an higher level of exercises. Left panel shows the results of both, dominant and non-dominant hands of the virtual BUTTERFLY for easy, medium and difficult tasks; and right panel shows the results of full, right and left ranges of the virtual posturographic BUTTERFLY for easy, medium and difficult levels (and P level of statistically significance of the observed differences in the selected ranges).
Test is a sensitive, valid, and reliable measure of hemispatial neglect and even better than classical clinic tests; research continues. Therefore, the authors concluded that the VR-LAT version with examiner-driven option may be useful assessment tool in research and clinical trials evaluating response to treatment or natural regenerative functions in the patient care. Similarly, the systematic review of 63 studies by Cogne’s group (Cogne et al., 2017) presented the contribution of virtual reality to the diagnosis of spatial navigation diseases and to the study of the role of navigational aids. The authors indicated that spatial navigation plays important integrative role in linking functions in the field of neurophysiology and neuropsychology such as learning, memory and cognition. The authors suggested that unlike classic clinical tests such as the pencil-and-paper test, virtual reality is useful to assess large-scale navigation strategies in patients with brain trauma or schizophrenia, also in the context of normal or pathological ageing, and dementia (e.g. Alzheimer-type dementia). Moreover, the review of many research showed that there is no ‘gold standard’ for the use of VR settings and procedures in medical practice or in daily activities of patients, nevertheless positive and beneficial effects are documented in numerous studies, but further research is still needed. It would also be useful for researchers/clinicians to recognize which types of VR tests and games, and which training devices may be of greater value to different subjects/patient groups. Llorens et al. (2016) demonstrated that the WBB-based posturography system is a very sensitivity in identifying stroke patients compared to healthy controls and noted the feasibility of the system as a clinical tool for assessing balance and postural control. Present research have explored the use and importance of VR in the effective recognition and testing of human functional lateralization in healthy conditions. The aim of the study was to assess the functional motor and postural control asymmetries (functional lateralization) by performing various tasks in the virtual reality environment, and additionally using the Wii Balance Board (WBB) platform. Healthy right-handed adults (80% of them were right-footed) completed an hour testing program with the NEUROFORMA system; the similar system was handed adults (80% of them were right-footed) completed an hour testing program with the NEUROFORMA system. The presented research have explored the use and importance of VR in the effective recognition and testing of human functional lateralization in healthy conditions. The aim of the study was to assess the functional motor and postural control asymmetries (functional lateralization) by performing various tasks in the virtual reality environment, and additionally using the Wii Balance Board (WBB) platform. Healthy right-handed adults (80% of them were right-footed) completed an hour testing program with the NEUROFORMA system; the similar system was applied in the upper limb rehabilitation of stroke patients in the Styla and Banas’ study and our previous research (Styla and Banas, 2016; Sokolowska and Sokolowska, 2019). The proposed virtual task sessions can help identify and assess the functional differences between the dominant and non-dominant side of the body. The best differentiation was observed at the advanced level of difficulty of the BUTTERFLY exercises. In the case of performing butterfly tasks with both hands the obtained mean score was very good (95.8 ± 2.4); with the right hand the score was only slightly lower (93.4 ± 3.4), although no promotion occurred in 14.3% of the exercises; and with left hand the score was already a significantly lower (90.1 ± 4.7) and no promotion increased to 33.3%. These results were statistically significant (P < 0.0001). In the case of virtual sessions on the WBB platform the differences among right-left postural deflections were pronounced. The performance level of the BUTTERFLY exercises in full range of motion with a crosshair (a posturographic marker on the monitor screen) which following the butterfly’s trajectory gave mean score 93.8 ± 2.6 and 9.5% no promotion. The performance of the exercises in the right-side field gave a lower score 90.7 ± 4 and 28.6% no promotion, while in the left-side field was observed the lowest score, i.e. 87.2 ± 5.5, and no progress in 47.6% of the tasks. These right-left differences were statistically significant (P = 0.00006). Note that in the training rehabilitation, the goal of the BUTTERFLY exercise is to improve hand-eye coordination and reaction speed, increase the muscle strength and range of limb motion, and better balance control. The presented results are consistent with other studies, which show that such the novel approach as cognitive-motor tasks/training in VR using the WBB platform are a sensitive tool for recognizing and assessing the functional differentiation/asymmetries of the right and left side of the body. Moreover, in the case upper/lower limbs taking into account the exercises for the dominant and non-dominant limbs additionally allows for a quantitative assessment and monitoring of their functionality.

Overall, this study demonstrate that: (a) performing virtual tasks by both hands is similar to the dominant hand, with a tendency to use the dominant one more often (this was especially noticeable at the advanced level of difficulty); (b) when the task requires some physical effort, fatigue is felt earlier and more clearly in the non-dominant hand; (c) similar tasks using the WBB-based posturography platform also are related to functional asymmetries of postural control, and better results of dominant body side were observed; (d) VR tasks are more willingly performed and motivated to achieve better results and progress in action by including various cognitive elements. In addition, it is important to emphasize the significant role played by research with the participation of healthy people, who are not only control groups (or the norm), but also an inspiration for the development of new directions of VR technology, including the discovering and testing of human capabilities with the determination of general safe limits for health and life related to VR applications.

4. Conclusions
In general, new virtual reality technologies are universal systems that can generally be used to study and evaluate performance/effectiveness of various human systems in health and disease. VR systems can constantly adapt to the capabilities and limitations of the practitioners. Inclusion of exercises with interesting cognitive elements additionally engages emotionally and motivates to continue the virtual tasks undertaken.

The presented research is part of the research area on the use of virtual reality as test tools assessing executive functions. It shows how to quantify test tasks, as well as how to increase the precision and credibility of the test itself in such an innovative approach, in a safe and attractive way for the participant.

This study particularly indicates the usefulness and effectiveness of virtual reality methods as a tool for the researching and assessment of functional lateralization. It shows which of the proposed test exercises turned out to be the most effective in such an assessment. It proposes a new analytical approach, taking into account the fact of creating virtual reality in the form of an interactive serious computer game. There are relatively few studies using VR as a method to quantify cognitive and/or motor functions compared to studies on the effects of VR in therapy and rehabilitation. This is partly due to the lack of developed standards for using the VR. Each area of VR applications still requires deeper and broader research, because there is no full knowledge of their potential possibilities, usefulness and limitations.

5. Methods and materials
5.1. Participants
Twenty-five healthy adults (13 women and 12 men), aged 31 ± 8 years (min−max 18–44), height 1.71 ± 0.7 m (min−max 1.55–1.89), weight 69 ± 14 kg (min−max 50–89) and BMI 23.3 ± 3.8 kg/m² (min−max 17–31) participated in this study. The dominant body side of motor skills was determined for each person based on: (1) an interview about their physical and professional active (participants declared: (a) no current and past health problems, likewise no disability; (b) daily exercise and/or recreational sports (jogging) to keep fit; (c) have studied or worked in various professions); (2) Violetta Florkiewicz’s lateralization test questionnaire/the test tool with picture cards (it is the illustrated test to examining the hand, eye, ear, leg preferences in various everyday situations [Florkiewicz, 2016]); and on (3) simple physical trials similar to those shown in the test questionnaire. All subjects were right-handed, 20 participants were right-footed and others had mutual dominance of lower limbs. They performed exercises with the virtual reality NEUROFORMA system using a posturographic platform of Wii Balance Board (WBB), as illustrated in Fig. 1. The WBB is portable force platform that enables users to interact with (video) games through
control of postural movement. After an initial phase of exercises and learning tasks in this system, the subjects practiced at least twice the virtual test training program for both hands, right (dominant) and left (non-dominant) hand, and the same exercises were performed in the full, right and left motion ranges on the WBB platform (in random order for each subject). In our laboratory, the NEUROFORMA computer system is a research tool in our studies (see also the next Section 5.2. Virtual Reality training sessions). Written informed consents were obtained from all participants.

5.2. Virtual reality training sessions

Training sessions were created using the NEUROFORMA system from Titanis Ltd, which is a specialized innovative system for hybrid (tele) functional motor-cognitive rehabilitation in virtual reality and dynamic feedback that indicates whether the exercise was done correctly (Fig. 1). The participants stood in front of the screen with a 3D-Kinect camera, saw own mirror image among VR objects (e.g. a butterfly, balls), and their task was to catch, evade, track and hit those visualizations.

The virtual exercise program was consisted of two modules, the first on the upper limbs (hands) and the second on balance control using the force platform, with the same three one-minute rounds of training sessions including the cognitive BALLS and motor BUTTERFLY exercises. The participants completed tasks for both, right and left body sides, at three different levels of difficulty: easy (denoted “easy”), average (“medium”) and high advanced (“difficult”). The virtual test lasted on average 60 min.

In the BALLS exercise, it was necessary to knock down colored balls, according to the rule displayed in a frame on the monitor screen. At higher difficulty levels, the task time was shorter and the number of balls were increased. The subjects received points every second for each correctly thrown ball. The BUTTERFLY exercise was following a butterfly’s trajectory, which was unpredictable and chaotic. There were also various distracters, i.e. distracting elements, which moved like the butterfly. The butterfly’s speed and trajectory varied with the difficulty level. The participants received points for every second in which they managed to keep the hand or crosshair (i.e. “posturographic marker”) on the moving butterfly.

5.3. Statistical analysis

The statistical analysis was performed using the STATISTICA 9.0 PL statistical package software. The distribution of variables was non-normal, as stated by the Shapiro-Wilk test. The Friedman (ANOVA) test (P < 0.05) with Wilcoxon as a post hoc test with Bonferroni correction (P < 0.003 was considered statistically significant) was used to compare the results for the different difficult levels of VR exercises of each range and also between different ranges. The χ2 test was applied to analyze of scoring distributions of VR exercises (Figs. 2 and 3). The data are expressed as mean and standard deviation.

Declaration of Competing Interest

The author declares that there are no known competing financial interests or personal relationships that could have influenced the work reported in this paper.

Acknowledgements

The study was carried out using the computational infrastructure of the Biocentrum-Ochota project (POIG.02.03.00-00-0030/09) and the NEUROFORMA’s virtual software of Titanis’ technologies. The investigation was realized as part of own scientific project on “Research of the Movement System using the Augmented and Virtual Reality”.

The author would like to thank Senior Professor Bogdan Lesnyg, Dr. Ewa Sokolowska and Dr. Teresa Sadura-Sieklucka for inspiration and motivation to undertake the presented research.

Founding

This research did not receive any specific grant from funding agencies in the public, commercial, or not-for-profit sectors.

References

Alonso, J., Besa, C., Pinto, F., Ribeiro, D., Moura, B., Rocha, T., Vinicius, M., Canario-Lozano, M., Prieto, R., Clemente, F.M., 2020. Asymmetry as a Foundational and Functional Requirement in Human Movement. From Daily Activities to Sports Performance. Springer Nature Singapore Pte Ltd. DOI:10.1007/978-981-15-2549-0.

Agosta, S., Magagna, D., Galante, E., Ferraro, F., Magherini, A., Di Giacopo, R., Micilì, G., Battelli, L., 2020. Lateralized cognitive functions in Parkinson’s patients: a behavioral approach for the early detection of sustained attention deficits. Brain Res. 1726, 146486. https://doi.org/10.1016/j.brainres.2019.146486.

Allen, H.N., Bohmar, H.J., Kolber, B.J., 2021. Left and right hemispheric lateralization of the amygdala in pain. Prog. Neurobiol. 196, 101891. https://doi.org/10.1016/j. pgeb.2020.101891.

Alqadah, A., Hsieh, Y.W., Morrissey, Z.D., Chuan, C.F., 2018. Asymmetric development of the nervous system. Dev. Dyn. 247, 124–137. https://doi.org/10.1002/dvdy.24595.

Annett, M., 2009. Patterns of hand preference for pairs of actions and the classification of handedness. Br. J. Psychol. 100, 491–500. https://doi.org/10.1348/ 000712608X357867.

Arlati, S., Colombo, V., Spoladore, D., Greco, L., Pedrosi, E., Serino, S., Cipresso, P., Goulene, K., Stramba-Badiale, M., Riva, G., Gaggioli, A., Fieringno, G., Sacco, M., 2019. A social virtual reality-based application for the physical and cognitive training of the elderly at home. Sensors (Basel) 19, 261–277. https://doi. org/10.3390/s19010261.

Babekh, K., Yoshizawa, M., Yoshida, Y., 2007. Simulating hemispatial neglect with virtual reality. J. Neuroeng. Rehabil. 4, 27–32. https://doi.org/10.1186/1743-0003- 4-27.

Bartolomeo, P., Thiebaud de Schotten, M., 2016. Let thy brain know what thy right brain doeth: inter-hemispheric compensation of functional deficits after brain damage. Neuropsychologia 93, 407–412. https://doi.org/10.1016/j. neuropsychologia.2016.06.016.

Barut, C., Ozer, C.M., Sevinc, O., Guvem, M., Yenstein, Z., 2007. Relationships between hand and foot preferences. Int. J. Neurosci. 117, 177–185. https://doi.org/10.1080/ 0020745900682013.

Berrettz, G., Wolf, O.T., Güntürkün, O., Ocklenburg, S., 2020. Atypical lateralization in neurodevelopmental and psychiatric disorders: what is the role of stress? Cortex 125, 215–232. https://doi.org/10.1016/j.cortex.2019.12.019.

Bishop, C., Turner, A., Read, P., 2018. Effects of inter-limb asymmetry on physical and sports performance: a systematic review. J. Sports Sci. 36, 1135–1144. https://doi.org/10.1016/j. british.2017.06.001.

Bogdanowicz, M., 1992. Left-Handedness in Children. WSiP Publisher, Warsaw (in Polish).

Brandler, W.M., Morris, A.P., Evans, D.M., Scerri, T.S., Kemp, J.P., Timpson, N.J., Stahl, D., Conley, A., Cooper, J., Sorg, O., 2017. Postnatal asymmetry of the amygdala in pain. Prog. Neurobiol. 93, 407–412. https://doi.org/10.1016/j. progneurol.2017.04.021.

Buchmann, I., Ziek, M., 2017. Assessment of postural sway at a given level of affect. J. Neurosci. 37, 123–130. https://doi.org/10.1523/jneurosci.2753-16.2017.

Buchanan, J., Randerath, J., 2017. Selection and application of familiar and novel tools in patients with left and right hemispheric stroke: psychometrics and normative data. Cortex 94, 49–62. https://doi.org/10.1016/j. cortex.2017.06.001.

Buxbaum, L.J., Dawson, A.M., Lindsey, D., 2012. Reliability and validity of the Virtual Reality Lateralized Attention Test in assessing hemispatial neglect in right-hemisphere stroke. Cortex 48, 440–411. https://doi.org/10.1016/j. cortex.2012.08.003.

Cameron, J.R., Megaw, R.D., Tatham, A.J., McGrory, S., MacGillivray, T.J., Doulab, F.N., Wardlaw, J.M., Trucco, E., Chandran, S., Dhillon, B., 2017. Lateralized thinking - interocular symmetry and asymmetry in neurovascular patterning, in health and disease. Prog. Retin. Eye Res. 59, 131–157. https://doi.org/10.1016/j. prethera.2017.04.003.

Cashmore, L., Uomini, N., Chapelain, A., 2008. The evolution of handedness in humans and great apes: a review and current issues. J. Anthropol. Sci. 86, 7–35.

Catanu, A., Apostu, A.P., 2017. The determination factors of left-right asymmetry disorders - a short review. Chujul. Med. 90, 139–146. https://doi.org/10.15286/ cjmed-701.

Cochet, H., 2016. Manual asymmetries and hemispheric specialization: Insight from developmental studies. Neuropsychologia 93, 335–341. https://doi.org/10.1016/j. neuropsychologia.2015.12.019.

Coddard Blythe, S., 2017. Attention, Balance and Coordination: The A.B.C. of Learning Success. Online ISBN:9781119116474 © 2017 John Wiley & Sons Ltd, Second Edition. DOI:10.1002/9781119116474.
home therapy after stroke. J. Neuroeng. Rehabil. 15, 88–100. https://doi.org/10.1186/s12984-018-0429-0.

Tront, Z., France, C., Anam, M., Shum, C., 2021. Virtual reality approaches to pain: toward a state of the science. Pain 162, 325–331. https://doi.org/10.1097/j.
pain.0000000000002060.

Utesch, T., Mentzel, S.V., Strauss, B., Büsch, D., 2016. Chapter 4 - measurement of laterality and its relevance for sports. In: Loffing, F., Hagemann, N., Strauss, B., MacMahon, C. (Eds.), Laterality in Sports. Theories and Applications. Elsevier Academic Press, pp. 65–86. https://doi.org/10.1016/b978-0-12-801426-4.00004-3.

Virk, S., McConville, K.M., 2006. Virtual reality applications in improving postural control and minimizing falls. Conf. Proc. IEEE Eng. Med. Biol. Soc. 2006, 2694–2697. https://doi.org/10.1109/EMBS.2006.260751.

Westerhausen, R., Kompus, K., Hugdahl, K., 2014. Mapping hemispheric symmetries, relative asymmetries, and absolute asymmetries underlying the auditory laterality effect. Neuroimage 84, 962–970. https://doi.org/10.1016/j.
neuroimage.2013.09.074.

Wittkopf, P.G., Lloyd, D.M., Coe, O., Yacoobali, S., Billington, J., 2020. The effect of interactive virtual reality on pain perception: a systematic review of clinical studies. Disabil. Rehabil. 42, 3722–3733. https://doi.org/10.1080/
09638288.2019.1610893.

Worthen-Chaudhari, L., 2015. Effectiveness, usability, and cost-benefit of a virtual reality-based telerehabilitation program for balance recovery after stroke: a randomized controlled trial. Arch. Phys. Med. Rehabil. 96, 418–425. https://doi.org/10.1016/j.
apmr.2014.10.019.

Yang, L.Z., Zhang, W., Wang, W., Yang, Z., Wang, H., Deng, Z.D., Li, C., Qiu, B., Zhang, D. R., Kadosh, R.C., Li, H., Zhang, X., 2020. Neural and psychological predictors of cognitive enhancement and impairment from neurostimulation. Adv. Sci. (Weinh) 7 (1902863), 1–13. https://doi.org/10.1002/advs.201902863.

Zajc-Lamparska, L., Wilkosi-Dubczyńska, M., Wojciechowski, A., Podshorecka, M., Polak-Szabelka, A., Warchol, E., Kędzierska-Kornatowska, K., Anaszkiewicz, A., Izdebski, P., 2019. Effects of virtual reality-based cognitive training in older adults living without and with mild dementia: a pretest-posttest design pilot study. BMC Res. Notes 12, 776–783. https://doi.org/10.1186/s13104-019-4810-2.