Unilateral Spatial Neglect After Stroke: Current Insights

Introduction: Unilateral spatial neglect (USN) is a disorder of contralesional space awareness which often follows unilateral brain lesion. Since USN impairs awareness of contralesional space/body and often of concomitant motor disorders, its presence represents a negative prognostic factor of functional recovery. Thus, the disorder needs to be carefully diagnosed and treated. Here, we attempted to present a clear and concise picture of current insights in the comprehension and rehabilitation of USN.

Methods: We first provided an updated overview of USN clinical and neuroanatomical features and then highlighted recent progresses in the diagnosis and rehabilitation of the disease. In relation to USN rehabilitation, we conducted a MEDLINE literature research on three of the most promising interventions for USN rehabilitation: prismatic adaptation (PA), non-invasive brain stimulation (NIBS), and virtual reality (VR). The identified studies were classified according to the strength of their methods.

Results: The last years have witnessed a relative decrement of interest in the study of neuropsychological disorders of spatial awareness in USN, but a relative increase in the study of potential interventions for its rehabilitation. Although optimal protocols still need to be defined, high-quality studies have demonstrated the efficacy of PA, TMS and tDCS interventions for the treatment of USN. In addition, preliminary investigations are suggesting the potentials of GVS and VR approaches for USN rehabilitation.

Conclusion: Advancing neuropsychological and neuroscience tools to investigate USN pathophysiology is a necessary step to identify effective rehabilitation treatments and to foster our understanding of neurofunctional bases of spatial cognition in the healthy brain.

Keywords: unilateral spatial neglect, rehabilitation, spatial attention, stroke

Introduction

The first attempt to define Unilateral Spatial Neglect (USN), a neuropsychological disorder of spatial awareness that often follows unilateral brain lesion, was made in the second half of the 19th century.1 A remarkable number of studies of USN have been published towards the end of the 20th century and the beginning of the current century. However, the last 10–15 years have witnessed a relative decrement in the number of neuropsychological papers investigating this syndrome. The reason might be twofold. Firstly, the advancement of neuroimaging and, more recently, brain stimulation methodologies has driven the interest (and preference) of cognitive neuroscientists toward the use of these innovative techniques to investigate the neurofunctional bases of spatial cognition in the healthy brain. Secondly, medical advances in the treatment of acute stroke have significantly improved individuals’ clinical and neuropsychological conditions. Nonetheless, USN is quite frequent...
since it occurs in about 25–30% of all stroke individuals and over 90% of people with USN have right-hemisphere lesions. In the acute phase, USN occurs in 43% of individuals with right-hemisphere lesion (RHL) and 20% of those with left-hemisphere lesions (LHL). At 3 months, it is still present in 17% and 5% of RHL and LHL individuals, respectively. Neglect per se, rather than overall stroke severity, predicts poor outcome in functional recovery. It may indeed entail longer hospitalization, functional dependency, long-term disabilities in activities of daily living and increased risk of falls.

Thus, USN is an important neuropsychological condition that needs to be carefully diagnosed and treated. Here, we attempt to provide a clear and concise picture of current insights in the comprehension and rehabilitation of USN. We briefly overview USN clinical and neuropsychological features and then highlight recent progresses in the diagnosis and rehabilitation of USN. In relation to the latter topic, we review recent findings on three of the most promising interventions for USN rehabilitation: prism adaptation (PA), non-invasive brain stimulation (NIBS), and virtual reality (VR).

**Clinical Manifestations**

Individuals affected by USN fail to explore, orient or respond to contents of the contralesional side of somatic and extrasomatic space. In the acute phase, they show an ipsilesional deviation of the head and the eyes and may respond to stimuli presented in the contralesional side as if they were in the “intact” side. During everyday activities, they may eat food only from the ipsilesional side of the plate, bump into objects located in the contralesional side when walking, and wash, shave, or apply cosmetics only to the ipsilesional side of the face/body.

**USN Is a Complex Syndrome**

There is a broad consensus among researchers on the heterogeneity of USN symptoms that is thought to reflect the complexity of neural correlates of spatial attention/representation. Building a coherent representation of space entails a complex integration of different sensory inputs and output-related factors, in relation to different portions of space and coordinates systems. Coherently with this assumption, USN symptoms can dissociate across sensory modalities, sectors of space (i.e., personal, peri-personal and extra-personal space), reference frames (egocentric vs allocentric neglect), and tasks. An often neglected dissociation concerns symptoms affecting perceptual and output stages of spatial processing. Some USN individuals are affected by a perceptual bias reflecting lateralized impairments in spatial representation/attention. However, in other individuals, USN reflects a “reluctance” to orient the response contralesionally. This type of neglect that has been called directional hypokinesia or intentional neglect, response bias or premotor neglect is rarely assessed, likely because it can only be detected by using few specific tasks, the most well-known being the landmark task. Another symptom affecting output stages of stimulus processing is motor neglect, whereby a dramatic reduction in the spontaneous use of contralesional limbs is not explained by motor impairment. Finally, not only the type of task but also task demands have been found to affect neglect severity.

Given the complexity of USN symptomatology, there is the need to use comprehensive assessment tools that minimize the risk to overlook its presence. The most reliable and commonly used assessment tests are two “paper and pencil” tasks: the line bisection and cancellation tasks. On these tasks, individuals with USN are asked to bisect a horizontal line or to search for spatially distributed targets. They mark the center of the line ipsilesionally and/or search exclusively for ipsilesional targets. Administration of both tasks is critical because USN can dissociate across them. Furthermore, other variables need to be kept into account when using these tasks. For example, line bisection performance is affected by the length of the line and by contextual factors. Lines of at least 18 or 20 degree of visual angle are necessary to reliably assess neglect. Short lines and very short lines produce a contralesional bisection bias that may even overshoot the end of the line (i.e., the crossover effect; see also Chatterjee et al for crossover effects in non-spatial tasks). Cancellation tasks are significantly affected by stimuli characteristics and task demands. USN tests or batteries (e.g., the Behavioral Inattention Test) often include also reading, copying and drawing tasks. In all these tests, individuals with USN omit (or may also “confabulate”) contents of contralesional space. However, canonical tests may not be sensitive enough to detect contralesional space disorders in subacute and chronic stages of the disease and more appropriate (and demanding) tasks are necessary to reveal their presence. For example, computerized methods may be more effective in detecting subtle symptoms than static paper-and-pencil tests.
conventional evaluation tests might not provide conditions consistent with real-life situations.

An accurate diagnosis of the specific symptoms that affect individuals with USN is fundamental to design tailored rehabilitation programs that may effectively overcome the limits posited by disrupted spatial awareness to functional recovery.

**Theoretical Models**

USN is not caused by elementary sensory or motor deficits and dissociates from deficits of intermediate vision.\(^{22,42–44}\) It is thought to derive from disruption of higher level spatial attention/representational processes.\(^7,8\) *Attentional theories* propose that USN is accounted for by a rightward lateralized bias in the orientation of spatial attention. Kinsbourne’s hemispheric rivalry account\(^45\) posits mutual transcortical inhibition between hemispheres in the normal brain and disruption of this balance in USN. It assumes the existence of two antagonist attentional vectors directed by each hemisphere toward the contralateral hemisphere. In physiological conditions, the left-hemisphere vector is stronger than the right-hemisphere one. A brain lesion would disrupt interhemispheric balance and symptoms would be explained not only by the inactivity of the lesioned area but also by the increased activity of homologous regions of the opposite hemisphere that are released by contralateral inhibition. Given the asymmetric strength of the attentional vectors, only a right-hemisphere lesion would produce a dramatic, lateralized ipsilateral bias in attentional orienting. Heilman and colleagues\(^8\) propose a complementary model, according to which the right hemisphere would direct attention to both hemispheres, while the left hemisphere exclusively to the right one. As a consequence, a right-hemisphere lesion would more frequently cause USN.\(^8\) *Representational accounts* of neglect instead propose that USN is a disorder of mental space representation,\(^46\) consisting in a left–right pathological anisometry of the medium for space representation: the left-side would be more relaxed and the right-side would be more contracted/compacted.\(^46\) The contralateral relaxation of the medium might still sustain “conscious” representation of contents in space, albeit with a horizontal size distortion. Beyond a critical point, the overrelaxed medium no longer sustains conscious representations. Bisiach’s theory\(^46\) also foresees that in some individuals, the disorder affects response level of stimulus processing (i.e., response bias). Another account referring to altered mechanisms of space representations is the *transformational hypothesis*.\(^47,48\) It suggests that USN is due to a failure of the transformation of sensory input into motor output, which is generally based on different reference frames. Since such coordinate transformation mainly occurs in the parietal cortex,\(^49,50\) a parietal lesion might impair this process.\(^47\) As a result, the egocentric representation of the surrounding environment would be deflected towards the ipsilesional side.

**Neural Correlates**

Early clinical observations pointed to damage to the right posterior parietal cortex (PPC), as the most likely correlate of USN symptoms.\(^51\) Anatomo-clinical correlation studies, based on CT or MRI, confirm a predominant role of the right inferior parietal lobe in association with USN symptoms.\(^52,53\) particularly of the angular gyrus (AG). Other findings suggest the right superior temporal gyrus (STG) as the main neural correlate for USN symptoms.\(^54\) Finally, USN is also observed after lesions to frontal and subcortical structures that are functionally connected to the posterior parietal lobe.\(^55\) Recently, neuroscientists have shifted their interest from trying to identify a single brain area to investigations of brain areas that are involved as sub-components of a more complex network, responsible for space attention and representation (see Hillis et al\(^55\) for a review). Studies using advanced neuroimaging techniques have concluded that USN symptoms heterogeneity can be explained by differences in the structures or circuit affected by the lesion. For instance, using PWI and DWI, Medina and colleagues\(^56\) found that functional inactivation of the right-supramarginal gyrus was most predictive of egocentric neglect, inactivation of posterior inferior temporal and lateral occipital areas was most predictive of stimulus-centered neglect, and, posterior middle/inferior temporal regions of object-centered neglect. Damage to intraparietal sulcus (IPS) and the temporoparietal junction (TPJ) have been further associated with egocentric and allocentric neglect, respectively.\(^57\) Finally, motor-intentional USN correlates to lesions of basal ganglia.\(^19,23\) Breakdown of functional connectivity between parietal and frontal regions linked by the superior longitudinal fasciculus (SLF) has been shown to play a critical role in the occurrence, severity and chronicity of egocentric USN symptoms.\(^2,57–62\)

**Rehabilitation Methods**

It is possible to distinguish between two types of neglect treatments: top-down and bottom-up approaches.\(^63\) The main difference between them concerns the extent of an individual’s awareness and active involvement. The
former approach aims to improve perceptual and behavioural bias by acting on disrupted awareness, thus on higher-level cognitive processes. Given USN features, this approach might be difficult to be applied in individuals with severe neglect. The latter is a physiological approach that aims to affect the sensory-motor level through passive sensorial manipulations or visuomotor adaptation. In this way, it is possible to override central awareness deficit and reach higher cognitive levels of spatial and action representation. Given that USN is a disorder of spatial awareness, bottom-up approaches have more frequently been proposed and investigated.

The most widely used top-down approach is visual scanning training (VST), during which the therapist encourages individuals to pay attention to and explore portions of space contralateral to the brain lesion. The standard procedure consists of different training tasks, such as visual search, digit detection, figure copying, picture exploring, reading and writing. The exploratory behaviour of contralosional contents of space is systematically strengthened by visual and verbal reinforcements, as well as compensatory strategies. Despite a wide variability of response to VST, overall, significant improvement of neglect has been reported following this intervention (for a review see Luauté et al). Some studies, comparing the efficacy of VST to that of bottom-up approaches, did not find any significant difference between them. Nonetheless, some RCT and single-case studies suggest that VST beneficial effects might be enhanced by the combination of this intervention with other techniques, such as, for example, left-hand somatosensory stimulation, limb activation or transcranial Direct Current Stimulation.

Over the years, a number of different techniques have been proposed to rehabilitate neglect symptoms. A large number of studies have been published for each approach. Since this is not a systematic review of neglect treatments, we will focus on the most promising recently proposed rehabilitation methods, although other effective – but less employed – techniques have been investigated to treat the disorder, such as eye-patching, caloric vestibular stimulation, visuomotor imagery, mirror therapy, TENS, Optokinetic Stimulation and the Constraint-induced movement therapy.

Specifically, we conducted a MEDLINE literature research on the use of prismatic adaptation, non-invasive brain stimulation and virtual reality in USN rehabilitation. To this end, we used the following combinations of words: “neglect”, “rehabilitation”, “prism adaptation”, “tDCS”, “galvanic vestibular stimulation”, “TMS”, “TBS”, “Virtual reality”. Reference lists from identified articles were also reviewed. Studies were selected according to the following exclusion criteria: nonintervention studies; theoretical, descriptive, or review papers; papers without adequate specification of interventions; subjects other than persons with stroke and USN; non-English language papers. The identified studies were classified according to the strength of their methods based on Cicerone et al’s recommendations. Specifically, three main levels of evidence were established. Studies were considered Class I evidence if they had well-designed, prospective, randomized controlled trials. Prospective studies with “quasi-randomized” assignment to treatment conditions were designed as Class Ia studies. Class II studies comprised prospective nonrandomized cohort studies, retrospective, nonrandomized case-control studies, or clinical series with well-designed controls (eg, multiple baseline across subjects). Studies were considered as Class III evidence if they consisted of clinical series without concurrent controls, or single-case studies with appropriate single-subject methods. All classifications were based on the agreement of at least two authors. The disagreement between reviewers was resolved by the evaluation of a third author.

**Prismatic Adaptation**

Prismatic Adaptation (PA) is one of the most widely studied and used bottom-up procedure for USN rehabilitation. Since the literature on this topic is very extensive and several reviews on this procedure have been published, here, we will present a non-exhaustive overview of recent relevant studies on PA for the treatment of USN (see Table 1). Standard PA procedure foresees that subjects wear the prismatic goggles, producing a visual shift, and perform different tasks to reach visual targets (e.g., pointing, reaching or throwing). These tasks are initially failed because of the deviation caused by the shift of the visual field that generates a mismatch between the perceptive object position and the arm movement trajectory. After a series of trials with visual feedback, the subjects adapt to optical displacement, improving their performance. After removing the prisms, movement trajectory deviates in the direction opposite to the visual shift, indicating a negative aftereffect. PA effects have been initially interpreted as due to a correction of the biased egocentric representation, in line with the transformational hypothesis. However, some studies suggested that PA may mainly affect motor-intentional “aiming” (response) neglect rather than perceptual levels of space representation. Finally, some
| Study          | Patients | Control | Protocol | Number of Sessions | Test                                                                 | Assessment                             | Results                                                                 | Design | Classification |
|---------------|----------|---------|----------|-------------------|----------------------------------------------------------------------|----------------------------------------|--------------------------------------------------------------------------------|--------|-----------------|
| Frassinetti et al<sup>63</sup> | 7 RH     | 6 RHI   | 10° RPA  | 20                | BIT; Bell cancellation; Reading; Fluff test; Room description; Object reaching | Pre, Post, Follow-up (2 days, 1 week and 5 weeks later) | Improvement after RPA, at least for 5 weeks | NRCT   | Class II        |
| Priftis et al<sup>67</sup>      | 31 RH    | None    | 10° RPA, or VST (visual scanning training), or LAT (limb activation treatment) | 20 | Comb and razor test; Fluff test; Picture scanning; Reading; Coin sorting; Ecological scale; Room description; CBS | Pre, Post, Follow-up (2 weeks later) | Improvement after each treatment, at least for 2 weeks later | Quasi-RCT | Class Ia        |
| Spaccavento et al<sup>69</sup> | 20 RH    | None    | 10° RPA or VST | 20 | Fluff test; Personal neglect scale; BIT; Extrapersonal neglect scale; CBS; FIM | Pre, Post (4 weeks later) | Improvement after both treatments in each test, except in the extrapersonal neglect scale | Pilot   | Class III       |
| Fortis et al<sup>64</sup>       | 5 RH     | None    | 12.4° RPA | 1 | LBT; Pointing | Pre, Post | Improvement on “aiming”, but not on “where” spatial bias | Pilot   | Class III       |
| Pisella et al<sup>85</sup>      | 2 RH     | None    | 10° RPA  | 1 | Straight-ahead; LBT | Pre, Post, Follow-up (72 hrs later) | Improvement at least for 4 days | Pilot   | Class III       |
| Rossetti et al<sup>87</sup>     | Exp1: 8 RH Exp2: 6 RH  | 5 Healthy subjects 6 RHI | 10° RPA and LPA | 1 | LBT;Cancellation test; Copying; Drawing from memory; Reading | Pre, Post, Follow-up (2 hrs later) | Improvement after RPA, at least for 2h | RCT    | Class I         |
| Farnè et al<sup>88</sup>        | 6 RH     | None    | 10° RPA  | 1 | Line, bell and letter cancellation; LBT; Visual scanning; Object-naming; Reading | Pre, Post, Follow-up (1 day and 1 week later) | Improvement after RPA, at least for 1 day | Pilot   | Class III       |

(Continued)
Table 1 (Continued).

| Study            | Patients | Control | Protocol          | Number of Sessions | Test                                                                 | Assessment | Results                                                                 | Design   | Classification |
|------------------|----------|---------|-------------------|--------------------|----------------------------------------------------------------------|------------|------------------------------------------------------------------------|----------|----------------|
| Serino et al,\(^8^9\) | 21 RH    | None    | 10° RPA           | 10                 | BIT; Bell cancellation; Reading; Fluff test; Room description; Object reaching; Tactile extinction test; Proprioceptive sensibility and standardized mobility scale | Pre, Post (1 week later); Follow-up (1, 3 and 6 months later) | Improvement in visuospatial abilities, tactile modality, but not for proprioception and motor functions. Persisted for 6 months | Pilot    | Class III      |
| Serino et al,\(^9^0\) | 10 RH    | 10 RH   | 10° RPA and NP (neutral pointing) | 10                 | BIT; Bell cancellation; Reading | Pre, Post, Follow-up (1 month later) | Improvement after RPA and NP, but stronger after RPA. Persisted for 1 month after RPA | Quasi-RCT | Class Ia       |
| Vaes et al,\(^9^1\) | 21 RH    | 22 RH   | 10° RPA or Placebo | 7                  | Digital visuospatial neglect test battery                          | Pre, Post, Follow-up (3 months later) | Improvement after RPA in drawing and bisection, navigation, visual extinction and non-motor memory. Improvement in navigation, drawing and memory persisted 3 months later | RCT      | Class I        |
| Mizuno et al,\(^9^2\) | 20 RH    | 18 RH   | 12° RPA or Neutral glasses | 20                 | BIT; CBS; ADL; FIM                                                  | Pre, Post, Follow-up (discharge) | Improvement in RM and CBS in mild USN-patients after RPA. Improvement in RM in prism group at the discharge | RCT      | Class I        |
| Nys et al,\(^9^3\) | 1 RH     | None    | 10° RPA           | 4                  | Star cancellation; Figure copying                                 | Pre, Post (after each session) | Improvement of neglect severity, but worsening of perseveration behaviour | Pilot    | Class III      |
| Turton et al,\(^9^4\) | 16 RH    | 10 RH   | 6° RPA or neutral glasses | 10                 | CBS; BIT                                                            | Pre, Post, Follow-up (8 weeks later) | Improvement of pointing bias, but not in CBS and BIT | RCT      | Class I        |
authors proposed that PA improves spatial cognition by inhibiting the PPC contralateral to the prismatic deviation, restoring, as a result, interhemispheric balance, in line with USN rivalry account. Although it is not clear yet the exact nature of the mechanisms underlying beneficial effects of PA in USN, this non-invasive procedure has showed its effectiveness in several studies and therefore researchers are currently exploring its potentials. For example, single rightward-PA sessions can improve USN from 2 hrs to few days. Likewise, two daily sessions of PA-treatment for 2 weeks may produce beneficial effects persisting for 1 to 6 months. Although several Randomized Control Trials (RCTs) have been published, the evidence supporting a systematic efficacy of PA for neglect rehabilitation is still controversial. For example, three studies reported significant improvement in 51 individuals with USN treated by PA compared to a placebo control group, both in standard neglect tests and in functional independence measures. Positive outcomes were also observed in studies comparing PA to VST, whereby the effectiveness of both approaches was found. However, mixed results have been reported in a brain-damaged woman suffering from USN who showed amelioration soon after 4 days of PA treatment, but not after 1 month at follow-up. Moreover, no beneficial effects by PA were observed in four RCT-studies treating overall 72 individuals affected by USN.

A possible explanation of negative findings might be that visuomotor adaptation (i.e., aftereffect) has to reach a critical threshold to affect performance in other tasks. Given the high intra- and interindividual variability of individuals with USN, visuomotor adaptation induced by low power prisms (i.e., shifting the visual field of 5°, 6° or 10°) – as those used in RCT studies that did not find any beneficial outcomes after PA might be too small to produce detectable effects in all patients. The fact that the critical threshold can only be reached with prisms of high power (i.e., shifting the visual field of 10° or 12°, as those used in the above studies that found significant PA effects) might explain some negative findings. Another suggestive possibility is that, as demonstrated by Fortis and collaborators, PA is more effective when USN affects the response level of stimulus processing. However, with the exception of few investigations, studies on PA never disentangle the two components of USN, not making possible to understand whether PA efficacy may depend on the stage (input vs output) affected by the lesion. Future investigations on PA rehabilitation (but also on other types of interventions) need to provide information on whether USN occurs at perceptual or response stages of

| Authors | Class | Test | Pre, Post | Follow-up | Conclusion |
|---------|-------|------|----------|-----------|------------|
| Mancuso et al. | I | CBS | Pre, Post | Improvement in the straight-ahead test, but no difference between the two groups 6 months later | No difference between the two groups |
| Rode et al. | I | FIM, BIT | Pre, Post (1, 2, 3, 4, 6 and 12 weeks later) | Pre, Post (1, 2, 3, 4, 6 and 12 weeks later) | No statistical difference between the two groups |
| Ten Brink et al. | I | CBS | Pre, Post | No difference between the two groups | No difference between the two groups |

Abbreviations: RH, Right Hemisphere; RPA, Rightward Prism Adaptation; LPA, Leftward Prism Adaptation; LBT, Line Bisection Task; BIT, Behavioural Inattention Test; FIM, Functional Independence Measure; CBS, Catherine Bergego Scale; ADL, Activities of Daily Living; RCT, Randomized Control Trial; NRCT, Non-Randomized Control Trial.
stimulus processing. Besides the power of prismatic goggle also this variable might explain the heterogeneity of findings. In general, tailoring PA treatment to specific forms of USN may result in a more successful rate of improvement. As shown in Table 1, on the basis of Cicerone et al\textsuperscript{83} classification, 9 out of 16 of selected works on PA were classified as class I (or Ia) studies.

Non-Invasive Brain Stimulation

NIBS may be effective in ameliorating cognitive and motor disorders in individuals affected by stroke\textsuperscript{99,100} or by other neurological disorders.\textsuperscript{101–103} The first attempts to treat neuropsychological symptoms using NIBS were made in individuals with USN.\textsuperscript{104,105} In line with the hemispheric rivalry account of neglect,\textsuperscript{45} according to which symptoms are not solely due to inactivity of the lesioned area, but also to increased activity of homologous regions of the opposite hemisphere, therapeutic effects in USN are typically obtained by down-regulating the PPC of the intact hemisphere and/or up-regulating the PPC of the affected hemisphere. It is worth noticing that the first NIBS studies for USN rehabilitation have been published less than 20 years ago. In Tables 2 and 3 are reported studies investigating the efficacy of different Non-Invasive Brain Stimulation (NIBS) techniques and protocols for the treatment of USN. The number and quality of studies reported in these Tables index a fast-growing interest and literature on this topic.

Transcranial Magnetic Stimulation (TMS)

In a proof of concept study, Brighina and collaborators were the first to apply a low-frequency (1 Hz) rTMS treatment (seven sessions over 2 weeks) to the healthy hemisphere of three individuals suffering from visuospatial neglect.\textsuperscript{104} Participants showed significant improvement on different tasks (landmark, line bisection, clock drawing) lasting up to 15 days from the intervention. Subsequent pilot\textsuperscript{105–108} and NRCT studies\textsuperscript{110} administering low-frequency rTMS to the left-hemisphere in small groups of individuals with left USN confirmed and extended preliminary findings. Furthermore, two RCT-studies corroborated the above outcomes.\textsuperscript{111,112} In recent years, researchers have also successfully applied inhibitory continuous Theta Burst Stimulation (cTBS) to the healthy hemisphere of individuals with USN in NRCT,\textsuperscript{113,114} as well as in RCT-studies\textsuperscript{115–118} observing long-lasting improved performance. Interestingly, Yang and colleagues\textsuperscript{119} conducted a RCT study to compare behavioural and brain plasticity effects in USN individuals undergoing low-frequency rTMS, high-frequency rTMS, or cTBS. The cTBS group exhibited the best outcome at 1 month after the end of treatments, followed by the low-frequency and high-frequency group. Interestingly, DTI evaluation showed a connectivity enhancement of the white matter tract network related to visual attention in the cTBS group.\textsuperscript{119} Table 2 reports TMS studies of USN treatments. On the basis of Cicerone et al\textsuperscript{83} classification, 50% of these studies (8 out of 16) were scored as high-quality studies (class I or IIa).

Transcranial Direct Current Stimulation (tDCS)

Only a few studies have been conducted using tDCS in the context of USN. Preliminary works administering a single session of excitatory stimulation (ie, anodal or a-tDCS) to the affected hemisphere\textsuperscript{120,121} or inhibitory stimulation (ie, cathodal or c-tDCS) to the intact one\textsuperscript{120} showed improved performance on line bisection and cancellation/visual search tasks. In a double-blind randomized cross-over study, Sunwoo and colleagues,\textsuperscript{122} comparing the effects of a dual-mode protocol (ie, a-tDCS of the affected hemisphere and c-tDCS of the intact hemisphere concurrently) to those of single-mode a-tDCS of the affected hemisphere, found that both single- and dual-mode tDCS were safe and effective for USN rehabilitation. Another double-blind, single-case, cross-over study,\textsuperscript{72} using a combined approach of biparietal tDCS (the anode was applied to the right PPC and the cathode to the left PPC) and cognitive training, showed greater USN improvement when using biparietal tDCS than standard therapy alone or sham. Beneficial effects were still observed at 3 months after treatment. However, a subsequent placebo-controlled study\textsuperscript{123} did not find any long-term USN improvement after parietal right-anodal and left-cathodal-tDCS of PPC. To our knowledge, only two studies used RCT designs. Yi and colleagues\textsuperscript{124} applied a-tDCS to the right-PPC and c-tDCS to the left-PPC and found beneficial effects on left-USN compared to sham-stimulation. The same protocol was applied by Bang & Bong\textsuperscript{125} in combination with Feedback Training (FT). Results showed greater improvement of symptoms after tDCS combined with FT than FT alone. In a recent NRCT study, Turgut and collaborators\textsuperscript{126} compared the efficacy of biparietal tDCS combined with optokinetic stimulation (eight sessions over 2 weeks) to that of a standard cognitive training, in 10 individuals with LHL and 6 with RHL suffering from USN. The authors showed greater efficacy of tDCS compared to standard treatment. Interestingly, RHL-participants showed improvement of allocentric
| Study | Participants | Protocol | Control | Stimulation | Coil | Number of Sessions | Tests | Assessment | Results | Design | Classification |
|-------|--------------|----------|---------|-------------|------|--------------------|-------|------------|---------|--------|----------------|
| Brighina et al.¹⁰⁴ | 3 RH | LF-rTMS over P5 | None | 900 pulses 1 Hz 90% MT | Figure-of-eight | 7 | LBT; Length judgment; Clock drawing | Pre (2 weeks); Post, Follow-up (2 weeks later) | Improvement at least for 15 days | Pilot | Class III |
| Oliveri et al.¹⁰⁵ | 5 RH 2 LH | HF-rTMS over contralesional hemisphere, P5 and P6 | Sham | 300 pulses 25 Hz 115% MT | Figure-of-eight | 1 | LBT; Length judgment | Pre, Post; Improvement after stimulation compared to sham | Pilot | Class II |
| Shindo et al.¹⁰⁶ | 2 RH | LF-rTMS over P5 | None | 900 pulses 0.9 Hz 90% MT | Figure-of-eight | 6 | BIT; BRS; BI; MMSE | Pre (2 weeks), Post; Follow-up (2, 4 and 6 weeks later) | Improvement in BIT and activities of daily living at least for 6 weeks | Pilot | Class III |
| Koch et al.¹⁰⁷ | 12 RH N+ 8 RH N- 10 Healthy participants | LF-rTMS over P3 | None | 600 pulses 1 Hz 90% MT | Figure-of-eight | 1 | Visual Chimeric Test | Pre, Post | LH hyperexcitability reduced in N+ patients; reduction of left-side omissions | Pilot | Class II |
| Song et al.¹⁰⁸ | 7 RH (TMS) 7 RH (Control) | LF-rTMS over P3 | None | 450 pulses 0.5 Hz 90% MT | Figure-of-eight | 20 (twice a day) | LBT and Cancellation Task | Pre (2 weeks), Post; Follow-up (2 weeks later) | Improvement in both tasks up to 2 weeks | Randomized controlled Pilot | Class Ia |
| Lim et al.¹⁰⁹ | 7 RH (TMS +BT) 7 RH (BT) | LF-rTMS over P5 | Behavioural Therapy (BT) | 900 pulses 1 Hz 90% MT | Figure-of-eight | 10 | LBT task; Albert Test | Pre (2 weeks), Post | Improvement in the line bisection task | Controlled open-label pilot | Class II |
| Agosta et al.¹¹⁰ | 6 RH | LF-rTMS over P3 | Sham Coil | 600 pulses 1 Hz 90% | Figure-of-eight | 2 | Visual tracking task; unilateral and bilateral task | Pre, Post, Follow-up (30 mins) | Improvement of sustained attention in the left visual field after rTMS, but not after sham | Crossover | Class II |

(Continued)
| Study       | Participants       | Protocol                                      | Control                                      | Stimulation                      | Coil                        | Number of Sessions | Tests                                         | Assessment | Results                                                   | Design | Classification |
|------------|--------------------|-----------------------------------------------|----------------------------------------------|------------------------------------|-----------------------------|----------------------|-----------------------------------------------|------------|----------------------------------------------------------|--------|-----------------|
| Kim et al. | 9 RH (HF-group)    | LF-rTMS over P3 + Standard Therapy            | Sham Coil + Standard therapy                | LF: 1200 pulses 1 Hz 90% MT       | Figure-of-eight             | 10                   | Motor-Free Visual Perception Test; LBT; Cancellation test; CBS; K-MBI | Pre (2 weeks), Post | HF-group improved in line bisection task. Both the HF- and LF-groups improved in K-MBI | RCT    | Class I        |
|            | 9 RH (LF-group)    | or HF-rTMS over P4 + Standard Therapy         |                                               | HF: 1000 pulses 10 Hz 90% MT      |                             |                      |                                               |            |                                                           |        |                 |
|            | 9 RH (sham-group)  |                                               |                                               |                                   |                             |                      |                                               |            |                                                           |        |                 |
| Cha & Kim | 15 RH (rTMS)       | LF-rTMS over P3 + Standard therapy            | Sham Coil + Standard therapy                | 1200 pulses 1 Hz 90 Hz           | Figure-of-eight             | 20                   | LBT; Box and block; Albert test; Grip strength test | Pre (4 weeks), Post | Improvement in every test after rTMS but not after sham stimulation | RCT    | Class I        |
|            | 15 RH (Sham)       |                                               |                                               |                                   |                             |                      |                                               |            |                                                           |        |                 |
|            | 15 RH (Both)       |                                               |                                               |                                   |                             |                      |                                               |            |                                                           |        |                 |
| Cazzoli et al. | 5 RH (cTBS)      | cTBS over P3                                  | Sham Coil                                   | 276 bursts (each contained 3 pulses at 30 Hz, repeated at 6 Hz) 100% MT | Round                       | 2                    | Visual search and two cancellation tasks with high or low attention load; Eye-tracking | Pre, Post | Improvement of neglect severity. Redeployment of visual fixations to the contralesional visual field; | RCT    | Class Ia       |
|            | 5 RH (Sham)        |                                               |                                               |                                   |                             |                      |                                               |            |                                                           |        |                 |
|            | 3 RH (Both)        |                                               |                                               |                                   |                             |                      |                                               |            |                                                           |        |                 |
| Hopfner et al. | 12 RH (SPT alone, SPT + cTBS, SPT + Sham) | cTBS over P3                                  | Sham Coil + SPT                           | 801 pulses 267 bursts (each including 3 pulses at 30 Hz, repeated at 6 Hz) 100% MT | Round                       | 1 (2 cTBS each day) | Bird cancellation task; | Pre, Post | Improvement of detection and cancellation score after cTBS + SPT compared to other conditions | NRCT   | Class Ia       |
|            | 6 RH (cTBS alone)  |                                               |                                               |                                   |                             |                      |                                               |            |                                                           |        |                 |
|            | 12 RH (cTBS + Sham)|                                               |                                               |                                   |                             |                      |                                               |            |                                                           |        |                 |
| Cazzoli et al. | 8 RH (cTBS + Sham) | cTBS over P3                                  | Sham Coil                                   | 801 pulses 30 Hz ISL 100 ms 100% MT | Round                       | 2 (4 cTBS each)  | CBS; Vienna test system; Picture test; Munich reading texts; short aphasia checklist | Pre (1 week); Post (1, 2 and 3 weeks later) | Improvement in every test only for real cTBS at least for 3 weeks | RCT    | Class I        |
|            | 8 RH (Sham + cTBS) |                                               |                                               |                                   |                             |                      |                                               |            |                                                           |        |                 |
|            | 8 (No stimulation) |                                               |                                               |                                   |                             |                      |                                               |            |                                                           |        |                 |
| Authors       | Hemisphere | Treatment | Coil | Parameters | Figure | Condition | Pre/Post/Follow-up | Description                                                                 | RCT Class |
|--------------|------------|-----------|------|------------|--------|-----------|-------------------|-----------------------------------------------------------------------------|-----------|
| Koch et al.  | RH (cTBS)  | cTBS over P3 | Sham Coil | 600 pulses | 50 Hz, ISI 200 ms, 80% MT | Figure-of-eight | Pre (2 weeks), Post, Follow-up (2 weeks later) | Improvement in BIT and reduced hyperexcitability of LH only after real cTBS for up to weeks after. | RCT Class I |
| Fu et al.    | RH (cTBS)  | cTBS over P5 | Sham cTBS + Standard Therapy | Three-pulse burst at 30 Hz, 80% MT | Figure-of-eight | Pre (14 consecutive days), Post, Follow-up (4 weeks) | Improvement in both tasks after cTBS, but not after Sham cTBS, at least for 4 weeks | RCT Class I |
| Fu et al.    | RH (cTBS)  | cTBS over P3 | cTBS over P3 | 600 pulses | 40% MT | Figure-of-eight | Pre (10 days), Post | Improvement in every test in both groups cTBS group showed lower connectivity in VAN after stimulation | RCT Class I |
| Yang et al.  | RH (LF-rTMS) | LF-rTMS or Sham rTMS | LF-rTMS 656 pulses, 1 Hz, 80% MT; HF-rTMS: 1000 pulses, 10 Hz, 80% MT; cTBS: 801 pulses, in bursts of 3 pulses at 30 Hz, 80% MT | Figure-of-eight | Pre, Post, Follow-up (1 month) | cTBS group displayed the best curative effect followed by 1 Hz and 10 Hz group; Enhanced connections in VAN after cTBS | RCT Class I |

Abbreviations: RH, Right Hemisphere; LF, Left Hemisphere; N+, Patients with Neglect; N+, Patients without Neglect; BT, Behavioural Therapy; rTMS, repetitive TMS; cTBS, continuous TBS; HF, High Frequency; LF, Low Frequency; MT, Motor Threshold; SPT, Smooth Pursuit eye movement Therapy; LBT, Line Bisection Task; BIT, Behavioural Inattention Test; BRs, Brunnstrom Recovery Stage; BI, Barthel Index; MMSE, Mini Mental State Examination; K-MBI, Korean version of Modified Barthel Index; CBS, Catherine Bergego Scale; DTI, diffusor tension imaging; RCT, Randomized Control Trial; NRCT, Non-Randomized Control Trial.
| Study         | Patients | Protocol                               | Control | Stimulation | Number of Sessions | Tests                                      | Assessment | Results                                                                 | Design      | Classification |
|--------------|----------|----------------------------------------|---------|-------------|--------------------|--------------------------------------------|------------|-------------------------------------------------------------------------|-------------|----------------|
| Brem et al,12 | 1 RH     | Single Mode: Anodal DC over P4         | Sham DC | 1 mA        | 10 (5 combined with standard therapy) | Covert attention test; LBT; cancelation and copy figures; ADL | Pre, Post, Follow-up (3 months) | Improvement in every test immediately after the treatment. Improvement only in ADL at the follow-up | Crossover   | Class III      |
| Ko et al,120  | 15 RH    | Single Mode: Anodal DC over P4         | Sham DC | 2 mA        | 1                  | Cancellation task; LBT                      | Pre, Post   | Improvement in every test                                               | Crossover   | Class I        |
| Sparing et al,121 | 10 RH | Cathodal over P3 or Anodal over P4 or Anodal over P3 | Sham DC | 1 mA        | 1                  | Subtests of Test Battery of Attentional Performance LBT | Pre, Post   | Improvement in LBT after Cathodal over P3 and Anodal over P4            | Crossover   | Class II       |
| Sunwoo et al,122 | 10 LH | Dual Mode: Anodal DC over P4 and Cathodal DC over P3 | Sham DC | 1 mA        | 1                  | LBT; Star cancellation task                 | Pre, Post   | Improvement in every test for dual and single mode. Dual mode was more effective than single | Crossover   | Class I        |
| Smit et al,123 | 5 RH     | Dual Mode: Anodal DC over P4 and Cathodal DC over P3 | Sham DC | 2 mA        | 5                  | Conventional tasks of BIT                   | Pre, Post, Follow-up (1 months) | No difference between the stimulation and sham condition                   | Placebo-controlled | Class I        |
| Yi et al,124  | 30 RH    | Single Mode: Anodal DC over P4 or Cathodal DC over P3 + Standard therapy | Sham DC + Standard therapy | 2 mA        | 15                 | Motor-free visual perception test (MVPT); LBT; Star cancellation task; CBS; m-BI | Pre, Post (1 weeks) | Improvement in MVPT, SCT, and LBT was greater in the anodal and cathodal groups than in the sham group | RCT         | Class I        |
| Study | Patient Characteristics | Intervention | Stimulation Parameters | Outcome Measures | Outcome Description | Study Design | Protocol |
|-------|-------------------------|--------------|------------------------|------------------|---------------------|--------------|----------|
| Bang and Bong | 12 RH (N+) | Dual Mode: Anodal DC over P4 and Cathodal over P3 + FT | FT alone, 2 mA, 20 min | MVPT, LBT, m-BI | Pre, Post | tDCS + FT decreased the symptoms of visuospatial neglect significantly more than FT alone | RCT | Class I |
| Turgut et al | 20 RH (N+) 12 LH (N-) | Dual Mode: Anodal DC over ipsilesional P4 and Cathodal DC over contralesional P3 + OKS | Standard therapy, 1.5–2.0 mA, 20 min | Spontaneous body orientation, LBT, Apples cancellation task, Clock drawing test, ADL | Pre, Post, Follow-up (6 days) | Improvement in spontaneous body orientation and in Clock Drawing Test | NRCT | Class II |
| GVS | Saj et al | 7 RH (N+), 5 RH (N-) | RC-GVS and Sham GVS | 1.5 mA (task time), 1 min | Subjective Vertical (SV) | Pre, Post | GVS induced a deviation toward the side opposite to the cathode in the three groups. LC-GVS stimulation can reduce the SV of N+ | NRCT Crossover | Class II |
| Nakamura et al | 7 RH | RC-GVS and Sham GVS | Below the ST (0.4–2.0 mA), 20 min | Line cancellation task | Pre, Post (10 min), Follow-up (20 min) | Improvement of cancellation score after LC-GVS at least for 20 mins | NRCT Crossover | Class II |
| Schmidt et al | 7 RH (N+), 15 RH (N-) | RC-GVS and Sham GVS | Below the ST (mean: 0.6 mA), 20 min | Horizontal Arm Position Sense (APS) | Pre, Post, Follow-up (20 min) | N+ showed impaired APS at baseline, which was improved after LC-GVS | NRCT Crossover | Class II |
| Zubko et al | 2 RH | RC-GVS | None | 1 mA and 1.5 mA, 20 min | Letter and Star cancellation task | Pre, Post, Follow-up (3 days) | Improvement in both tasks at least for 3 days | Pilot | Class III |
| Utz et al | 6 RH (N+), 11 RH (N-) | RC-GVS and Sham GVS | 1.5 mA, 20 min | LBT | Pre, Post | Both RC-GVS and LC-GVS lead to a reduction of rightward bias in N+ compared to N-, but it was larger after RC-GVS | NRCT Crossover | Class II |
Table 3 (Continued).

| Study             | Patients Description | Protocol | Control | Stimulation | Number of Sessions | Tests                        | Assessment | Results                                                                 | Design | Classification |
|-------------------|----------------------|----------|---------|-------------|-------------------|--------------------------|-------------|--------------------------------------------------------------------------|--------|----------------|
| Wilkinson et al.  | 15 RH (1 GVS – 9 Sham) | RC-GVS   | Sham GVS| Below the ST (0.5–1.5 mA) 25 min | 10 | BIT | Pre, Post, Follow-up (1 months) | Improvement after all conditions at least for 1 months | RCT | Class I |
|                   | 18 RH (5 GVS - 5 Sham) |          |         |             |                   |                          |             |                                                                          |        |                |
|                   | 16 RH (10 GVS)        |          |         |             |                   |                          |             |                                                                          |        |                |
| Oppenländer et al.| 11 RH (N+)  13 RH (N-) | RC-GVS and LC-GVS | Sham GVS| Below the ST (mean: 0.7 mA) 20 min | 3 | Digit cancellation; text copying; copy of symmetrical figures: LBT | Pre, Post | L-GVS improved egocentric neglect, R-GVS results in an amelioration of the allocentric neglect | NRCT Crossover | Class II |
| Volkering et al.  | 24 RH                | RC-GVS and LC-GVs + SPT and VST | Sham GVS + SPT and VST | 1.5 mA 20 min | 10-12 | Neglect test, visuo-tactile search task, SV and tactile vertical | Pre, Post, Follow-up (2 and 4 weeks) | Neither SPT nor the combination of SPT, VST and GVS improved neglect symptoms | RCT | Class I |
| Ruet et al.       | 4 RH                 | RC-GVS and LC-GVS | Sham GVS | 1.5 mA 20 min | 1 | LBT and star cancellation task | Pre, Post (after 10 min GVS) | No significant differences in the performance of either task following GVS | RCT crossover | Class I |

**Abbreviations:** RH, Right Hemisphere; LF, Left Hemisphere; N+, Patients with Neglect; N-, Patients without Neglect; DC, Direct Current; OKS, Optokinetic Stimulation; RC= Right Cathodal; LC, Left Cathodal; ST, Sensory Threshold; SPT, Smooth Pursuit eye movement Training; VST, Visual Scanning Training; FT, Feedback Training; LBT, Line Bisection Task; BIT, Behavioural Inattention Test; m-BI, modified Barthel Index; MMSE, Mini Mental State Examination; CBS, Catherine Bergego Scale; ADL, Activities of Daily Life; RCT, Randomized Control Trial; NRCT, Non-Randomized Control Trial.
symptoms, while the ones with LHL improved their egocentric symptoms. Findings from this study indicate that differences between egocentric and allocentric symptoms need to be considered in future brain stimulation studies. As shown in Table 3, 5 out of 8 tDCS studies provide class I (or Ia) evidence.83

Galvanic vestibular stimulation (GVS) is a variant of tDCS that consists in applying a weak direct percutaneous current through an anode and a cathode positioned over the right and the left mastoids. Cathodal currents induce an increase and anodal currents a decrease in the firing rate of the vestibular nerve.127–129 Some NRCT-studies applying R-GVS (ie, right anodal/left cathodal stimulation) showed beneficial effects on perceptual130,131 and arm-position symptoms132 of neglect. On the contrary, in other pilots,133 NRCT-134 and RCT-studies,135 L-GVS (ie, left anodal/right cathodal stimulation) has been found to ameliorate USN and the effects persist up to a month when stimulation was applied for several (10) sessions.135 A recent NRCT-study tested repetitive-GVS in right-brain-damaged people with neglect syndrome, by comparing the effects of R-GVS, L-GVS and sham stimulation.136 While previous studies showed vestibular stimulation effects on egocentric spatial neglect symptoms, authors interestingly reported that L-GVS significantly improved egocentric neglect (assessed by line bisection and text copying task) whereas R-GVS results in amelioration of allocentric neglect (evaluated by figure copying and digit cancellation tasks). However, two recent RCT-studies, using repeated sessions of stimulations (10–12 sessions)137 did not observe any post-treatment effects by GVS on neglect symptomatology.137,138 Future studies are necessary to better understand the specific influence of GVS on disorders of spatial awareness and its potential in neglect rehabilitation. As shown in Table 3, only 3 out of 9 studies were classified as class I investigations.

Virtual Reality

Computerized methods may provide a proper alternative approach to standard methods not only for the assessment but also for the rehabilitation of neglect.39 One of the most advanced tools recently implemented in clinical treatments is Virtual Reality (VR). In Table 4 are reported the most significant or recent studies on the use of VR for USN treatment. The VR can simulate relevant situations of everyday life and the possibility to control for head, eyes and limbs movements or postural shifts, provide a key feature for an optimal research setting.41 To our knowledge, the only RCT-study using VR on USN-rehabilitation was conducted by Kim and colleagues.139 Twelve people suffering from USN were asked to accomplish the following three tasks: 1) “Bird and Ball”, where they had to touch flying balls to turn them into a bird; 2) “Coconut”, where they had to grab a coconut falling down from a tree; and 3) the “Container”, where they had to relocate an object from one side to the other. The authors compared the outcomes of the experimental group to those of a control group undergoing standard training. Treatments were administered for 15 days over 3 weeks. Although both groups showed improvement after intervention, the VR-group had higher scores in star cancellation test and the Catherine Bergego Scale compared to controls. Another contribution to the use of VR in neglect rehabilitation is a single case study using the “Duckneglect” platform,140 in which the participant was asked to reach various targets in conditions requiring different levels of difficulty. The virtual environment was arranged in ecological settings representing everyday life situations. Authors administered the videogame-like task to a man affected by neglect, 5 days a week for a month. Results showed improvement of neglect on several standard evaluations and in daily-life activities persisting up to 5 months. A third low-cost VR-system for training street-crossing was validated by Navarro and colleagues.141 Fifteen USN individuals were recruited and compared to 17 post-stroke individuals without USN and 15 healthy participants. Interestingly, results showed that USN-group had more difficulties crossing the street avoiding accidents than the non-USN control group and healthy controls. Furthermore, a correlation between the scores of standard neuropsychological tests and those of the virtual street-crossing system was observed, suggesting the potential of the VR approach for USN rehabilitation. Another novel VR-training method is the RehAtt.142 The software consisted in visual scanning training with multi-sensory stimulation in a VR-environment. Fifteen post-stroke individuals suffering from chronic neglect were trained for 15 sessions over 5 weeks. Results showed that the VR-training improved visuospatial deficits and activities of daily living.142 Interestingly, 2 years later, authors used fMRI to evaluate changes in brain activity during Posner’s Cueing Task after RehAtt™ rehabilitation. The amelioration of neglect symptoms was associated with increased brain activity in the pre-frontal and temporal cortex during attentional cueing,143 suggesting enhancement of top-down strategies, and increased inter-hemispheric resting-state functional connectivity of the dorsal attentional
| Study          | Participants | Control          | VR Training                                      | Number of Sessions | Tests                                      | Assessment | Results                                                                 | Design   | Classification |
|---------------|--------------|------------------|------------------------------------------------|-------------------|--------------------------------------------|------------|-------------------------------------------------------------------------|----------|----------------|
| Kim et al     | 24 RH (12 VR-Group and 12 Control Group) | Standard therapy | Bird and Ball (touch a flying ball); Coconuts (catch falling coconuts); Container (move a box from one side to another) | 15 sessions of 30 mins | Star Cancellation task; LBT; CBS; K-MBI   | Pre, Post  | Improvement in CBS and in star cancellation task after VR training  | RCT      | Class I        |
| Mainetti et al | 1 RH          | None             | Duckneglect (reach targets with an increasing level of difficulties) | 20 sessions of 30 mins | Albert Test; Letter Cancellation Test; LBT; MMSE; Attentional Matrices and the Token Test | Pre, Post, Follow-up (5 months later) | Improvement in MMSE, Attentional matrices, Albert test and LBT, at least for 5 months  | Single-case | Class III      |
| Fordell et al | 15 RH         | None              | VST and multi-sensory stimulation               | 15 of 1 hr         | VR-Star cancellation; VR-Baking tray task; VR-LBT; VR-Extinction; VR-Posner Task; CBS | Pre, Post, Follow-up (6 months) | Improvement in Star cancellation, Baking tray, Extinction and Posner Task; Improvement in CBS at least for 6 months  | Pilot    | Class III      |
| Ekman et al   | 12 RH         | None              | VST and multi-sensory stimulation               | 15 of 1 hr         | VR-Posner Task; fMRI                      | Pre (1 week), Post (1 week) | Improvement in Posner performance. Increase in after VR-training in frontal and temporal activity during attentional cueing  | Pilot    | Class III      |
| Wählin et al  | 13 RH         | None              | VST and multi-sensory stimulation               | 15 of 1 hr         | VR-Posner task; rs-fMRI                    | Pre (1 week), Post (1 week) | Increase in DAN connectivity                                            | Pilot    | Class III      |

**Abbreviations:** RH, Right Hemisphere; VST, Visual Scanning Training; LBT, Line Bisection Task; K-MBT, Korean version of Modified Barthel Index; MMSE, Mini Mental State Examination; CBS, Catherine Bergego Scale; DAN, Dorsal Attention Network; RCT, Randomized Control Trial.
A final promising protocol was tested in a single-blind dose–response study in healthy subjects, by using VR as an alternative to real prisms. Authors progressively induced a displacement of the visual field following the virtual PA procedure, making difficult for the subject to become aware of the experimental manipulation. Results showed that large rightward deviations may affect sensorimotor performance in healthy participants similarly to neglect patients without generating discomfort linked to the large visual shift. However, results need to be replicated in stroke individuals with USN. Taken together, these studies suggest that VR-systems may represent a suitable alternative to standard rehabilitation techniques. By involving multisensory online feedbacks in real-like situations, virtual approaches may provide novel powerful tools for neglect rehabilitation. As shown in Table 4, only one out of five studies was classified as class I investigation. However, VR is one of the most recent and innovative approaches of USN rehabilitation and, up to now, its potentials have been only minimally explored.

Conclusions and Future Directions
Investigations of USN have provided most of the knowledge we currently have on the neural mechanisms of spatial attention and representation and their interaction with the response system. Nonetheless, correlating brain lesion localization with behavioral impairment presents a series of limitations (i.e., the extent of natural lesions which often involve more than one structure, the effects of the diaschisis and brain reorganization). Moreover, individuals’ clinical and cognitive conditions may posit practical constraints on recruitment and testing. In the last 20 years, cognitive neuroscientists have used TMS to induce neglect-like behaviors in healthy volunteers and overcome the above limits. These studies have disentangled previous controversies on neglect neuroanatomy, confirming a causal role of the right PPC in visuospatial attention during performance of stimulus detection and line bisecting/landmark tasks, and a role of superior temporal cortex in the performance of visual conjunction search task. These findings, in line with the observation that USN may dissociate across tasks, further highlight the importance of using diverse types of assessment tools to reliably evaluate neglect symptomatology for both clinical and experimental purposes. Consistent with recent studies on neglect neuroanatomy, single-pulse TMS applied to the right PPC inside the scanner, shows that neglect-like bias on the landmark task is associated with decreased activity of right parieto-frontal areas corresponding to those connected by SLFII. In contrast to the rivalry account of USN and in line with Heilmann’s hypothesis, these TMS/fMRI findings also show decreased activity of contralateral PCC (see Bagattini et al for similar findings), suggesting that unbalanced inter-hemispheric activity might worsen neglect symptomatology but not be necessary for its emergence. Future TMS and neuroimaging studies in the healthy brain may help to clarify the nature of neglect symptoms and the possibilities offered by brain stimulation, PA and other techniques to modulate them. As described in the present paper, high-quality studies have already demonstrated the efficacy of PA, TMS and tDCS interventions for the treatment of USN. In addition, preliminary investigations are suggesting the potentials of GVS and VR approaches for UNS rehabilitation. However, optimal protocols for USN rehabilitation still need to be defined.

To sum up, the application of advanced neuroimaging and brain stimulation techniques in healthy individuals and in individuals with USN may help to overcome parts of the limits posited by classical neuropsychological studies. On the other hand, only high-quality neuropsychological investigations of individuals with USN may provide unique insights into the syndrome and, consequently, into the mechanisms underpinning conscious space representations in the healthy brain.

Funding
This work was supported by MIUR (RICR_RILO_17_01) and Molo Foundation (BERA_CONTR FINA_15_01) grants.

Disclosure
The authors declare no conflicts of interest.

References
1. Bisiach E. Unilateral neglect and related disorders. In: Denes G, editor. Handbook of Clinical and Experimental Neuropsychology. Hove, East Sussex: Psychology Press; 1999:479–496.
2. Corbetta M, Kincade M, Lewis C, Snyder AZ, Sapir A. Neural basis and recovery of spatial attention deficits in spatial neglect. Nat Neurosci. 2005;8:1603–1610. doi:10.1038/nn1574
3. Ringman JM, Saver JL, Woolson RF, Clarke W, Adams JH. Frequency, risk factors, anatomy, and course of unilateral neglect in an acute stroke cohort. Neurology. 2004;63(3):468–474. doi:10.1212/01.WNL.0000133011.10689.CE.
4. Di Monaco M, Schintu S, Dotta M, Barba S, Tappero R, Gindri P. Severity of unilateral spatial neglect is an independent predictor of functional outcome after acute inpatient rehabilitation in individuals with right hemispheric stroke. Arch Phys Med Rehabil. 2011;92(8):1250–1256. doi:10.1016/j.apmr.2011.03.018

Neuropsychiatric Disease and Treatment 2020:16

Dovepress
44. Bisiach E, Ricci R, Lai E, De Tanti A, Inzaghi MG. Unilateral neglect and disambiguation of the Necker cube. Brain. 1999;122(1):131–140. doi:10.1093/brain/122.1.131

45. Kinsbourne M. Hemi-neglect and hemisphere rivalry. Adv Neurol. 1977;18:41–49.

46. Bisiach E, Ricci R, Módona MN. Visual awareness and anisomtery of space representation in unilateral neglect: a panoramic investigation by means of a line extension task. Conscious Cogn. 1998;7(3):327–355. doi:10.1006/ccog.1998.0361

47. Karnath HO. Spatial orientation and the representation of space with parietal lobe lesions. Philos Trans R Soc Lond B Biol Sci. 1997;352(1360):1411–1419. doi:10.1098/rstb.1997.0127

48. Vallar G, Guariglia C, Magnotti L, Pizzagalli L. Optokinetic stimulation affects both vertical and horizontal deficits of position sense in unilateral neglect. Cortex. 1995;31(4):669–683. doi:10.1016/S0010-9452(13)80019-6

49. Andersen RA. Encoding of intention and spatial location in the posterior parietal cortex. Cereb Cortex. 1995;5(5):457–469. doi:10.1093/cercor/5.5.457

50. Andersen RA, Snyder LH, Bradley DC, Xing J. Multimodal representation of space in the posterior parietal cortex and its use in planning movements. Ann Rev Neurosci. 1997;20:303–330. doi:10.1146/annurev.neuro.20.1.303

51. Critchley M. The phenomenon of tactile inattention with special reference to parietal lesions. Brain. 1949;72(4):538–561. doi:10.1093/brain/72.4.538

52. Mort DJ, Mallotta P, Mannan SK, et al. The anatomy of visual neglect. Brain. 2003;126(9):1985–1997. doi:10.1093/brain/awg200

53. Vallar G. Extrapersonal visual unilateral spatial neglect and its neuroanatomy. NeuroImage. 2001;14(1 II):52–58. doi:10.1006/nimg.2001.0822

54. Karnath HO, Ferber S, Himmelbach M. Spatial awareness is a function of the temporal not the posterior parietal lobe. Nature. 2001;411(6840):950–953. doi:10.1038/35082075

55. Hillis AE. Neurobiology of unilateral spatial neglect. Neuroscientist. 2000;6(2):153–163. doi:10.1177/1073858400284257

56. Medina J, Kannan V, Pawlak MA, et al. Neural substrates of visuospatial processing in distinct reference frames: evidence from unilateral spatial neglect. J Cogn Neurosci. 2009;21:2073–2084. doi:10.1162/jocn.2008.21160

57. Chechclaz M, Rotstein P, Bickerton WL, Hansen PC, Deb S, Humphreys GW. Separating neural correlates of allocentric and egocentric neglect: distinct cortical sites and common white matter disconnections. Cogn Neurosci. 2010;27(3):277–303. doi:10.1080/20448294.2010.519699

58. Bartolomeo P, Thieubert De Schotten M, Doricchi F. Left unilateral neglect as a disconnection syndrome. Cereb Cortex. 2007;17(11):2479–2490. doi:10.1093/cercor/bhl181

59. Doricchi F, Tomaiuolo F. The anatomy of neglect without hemianopia. NeuroReport. 2003;14(17):1–5. doi:10.1097/0001756-200312200-00002

60. Ricci R, Salatino A, Li X, et al. Imaging the neural mechanisms of TMS neglect-like bias in healthy volunteers with the interleaved TMS/MRI technique: preliminary evidence. Front Hum Neurosci. 2012;6(December):1–13. doi:10.3389/fnhum.2012.00326

61. Molenberghs P, Sale MV, Mattingley JB. Is there a critical lesion site for unilateral spatial neglect? A meta-analysis using activation likelihood estimation. Front Hum Neurosci. 2012;6(April):1–10. doi:10.3389/fnhum.2012.00078

62. Lunven M, Bartolomeo P. Attention and spatial cognition: neural and anatomical substrates of visual neglect. Ann Phys Rehabil Med. 2017;60(3):124–129. doi:10.1016/j.rehab.2016.01.004

63. Frassinetti F, Angeli V, Meneghelli F, Avanzi S, Ladavas E. Long-lasting amelioration of visuospatial neglect by prism adaptation. Brain. 2002;125(3):608–623. doi:10.1093/brain/awf856

64. Rode G, Pisella L, Rossetti Y, Farnè A, Boisson D. Bottom-up transfer of sensory-motor plasticity to recovery of spatial cognition: visuomotor adaptation and spatial neglect. Prog Brain Res. 2003;142:273–287. doi:10.1016/S0079-6123(03)42019-0

65. Antonucci G, Guariglia C, Judica A, et al. Effectiveness of neglect rehabilitation in a randomized group study. J Clin Exp Neuropsychol. 1995;17(3):383–389. doi:10.1080/01688639508405131

66. Luauté J, Halligan P, Rode G, Rossetti Y, Boisson D. Visuo-spatial neglect: a systematic review of current interventions and their effectiveness. Neurosci Biobehav Rev. 2006;30(7):961–982. doi:10.1016/j.neubiorev.2006.03.001

67. Pritiš K, Passarini L, Pilosio C, Meneghello F, Pitteri M. Visual scanning training, limb activation treatment, and prism adaptation for rehabilitatiing left neglect: who is the winner? Front Hum Neurosci. 2013;7(July):1–12. doi:10.3389/fnhum.2013.00360

68. Salatino A, Barba S, Vigna F, et al. Prism adaptation and visual scanning training treatments in unilateral spatial neglect. Neuro Sci. 2015;36(1998):194.

69. Spaccavento S, Cellamare F, Cafforio E, Loverre A, Craca A. Efficacy of visual-scanning training and prism adaptation for neglect rehabilitation. Appl Neuropsychol Adult. 2016;23(5):313–321. doi:10.1080/23270905.2015.1038386

70. Polanowska KE, Seniów JB, Paprot E, Lesiński MM, Czonkowska A. Left-hand somatosensory stimulation combined with visual scanning training in rehabilitation for post-stroke hemineglect: a randomised, double-blind study. Neuropsychol Rehabil. 2009;19(3):364–382. doi:10.1080/09602010802268856

71. Bailey MJ, Riddoch MJ, Crome P. Treatment of visual neglect in elderly patients with stroke: a single-subject series using either a scanning and cueing strategy or a left-limb activation strategy. Phys Ther. 2002;82(8):782–797. doi:10.1093/ptj/82.8.782

72. Brem A, Unterberger E, Speight I, Jäncke L. Treatment of visuospatial neglect with biparietal tDCS and cognitive training: a single-case study. Front Syst Neurosci. 2014;8:doi:10.3389/fnsys.2014.00180.

73. Smania N, Fonte CS, Picelli A, Gandolfi M, Varalta V. Effect of eye patching in rehabilitation of hemispatial neglect. Front Hum Neurosci. 2013. doi:10.3389/fnhum.2013.00527

74. Bottini G, Gandola M. Beyond the non-specific attentional effect of caloric vestibular stimulation: evidence from healthy subjects and patients. Multisensory Res. 2015;28(5–6):591–612. doi:10.1111/22138408-0002504

75. Wellfringer A, Leifert-Fiebach G, Babinsky R, Brandt T. Visuomotor imagery as a new tool in the rehabilitation of neglect: a randomised controlled study of feasibility and efficacy. Disabil Rehabil. 2011;33(21–22):2033–2043. doi:10.3109/09638288.2011.556208

76. Dohle C, Püllen J, Nakaten A, Käst J, Rietz C, Karbe H. Mirror therapy promotes recovery from severe hemiparesis: a randomized controlled trial. Neurorehabil Neural Repair. 2009;23(3):209–217. doi:10.1177/1545968308324786

77. Pitzalis S, Spinelli D, Vallar G, Russo FD. Transcutaneous electrical nerve stimulation effects on neglect: a visual-evoked potential study. Front Hum Neurosci. 2013;7:doi:10.3389/fnhum.2013.00111.

78. Kerrhoffer G, Reinhart S, Ziegler W, Artinger F, Marquardt C, Helmchen C. Randomized controlled trial on hemifield eye patching and optokinetic stimulation in acute spatial neglect. Stroke. 2014;45(8):2465–2468. doi:10.1161/STROKEAHA.114.006059
80. von der Gablentz J, Königsmund I, Sprenger A, et al. Brain activations during optokinetic stimulation in acute right-hemisphere stroke patients and hemispatial neglect: an fMRI study. *Neuropsychiatr Dis Treat*. 2017;13:821–832. doi:10.2147/NDT.S126582

81. Kwakkel G, Zeijlmans van Enckevort F, de Vet HC, et al. Constraint-induced motor therapy after stroke. *Lancet Neurol*. 2013;12(2):101–108. doi:10.1016/S1474-4422(13)70203-4

82. Corbetta D, Sieroti V, Castellini G, Moja L, Gatti R. Constraint-induced movement therapy for upper extremities in people with stroke. *Cochrane Database Syst Rev*. 2015;(10):Art No.: CD004433. doi:10.1002/14651858.CD004433.pub3

83. Cicerone KD, Dahlberg C, Kalmar K, et al. Evidence-based cognitive rehabilitation: recommendations for clinical practice. *Arch Phys Med Rehabil*. 2000;81(12):1596–1615. doi:10.1053/apmr.2000.19240

84. Fortis P, Chen P, Goedert KM, Barrett AM. Effects of prism adaptation on motor-intentional spatial bias in neglect. *Neuroreport*. 2011;22(14):700–705. doi:10.1097/WNR.0b013e328353a3e20

85. Pisella L, Rode G, Farne A, Tilikete C, Rossetti Y. Prism adaptation in the rehabilitation of patients with visuo-spatial cognitive disorders. *Curr Opin Neurol*. 2006;19(6):534–542. doi:10.1097/WCO.0b013e328010924b

86. Martin-Arvalo E, Schintu S, Farne A, Pisella L, Reilly KY. Adaptation to leftward shifting prisms alters motor interhemispheric inhibition. *Cereb. Cortex*. 2018;28(2):528–537. doi:10.1093/cercor/bhw386

87. Rossetti Y, Rode G, Pisella L, et al. Prism adaptation to a rightward optical deviation habituates left hemispatial neglect. *Nature*. 1998;395(6708):166–169. doi:10.1038/25988

88. Farne A, Rossetti Y, Toniolesi S, Ladasav A. Ameliorating neglect with prism adaptation: visuo-manual and visuo-verbal measures. *Neuropsychologia*. 2002;40(7):718–729. doi:10.1016/S0028-3932(01)00186-5

89. Serino A, Bonifazi S, Pierfederici L, Làdavas E. Neglect treatment by prism adaptation: what recovers and for how long. *Neuropsychol Rehabil*. 2007;17(6):657–687. doi:10.1080/09602010601052006

90. Serino A, Barbiani M, Rinaldesi ML, Ladasav A. Efferentness of prism adaptation in neglect rehabilitation. *Stroke*. 2009;40(4):1392–1398. doi:10.1161/strokeaha.108.530485

91. Vaes N, Nys G, Lafosse C, et al. Rehabilitation of visuo-spatial neglect by prism adaptation: effects of a mild treatment regime. A randomised controlled trial. *Neuropsychol Rehabil*. 2018;28(6):899–918. doi:10.1080/09602011.2018.1208617

92. Muzzo K, Tsuchiya T, Takebayashi T, Fujitani T, Hase K, Liu M. Prism adaptation therapy enhances rehabilitation of stroke patients with unilateral spatial neglect: a randomized, controlled trial. *Neuropsychol Rehabil. 2011;25(8):711–720. doi:10.1177/1545693111407516

93. Nys GMS, Seurinck R, Dijkerman HC. Prism adaptation moves neglect-related perseveration to contralesional space. *Cognit Behav Neurol*. 2008;21(4):249–253. doi:10.1097/WNN.0b013e31818aa5e1

94. Turton AJ, O’Leary K, Gabb J, Woodward R, Gilchrist ID. A single blinded randomised controlled pilot trial of prism adaptation for improving self-care in stroke patients with neglect. *Neuropsychol Rehabil*. 2010;20(2):180–196. doi:10.1080/0960201090340683

95. Mancuso M, Pacini MJ, Gemignani P, et al. Clinical application of prismatic lenses in the rehabilitation of neglect patients. A randomized controlled trial a randomized controlled trial. *Eur J Phys Rehabil Med*. 2012;48(2):197–208.

96. Rode G, Lacour S, Jaquin-Courtois S, et al. Long-term sensorimotor and therapeutical effects of a mild regime of prism adaptation in spatial neglect. A double-blind RCT essay. *Ann Phys Rehabil Med*. 2015;58(2):40–53. doi:10.1016/j.jrehab.2014.10.004

97. Ten Brink AF, Visser-Meily JMA, Schut MJ, Kouwenhoven M, Eijsackers ALH, Nijboer TCW. Prism adaptation in rehabilitation? No additional effects of prism adaptation on neglect recovery in the subacute phase poststroke: a randomized controlled trial. *Neuropsychiatr Dis Treat*. 2017;13(12):1017–1028. doi:10.2147/NDT.S15456931744277

98. Gammeri R, Turri F, Ricci R, Ptak R. Adaptation to virtual prisms and its relevance for neglect rehabilitation: a single-blind dose-response study with healthy participants. *Neuropsychol Rehabil*. 2018;1–14. doi:10.1080/09962011.2018.1590267

99. Salatino A, Berra E, Troni W, et al. Behavioral and neuroplastic effects of low-frequency rTMS of the unaffected hemisphere in a chronic stroke patient: a concomitant TMS and fMRI study. *Neurocase*. 2014;20(6):615–626. doi:10.1080/135545794.2013.826691

100. D’Agata F, Peila E, Cicerale A, et al. Cognitive and neurophysiological effects of non-invasive brain stimulation in stroke patients after motor rehabilitation. *Front Behav Neurosci*. 2016;10. doi:10.3389/fnbeh.2016.00135

101. Ricci R, Salatino A, Siebner HR, Mazzeo G, Nobili M. Normalizing biased spatial attention with parietal rTMS in a patient with focal hand dystonia. *Brain Stimul*. 2014;7(6):912–914. doi:10.1016/j.brs.2014.07.038

102. Salatino A, Momo N, Nobili M, Berti A, Ricci R. Awareness of symptoms amelioration following low-frequency repetitive transcranial magnetic stimulation in a patient with Tourette syndrome and comorbid obsessive-compulsive disorder. *Brain Stimul*. 2014;7(2):341–343. doi:10.1016/j.brs.2014.01.002

103. Salatino A, Boccia G, Dardanello D, et al. Acute and cumulative effects of rTMS on behavioural and EMG parameters in focal hand dystonia. *Heliyon*. 2019;5(11):e02770. doi:10.1016/j.heliyon.2019.e02770

104. Brighina F, Bisiach E, Oliveri M, et al. 1 Hz repetitive transcranial magnetic stimulation of the unaffected hemisphere ameliorates contralesional visuospatial neglect in humans. *Neurosci Lett*. 2003;336(3):131–133. doi:10.1016/s0304-3900(02)01283-1

105. Oliveri M, Bisiach E, Brighina F, et al. rTMS of the unaffected hemisphere transiently reduces contralesional visuospatial heineglect. *Neurology*. 2001;57(7):1338–1340. doi:10.1212/WNL.57.7.1338

106. Shindo K, Sugiyama K, Huaibo L, Nishijima K, Kondo T, Izumi SI. Long-term effect of low-frequency repetitive transcranial magnetic stimulation over the unaffected posterior parietal cortex in patients with unilateral spatial neglect. *J Rehabil Med*. 2006;38(1):65–67. doi:10.1650/165197050441807

107. Koch G, Oliveri M, Chee R, BJ, et al. Hyperexcitability of parietal-motor functional connections in the intact left-hemisphere of patients with neglect. *Brain*. 2008;131(Pt 12):3147–3155. doi:10.1093/brain/awn273

108. Song W, Du B, Xu Q, Hu J, Wang M, Luo Y. Low-frequency rTMS alters motor interhemispheric parietal-motor functional connections in the intact left-hemisphere of patients with neglect: a concomitant TMS and fMRI study. *Neuropsychiatr Dis Treat*. 2020;16:276. doi:10.2147/NDTT.S244489

109. Agosta S, Herpich F, Miceli G, Ferraro F, Battelli L. Contralesional rTMS relieves visual extinction in chronic stroke. *Neuropsychologia*. 2014;62:269–276. doi:10.1016/j.neuropsychologia.2014.07.026

110. Kim BR, Chen MH, Kim D, Lee SJ. Effect of high- and low-frequency repetitive transcranial magnetic stimulation on visuospatial neglect in patients with acute stroke: a double-blind, sham-controlled trial. *Arch Phys Med Rehabil*. 2013;94(5):803–807. doi:10.1016/j.apmr.2012.12.016
112. Cha HG, Kim MK. Effects of repetitive transcranial magnetic stimulation on arm function and decreasing unilateral spatial neglect in subacute stroke: a randomized controlled trial. Clin Rehabil. 2016;30(7):649–656. doi:10.1177/0269215515599817

113. Cazzoli D, Rosenthal CR, Kennard C, Zito GA, Nyffeler T. Theta burst stimulation improves overt visual search in spatial neglect independent of attentional load. Cortex. 2015;73:317–329. doi:10.1016/j.cortex.2015.09.009

114. Hopfner S, Cazzoli D, Müri RM, Nef T, Nyffeler T. Enhancing treatment effects by combining continuous theta burst stimulation with smooth pursuit training. Neuropsychologia. 2015;74:145–151. doi:10.1016/j.neuropsychologia.2014.10.018

115. Cazzoli D, Müri RM, Schumacher R, et al. Theta burst stimulation reduces disability during the activities of daily living in spatial neglect. Brain. 2012;135(11):3426–3439. doi:10.1093/brain/awz182

116. Koch G, Bonni S, Giacobbe V, et al. 0-burst stimulation of the left hemisphere accelerates recovery of hemispatial neglect. Neurology. 2012;78(1):24–30. doi:10.1212/WNL.0b013e31823d08f

117. Fu W, Song W, Zhang Y, et al. Long-term effects of continuous theta-burst stimulation in visuospatial neglect. J Int Med Res. 2015;43(2):196–203. doi:10.1177/0300060514539863

118. Fu W, Cao L, Zhang Y, et al. Continuous theta-burst stimulation may improve visuospatial neglect via modulating the attention network: a randomized controlled study. Top Stroke Rehabil. 2017;24(4):236–241. doi:10.1080/10749357.2016.1253139

119. Yang W, Liu T, Song X, Zhang Y, Liu J. Comparison of different stimulation parameters of repetitive transcranial magnetic stimulation for unilateral spatial neglect in stroke patients. J Neurosci. 2015;35(9):219–225. doi:10.1016/j.jns.2015.08.1541

120. Ko MH, Han SH, Park SH, Seo JH, Kim YH. Improvement of visual scanning after DC brain polarization of parietal cortex in patients with stroke neglect. Neurosci Lett. 2008;448(2):171–174. doi:10.1016/j.neulet.2008.10.050

121. Sparing R, Thimm M, Hesse MD, Küst J, Karbe H, Fink GR. Bidirectional alterations of interhemispheric parietal balance by non-invasive cortical stimulation. Brain. 2009;132(11):3011–3020. doi:10.1093/brain/aws154

122. Sunwoo H, Kim YH, Chang WH, Noh S, Kim EJ, Ko MH. Effects of dual transcranial direct current stimulation on post-stroke unilateral visuospatial neglect. Neurosci Lett. 2015;554:94–98. doi:10.1016/j.neulet.2015.08.064

123. Smut M, Schutter DJ, Nijboer TC, Visser-Meily JM, Dijkerman HC. Transcranial direct current stimulation to the parietal cortex in hemispatial neglect: a feasibility study. Neuropsychologia. 2015;74:152–161. doi:10.1016/j.neuropsychologia.2015.04.014

124. Yi YG, Chun MH, Do KH, Song EJ, Kwon YG, Kim DY. The effect of transcranial direct current stimulation on neglect syndrome in stroke patients. Ann Rehabil Med. 2016;40(2):223–229. doi:10.5535/arm.2016.40.2.223

125. Bang D, Bong S. Effect of combination of transcranial direct current stimulation and feedback training on visuospatial neglect in patients with subacute stroke: a pilot randomized controlled trial. J Phys Ther Sci. 2015. doi:10.1589/jpts.27.2759

126. Turgut N, Chun MH, Do KH, Song EJ, Kwon YG, Kim DY. The effect of transcranial direct current stimulation on neglect syndrome in stroke patients. Ann Rehabil Med. 2016;40(2):223–229. doi:10.5535/arm.2016.40.2.223

127. Utz KS, Koehler B, Kerkhoff G. Galvanic vestibular stimulation reduces the pathological rightward line bisection error in neglect—a sham stimulation-controlled study. Neuropsychologia. 2011;49:1219–1225. doi:10.1016/j.neuropsychologia.2011.02.046

128. Wilkinson D, Zubko O, Sakel M, Coulton S, Higgins T, Pullicino P. Galvanic vestibular stimulation in hemispatial neglect. Front Integr Neurosci. 2014;8(January):1–12. doi:10.3389/fint.2014.00004

129. Oppenländer K, Utz KS, Reinhart S, Keller I, Kerkhoff G, Schaadt AK. Subliminal galvanic-vestibular stimulation recalibrates the distorted visual and tactile subjective vertical in right-sided stroke. Neuropsychologia. 2015;74:178–183. doi:10.1016/j.neuropsychologia.2015.03.004

130. Volkening K, Kerkhoff G, Keller I. Effects of repetitive galvanic vestibular stimulation on spatial neglect and verticality perception—a randomised sham-controlled trial. Neuropsychol Rehabil. 2018;28(7):1179–1196. doi:10.1080/09602011.2016.1248446

131. Ruet A, Jokie C, Denise P, Leroy F, Azouvi P. Does galvanic vestibular stimulation reduce spatial neglect? A negative study. Ann Phys Rehabil Med. 2014;57(9–10):570–577. doi:10.1016/j.rehab.2014.09.009

132. Kim YM, Chun MH, Yun GJ, Song YJ, Young HE. The effect of virtual reality training on unilateral spatial neglect in stroke patients. Ann Rehabil Med. 2011. doi:10.5535/arm.2011.35.3.309

133. Mainetti R, Sedda A, Ronchetti M, Bottini G, Borghese NA. Duckneglect: video-games based neglect rehabilitation. Technol Health Care. 2013;21(2):97–111. doi:10.3233/THC-120717

134. Navarro M, Lloréns R, Noé E, Ferri J, Alcañiz M. Validation of a low-cost virtual reality system for training street-crossing. A comparative study in healthy, neglected and non-neglected stroke individuals. Neuropsychol Rehabil. 2013;23(4):597–618. doi:10.1080/09602011.2013.806269

135. Fordell H, Bodin K, Eklund A, Malm J. RehAtt – scanning training for neglect enhanced by multi-sensory stimulation in virtual reality. Top Stroke Rehabil. 2016;23(3):191–199. doi:10.1080/10749357.2016.1138670

136. Ekman U, Fordell H, Eriksson J, et al. Increase of frontal neuronal activity in chronic neglect after training in virtual reality. Acta Neurol Scand. 2018;138(4):284–292. doi:10.1111/ane.12955

137. Wählin A, Fordell H, Ekman U, Lenfeldt N, Malm J. Rehabilitation in chronic spatial neglect strengthens resting-state connectivity. Acta Neurol Scand. 2019;139(3):254–259. doi:10.1111/ane.13048
145. Rose NS, Rendell PG, Hering A, Kliegel M, Bidelman GM, Craik FIM. Cognitive and neural plasticity in older adults’ prospective memory following training with the virtual week computer game. *Front Hum Neurosci*. 2015;9(October):1–13. doi:10.3389/fnhum.2015.00592

146. Hilgetag CC, Théoret H, Pascual-Leone A. Enhanced visual spatial attention ipsilateral to rTMS-induced ‘virtual lesions’ of human parietal cortex. *Nat Neurosci*. 2001;4:953–957. doi:10.1038/nn0901-953

147. Fierro B, Brighina F, Piazza A, Oliveri M, Bisiach E. Timing of right parietal and frontal cortex activity in visuo-spatial perception: a TMS study in normal individuals. *NeuroReport*. 2001;12(11):2605–2607. doi:10.1097/00001756-200108080-00062

148. Giglia G, Pia L, Folegatti A, Puma AL, Brighina F. Far space remapping by tool use: a rTMS study over the right posterior parietal cortex. *Brain Stimul*. 2015;8:795–800. doi:10.1016/j.brs.2015.01.412

149. Giglhuber K, Maurer S, Zimmer C, Meyer B, Krieg SM. Evoking visual neglect-like deficits in healthy volunteers – an investigation by repetitive navigated transcranial magnetic stimulation. *Brain Imaging Behav*. 2017;11(1):17–29. doi:10.1007/s11682-016-9506-9

150. Bjoertomt O, Cowey A, Walsh V. Near space functioning of the human angular and supramarginal gyri. *J Neuropsychol*. 2009;3(1):31–43. doi:10.1348/174866408X394604

151. Brighina F, Bisiach E, Piazza A, et al. Perceptual and response bias in visuospatial neglect due to frontal and parietal repetitive transcranial magnetic stimulation in normal subjects. *Neuroreport*. 2002;13(18):2571–2575. doi:10.1097/01.wnr.0000052321.62862.7e

152. Salatino A, Poncini M, George MS, Ricci R. Hunting for right and left parietal hot spots using single-pulse TMS: modulation of visuospatial perception during line bisection judgment in the healthy brain. *Front Psychol*. 2014;1–7. doi:10.3389/fpsyg.2014.01238

153. Salatino A, Chillemi G, Gontero F, et al. Transcranial magnetic stimulation of posterior parietal cortex modulates line-length estimation but not illusory depth perception. *Front Psychol*. 2019;1–8. doi:10.3389/fpsyg.2019.01169

154. De Schotten MT, Dell’Acqua F, Forkel SJ, et al. A lateralized brain network for visuospatial attention. *Nat Neurosci*. 2011;14:1245–1246. doi:10.1038/nn.2905

155. Bagattini C, Mazzi C, Savazzi S. Waves of awareness for occipital and parietal phosphenes perception. *Neuropsychologia*. 2015;70:114–125. doi:10.1016/j.neuropsychologia.2015.02.021