



Systematic Review of Sensory Stimulation Programs in the Rehabilitation of Acquired Brain Injury

Joana O. Pinto¹ , Artemisa R. Dorés², Bruno Peixoto^{3,4}, Andreia Geraldo¹, and Fernando Barbosa¹

¹Laboratory of Neuropsychophysiology, Faculty of Psychology and Education Sciences, University of Porto, Portugal

²School of Health, Polytechnic Institute of Porto, Portugal

³CESPU, University Institute of Health Sciences, Gandra, Portugal

⁴NeuroGen – Center for Health Technology and Services Research (CINTESIS), Porto, Portugal

Abstract: Acquired Brain Injury (ABI) can lead to sensory deficits and compromise functionality. However, most studies have been focused on motor stimulation in stroke and traumatic brain injury (TBI). Sensory stimulation in stroke and mild/moderate TBI has received reduced interest. The main objective of this review is to know the methodological characteristics and effects of sensory programs in ABI. Studies with the purpose of testing the efficacy of those programs were identified through a literature search, following the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) and the Cochrane Collaboration Guidelines. Twenty-three studies were included in this review. The results show that in most studies sensory stimulation started within 12 months after injury and there is no consensus regarding frequency, duration and number of sessions, duration of intervention, and instruments used to assess outcomes. Most programs involved unisensory stimulation, and vision was the predominant target. The most used methods were compensation and somatosensory discrimination training. Most studies used a pre- and post-intervention assessment, with few studies comprising follow-up assessment. Regarding the studies revised, the interventions with positive outcomes in ABI are: compensation, cognitive training, vestibular intervention, somatosensory discrimination training, proprioceptive stimulation with muscle vibration, and sustained attention training with olfactory stimulation. Available findings suggest that sensory stimulation has positive results with immediate and long-term improvements in sensory functioning. This review provides useful information to improve rehabilitation and to design future investigation.

Keywords: sensory stimulation, acquired brain injury, systematic review, PRISMA

Acquired Brain Injury (ABI) is defined as brain damage not related to a congenital defect nor degenerative disease that may cause temporary or permanent dysfunctions and poor psychosocial adjustment (World Health Organization [WHO], 1996). The most prevalent causes for ABI worldwide are traumatic brain injury (TBI) and stroke, which in turn are relevant causes of death and incapacity (Feigin et al., 2017; Hawryluk & Bullock, 2016). Depending on the nature and location of the lesion, sensory, cognitive, motor, behavioral, and emotional deficits can emerge. These alterations may have impacts in activities of daily living, social participation, and occupational re-integration. Therefore, rehabilitation should be initiated as soon as possible, targeting motor, sensory, cognitive, and affective functioning. However, the clinical heterogeneity of the

ABI groups and of the interventions used, pose a serious challenge to the research and intervention in this field (Turner-Strokes, 2003).

About 60% of the individuals present sensory deficits after ABI (Carey, 1995). ABI severity is positively correlated with the severity of the sensory compromise (Tyson et al., 2008). Connell (2007) points that 46–71% of the variance regarding recuperation is explained by the severity of the ABI, sensory commitment, and daily living functionality, suggesting that cognitive factors and perceptive ability affect this result.

TBI may lead to damage of sensory receptors and sensory pathways (Folmer et al., 2011). Despite the higher prevalence of mild and moderate TBI in comparison to severe TBI (Li et al., 2016), there is a lesser interest in the

sensory stimulation in the two first forms. Padilla and Domina (2016) found evidence that multimodal stimulation improves arousal and clinical outcomes of comatose patients or in persistent vegetative state. As a result, these authors recommend the early implementation of sensory stimulation, with intensive frequency (3–5 times/day, 20 min sessions) and increasing complexity of the programs, adjusting the stimuli to patient's pre-morbid preferences.

Sensory stimulation consists in the controlled exposition to specific sensory stimuli or environments through different procedures (Padilla & Domina, 2016). Most of the intervention protocols for persons with consciousness disorders encompass simple, frequent, and repetitive stimuli, which may have emotional or autobiographical content. The use of natural or virtual environments with complex stimuli is considered as being more effective than artificial environments, as the former require cognitive processing of input and output information and allow the introduction of emotional and autobiographical contents (Abbate et al., 2014).

The stimulation strategies can be directed to one sense only (unimodal or unisensory stimulation) or several senses (multimodal or multisensory stimulation). Senses can be divided in primary modalities, such as touch, pressure, pain, temperature, position, and vibration, and secondary modalities, such as tactile discrimination, stereognosis, graphesthesia, tactile localization, among others. Regarding vision and hearing, a lesion in the primary visual cortex or in the primary auditory cortex often originates sensory-perceptive disturbances, and lesions in the association cortices may cause incapacity to recognize and interpret stimuli (Campbell, 2013).

Concerning visual rehabilitation, three methods are usually considered: (a) adaptation or compensation; (b) substitution; and (c) restoration (Zangwill, 1947). Compensation aims to adapt patients to the loss of visual field, namely through the training of visual search strategies. Substitution strategies aim to change visual field using apparatus such as prisms, eye-patches, and magnifying glasses (Rowe et al., 2013). Restoration is mostly achieved by the stimulation of the neural areas in the transition between the compromised and intact visual fields (Bergsma et al., 2012).

Hemineglect is one of the common sequelae of both stroke and TBI. The treatment approaches can be divided into extrinsic or top-down, intrinsic or bottom-up, and combined. The top-down approaches make use of external orientations in order to elicit active, conscious, and meaningful participation of the patient; bottom-up approaches do not require patients' active participation, once these approaches are based on the manipulation the characteristics of the stimuli or direct activation of the brain itself. Top-down approaches include training of visual scanning, sustained attention, and mental imagery, while bottom-up include prism glasses, phasic alert, torso rotation,

eye-patches, limb activation, optokinetic and thermal stimulation, transcutaneous electric stimulation, neck muscles vibration, and direct cerebral stimulation. Combined strategies are also possible, for example including prism adaptation and visual search training (Marshall, 2009).

The need for sensory intervention has been justified with several factors. Sensory deficits compromise the ability to explore the environment (Carey et al., 1993), the functionality in activities of daily living (Nelles et al., 2010), are related to a reduction in social participation (Carey et al., 2018; Rowe et al., 2013), and associated with cognitive deficits (Schubert et al., 2017). For example, not only visual and auditory deficits have a negative impact on cognitive functioning, but reduction in processing speed and executive deficits also have a negative influence on visual and auditory processing (Lew et al., 2010). Thus, authors like Sullivan and Hedman (2008) point to the need of further studies, namely to determine methodological issues such as the dose-response ratio in sensory stimulation in order to better adjust the rehabilitation programs.

Summing-up, previous systematic reviews assessed the effects of: (a) multisensory stimulation after ABI on low- and higher-level sensory deficits (Tinga et al., 2016); (b) multimodal stimulation in persistent vegetative state or comatose patients (Padilla & Domina, 2016); (c) different therapies for hemineglect after ABI (Bowen et al., 2013; Kashiwagi et al., 2018; Lisa et al., 2013; Yang et al., 2013); (d) sensory stimulation on motor recuperation (Grant et al., 2018; Laufer & Elboim-Gabyzon, 2011).

To our knowledge this is the first systematic review aiming to analyze the methodological characteristics of sensory stimulation programs for the rehabilitations of ABI patients. The present work also intended to systematically review the effects of sensory stimulation on cognitive rehabilitation and to determine the most frequent clinical conditions in which they are used. Regarding the impact of the sensory deficits the review focused on programs directed to the stimulation of primary and secondary sensory modalities. The description of these programs could be useful for the identification of the dose-response ratio in order to adjust the clinical practice and give directions to future research. The following research questions were formulated:

Research Question 1 (RQ1): How long after the ABI the sensory stimulation is usually initiated?

Research Question 2 (RQ2): What are the most frequently used methods in sensory stimulation programs and what are the most simulated senses?

Research Question 3 (RQ3): What is the usual frequency, duration, number of sessions, and length of sensory stimulation programs?

Regarding intervention outcomes, research questions were the following:

Research Question 4 (RQ4): Which assessment instruments are most frequently used to evaluate the efficacy of sensory stimulation?

Research Question 5 (RQ5): What are the immediate and long-term outcomes of the sensory stimulation programs?

Research Question 6 (RQ6): Are the outcomes of the stimulation programs generalizable to cognitive functioning or activities of daily living?

Method

The protocol of the systematic review followed the recommendations of the Preferred Systematic Review and Meta-analysis (PRISMA; Moher et al., 2009; Shamseer et al., 2015).

Search Strategy

Studies were identified through a search on EBSCO, PubMed and OTseeker. The following EBSCO databases were selected: MEDLINE, MEDLINE with full text, Academic Search Complete, PsycInfo, PsycArticles, CINAHL Plus with full text and Psychology and Behavioral Sciences Collection. Furthermore, references of the selected studies were reviewed in order to identify other relevant studies. A manual search was performed to prevent source selection bias.

The search strategy comprised three types of terms related to the population, sensory component and intervention. The search equation was: brain injur* OR brain damag* OR tbi OR head trauma OR cerebrovascular disorders OR cerebrovascular accident* OR cva OR stroke OR poststroke AND multisensor* OR sensor* OR multimodal OR visual* OR tactile* OR vestibular OR audio* OR olfactory OR Somatosens* OR percep* OR visuo* OR audit* OR neglect OR propriocep* AND rehabilitation OR remediation OR education OR *training OR treatment* OR therapy OR stimulation OR integration. All expressions were limited to the titles.

Studies Selection

Inclusion criteria were: (a) adult participants (+18 years) with ABI; (b) empirical studies aiming to assess the methodology used in sensory stimulation programs; (c) human studies only; (d) publications in English language only.

The following constituted exclusion criteria: (a) literature reviews; (b) studies with only motor stimulation or presenting only motor outcomes; (c) studies with no relevance for the theme; (d) studies using only cerebral stimulation techniques; (e) case studies; (f) studies including only participants in coma or in vegetative persistent state.

After the elimination of duplicate articles, the selection of studies for full-text analysis was performed by two independent reviewers in accordance with the Cochrane Collaboration's recommendations (Higgins & Green, 2011). A third reviewer was consulted to decide dissent cases in article selection. After full-text analysis, articles previous to 1990 were also eliminated due to methodological limitations, such as reduced number of participants, unclear intervention description, or lack of outcomes of the intervention.

Results

A total of 774 papers were identified (EBSCO: $n = 278$, PubMed: $n = 436$, OTseeker: $n = 60$). Three papers were included through manual search. After the exclusion of duplicate papers, the analysis of titles and abstracts of 554 papers was carried by two researchers. Sixty-five studies were retained for full-text analysis, while 489 papers were excluded, either because they were out of scope, or were not empirical studies. A Cohen's κ coefficient of .878 was obtained with regard to inter-reviewer agreement in the assessment of titles and abstracts, indicating an almost perfect agreement between reviewers (Landis & Koch, 1977).

After full-text analysis, 45 studies were further excluded for the following reasons: publication before 1990 ($n = 9$); sample comprising patients in coma or in vegetative persistent state ($n = 3$); sample with subjects under 18 years old ($n = 2$); without intervention description ($n = 8$); use of electrostimulation ($n = 3$); research with focus on motor stimulation or other than sensory stimulation ($n = 17$); without the outcomes of intervention ($n = 3$). Thus, 23 papers fulfilled the eligibility criteria in the systematic review process (Figure 1).

Studies Characteristics

The analysis of the methodological quality of the studies was performed according to the classification of Cicerone et al. (2000). Class I was given to nine studies with a prospective design, randomized, and controlled. Two studies presented a prospective design, quasi-randomized to treatment conditions, and were classified as Class Ia. Class II comprised three prospective, non-randomized, cohort

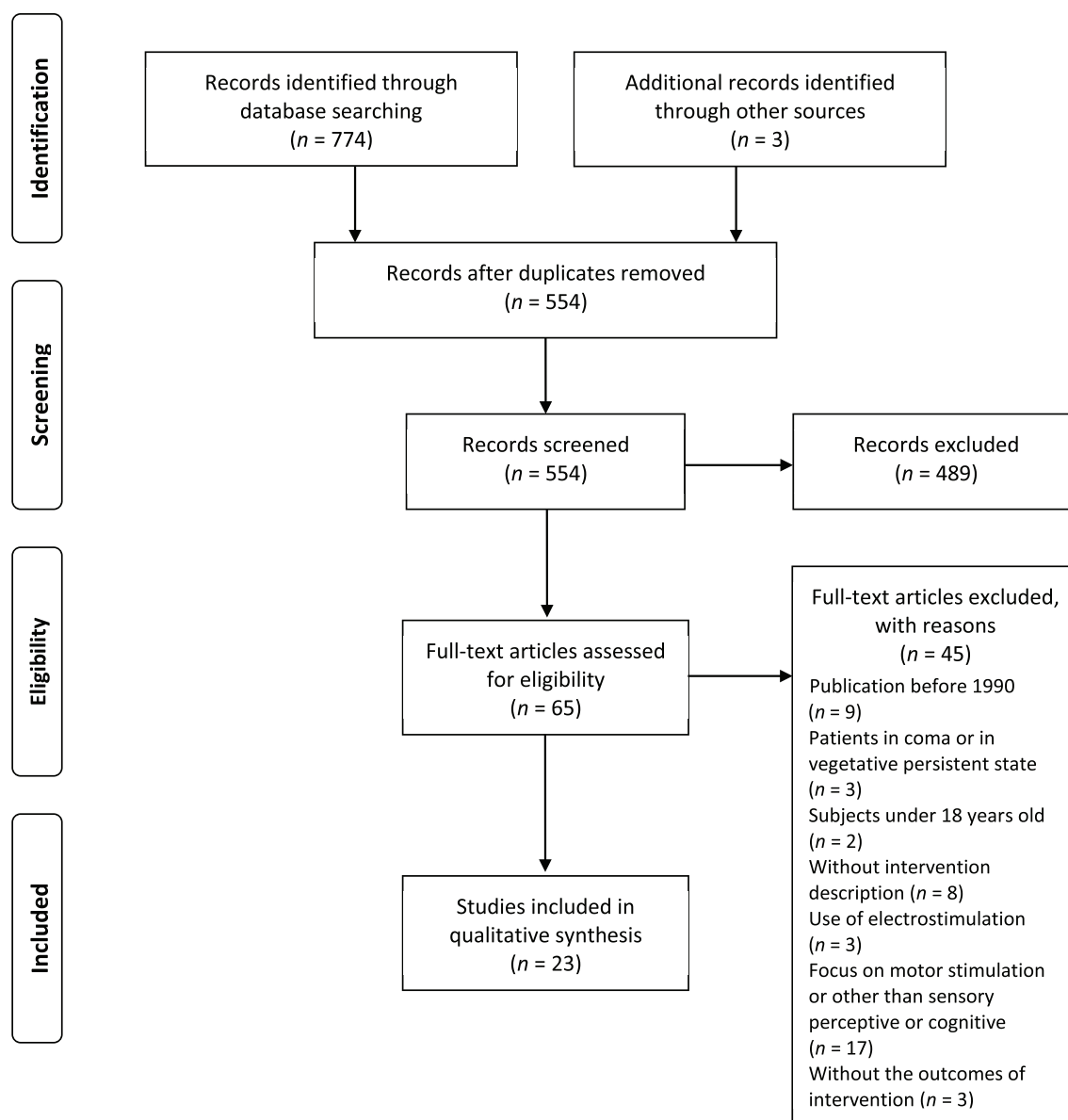


Figure 1. Flow diagram of literature search.

studies, or clinical studies enabling group comparisons according to different treatment conditions. Nine studies were classified as Class III, since they constitute clinical series without control group.

The reviewed studies included 621 participants ($M = 27.0$; $SD = 17.8$; $Min = 7$; $Max = 69$), of which 194 were female (31%). Study #17 only states that two participants in the experimental group were female. Participants' age ranged between 19 and 89 years. Stroke was more frequent ($n = 18$ studies; 78%) than TBI ($n = 5$ studies; 22%).

Studies were published in 15 different journals. Journals with higher number of records included in this review were *Neurorehabilitation and Neural Repair* ($n = 6$) and *Topics in Stroke Rehabilitation* ($n = 3$).

Intervention Characteristics

The sensory stimulation programs of the reviewed studies were initiated 1 month to 8 years after the lesion. The only exception is study #23, which included participants with more than 8 years over the lesion. Study #21 did not provide this information (Table 1).

Multisensory stimulation programs were applied in 17 studies. Vision is the most frequently stimulated sense ($n = 13$; studies #1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13), followed by touch ($n = 2$; studies #15, 16). Vestibular function ($n = 1$; study #14), proprioception ($n = 1$; study #17), smell ($n = 1$; study #20), and hearing ($n = 1$; study #21) were also stimulated. Four multisensory stimulation programs were

Table 1. Methodology used in the assessment of the efficacy of sensorimotor and cognitive programs

First Author	Class	Etiology	Age <i>M</i> ± <i>SD</i> [<i>Min</i> , <i>Max</i>]	Time after injury	Sensory modality stimulated / cognitive functions	Treatment	Frequency of stimulation	Sessions length	Intervention length	Total number of sessions	Assessment moments	Variables measured	Instruments	Main results
1 Mollen (2012)	I	Stroke	RT: <i>M</i> = 58.3 ± 11.4 CT: <i>M</i> = 57.1 ± 8.3 OT: <i>M</i> = 59.0 ± 11.1	<i>M</i> = 4 wks	Vision (hemianopia)	Restorative Training (RT) Compensation Training (CT) Occupational Therapy (OT)	Daily	30 min	NA	15	Pre Post	Visual scanning, attention and visual perimetry – visual conjunction search Visual exploration Reading ability Independence in ADL	TAP BIT – LCT, SCT, LC WMT EBI	Visual field enlargement – ↑ CT, RT Visual exploration – ↑ CT, RT Performance in reading – ↑ CT Attention – ↑ CT, RT Visual conjunction search – ↑ TC
2 Funk et al. (2013)	III	Stroke	[23–60]	<i>M</i> = 20.7 wks	Vision	Feedback-based perceptual training Monocular training	NA	NA	4 wks	<i>M</i> = 11	Baseline 1 Baseline 2 Post Follow-up (8 wks)	Visual orientation discrimination Visuospatial ability Visuoconstruction Visuoperception Spatial dysgraphia Visual performance unrelated to orientation perception Spatial contrast sensitivity Text reading Visual search performance	CVSP JLOT MLT CRT HW Visual tests unrelated to orientation perception: CLCG Reading test Search task on large visual display	Errors in CVSP – baselines > post Post = follow-up Post < baseline – errors in JLOT, MLT, CRT and deviations in HW Visuospatial tests related to orientation perception – baselines = post
3 Nelles (2001)	II	Stroke	EG: <i>M</i> = 59.2 ± 3.5 CG: <i>M</i> = 63 ± 3.2	<i>M</i> = 1.5 mos [0.5–24]	Vision (hemianopia)	Compensation visual field training (saccadic training) Condition A – eyes fixating Condition B – exploratory eye movements	2 × d	30 min	4 wks	NA	Pre Post Follow-up (8 mos)	Visual field Detection of a visual stimulus Reaction time Functional ability for ADL	TAP Response to a visual stimulus Time between onset of stimulus presentation and response NA	↑ Detection of a visual stimulus and ↓ reaction time Condition B = follow-up ↑ ADL
4 Bergsma (2014)	III	Stroke	[40–68]	<i>M</i> = 32.6 mos	Vision (hemianopia)	Visual Restoration Training	5 × wk	1 h	13 wks	NA	Pre Post	Visual field defect Cortical tissue allocated to a part of the visual field Functionality	DGP CMF	↑ Visual field enlargement ↑ GAS
5 Nelles (2010)	II	Stroke	[53–68]	8 wks	Vision (hemianopia)	Compensation eye-movement training	Daily	30 min	4 wks	NA	Pre Post Follow-up (4 wks)	Visual field perimetry Brain activation pattern	TAP fMRI – Fixation task	↑ Activation of the extrastriate in the contralateral hemisphere in the follow-up

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Table 1. (Continued)

No	First Author	Class	Etiology	Age M ± SD [Min, Max]	Sensory modality stimulated / cognitive functions	Treatment	Frequency of stimulation	Sessions length	Intervention length	Total number of sessions	Assessment moments	Variables measured	Instruments	Main results
6	Katz (2005)	la	Stroke	EG: M = 62.4 ± 14.0 CG: M = 63.3 ± 10.8	Vision (unilateral spatial neglect)	Virtual Environment Interactive, Immersive Computer based visual scanning tasks	3 sessions per wk	45 min	9 h (4 wks)	NA	Pre Post	Functional independence Neglect measures ADL Performance in street crossing test – VR	FIM Star CT (BIT); MSC ADL checklist VRSC Number of times looked to the left and to the right, total time to complete each level and number of accidents Time taken to decide to cross the road/number of vehicles that passed during that time, number of times looked to the left and to the right	VRSC ↑EG –Number of times looked to the left ↓EG – accidents
7	Yasuda (2017)	III	Stroke	[45–85]	Vision (neglect)	Virtual Reality	NA	30 min	NA	1	Pre Post	Near space neglect (tests presented in front of the patients) and far (tests projected on the wall at 240 cm)	BIT, LCT, LBT, SCT, LC	↑ Far space neglect
8	van Kessel (2013)	la	Stroke	EG: M = 61.86 ± 7.75 [52–77] CG: M = 59.07 ± 6.08 [48–71]	Vision (neglect)	VE Scanning Training (EG, CG) VE Scanning Training + Lane tracking (EG, CG) VE Scanning Training + Dual ask (EG)	5 d a wk	1 h	6 wks	30 sessions	Pre (2 sessions) Post	Neglect Extrapersonal neglect Personal neglect Performance on driving simulator	LCT, LC, BCT, LBT, WRT, Gray scales, BITT Semi-structured scale Subjective neglect questionnaire "Lane tracking, Single detection task, Dual task"	↑ EG, CG

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Table 1. (Continued)

First No. Author	Class	Etiology	Age M ± SD [Min, Max]	Time after injury	Sensory modality stimulated / cognitive functions	Treatment	Frequency of stimulation	Sessions length	Intervention length	Total number of sessions	Assessment moments	Variables measured	Instruments	Main results
9 Mizuno (2011)	I	Stroke	EG: M = 66.0 ± 11.5 CG: M = 66.6 ± 7.7	EG: 67.1 ± 18.4 d CG: 64.4 ± 20.9 d	Vision (neglect)	Prism Adaptation Therapy	2 × d – 5 d per wk	20 min	2 wks	20	Pre Post Follow-up at discharge (96.5 ± 41.2 d after treatment in EG and 99.3 ± 49.0 in CG)	Spatial neglect Neglect in ADL ADL Stroke impairment Global cognitive functioning	BIT-C; BIT-B CBS FIM SIAS MMSE	EG > FIM > CG EG with mild neglect > BIT-C > CG
10 Brink (2017a)	I	Stroke	PA: M = 59.31 ± 14.45 SA: M = 61.48 ± 13.37	PA: M = 41.50 ± 39.00 d SA: M = 37.00 ± 37.00 d	Vision (neglect)	Prism Adaptation (PA) vs. Sham Adaptation (SA) Standard treatment Neglect treatment	1 × d (working d) 1 h per wk	NA	2 wk 1–6 wks (3 on average)	10	Baseline 1, 2, 3, 4, 6, 14 wks from the start of treatment MAC – baseline, 2, 4, and 14 wks	Neglect in ADL Neglect Targets detection in dynamic task Global cognitive functioning Quality of communication Muscle strength Independence in ADL Independence in walking	CBS SCT, LBT MAC MMSE or MoCA SAN MI BI FAC	↑ CBS, MAC and SCT – PA and SA
11 Fordell (2016)	III	Stroke	M = 72.8 ± 5.7 [62–82]	M = 41 ± 27 Visual mos [6–120] (hemineglect)	Visual	RehAtt – visual scanning training with multi-sensory stimulation in 3D virtual reality (VR) game environment	3 × wk	1 h	15 h, 5 wk	NA	Baselines 1, 2, 3 Post Follow-up (6 mos)	Global cognitive functioning Functionality Neglect Stroke severity ADL	MMSE BI VR – DISTRO: Star CT, BTT, LBT, ET, PT NIHSS CBS	↑ SCT, BTT, ET ↑ CBS in self-report and observer assessment
12 Aparicio- López (2015)	I	Stroke	M = 48.08 ± 9.07	90 ± 46,79 d Visuo- spatial attention (neglect)	Visuo- spatial attention (neglect)	Computer-based cognitive rehabilitation (Guttman- Trainer) and right hemifield eye- patching Guttman- NeuroPersonal Trainer – single treatment	M = 3.08 ± 0.66 wk sessions	1 h	M = 15,17 ± M = 15 1,11 h	15	Pre Post	Visuospatial attention Neglect in ADL	BCT, FCO, LBT, BTT, RT, CBS	Guttman- NeuroPersonalTrainer: ↑ LBT Combined treatment: ↑ BCT, LBT Reading test: Combined Treatment > Guttman- NeuroPersonalTrainer

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Table 1. (Continued)

No	First Author	Class	Etiology	Age <i>M</i> ± <i>SD</i> [<i>Min</i> , <i>Max</i>]	Time after injury	Sensory modality stimulated / cognitive functions	Treatment	Frequency of stimulation	Sessions length	Intervention length	Total number of sessions	Assessment moments	Variables measured	Instruments	Main results
13	Piccardi (2006)	III	Stroke	[63–77]	2 ± 0.69 mos	Vision (neglect) and attention deficit (no-lateralized disorder)	Standard neglect treatment based on visuospatial rehabilitation	5 d per wk	45 min	2 mos	NA	Pre Post	Neurological disorders Neglect Functional evaluation of hemineglect Attentional abilities	MR, CAT LCT; LC; Word and non-word reading test; BCT Semi-structured scale TEA-CBA: alertness test, Go/No-Go test, vigilance test	↑ Ability of visuospatial exploration ↑ Functionality Intervention did not improve attentional performance
14	Dai (2013)	I	Stroke	<i>M</i> = 60.88 ± 13.87 [30–87]	<i>M</i> = 65.38 ± 38.95 d [15–155]	Vestibular (neglect)	Vestibular Rehabilitation – Cawthorne–Cooksey exercises with registered nurse (RVN) and with primary caregiver (RVC) Conventional rehabilitation	RVN – 1 x d RVC – NA	RVN – 30 min RVC – NA	RVN – 2 wks RVC – 2 wks	RVN – 10 RVC – NA	Pre Day 14 (2nd wk of intervention) Day 28 (4th wk)	Neglect ADL Balance Falls	BIT-C FIM PASS Number of falls	↑ BIT-C, FIM, PASS – EG and CG Interaction EG x day 14 and day 28 – ↑ BIT-C, FIM, PASS
15	Carey (2011)	I	Stroke	<i>M</i> = 61.02 ± 12.75	<i>M</i> = 48.14 wks	Touch	Somatosensory discrimination training Repeated exposure to sensory stimulæ	3 x wk	60 min	NA	10	Pre End of phase 1 End of phase 2 Follow-up (6 wk and 6 mos)	Hand dominance Side and site of lesion Severity of neurological impairment Functionality Somatosensory impairment – touch Texture discrimination Limb position sense Temperature discrimination Tactile object recognition Hand function	AQ CAT or MR NIHSS BI WEST-hand monofilaments TDT and FMT WPST and FPS RDK fTORT SODA, MAL	EG > CG in sensory discrimination 6 wk: •31% – performance within the healthy range •69% ↓ deficit by 50% or + •83% ↓ deficit of >=25% 6 mos: •38% – performance within the healthy range •59% – ↓ deficit by 50% or + •86% – ↓ deficit of >=25%
16	Carey (2016)	III	Stroke	[40–79]	6 mos	Touch	Touch discrimination training	3 x wk	45–60 min	6 wks	15	Pre Post	Severity of neurological impairment Hand function Touch detection Tactile Discrimination Limb position sense Tactile object recognition Temperature discrimination Brain activation pattern	NIHSS ARAT WEST – hand monofilaments TDT WPST fTORT RDK fMRI: TSP	TDT – post>pre

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Table 1. (Continued)

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17	Müller (2002)	I	TBI	<i>M</i> = 32 [19–59]	<i>M</i> = 6.4 ± 3.2 mos	Pro-prioception	Muscle vibration (Passive or choice-reaction-time task with or without vibration of left forearm)	NA	NA	NA	Training sessions + 10 experimental mental sessions	During the intervention	Electrical brain activity Ocular movements Behavior during the task	ERP proprioception Electro-oculogram Reaction time, % correct responses, <i>d</i> values – hits, misses, false alarms WAIS-R RFT, AVLT d2 Stroop test, working memory and flexibility subtests of CBA	EG > correct detections with vibration EG < hit rate < CG EG > reaction time (with or without vibration) > CG EG < reaction time with vibration < reaction time without vibration EG > P300 latency < CG EG – vibration sped up the offset of the P300 EG – WAIS-R, RFT, AVLT, and d2 – normal; cognitive slowing, mild impairment of EF
18	Carey (1993)	III	Stroke	[34–75]	5–26.5 wks	Touch and proprioception	Texture discrimination training Limb position discrimination of the wrist Usual rehabilitation program	48–72 h between sessions	Baseline: 15–30 min	Study 1: 9–13 wks Study 2: 13–16 wks	Study 1: 10 sessions Study 2: 20 sessions	Study 1: 10 baseline sessions Intervention Follow-up (9–13 wks) Study 2: 10 baseline sessions Intervention Follow-up (13–16 wks)	Tactile discrimination Proprioceptive discrimination	TDT PDT	↑ Texture and limb position discrimination
19	Carey (2005)	III	Stroke	[44–88]	4.5–52 wks	Touch and proprioception	Stimulus-specific training (Study 1) Stimulus-generalization training (Study 2)	Study 1: 3 x wk	Study 1: 40–60 min	Study 1: 12–14 wks 40–60 min	3 phases with 10 sessions each	Baseline assessments with 48–72 hr of interval Follow-up (12–14 wks)	Study 1 Tactile-discrimination: Proprioception Study 2: Tactile-discrimination Texture-grid matching ability	Study 1: TDT, FMT, WPST Study 2: FMT, GMT	Study 1: FMT and WPST – normal performance, comparable to the unaffected hand Study 2: GMT – normal performance
20	Sullivan (1998)	I	TBI	<i>M</i> = 23.78	EG: <i>M</i> = 8.30 ± 4.85 mos CG: <i>M</i> = 8.70 ± 4.80 mos	Olfact and sustained attention	Olfactory stimulation (fragrance delivery) Attentional task of stimulus detection	NA	30 min	NA	EG: <i>M</i> air = 1.7, <i>M</i> pepper-mint = 2.10 CG: <i>M</i> air = 1.3, <i>M</i> pepper-mint = 1.4	Pre During the intervention Sustained attention	Severity of lesion Anosmia Sustained attention	GCS Anosmia Screening test Percentages of correct detections and false alarms	EG – rate of detection EG ≅ CG ↑EG – false alarm > CG ↓EG – false alarm over the course in the presence of unscented air ↓CG – false alarm over time EG ≅ CG – in peppermint air

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Table 1. (Continued)

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21 Dundon (2015)	I	TBI	M = 38.96 ± 10.13 [19–58]	NA	Hearing/Selective attention	Cognitive training based on Attention Process Training with background noise adaptive (Adaptive Group – AG) and Non- adaptive (NAG)	NA	1 h	NA	8	Pre Post	Auditory selective attention Immediate and delayed recall Distraction Perceived stress Symptoms of somatic stress Electrophysiological activity Attention to speech in noisy	TEA: EC, EC-d, EC-r, TS RBMT: RI and RD	1 AG and NAG – DL CG > NAG > AG – pre and post in EC-r EG (AG and NAG) – f EC-d, TS, RI, RD and EC-r DL performance in post- training correlated with pre-training SQ, Dist and C-SOSI NAG and AG > P3b amplitude from pre/post > CG
22 Dworkin (2013)	III	TBI	M = 37.8 ± 17.9 15.6 wks	M = 10.3 ± 15.6 wks	Visuo-haptic/ attention	Virtual Reality with robotic haptic stimulation – 3 conditions: no haptic feedback, break- through force or gentle pulse of force	NA	6 blocks of trials, each lasting 4 min, with unlimited number of trials	2 d	2	During the intervention	Cognitive functioning Spatial and temporal kinematic parameters of the reach movement	RLA Total trial time, hand patch, velocity and distance from target, duration of pauses during the movement, number of targets acquired in a block	2nd session < pauses and duration of pause < 1st session 1 Acquired targets 1st session – no feedback and break-through force < acquired targets < gentle pulse of force 2nd session – no feedback and gentle pulse of force > targets > break-through force Time trial > break-through force ↓ Median frequency in the right central and temporal EEG electrodes
23 Gómez (2016)	II	TBI	EG: M = 38.06 ± 8.25 CPG: M = 44.61 ± 10.89 CG: M = 37.56 ± 5.58	0.5–4 yr – 5 4–8 yr – 8 > 8 yr – 5	0.5–4 yr – 5 Vision, audition	Snoezelen	NA	18 min	NA	1	Pre Post	Problem behavior Electrical brain activity	PBC EEG	↓ Median frequency in the right central and temporal EEG electrodes

Notes. M = Mean; h = Hour; min = Minutes; wks = Weeks; d = Day; mos = Months; yr = Year; NA = Not Available; Pre = Pre-Intervention; Post = Post-Intervention; ADL = Activities of Daily Living; TAP = Test Battery of Attentional Performance; BIT = Behavioral Inattention Test; LCT = Line Cancellation Task; Star CT = Star Cancellation Task; Star CT = Star Cancellation Task; WMT = Wechsler Memory Test; EBI = Extended Barthel Index; CVSP = Computerized Visual-Spatial Perception Program; JLOT = Judgment of Line Orientation Test; MTL = Mack-Levine test; CRT = Clock-Reading Test; HW = Horizontal Writing; CLCG = Cambridge Low Contrast Gratings; EG = Experimental Group; CG = Control Group; TA = Tubinger Automatic Perimeter; DGP = Dynamic Goldmann perimeter; CMF = Cortical Magnification Factor; GAS = Goal Attainment Scaling; fMRI = Functional Magnetic Resonance Imaging; VR = Virtual Reality; FIM = Functional Independence Measure; MSC = Mesulam Symbol Cancellation Test; VRSC = VR Street Crossing Test; LBT = Line Bisection Task; VE = Visuospatial; BCT = Bells Cancellation Test; WRT = Word Reading Task; BIT = Baking Tray Task; BIT-C = Behavioral Inattention Test – Conventional Test; BIT-B = Behavioral Inattention Test – Behavioral test; CBS = Catherine Bergego Scale; SIAS = Stroke Impairment Assessment Set; MMSE = Mini-Mental State Examination; SCT = Shape Cancellation Task; MAC = Mobility Assessment Course; MoCA = Montreal Cognitive Assessment; SAN = Stichting Afasie Nederland Test; MI = Motricity Index; FAC = Functional Ambulation Categories; ET = Extinction test; PT = Posner Task Unified Index; NIHSS = National Institutes of Health Stroke Scale; FCO = Figure Copying of Odgen; MR = Magnetic Resonance; CAT = Computerized Axial Tomography; TEA-CBA = Computerized Screening Battery of Attentional Disorders; PASS = Postural Assessment Scale for Stroke Patients; AQ = Annett Questionnaire; WEST = Weinstein Enhanced Sensory Test; TDT = Tactile Discrimination Test; FMT = Fabric Matching Test; WPST = Wrist Position Sense Test; FPS = Finger Position Sense; RDK = Roylan Hot and Cold Discrimination Kit; fTORT = functional Tactile Object Recognition Test; SODA = Sequential Occupational Dexterity Assessment; MAL = Motor Activity Log; ARAT = Action Research Arm Test; TSP = Touch Stimulation Paradigm; IQ = Intelligence Quotient; ERP = Event-Related Potentials; WAIS-R = Wechsler Adult Intelligence Scale – Revised; RFT = Recurring Figures Test; AVL = Auditory Verbal Learning Test; CBA = Computerized Battery for the Assessment of attention deficits; EF = Executive Functions; PDT = Proprioceptive Discrimination Test; GMT = Grid Matching Test; GCS = Glasgow Coma Scale; TEA = Test of Everyday Attention; EC = Elevator Counting; EC-d = Elevator Counting with distraction; EC-r = Elevator Counting with reversal subtests; TS = Telephone Search; RBMT = Rivermead Behavioral Memory Test – Immediate Recall (RI) and Delayed Recall (RD); Dist = Distractibility Questionnaire; PSQ = Perceived Stress Questionnaire; C-SOSI = Calgary Symptoms of Somatic Stress; DL = Dichotic Listening; RLA = Rancho Los Amigos Scale; PBC = Problem Behavior Checklist Adapted From the Agitated Behavior Scale; CPG = Cerebral Palsy Group; EEG = Electroencephalogram.

included, two directed to touch and proprioception (studies #18 and 19), one for vision and touch (study #22), and other for vision and hearing (study #23).

The frequency of stimulation ranged between twice-a-week to twice-a-day. This information was not provided in seven studies (#2, 7, 17, 20, 21, 22, 23).

The average duration of sessions was 41.75 min ($SD = 16.09$). Three studies did not provide this information (studies #2, 10, 17) and three studies reported an interval of duration (studies #16, 18, 19).

The intervention length ranged between 2 days (study #22) and 13 weeks. One study (#12) reported the intervention length in hours ($M = 15.17 \pm 1.1$). This information was not provided in seven studies (#1, 7, 15, 17, 20, 21, 23).

The intervention programs ranged between 1 session (studies #7, 23) and 30 sessions (studies #8, 19). The number of sessions was not considered in seven studies (#3, 4, 5, 6, 11, 13, 14).

Intervention Method and Outcomes

In regard to visual stimulation, study #1 comprised restoration and compensation methods and occupational therapy. Compensation methods were used in six studies (#3, 5, 6, 7, 8, 11), virtual reality was used for compensation purposes in three (studies #6, 7, 11), four of them aimed to treat hemineglect by using top-down (studies #6, 7, 8) or bottom-up and top-down approaches combined (study #11).

Restoration method was employed in one study (#4).

Substitution method was used in one study (#9) and other compared the results of substitution method with those of compensation method in the treatment of hemineglect (study #10). In accordance to Marshall (2009), these approaches can be classified as bottom-up.

Five studies applied sensory and cognitive stimulation (#2, 12, 13, 20, 21); substitution methods were also used in two studies (#2, 12).

Concerning restoration, Mödden and collaborators (2012) showed different colored targets at different positions from the visual field limit without ocular movement. Bergsma and colleagues (2014) used a computerized program for visual restoration.

For compensation Mödden and collaborators (2012) used the exploration task from the Rehacom (HASOMED GmbH, Magdeburg, Germany), where patients were instructed to follow a moving ring and to identify a target-stimulus by pressing a key. The compensation of the visual field in the study by Nelles and colleagues (2001) was performed by using a square with red lights and both sides inward oriented. Head movements were not allowed. In the A condition patients had to stare to a point in the middle of the square; in condition B they had to perform

exploratory eye movements in order to identify target-stimuli. Nelles et al. (2010) focused only on task B. The condition B led to an improvement in the detection of stimulus in the left and right hemianopia ($p = .02$; $p = .003$) and shorter reaction time in the hemianopic visual field ($p = .02$), kept in the 8 months follow-up assessment (Nelles et al., 2001) in stroke patients. In addition, it was reflected in the activation of the extra-striate cortex in the contralesion hemisphere ($p < .001$), which was maintained after training and 1 month follow-up (Nelles et al., 2010).

Compensation and restoration methods showed positive outcomes in hemianopia and visual field enlargement ($p = .013$ and $p = .003$, respectively), visual exploration ($p = .003$ and $p = .005$) and in attention ($p = .001$ and $p = .033$). Only the compensation method resulted in improvements in reading performance ($p = .016$) and visual conjunction search ($p = .001$), being considered the treatment of choice for the neglect (Mödden et al., 2012). Bergsma and colleagues (2014) also showed the efficacy of visual restoration in visual field enlargement ($p < .005$).

Virtual reality was employed: (1) to simulate a crossroad environment (Katz et al., 2005); (2) to present an visual identification task where objects flash from right to left at a distance and a touch task at close range with a virtual hand (Yasuda et al., 2017); (3) to use a robot arm in direction of target-stimuli creating haptic sensation (Dvorkin et al., 2013); (4) to multisensory stimulation using program RehAtt (Brain Stimulation AB, Holmsund, Sweden). RehAtt contemplated three tasks: (a) mental rotation, requiring moving figures from left to right side; (b) visual motor exploration, by allocating 3D cubes in three directions; (c) visual spatial and search task, aiming to move or fix moving targets with increasing speed (Fordell et al., 2016).

Participation in visual scanning training resulted in significant improvements in hemineglect, assessed with Mesulam Cancellation (Mesulam, 1985) ($p < .01$) and less time spent at the second assessment moment, but the percentage of improvements in time to complete the test was two times higher in the virtual reality group in comparison to the control group who received conventional visual scanning training. There were significant improvements in the activities of daily living in both groups ($p < .05$), but in the virtual reality group the numbers of times participants looked to the left was higher ($p < .05$) and accidents were fewer ($p < .035$) than in the control group, in the virtual reality environment. Moderate correlations were found between the decision time for real street crossing in the post-intervention and the activities of daily living, ($r = -.49$, $p < .05$) (Katz et al., 2005).

The second training led to improvements in the post-intervention assessment of hemineglect with Behavioural Inattention Test (Wilson et al., 1987) ($p = .002$) and respective subtests (all $p < .003$) (Yasuda et al., 2017).

In the second session with robot-rendered haptic stimulation, TBI participants took less pauses ($p < .001$), showed shorter reaction time ($p = .007$) and acquired more targets ($p < .0001$), compared to the first session (Dvorkin et al., 2013).

RehATT – scanning training for stroke patients with hemineglect resulted in significant post-intervention improvements in the Star cancellation test (Wilson & Halligan, 1987) ($p = .006$), Baking Tray Task (Tham, 1996) ($p < .001$), and Extinction test (Geeraerts et al., 2010) ($p = .05$). Post-intervention improvements were also found in the Catherine Bergego Scale (Bergego et al., 1995), both in self-report ($p = .002$) and observer assessment ($p = .01$), which were maintained in a 6-month follow-up assessment ($p = .21$) (Fordell et al., 2016).

The visuospatial training, also known as feedback based perceptive training, included tasks such as digits detection, drawings copy, reading and copying phrases, and image description (Piccardi et al., 2006; van Kessel et al., 2013). Hemineglect stroke patients received Visuospatial Scanning training for 3 days a week and combined treatment (Visuospatial Scanning training and lane tracking drive simulator) for 2 days a week during 3 weeks. Then, experimental condition received Visuospatial Scanning training and dual task and control condition continued with combined treatment for 3 weeks. Dual task consisted of a computerized visual reaction time task using virtual reality where the participants had to maintain their driving position while performing visuospatial scanning task. Participants in both groups had improvements between before and after training assessments in: Line cancellation (Albert, 1973) ($p < .01$); Letter cancellation (Diller & Weinberg, 1977), extrapersonal neglect (Zoccolotti et al., 1992) (all $p < .001$); personal neglect (Zoccolotti et al., 1992), subjective neglect (Towle & Lincoln, 1991), Bells test (Gauthier et al., 1989), Reading (all $p < .005$); Gray scales index (Tant et al., 2002) ($p < .05$). In addition both groups had improvements in lateral position in line tracking and in dual task – single detection task and lane tracking (all $p < .05$); omissions ($p = .057$) in the single detection task; reaction time to the left ($p < .05$) in single detection task; reaction time for middle ($p < .05$) and right stimuli ($p = .058$) on the previous mentioned dual task (van Kessel et al., 2013). Piccardi and collaborators (2006) also showed improvements in visuospatial exploration (Line cancellation, Letter cancellation, Bells test, Reading test) after Visuospatial training ($p < .001$), as well as increased functionality (semi-structured scale for the functional neglect assessment; Zoccolotti & Judica, 1991) ($p < .01$). The intervention had no effect on attention performance of stroke patients with hemineglect and attention disorders.

The adaptation of the prismatic goggles is a substitution method in which the participants are placed in front of a

semicircular desk and asked to point to three targets for improving hemineglect. In the study by Mizuno and colleagues (2011) the task was repeated with prismatic goggles displacing the visual field 12° to the right. Brink, Visser-Meily, Schut, et al. (2017) used the same method to displace the visual field 10° to the right. The treatment of hemineglect also comprised psychoeducation and visual search tasks such as reading. Hemineglect patients who participated in this therapy obtained better results in the Functional Independence Measure (Uniform Data System for Medical Rehabilitation, NY, USA) between the post-intervention and follow-up, compared to controls who received the same treatment with neutral plastic glasses ($p < .05$). Specifically, the experimental group obtained higher scores in the Functional Independence Measure in the post-intervention ($p < .05$) and follow-up ($p < .01$), compared to the control group, as well as higher results in Behavioural Inattention Test – conventional test (Wilson et al., 1987) ($p < .05$) (Mizuno et al., 2011). Prismatic goggles and sham adaptation with plain lenses also led to improvements in performance over time in the Catherine Bergego Scale, Mobility Assessment Course (Brink, Visser-Meily, & Nijboer, 2017), and static shape cancellation task ($p < .001$). However, the prismatic goggles adaptation did not show greater effect than the simulated adaptation (Brink, Visser-Meily, Schut, et al., 2017).

Funk and colleagues (2013) implemented a perceptive training based on feedback through a computerized visual discrimination task concerning line orientation with stroke patients. In this task two oblique lines were presented and then rotated until the participants considered that they had the same orientation. A monocular training program based in the same task was also implemented, with the participants wearing an eye-patch to test if there was transfer of training from one eye to the other. This training had effects on constant errors and uncertainty intervals (both $p < .001$) in post-training compared to baseline, and the effects for 45° and 135° orientations were maintained at follow-up ($p > .40$). Furthermore, a decrease in the number of errors in the post-training compared with baselines were found in the Judgment of Line Orientation Test (Benton et al., 1983) and clock reading, as well as smaller deviations in a horizontal line and increase in the number of correct items in Marck-Levine test (Mack & Levine, 1981) (all $p < .01$) (Funk et al., 2013).

A platform named Guttman-NeuroPersonalTrainer (BrainHealth Solutions SL, Badalona, Spain), was used for the cognitive training of attention, memory, and executive functioning. The cognitive training was applied as usual, and with right eye-patching for visuospatial neglect. This training led to improvements in the Line bisection task (Schenkenberg et al., 1980) ($p = .039$), and combined with right hemifield eye-patching resulted in improvements both

in the Line bisection task and in the Bells test (all $p = .043$). In the pre- and post-intervention comparison between stroke groups, patients who received the combined treatment had better performance in the Reading Task ($p = .048$), than patients only received cognitive training (Aparicio-Lopez et al., 2015).

The *Cawthorne-Cooksey exercises* (Cooksey, 1946) were used by Dai and colleagues (2013) to vestibular rehabilitation of stroke patients with hemineglect. These exercises encompass several steps: (a) to move the head up and down and to both sides with eyes open; (b) same as previous with eyes shut; (c) same as previous while looking at a moving target. It was observed an interaction between the group (experimental, control) and results at the 2nd and 4th weeks of intervention of the Behavioural Inattention Test – conventional test ($p = .011$; $p = .009$), Functional Independence Measure ($p = .011$; $p = .011$) and Postural Assessment Scale for Stroke patients (Benaim et al., 1999) ($p = .001$; $p = .003$) (Dai et al., 2013).

A somatosensory discrimination method was used in four studies (#15, 16, 17, 18, 19) and a bottom-up approach for the stimulation of proprioception was used in one study (#17).

The discriminative training used touch and involved the exploration and the discrimination of an unusual texture among other textures (Carey et al., 1993, 2016). A proprioceptive discriminative training as also applied, requiring participants to identify the perceived position of the fist in several predefined angles (Carey et al., 1993). After these training, stroke patients with impairment in proprioception and/or tactile discrimination revealed improvements in the affected hand ($p = .003$), resulting in comparable performance to the normal hand (Carey et al., 1993; Carey & Matyas, 2005).

Carey and Matyas (2005) followed the procedure of Carey and collaborators (1993) with texture grids, but other materials like glass, paper, leather, rubber and superficies with different degrees of roughness were used in order to favor stimuli generalization. Participants who performed this training revealed transference of the results to untrained related stimulus within the same modality (Carey & Matyas, 2005).

Besides the texture and limb position, the tactile recognition of objects focused on shape, size, weight, hardness and temperature were other tasks included in somatosensory discrimination training (Carey et al., 2011). The non-specific repeated exposure to sensory stimulus with diversified characteristics was performed through grasping of common objects and passive movements of the upper limb (Carey et al., 2011). After this training, stroke patients with impaired texture discrimination, limb position sense, and/or tactile object recognition obtained better results in sensory discrimination, compared to those who received

repeated exposure to sensory stimulus ($p = .004$). The improvements were maintained 6 weeks and 6 months after the intervention (Carey et al., 2011).

The proprioceptive stimulation was also performed through a choice-reaction-time task. This task involved digit discrimination, and pressing a button with two different fingers in the case of even or odd numbers. This task was also performed with the vibration of the left extensor radialis muscle during the presentation of stimulus to study its effects on cognitive processes. TBI patients presented a higher number of correct detections of non-masked stimulus ($p = .001$) and in the vibration condition ($p = .001$). Compared to the healthy control group, they presented a lower hit rate of targets ($p < .01$) and longer reaction time ($p < .0001$). The experimental group showed shorter reaction times to target stimuli in the vibration condition, compared to the condition without vibration ($p = .01$). The latency of the P300, a brain potential evoked by vibratory stimuli, in this case, was higher in the experimental group in the condition without vibration ($p = .01$), compared to the controls. The experimental group showed normal performance on the Wechsler Adult Intelligence Scale – Revised (Wechsler, 1981), Recurring Figures Test (Rixecker & Hartje, 1980), Auditory Verbal Learning Test (Rey, 1958) and d2 (Brickenkamp & Zillmer, 1998), despite moderate cognitive slowness and impairment on executive functions (Müller et al., 2002).

The olfactory stimulation was performed through modified oxygen masks, which delivered peppermint fragrance in the experimental condition and unscented air in the control condition. This stimulation was provided during an attention task, in which pairs of lines with different distances from a central dot should be detected (Sullivan et al., 1998). Brain injury participants presented a detection rate similar than revealed by the healthy control group, but obtained a higher false alarm percentage in the unscented air condition (Sullivan et al., 1998).

The selective attention tasks (simple target detection and palindromes detection) of the Attention Process Training Program (Sohlberg & Mateer, 1987) were modified by manipulating background noise to improve selective attention using auditory stimuli, with an increase of decibel level along training. For the adaptive condition, the progression of noise was based on cognitive performance and in non-adaptive condition, participants did not adjust to the increasing noise, but were exposed to each noise level for the same period as the previous condition (Dundon et al., 2015). In the TBI group (adaptive and non-adaptive training) had positive effects on a dichotic listening task ($p = .003$), while in a healthy control group performance did not change over time ($p = .34$). Considering post-intervention assessment, in the Elevator Counting (Robertson et al., 1994) the control group obtained better results than

the adaptive group ($p = .000$) and non-adaptive group ($p = .036$). The experimental group presented better results in post-intervention in the Elevator Counting with distraction and with reversal ($p = .002$ and $p = .059$), Telephone Search (Robertson et al., 1994) ($p = .009$), Rivermead Behavioral Memory Test – immediate and delayed recall (Wall et al., 1994) ($p = .002$ and $p = .000$), compared to the pre-intervention assessment. The performance in the post-training dichotic listening task correlated with the results obtained in the Perceived Stress Questionnaire (Cohen et al., 1983) ($R^2 = .50$, $p = .002$), distractibility questionnaire ($R^2 = .32$, $p = .018$) and with Calgary symptoms of somatic stress (Carlson & Thomas, 2007) ($R^2 = .28$, $p = .030$) in pre-training. The amplitude of P3b, a subcomponent of the P300, increased from the pre- to post-intervention assessment in the adaptive group ($p = .007$) and non-adaptive group ($p = .041$) in response to infrequent targets in an oddball paradigm. The same did not happen in the control group ($p = .598$) (Dundon et al., 2015).

Snoezelen multisensory stimulation was used in one study (#23). The intervention comprised auditory and visual stimulation with colored bubble tubes, optic fiber bundles, rotating mirror ball, projector display, and sounds of nature (Gómez et al., 2016). Participation in one *Snoezelen* session led to a decrease in the median frequency (frequency that comprises 50% of the power spectral density) recorded by Encephalography ($p = .04$) in central and right temporal electrodes, suggesting deceleration of oscillatory activity (Gómez et al., 2016).

Assessment Procedures

Most studies ($n = 10$) followed a pre-and post-intervention design (studies #1, 4, 6, 7, 8, 12, 13, 16, 21, 23). Five studies conducted pre/post-intervention and follow-up assessments (studies #2, 3, 5, 9, 11). The assessment was performed only during the intervention in two studies (#17, 22) while in other two, it was conducted an assessment previously to the intervention, during the intervention, and at follow-up ($n = 2$; studies #18, 19). Other studies encompassed the following assessment moments: pre-intervention and during the intervention ($n = 1$; study #20); pre-intervention, during the intervention and post-intervention ($n = 1$; study #14); pre-intervention, during the intervention and at follow-up ($n = 1$; study #15); pre-intervention and during the intervention ($n = 1$; study #10).

The follow-up assessment was conducted from 4 weeks (study #5) up to 8 months (study #3) after the end of the intervention.

In the studies included in this review, sensory stimulation programs focus on different sensory modalities and cognitive functions. Hence, the authors considered different outcome variables.

Attention was considered in six studies and evaluated through the: Test Battery of Attentional Performance (Zimmermann & Fimm, 2002) (study #1); reaction time between stimulus presentation and response (study #3); Computerized Screening Battery of Attentional Disorders (Zimmermann & Fimm, 1995) (studies #13, 17); d2 (study #17); percentage of correct detections and false alarm (study #20); Test of Everyday Attention (Robertson et al., 1994) (study #21); and dichotic listening (study #21).

Five studies considered the dysfunction and severity of ABI, using the National Institutes of Health Stroke Scale (Brott et al., 1989) (studies #11, 15, 16), the Stroke Impairment Assessment Set (Chino et al., 1996) (study #9), and the Glasgow Coma Scale (Teasdale & Jennett, 1974) (study #20).

Four studies presented an evaluation of the global cognitive functioning through the Mini Mental State Examination (Folstein et al., 1975) (studies #9, 10, 11) and the Rancho Los Amigos scale (Hagen et al., 1979) (study #22).

One study tested the premorbid intelligence quotient with Wechsler Adult Intelligence Scale – Revised (study #17). Memory was assessed through the Recurring Figures Test (study #17), Auditory Verbal Learning Test (study #17), and Rivermead Behavioral Memory Test (study #21).

Visuoconstructive and perceptive abilities were considered in study #2. Visual orientation was assessed with the computerized visual-spatial perception program (Kerkhoff & Marquardt, 1995), the visuospatial ability with the Judgment of Line Orientation Test, the visuoconstruction with the Mack-Levine test, the visuoception with the analog clock reading task, and the spatial contrast sensitivity with the Cambridge Low Contrast Gratings (Wilkins et al., 1988) (study #2).

Hemineglect was a widely considered variable (studies #1, 2, 3, 6, 7, 8, 9, 10, 11, 12, 13, 14). The instrument that gathered more consensus to assess this condition was the Behavioural Inattention Test. This test or some of its scales were used in nine studies (#1, 6, 7, 8, 9, 10, 12, 13, 14). Three studies used Bells test (studies #8, 12, 13), two studies used Baking Tray Task (studies #8, 12). Two studies used assessment protocols adjusted to certain task (studies #6 and 8). Specifically, study #6 considered the individuals' performance when crossing streets both in virtual reality environment and in the real streets. In study #8 the performance was assessed in a driver simulator. One study used the Virtual Reality – DiSTRO (Brain Stimulation AB, Holmsund, Sweden) (study #11), a hemineglect assessment battery in virtual reality. Other studies used were the Mesulam Symbol Cancellation test (study #6), Gray scales (study #8). Hemineglect was also assessed through: discrimination tasks on large visual displays (study #2); response to visual stimulus (study #3); shape cancellation (study #10); Figure Copying of Ogden (Ogden, 1985) (study

#12); detection of targets on a dynamic task with Mobility Assessment Course (study #10). Finally, in study #8, the extrapersonal and personal neglect were assessed through a semi-structured scale and a subjective neglect questionnaire.

Reading was considered in five studies aimed at stimulating vision (studies #1, 2, 8, 12, 13), and considered a measure of hemineglect in three studies (#8, 12, 13). It was assessed through reading task (studies #2, 8, 12), subtests of the Wechsler Memory Test – Revised (Wechsler, 2004) (study #1), and reading of words and non-words task (study #13).

One study assessed the spatial dysgraphia through horizontal writing task (study #2).

The assessment of the visual field was considered in three studies, which administered the: Tubinger automatic perimeter (study #3); Dynamic Goldmann perimetry (study #4); and an automatic computerized system (study #5).

One study evaluated smell through the anosmia screening test (International Flavors and Fragrances Corporation, New York, United States of America) (study #20).

The somatosensory deficits were considered in four studies (#15, 16, 18, 19). For touch and texture discrimination or tactile recognition, the following assessment instruments were used: the Tactile Discrimination Test (Carey et al., 1997) (studies #15, 16, 18, 19); the Weinstein Enhanced Sensory Test (Weinstein, 1996) (studies #15, 16); the Fabric Matching Test (Carey, 1995) (studies #15, 19); the functional Tactile Object Recognition Test (Carey, 2006) (studies #15, 16); and the Grid Matching Test (Carey, 1995) (study #19). The Roylan hot and cold discrimination kit (studies #15, 16) was used for the temperature discrimination. Proprioception was assessed through the Wrist Position Sense Test (Carey et al., 1996) (studies #15, 16, 19), the Finger Position Sense (Carey, 1995) (study #15) and the Proprioceptive Discrimination Test (Carey et al., 1993) (study #18).

One study directed to the proprioceptive stimulation used a task-adjusted evaluation protocol, which included the reaction time to targets, the percentage of correctly detected targets, hits, misses, and false alarms (study #17). A task-adjusted evaluation protocol was also used in study #22, which considered spatial and temporal kinematic parameters of the hand movement (total trial time, hand path, velocity and distance from the target, duration of pauses, and number of targets acquired).

The analysis of brain structure and functioning was considered in seven studies (#4, 5, 13, 15, 16, 17, 21, 23). It was assessed through functional Magnetic Resonance Imaging (studies #4, 5, 16); Magnetic Resonance Imaging and Computerised Axial Tomography (studies #13, 15); and Event-related Potentials (studies #17, 21); and Electroencephalography (study #23).

Independence in activities of daily living was considered in eight studies (#1, 4, 6, 9, 10, 11, 14, 15). It was assessed with the: conventional or extended Barthel Index (Mahoney & Barthel, 1965) (studies #1, 10, 11, 15); Functional Independence Measure (studies #6, 9, 14); Activities of Daily Living checklist (study #6); Functional Ambulation Categories (Holden et al., 1984) (study #10); Goal Attainment Scaling (Kiresuk & Sherman, 1968) (study #4). The impact of the hemineglect on activities of daily living was assessed with the Catherine Bergego Scale (studies #9, 10, 11, 12). Unspecified instruments were used in two studies (#4, 13).

Other variable assessed were handedness – Annett Questionnaire (Annett, 1970) (study #15).

Discussion

ABI can lead to sensory and cognitive deficits, impaired ability to explore the environment and, consequently, the lower functionality in activities of daily living. Despite the recognized impact of sensory deficits, the literature has focused on motor rehabilitation in stroke and sensory stimulation in altered states of consciousness in TBI. The sensory stimulation in stroke and mild to moderate TBI has deserved low interest of the literature. Therefore, the relationship between dose-response to sensory stimulation and clinical predictors need to be studied to adjust neurorehabilitation programs in ABI (Sullivan & Hedman, 2008).

The main objective of this review was to produce knowledge on the methodological characteristics of sensory stimulation programs in ABI and its results.

For the reasons described above, we did this review with the purpose of answering the following questions about the characteristics of the intervention: (RQ1) how long after the injury the sensory stimulation usually is initiated?; (RQ2) what are the most frequently used methods and what senses are stimulated?; (RQ3) what is the frequency, duration and average number of sessions and length of sensory stimulation programs?

Regarding the intervention results, we intend to answer the following questions: (RQ4) which assessment instruments are frequently used to evaluate the efficacy of sensory stimulation?; (RQ5) what are the immediate and long-term outcomes?; and (RQ6) are the outcomes of the stimulation programs generalized to cognitive functioning or activities of daily living?

Thus, a systematic review of literature was conducted in accordance with the principles of PRISMA (Moher et al., 2009; Shamseer et al., 2015) and Cochrane Collaboration's recommendations (Higgins & Green, 2011).

Concerning the methodological quality of the revised studies, less than half of them were included in Class I. This

means that most of the studies have methodological limitations and reported findings do not provide robust evidence.

Regarding the sample characteristics, there was a higher prevalence of stroke patients and males.

Answering RQ1, sensory stimulation was initiated within 12 months after the injury in most studies.

Considering the most frequently used methods and stimulated senses (RQ2), we found that sensory stimulation programs were mostly unisensory and the most frequently stimulated sense was vision. No program included taste stimulation. The most frequently used method in vision stimulation was compensation, with computerized tasks (Bergsma et al., 2014; Mödden et al., 2012) and boards for stimuli detection (Nelles et al., 2001, 2010). In visual substitution the most used method was the prismatic lens adaptation (Brink, Visser-Meily, Schut, et al., 2017; Mizuno et al., 2011). The hemineglect treatment was accomplished mainly with top-down approaches, and using virtual reality (Fordell et al., 2016; Katz et al., 2005; Yasuda et al., 2017). Sensory and cognitive stimulation were applied in a small number of studies, which used computerized tasks, among others (Aparicio-Lopez et al., 2015; Funk et al., 2013) and a program based on Attention Process Training (Dundon et al., 2015). Regarding somatosensory stimulation, the most frequently used methods were texture discrimination training and proprioceptive discrimination training (Carey & Matyas, 2005; Carey et al., 1993, 2011, 2016).

Concerning RQ3, studies are not consensual about the frequency, duration, number of sessions and length of sensory stimulation programs, and not all reported this information. Most frequent data were: stimulation frequency of three times a week; session duration of 30 min; intervention duration of 4 weeks; intervention length between 10 and 15 sessions.

In the majority of the studies, a pre- and post-intervention assessment design was applied. However, follow-up assessments were conducted in less than half of the studies.

With regard to assessment instruments (RQ4), we concluded that they were diversified, because of many variables considered. Hemineglect was the most widely considered variable and the most used instrument was Behavioural Inattention Test. The cognitive domain most assessed in pre- and post-intervention moments was attention, but all studies used different assessment instruments. In visual function assessment, sophisticated instruments were used that required specialized technical knowledge. In the assessment of somatosensory deficits, the most frequent instruments were the Tactile Discrimination Test and Wrist Position Sense Test. The ABI severity assessment was reported in a small number of studies, in spite of being considered central to neurorehabilitation program planning (Ślusarz et al., 2015). Assessments of general cognitive function, memory, and executive functions were performed in a

small number of studies, mostly with the purpose of sample characterization. The structure and brain functioning were analyzed only in one third of the studies, using several techniques: magnetic resonance imaging; functional magnetic resonance imaging; computerized axial tomography; and event-related potentials. The use of different instruments and assessment protocols depending on the intervention programs prevents the comparison of their efficacy.

The included studies focused their assessment in the sensory modality targeted by the intervention. However, notions that sensory processing in the brain is unimodal and activity of a sensory system has little influence on others have been contradicted (Baier et al., 2006). For example, when auditory and visual stimuli are randomly combined, the sensory system relevant to the ongoing task is activated and the other is suppressed (Baier et al., 2006) showing an interaction between sensory modalities. However, when there is an association between auditory and visual information, both systems are activated. According to Theeuwes and collaborators (2007), we have different resources for perception, one for vision and other for auditory, but at a cognitive level, particularly in working memory, there is no separation. Thus, we considered important to include a battery of cognitive tests in the evaluation of programs efficacy.

Neuropsychology shows a growing concern regarding the development of assessment instruments and rehabilitation programs with ecological validity. This can be defined as the relationship between cognitive performance in neuropsychological assessment and behavior in activities of daily living (Spooner & Pachana, 2006). Ecological validity may be enhanced through the inclusion of functionality measures in real life environments. Few of the considered studies used instruments as the Test of Everyday Attention and the Catherine Bergego Scale, which enable to understand the impact of the interventions on participants' ability to perform daily tasks. In this context, virtual reality is a methodology with potential to approximate the programs to the real contexts, hence allowing to reproduce the activities of daily living functioning (Parsons, 2015). Virtual reality can be useful in assessment and intervention, since it allows the accuracy of laboratory measures, through controlled and precise presentation of stimuli, with content similar to real life (Abbate et al., 2014; Parsons, 2015).

Affective disorders are common in ABI (Hackett et al., 2005; van Reekum et al., 2000), but none of the studies included measures of such disorders, even if multisensory stimulation has demonstrated a positive effect on depression and anxiety (Ozdemir & Akdemir, 2009).

Quality of life assessment is also used as an indicator of rehabilitation efficacy (Neznanov & Petrova, 2002). Again, none of the studies assessed this parameter.

Regarding the outcomes of the intervention programs (RQ5), Class I studies showed evidence of immediate

improvement of vision (hemianopia) with compensation method (Mödden et al., 2012), hemineglect using vestibular intervention – *Cawthorne-Cooksey exercises* (Dai et al., 2013), cognitive functioning using proprioceptive stimulation – muscle vibration (Müller et al., 2002), sustained attention using olfactory stimulation (Sullivan et al., 1998) and an adapted version of Attention Process Training Program (Dundon et al., 2015). Immediate and long-term improvements were found on somatosensory discrimination using this intervention (Carey et al., 2011) and hemineglect using Guttman-NeuroPersonalTrainer with and without eye-patching (Aparicio-Lopez et al., 2015). Only one study of Class III used a stimulus-generalization training. However, studies of Class I showed generalization (RQ6) of compensation method effects to reading task (Mödden et al., 2012), prism adaptation therapy to functionality (Mizuno et al., 2011), Prismatic goggles and sham adaptation with plain lenses to activities of daily living (Brink, Visser-Meily, Schut, et al., 2017), *Cawthorne-Cooksey exercises* to functionality (Dai et al., 2013), selective attention training with auditory stimulation to immediate and delayed recall (Dundon et al., 2015).

The studies of efficacy of prismatic lens in the subacute period of stroke showed contradictory results. Mizuno and collaborators (2011) showed an improvement, with maintenance of results in follow-up, while Brink and collaborators (Brink, Visser-Meily, Schut, et al., 2017) found that prismatic lens adaptation had not greater effect than simulated adaptation.

The studies included in this review have several limitations, such as: (a) small samples in half of the studies (less than 30 participants); (b) lack of a control group in 9 studies; (c) lack of randomization procedures in 12 studies; (d) lack of follow-up to examine the maintenance of the results in 15 studies; (e) small number of intervention sessions; (f) implementation of conventional rehabilitation simultaneously to the intervention being studied, producing confounding effects.

This literature review also has limitations. Only papers in English language and published after 1990 were included. Anyhow, it is worth mentioning that most of the studies that met the criteria had been published in the after 1990.

From this review, future studies on sensory stimulation in ABI should considered: (a) better sample characterization, for example, regarding educational level, ABI severity, biological variables as handedness, and pharmacological treatment; (b) performing cognitive assessment pre- and post-intervention; (c) using of an expanded assessment battery of sensory functioning, not only directed to the target sensory modality, due to interactions between sensory modalities; (d) measures of functionality, quality of life, affective disorders and emotional well-being, to enhance the ecological validity of the protocols; (e) performing follow-up

assessments, to provide information about the maintenance of intervention outcomes; (f) inclusion of active and passive control groups; (g) whenever the intervention programs begin in the first months after the injury control groups are paramount to dissociate the spontaneous recovery from the effects of the rehabilitation programs; (h) using structural and functional brain measures to provide neurobiological evidence of intervention efficacy.

Considering the findings and shortcomings mentioned above, this review suggests that sensory stimulation has positive outcomes in ABI, including at cognitive and affective levels, with potential benefits to patients functionality in activities of daily living, but future studies may consider methodologies that provide stronger evidence, enhance the generalization of outcomes, and allow comparative analysis between studies. The recommendations presented here are important to achieve these goals.

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ORCID

Joana Pinto

 <https://orcid.org/0000-0002-0643-8439>

Joana Pinto

Faculty of Psychology and Education Sciences
University of Porto
Rua Alfredo Allen
4200-135 Porto
Portugal
joanaftopinto@gmail.com



Joana Pinto has a master's degree in clinical neuropsychology and specialization in Clinical and Health Psychology. Currently, she is a PhD student at Laboratory of Neuropsychophysiology with a project in cognitive and affective neurosciences field. Her main research interests includes neurocognitive rehabilitation, and neurodegenerative diseases.



Artemisa R. Does (PhD in cognitive neurosciences) is a specialist in Clinical and Health Psychology, and in Neuropsychology. Artemisa R. Does is Professor at the Polytechnic of Porto, School of Health, and member of the Rehabilitation Research Center (ESS – P. Porto) and of the Neuropsychophysiology Laboratory (FPCEUP).



Bruno Peixoto holds a Doctorate degree in Psychology (Psychobiology) and advanced specialization in Neuropsychology. He is Professor and researcher at CESPU, University Institute of Health Sciences in the fields of Neuroanatomy and Neuropsychology. His main research interests are dementia and neuropsychology of medical conditions. He is a research collaborator with CINTESIS.



Andreia Geraldo is a specialist in clinical and health psychology, with pre-specialization in neuropsychology. She is a PhD student with a project within cognitive and affective neurosciences. Her main research interests involve the use of new ICTs across neuropsychological assessment and rehabilitation, ABI and other neurodegenerative disorders, and gambling/gaming.



Fernando Barbosa is a Clinical Psychologist with specialization in Neuropsychology and PhD in Neuroscience. He is Professor at the University of Porto, Portugal and Coordinator of the Laboratory of Neuropsychophysiology. He is Founding member of the European Society for Cognitive and Affective Neuroscience, and member of the Standing Committee on Clinical Neuropsychology of the European Federation of Psychologists' Associations.