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Review

A systematic literature review of the theoretical foundations of therapeutic and recuperative approaches through physiatry interventions involving prism adaptation in unilateral spatial neglect after brain injuries

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Abstract: Unilateral Spatial Neglect (USN) is a neurological disorder where individuals do not recognize objects or events in the hemispace opposite the brain lesion, focusing instead on items in the ipsilesional visual-spatial area hemifield [1, 2]. USN occurs in approximately 50% of individuals following a stroke that affects the right cerebral hemisphere and may persist in 75% of these individuals during the chronic phase. It can also develop after other brain injuries[3]. This syndrome significantly impacts the individual's quality of life and level of functionality. Several rehabilitative interventions have been designed to enhance or resolve USN, with prism adaptation gaining increased focus in recent years. [4] The study aims to emphasize the therapeutic effects of Prism Adaptation Therapy (PAT) in addressing Spatial Neglect (SN) following brain damage. We conducted a comprehensive literature review to assess the current state of research and the knowledge level related to the selected topic. The internationally recognized Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) method was used to select and filter material. As a result, we used search keywords and keyword combinations in the following four international databases: Elsevier [5], PubMed [6], PMC [7], and PEDro [8]. These articles were published in English in ISI Web of Knowledge/Science indexed journals from January 1, 2021, to December 31, 2023. We selected this timeframe because we noticed a significant increase in the density and concreteness of related studies after 2020. After using the PRISMA system, eliminating duplicates, and applying the inclusion and exclusion criteria, 14 studies were included in the systematic literature review. No research on the selected topic has been highlighted in the Romanian literature. This research study will allow us to evaluate the beneficial contribution of treatment with prism lenses for USN following brain injuries. Thus, we hope it will enhance the quality of life for these patients and support a more comprehensive and effective recovery program for them. Participating in optimizing evaluation and treatment algorithms for patients with these conditions will hopefully lead to a more effective therapeutic approach that maximizes efficacy, benefiting both the patient and the healthcare and social systems.

Keywords: unilateral spatial neglect, prism adaptation treatment, brain injuries, stroke, hemineglect, spatial neglect, prism lenses, hemispatial neglect, neurorehabilitation;

1. Introduction

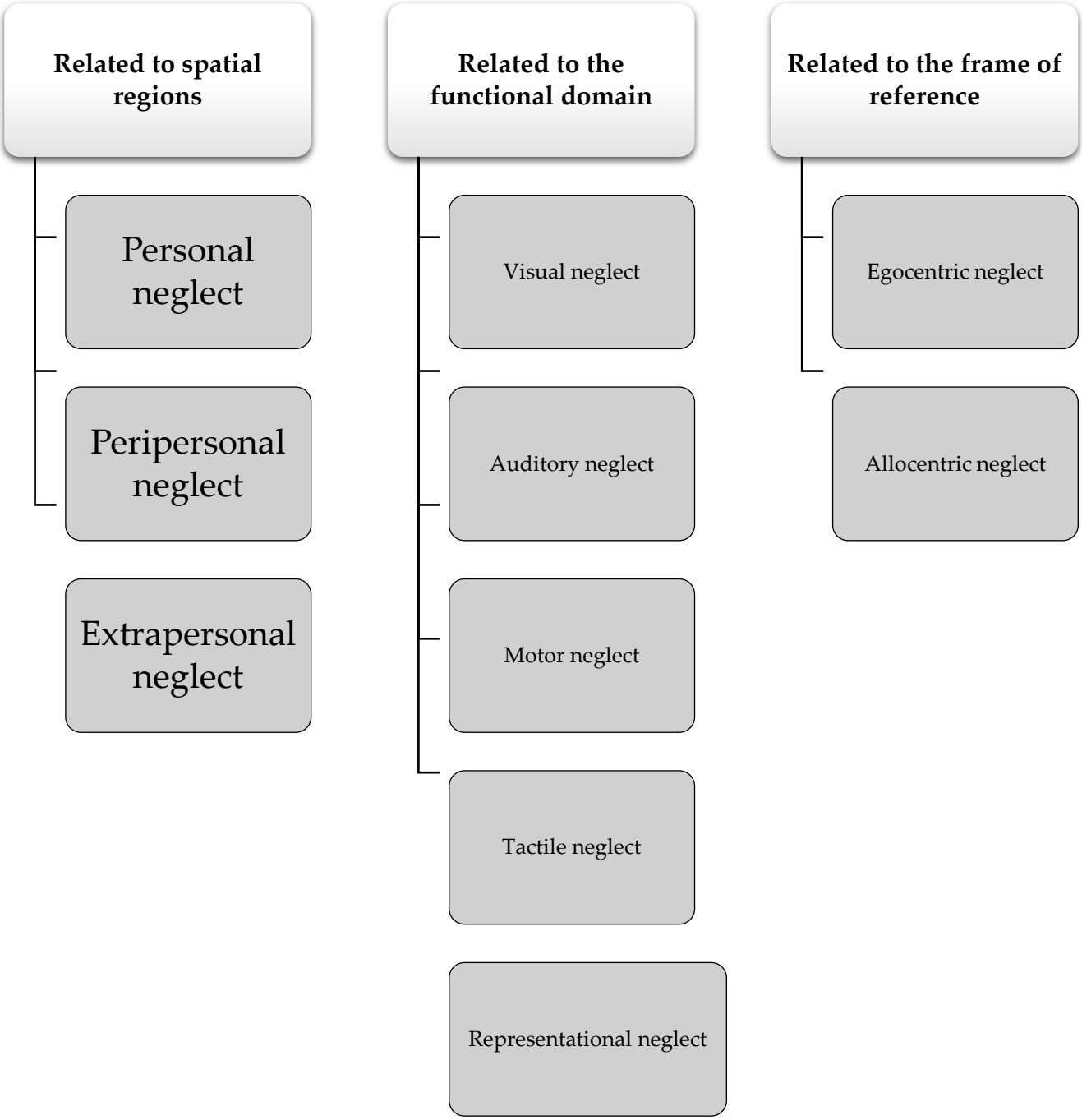
The full definition of USN is a failure to report, respond to, or orient to stimuli that are either presented or mentally represented in a spatial location, usually contralateral to the injured cerebral hemisphere, regardless of primary sensory or motor

function defects. [9] Brain injuries result in the dysfunctional destruction or degeneration of nerve cells or connectivity elements, which, in the case of SN, affects spatial attention as well as cognitive and motor functions. [10, 11] Brain injuries can result from a variety of internal and external factors and stem from different conditions: stroke, Traumatic Brain Injury (TBI), Tumors, genetic disorders, and infections. [10,12] USN primarily results from the occlusion of the right middle cerebral artery. The affected areas in the right hemisphere include the right posterior parietal cortex, particularly the inferior parietal lobe (IPL) and temporoparietal junction (TPJ) [13]. Visual impairment and anosognosia typically involve the perisylvian regions of the right hemisphere. The line bisection test (incorrect) and visual extinction are due to the involvement of the IPL and TPJ [13,14,15]. In affecting subcortical regions, SN may develop indirectly through its effects on cortical areas. The primary part of the subcortex involved is the superior longitudinal fasciculus, while the basal ganglia, thalamus, and cingulate cortex are less involved [15,16]

USN after right brain injury is more prevalent and severe than after left brain injury. Additionally, the symptomatology of left-sided USN has a more pronounced impact on the patient's functionality than right-sided USN, which can often go unnoticed [17]. The explanation may relate to the neural networks essential for spatial attention, mainly located in the right hemisphere. [11]

Depending on the symptoms exhibited by the SN patient, they can be classified into three subtypes (Figure 1). The first subtype considers the distance from the patient's body, leading to three cases: symptoms involving neglect of the patient's body, implicitly including activities such as shaving or combing (Personal Neglect); symptoms that target the space close to the patient, typically affecting the location of objects such as cutlery during meals (Peripersonal Neglect); and symptoms that refer to considerable distances from the patient, which involve difficulty in localizing distant stimuli (Extrapersonal Neglect). [18, 19, 20, 21] The second category pertains to functional domains and is subclassified into five types of hemineglect: Visual neglect (the patient may not respond to visual stimuli from the neglected side), Auditory neglect (the patient may „ignore" sounds from the neglected side), Motor neglect (the patient does not use limbs on the contralateral side, even if there are no apparent motor deficits), Tactile neglect (inattention to tactile stimuli on one side of the body), and Representational neglect (involving representations or visualizations of a task, actions, or mental environments "halfway"). . [18, 19, 20, 21] The last subtype relates to the frame of reference and is classified as either Egocentric neglect (symptoms directed at one's own person) or Allocentric neglect (symptoms referring to an object or stimulus).[18, 19, 20, 21]

Figure 1 Subtypes of SN [18, 19, 20, 21]



Regarding the therapeutic methods for approaching SN, we refer to:

• Neuropsychological recovery: Techniques aimed at helping the patient regain awareness of the neglected area. [22]

• Multisensory stimulation: Employing visual (including VR), auditory, and tactile stimuli to capture the patient's attention towards the neglected area.[23]

• Drugs with a neurotrophic effect: In certain instances, medications can enhance cognitive function. [24]

• Non-invasive, modern brain stimulation techniques (rTMS).[25]

Various remedial interventions have been implemented for SN. Generally, they fall into two categories:

1. *Interventional approaches from top to bottom (remediation through endogenous capacity)* aim for patients to acquire strategies that allow them to compensate for their hemineglect-type deficits voluntarily. These require full cooperation from the affected individual to become aware of the space they neglect (examples include visual scanning and mental imagery). [4,26,27]

2. *Bottom-up interventional approaches (compensators/exogenous facilities)* are designed to adapt to the external environment or apply sensory stimulation. [4] They focus on correcting information intended to enhance patients' perception of the neglected hemispace, such as prism adaptation, active limb exercises, optokinetic stimulation, specific feedback training, cervical muscle vibration therapy, virtual reality (VR), rTMS [28]

Some types of *virtual therapy* that may enhance the symptoms of a patient with SN include:

1. Immersive VR—Patients utilize head-mounted displays to interact with 3D environments. These environments can be modified to promote focus on the neglected side through engaging and repetitive tasks. [4,29,30]
2. Non-immersive VR: Utilizing computer screens or tablets to display virtual environments where patients engage in tasks that require focus on the neglected area.[4,29,30]
3. Play therapy: Customized games that encourage movement or focus on the neglected part can be more engaging and enjoyable for patients, boosting their motivation and adherence to therapy. [32]
4. Augmented Reality (AR): Merging real-world settings with computer-generated information or stimuli to motivate patients to interact with the neglected space. This may involve visual or auditory cues that attract attention to the neglected side. [4,30]

As will be observed, the attempt to systematize cannot categorically separate the different modalities of therapeutic-recovery interventions.

Other therapeutic-recuperative interventions can be used in USN:

1. Cognitive and behavioral techniques

• Cognitive training techniques: Exercises designed to enhance attention and awareness. (I)

• Visual feedback techniques: Utilizing visual feedback to improve movements and posture. (II) [32, 33]

2. Techniques and Specific Exercises

- Visual Orientation Exercises: Directing the patient to focus his gaze on the affected side. (I)
- Use of Mirrors: Mirrors can facilitate visual awareness of the affected area. (I) [34]
- Motor Recovery Exercises: Training the muscles on the affected side through active and passive movements. (II)
- Coordination Exercises: Enhancing coordination between the affected and unaffected sides. (II) [35]
- Sensory Stimulation Techniques: Applying stimuli to the neglected side, such as touch, vibrations, and visual cues. (II) [36]

3. Environmental Adaptation

• Adapting the Environment and Tasks: The environment and exercises in the rehabilitation program must be modified to suit the patient's needs and abilities. This may involve using specialized rehabilitation devices and adjusting tasks to make them more accessible and comprehensible for the patient. [37]

• Modifying the Home Environment: Rearranging furniture and space to facilitate the use of the affected area. [38]

• Assistive Devices

4. Educating the patient and their family.

• Encouraging family and caregiver involvement: Involving family members and caregivers can significantly support the patient's recovery outside therapy sessions. They can help by practicing recommended exercises and promoting the use of skills in everyday life. [39]

• Education and psychological support: It is important to inform both the patient and the family about spatial neglect and the strategies for managing the daily challenges created by the associated disability.[40]

• Repetition and constant feedback: Repeating exercises and providing continuous feedback are critical for reinforcing progress and enhancing performance. The physician and therapist should offer ongoing guidance and support throughout the recovery program. [41]

5. Monitoring and Evaluation

• Continuous monitoring and adjustments: The program should be monitored and adjusted as the patient's progress and condition changes. Adapting therapy is essential to meet the patient's evolving needs. [42]

• Regular evaluations: Track the patient's progress and modify the recovery program accordingly.

• Adjusting goals: Review and revise goals as the patient advances.

6. Prism adaptation

Prism adaptation treatment (PAT) is a promising therapeutic-recuperative intervention for improving USN and performance in daily living activities.[43,44] The most recent American Heart Association/Stroke Guidelines for Stroke Rehabilitation and Recovery in Adults recommend PAT because it is supported by type A level evidence (multiple populations assessed using randomized controlled trials or meta-analyses) and class IIa effect size (benefit outweighs risk). [45]

Two mechanisms have been proposed to explain the effects of PAT:

1. Recalibration – a strategic cognitive process that occurs in the early stages of PAT. It has been suggested that the parietal lobe primarily facilitates recalibration.

2. Realignment – a fully automatic reorganization of spatial maps that manifests later and more gradually over time. Realignment is believed to be carried out by the cerebellum.[46]

Glasses with prism lenses are optical devices that alter the direction of light and its information, consequently affecting the wearer's visual perception. In the context of

neurological recovery, prism glasses redirect the visual field of patients with USN, assisting them in regaining spatial awareness of their hemineglect environment.

By utilizing these glasses, patients can learn to explore the neglected parts of space, thereby enhancing the acquisition of visual information related to motor and cognitive functions. [1,3] Prism adaptation induces a change in how spatial information is transformed from retina-based perceptual coordinates for representing the position of objects in space to proprioceptive and motor of-the-body coordinates for representing the location of objects. Patients with SN who wear prism lenses that localize visual information to the right must make reaching movements to the left of where an object "appears" to reach its current location. In USN patients, this progression/extension of leftward motion perception persists after the prism lens-induced adaptation period and may generalize in utility to tasks of daily living. [47] Prism adaptation is dependent on repetitive use and accumulated perceptual experience. Thus, wearing prism adaptation lenses offers multiple opportunities for learning, including errors. The “neuroanatomical-neuropharmacological paradigms” supporting prism adaptation effects in SN are unclear. Still, they may operate on the same principles that underpin implicit motor learning and thus could provide optimal support for the recovery of spatial motor "targeting." [47] Emerging research indicates that PAT primarily and specifically ameliorates motor-intentional deficits rather than perceptual-attentional ones. Therefore, there is a possibility that the visual perception of "where" does not improve following adaptation therapy with prism lenses; at a level of attention to the hemi-neglected area, this therapy focuses on spatial motor function. [47] Unlike prism treatment for diplopia, both lenses should induce the same degree and direction of perceived displacement. Although the literature does not provide "dose-response" specifications for a certain degree of prismatic displacement, such lenses are found in literature measuring 20 diopters at 5.7°-20° [47, 48, 49]

2. Materials and Methods

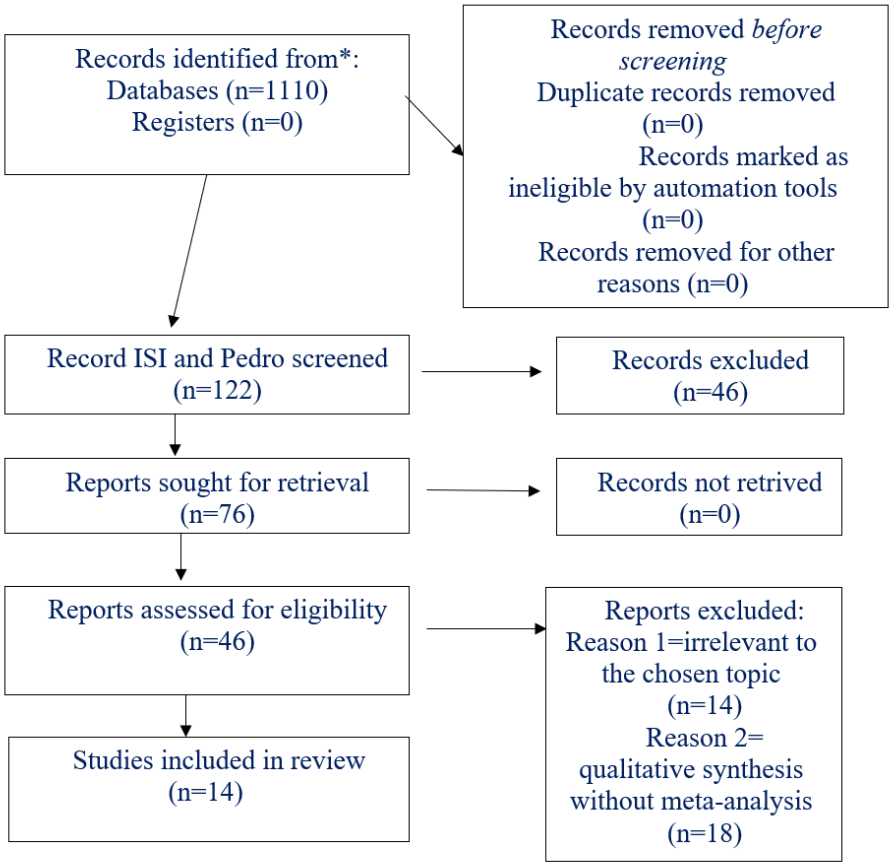
We previously carried out a systematic literature review to understand our chosen topic's current research and knowledge. We followed the internationally recognized Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) guidelines for material selection and filtering. As a result, we used specific keywords and combinations (Table 1) in these international databases: Elsevier [5], PubMed [6], PMC [7], and PEDro [8]. The articles reviewed are published in English in ISI Web of Knowledge/Science indexed journals between January 1, 2021, and December 31, 2023. Historically, some medical initiatives for this purpose trace back to the onset of this millennium; however, we found that the density and concreteness of related studies increased significantly after 2020. This is why we selected the most impactful works in the field according to the PRISMA method. There has been no research on this topic identified in the Romanian literature.

Table 1 Keywords and keyword combinations used in the PRISMA reporting system

Keywords and keyword combinations	Elsevier	PubMed	PMC	PEDro	Total
"stroke" + "hemineglect" + "prism adaptation" + "rehabilitation"	0	0	41	0	41
"stroke" + "hemineglect" + "optokinetic stimulation" + "rehabilitation"	0	0	18	0	18
"stroke" + "unilateral spatial neglect" + "prism adaptation" + "rehabilitation"	0	6	69	0	75
"stroke" + "unilateral spatial neglect" + "optokinetic stimulation" + "rehabilitation"	0	0	23	0	23
"stroke" + "unilateral spatial neglect" + "prism therapy" + "rehabilitation"	0	0	3	0	3
"stroke" + "unilateral neglect" + "prism adaptation" + "rehabilitation"	0	3	69	0	72
"stroke" + "unilateral neglect" + "optokinetic stimulation" + "rehabilitation"	0	0	21	0	21
"stroke" + "unilateral neglect" + "prism therapy" + "rehabilitation"	0	0	3	0	3
"stroke" + "spatial neglect" + "prism adaptation" + "rehabilitation"	3	22	92	1	118
"stroke" + "spatial neglect" + "optokinetic stimulation" + "rehabilitation"	0	4	26	0	30
"stroke" + "spatial neglect" + "prism therapy" + "rehabilitation"	2	0	3	0	5
"stroke" + "hemineglect" + "prism adaptation" + "recovery"	0	0	40	0	40
"stroke" + "hemineglect" + "optokinetic stimulation" + "recovery"	0	0	17	0	17
"stroke" + "unilateral spatial neglect" + "prism adaptation" + "recovery"	0	2	62	0	64
"stroke" + "unilateral spatial neglect" + "optokinetic stimulation" + "recovery"	0	0	20	0	20
"stroke" + "unilateral spatial neglect" + "prism therapy" + "recovery"	0	0	3	0	3
"stroke" + "unilateral neglect" + "prism adaptation" + "recovery"	0	0	62	0	62
"stroke" + "unilateral neglect" + "optokinetic stimulation" + "recovery"	0	0	18	0	18
"stroke" + "unilateral neglect" + "prism therapy" + "recovery"	0	0	3	0	3
"stroke" + "spatial neglect" + "prism adaptation" + "recovery"	0	5	81	0	86
"stroke" + "spatial neglect" + "optokinetic stimulation" + "recovery"	0	0	23	0	23
"stroke" + "spatial neglect" + "prism therapy" + "recovery"	0	0	3	0	3
"stroke" + "hemineglect" + "prism adaptation" + "assessment"	0	0	40	0	40

We conducted a keyword search across four international databases using eleven keyword sets. Following this, we eliminated duplicate entries—articles appearing in multiple databases. We confirmed that all included articles were published in ISI-indexed journals without excluding any. Subsequently, we applied a PEDro-inspired algorithm to indirectly classify the articles' quality. We then performed a full-text eligibility analysis on the remaining articles, which led to the exclusion of 32 articles for specific reasons. The articles that passed all previous filtering criteria and PRISMA stages were chosen for qualitative synthesis, excluding meta-analysis. Fourteen studies were included in the review. (Figure 2)

Figure 2. PRISMA diagram related to our systematic literature review



Studies generally show that PAT is an effective treatment for spatial neglect, with effect sizes typically ranging from moderate to large, depending on dosage and protocol [50, 51]. There is significant variability in PAT protocols, including differences in treatment duration, frequency, and whether it is combined with other therapies [52, 53]. This variability can influence the consistency of results. Some studies [54] found that passive exposure to prisms without active adaptation has minimal lasting effects, suggesting that active engagement is necessary for effective outcomes. The role of passive exposure remains unclear and contradictory in some studies. Combining PAT with other interventions, such as visual scanning training [51] or brain stimulation [55], has shown potential for enhancing outcomes, though the optimal combination of treatments remains to be fully defined.

We aim to evaluate three groups of patients diagnosed with USN:

1. The prospective study group (Group 1) consists of approximately 50 patients who will exclusively benefit from PAT. This group will also utilize standard treatments such as physical therapy, physiotherapy, and speech therapy.

2. A prospective study group (Group 2) of around 50 patients will receive specific treatment for SN, including exercises like visual scanning training, limb activation, mental imagery, mirror therapy, and guided feedback, excluding PAT. Similar to the first group, standard treatments will also be provided, including physical therapy, physiotherapy, and speech therapy.

3. A prospective control group (Group 3) of about 50 patients will not receive therapy that involves prism lenses or specific treatment for SN but will only participate in standard treatments such as physical therapy, physiotherapy, and speech therapy.

Inclusion criteria: age over 18 years, newly diagnosed stroke in the right hemisphere, presence of spatial neglect syndrome, obtaining informed consent, and a medical

history that includes a brain injury affecting the right side of the brain, such as ischemic or hemorrhagic stroke, or one or more brain or cerebellar tumors post-surgery. Exclusion criteria: age under 18 years, refusal to participate in the study, inability to obtain the patient's informed consent, associated psychiatric disorders that may adversely affect the scientific integrity of the study (such as schizophrenia, dementia, and severe depression), a significant communication deficit, visual impairment or blindness of any kind that cannot be corrected optically in one or both eyes, cognitive impairment that hampers the ability to recall information, and a diagnosis of left-sided stroke or any left hemisphere injury.

Protocol for using prism glasses (Group 1): Both lenses will produce the same level and direction of perceived displacement. The prisms will have a power of 20 diopters and 10°. During the session, patients repeatedly point at targets or perform continuous manual tasks, partially obstructing their view of arm movements. Initially, patients will mispoint toward the direction of optical displacement (to the right), but if the therapy is effective, they will be seen pointing accurately after more than 50 trials. Upon removing the lenses, participants typically show an aftereffect by mispointing the target in the opposite direction (to the left) following the therapy session. There will be 10 daily therapy sessions utilizing the prismatic lenses, with each training session lasting briefly (15–30 minutes). Throughout PAT, a doctor or therapist will constantly supervise the patient. The prism lenses are only utilized during therapy sessions, avoiding use in other activities or rehabilitation therapies. Few adverse effects have been noted in the literature; clinicians have occasionally reported discomfort or dizziness. Optimizing the methodology identified in the literature based on accumulated clinical experience is possible during the doctoral clinical study.

Regarding study group no. 2: There will be 10 daily therapy sessions utilizing exercises such as visual scanning training, mental imagery, and mirror therapy. The training sessions will be brief (15–30 minutes, depending on the patient's general condition, comorbidities, and the severity of the underlying pathology) and similar to PAT's. During prismatic adaptation therapy, the patient will be continuously supervised by a doctor or therapist.

The assessment methods that will be used include the Sunnybrook Neglect Assessment Procedure (SNAP), Montreal Cognitive Assessment (MOCA) scale, Activities of Daily Living (ADL) scale, Functional Independence Measure (FIM), and Functional Assessment Measure (FAM) scale, Catherine Bergego Scale, and the World Health Organization Quality-of-Life Scale (WHOQOL-BREF).

The study will be conducted in the Clinical Department of Neuromuscular Recovery of the Teaching Emergency Clinical Hospital" Bagdasar-Arseni" (TECHBA), Bucharest. The patient or their legal representative will consent to gather and utilize data for research, ensuring confidentiality in line with existing laws. This doctoral research will be conducted with the approval of the Bioethics Commission of TECHBA. Statistical analysis will utilize SPSS version 24 (Statistical Package for Social Sciences) and Microsoft Excel 2007. The analysis will cover demographic data, descriptive statistics, comparative tests, and parametric or non-parametric tests based on data normality. Correlation tests and visual representations using diagrams and histograms may also be included. Statistical significance will be established with $p < 0.05$. We will also consider the 95% confidence level and confidence intervals associated with particular calculations.

3. Results

By using PAT in SN patients, we aim to achieve several objectives: improve visuospatial attention, allowing patients to exhibit an increased capacity to manage

and become aware of the "neglected" body parts; enhance motor response, evidenced by touching objects in the affected area, moving towards this direction, and increasing the frequency of episodes of obstacle avoidance on the neglected side; augment the affected visual field; induce changes in neural activation through prismatic adaptation to promote neural plasticity and facilitate the recovery of neural functions in brain areas involved in visuospatial attention and motor planning; and ultimately enhance quality of life.

3. Discussion

One-third of stroke survivors develop hemineglect syndrome, which increases the risks of prolonged hospitalization, related conditions due to the acquired disability, minimal improvement in motor function, the inability to return to work, subsequent admissions to long-term care facilities, potential psycho-cognitive decline, and significant deterioration of quality of life. PAT is an essential tool for achieving this goal and may demonstrate potential in alleviating symptoms of SN, potentially maximizing the rehabilitation program's results, and allowing patients to regain a certain level of independence. Effective treatment for individuals diagnosed with this syndrome can reduce long-term care needs and healthcare expenses. By improving patient outcomes, the "efforts" of health systems and care systems can be lessened. However, there is a significant gap in Romanian research on PAT, creating an opportunity to explore its effectiveness, customize treatment methods, and improve the wider scientific understanding. Future research should focus on mechanistic studies to uncover how PAT operates at the neural level, while also emphasizing the importance of standardized protocols to ensure treatment consistency.

5. Conclusions

Through this research study, we aim to objectively evaluate the positive impact of prism lens treatment for USN following brain injury injuries. Thus, we hope it will enhance the quality of life for these patients and support the development of a more comprehensive recovery program. Involvement in optimizing evaluation and treatment algorithms for patients with such conditions will lead to a more effective therapeutic approach that maximizes its benefits for both the patients and the healthcare system—social systems.

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