

**Supplemental Table 1. Evidence for the Effectiveness of Sensory Stimulation to Improve Arousal and Alertness of People in a Coma or Persistent Vegetative State After Traumatic Brain Injury**

Author/Year	Level/Design/Participants	Intervention	Outcome Measures	Results
Abbasi, Mohammadi, & Sheaykh Rezayi (2009)	Level I RCT  <i>N</i> = 50 adults age 18–45 with newly acquired comatose head injury and GCS score of 6–8; people with opium or drug addiction excluded.  Intervention group, <i>n</i> = 25 (22 men, 3 women).  Control group, <i>n</i> = 25 (21 men, 4 women).	<i>Intervention group:</i> Training for family members in protocol for 15-min visits with patient: In the 1st 5 min of visit, sit on the chair near the bed, call the patient using normal intonation, introduce oneself, hold the patient's hands, touch the patient gently, talk to the patient about all the measures that had been taken for the patient's improvement, and wait for 1 min. In the 2nd 5 min of the visit, touch the patient's hands and face, make the patient familiar with the time and place, and wait again for 1 min. In the 3rd 5 min, touch the patient again, say goodbye, and finally state the time of the next visit (over 6 consecutive days)  <i>Control group:</i> No program was provided.	GCS	Consciousness levels (GCS scores) differed significantly between groups after 6 days of intervention ( $p = .001$ ).
Cheng et al. (2013)	Level III  Single group, single exposure  <i>N</i> = 86 adults (67 men, 19 women; <i>M</i> age = 46) recovering from coma, free of sedative drugs; 47 in VS, 39 in MCS; traumatic etiology in 53, nontraumatic in 33 (median time between injury and assessment = 5 mo).	Auditory stimulus (bell and patient's name) presented from the right and left side while the patient sat upright and the examiner stood next to the patient but out of view; stimuli matched for intensity and duration of presentation and presented twice for each side  <i>Advanced Care Protocol</i> <i>Phase 1:</i> Targeted, sequential, and cumulative pharmaceutical treatment to optimize or potentiate neurotransmitter function <i>Phase 2:</i> Addition of median nerve stimulation to enhance ability of medications to regulate neurotransmitter stability <i>Phase 3:</i> Addition of nutraceutical treatment to support neurotransmitter production and metabolism, in addition to daily standard nursing care for SDOC patients and combination of physical, occupational, and speech therapy $\geq 3$ hr/weekday and modified weekend schedule	GCS  • Localization to auditory stimulus (orientation of head or eyes toward the stimulus on both trials for at least 1 side) • CRS–R	43% of participants showed localization to auditory stimulation. More MCS patients oriented the head or eyes to their own name than to sound ( $p < .001$ ); this difference was not significant for the VS group.
Defina et al. (2010)	Level IV  Within-subjects retrospective case series  <i>N</i> = 41 hospitalized adults with SDOC: 14 in VS after TBI, 18 in VS after nontraumatic brain injury, 7 in MCS after TBI, and 2 in MCS after nontraumatic brain injury (29 men, 12 women; age at admission 26.3–53.3; time from injury = 1 mo to 1 yr).		• Standard neurological exam and physical, occupational, and speech therapy assessments • Disability Rating Scale • FIM™ • GCS • CRS–R	Intervention participants showed significantly greater improvement in disability than patients who received standard treatment matched on injury type and level of consciousness from published literature.

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**Supplemental Table 1. Evidence for the Effectiveness of Sensory Stimulation to Improve Arousal and Alertness of People in a Coma or Persistent Vegetative State After Traumatic Brain Injury (cont.)**

Author/Year	Level/Design/Participants	Intervention	Outcome Measures	Results
Di Stefano, Cortesi, Masotti, Simoncini, & Piperno (2012)	Level III Pretest-posttest <i>N</i> = 12 noncommunicative adults (age range = 21–47) with brain injury >3 mo postinjury, 6 in VS and 6 in MCS (1 unable to complete protocol because of clinical complications).	Phase A: Assessment of active behaviors during hygiene care performed by staff with verbal instructions only Phase B: Assessment during stimulation with personally salient objects Phase C: Assessment during enriched stimulation with same personal objects in augmented environment (1 wk/phase over 5 wk)	Wessex Head Injury Matrix	The number of responses increased significantly from Phase A to Phase B and from Phase B to Phase C ( <i>p</i> ≤ .01). Increased behavioral response resulted from complexity rather than intensity of stimuli.
Megha, Harpreet, & Naveem (2013)	Level I RCT 30 comatose adults (age range = 25–55) with TBI, GCS score <8, and duration of coma <8 days and free of sedative drugs Group A, <i>n</i> = 10. Group B, <i>n</i> = 10. Group C, <i>n</i> = 10.	<i>Multimodal Coma Stimulation</i> : Stimulation of each of the 5 sensory systems in an established sequence, with a rest period of 2 hr in between. <i>Group A</i> : Intervention for 20 min, 5×/day, for 5 consecutive weekdays over 2 wk <i>Group B</i> : Intervention for 50 min, 2×/day for 5 consecutive weekdays over 2 wk <i>Group C</i> : Conventional physiotherapy 2×/day, for 5 consecutive weekdays over 2 wk	• GCS • WNSSP	Multimodal Coma Stimulation was effective in improving consciousness levels in treatment participants compared with control participants. Administration 5×/day for 20 min/session showed better results than administration 2×/day for 50 min/session. WNSSP scores differed significantly between Groups A and B, but GCS scores did not.
Meyer et al. (2010)	Level I Systematic review <i>N</i> = 18 studies with ≥50% participants with ABI, intervention targeting arousal of patients in prolonged coma; 100% of patients in coma or VS ≥48 hr at initiation of intervention; and Rancho Los Amigos Levels ≤III, GCS scores ≤8, and Disability Rating Scale scores ≥22.	Dopamine targeting agents, sensory stimulation, music therapy, median nerve electrical stimulation	PEdro scoring system to generate methodological quality	The evidence indicates that amantadine improves arousal in children and adolescents postinjury, but findings were inconclusive for adults. Bromocriptine may improve functional and cognitive recovery from coma in conjunction with other rehabilitative strategies, and levodopa/carbidopa administration may improve level of consciousness in comatose ABI patients. Sensory stimulation may improve clinical outcomes, physiological parameters, and behaviors indicating arousal from coma. No evidence was found that music therapy alone improves consciousness, but it may improve awareness in patients with ABI when used with multimodal stimulation. Further study is warranted.

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**Supplemental Table 1. Evidence for the Effectiveness of Sensory Stimulation to Improve Arousal and Alertness of People in a Coma or Persistent Vegetative State After Traumatic Brain Injury (cont.)**

Author/Year	Level/Design/Participants	Intervention	Outcome Measures	Results
Noé et al. (2012)	Level III Single cohort pretest-posttest <i>N</i> = 32 adults with ABI (22 men, 10 women; <i>M</i> age = 39.9, range = 16–64), 15 with TBI, 12 with hemorrhage, and 5 with anoxia; 12 in VS and 20 in MCS; <i>M</i> days from injury to inclusion = 144.9, range = 38–360.	Integrative multisensory program comprising daily physical rehabilitation procedures and multimodal sensory stimulation (over 6 mo or until patient emerged from MCS)	Spanish version of the CRS–R	Eight participants (25.8%) emerged from MCS during the 6-mo follow-up period. Patients admitted in VS were less likely to emerge from MCS than those admitted in MCS. Time from injury to enrollment was slightly but significantly ( $p = .04$ ) shorter for participants who emerged from MCS compared with those who did not. None of the 12 patients for whom time from injury to enrollment was $\geq 6$ mo emerged from MCS during follow-up.
Oh & Seo (2003)	Level III Single experimental group, interrupted time series <i>N</i> = 5 men (ages 39–60) $\leq 3$ mo after brain injury (1 traumatic, 4 hemorrhagic) with GCS score of 3–10 (indicating coma, semicomatose, or confusion) and no past history of brain injury, 4 with ventriculoperitoneal shunts and 3 with extraventricular drainage.	Sensory stimulation selected using stimuli in accordance with patients' past preferences: visual (e.g., colored papers, faces of family), auditory (e.g., music, voice of family member), olfactory (e.g., perfume, vinegar), gustatory (e.g., salty, sweet, oral care), and tactile (e.g., touch, temperature), first provided 2x/day, 5 days/wk over 4 wk, followed by 4-wk recession period (i.e., usual care), then repeated, followed by 4-mo recession period	GCS	Significant alterations in consciousness levels were found 2 wk after the first intervention period started. This effect increased gradually and was maintained for 3–4 wk. Consciousness levels began to continually decrease after 2 wk of recession after 1st intervention. Consciousness levels began to increase 2 wk after initiating 2nd intervention and continued for 2 wk after initiating 2nd recession. These results suggest that an intervention program should be applied for $\geq 1$ mo to achieve a permanent effect on consciousness levels and that $\geq 2$ wk are required for any significant effect.
Urbenjaphol, Jitpanya, & Khaoropthum (2009)	Level II 2 group randomized quasi-experimental <i>N</i> = 40 adults with GCS scores of 3–8. Group 1 (control), <i>n</i> = 20 (male:female ratio = 14:6; <i>M</i> age = 34.7). Group 2 (SSP), <i>n</i> = 20 (male:female ratio = 14:6; <i>M</i> age = 33.4).	<i>Group 1:</i> Routine nursing care and rehabilitation services for TBI <i>Group 2:</i> Routine nursing care and rehabilitation services for TBI plus SSP including tactile, gustatory, olfactory, auditory, and visual stimuli selected on the basis of past preferences and familiarity; sequential stimulation of all 5 senses provided daily for 30-min episodes at 2-hr intervals from 8 a.m. to 4 p.m. for 14 consecutive days	<ul style="list-style-type: none"> <li>• GCS</li> <li>• SMART score, modified to include all 5 modalities</li> </ul>	Compared with Group 1 (control), Group 2 showed higher mean and total modified SMART scores on Day 14 of the study. Providing repetitive SSP over 2 wk can enhance arousal from coma for patients with TBI.

*Note.* ABI = acquired brain injury; CRS–R = Coma Recovery Scale–Revised; GCS = Glasgow Coma Scale; *M* = mean; MCS = minimally conscious state; PEDro = Physiotherapy Evidence Database; RCT = randomized controlled trial; SDOC = severe disorder of consciousness; SMART = Sensory Modality Assessment and Rehabilitation Technique; SSP = sensory stimulation program; TBI = traumatic brain injury; VS = vegetative state; WNSSP = Western Neuro Sensory Stimulation Profile.

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**Supplemental Table 2. Risk of Bias for Studies Included in the Review (Except Systematic Review)**

Citation	Selection Bias		Performance Bias		Blinding of Outcome Assessment (Detection Bias)			Incomplete Outcome Data (Attrition Bias)		Reporting Bias
	Random Sequence Generation	Allocation Concealment	Blinding of Participants and Personnel		Patient-Reported Outcomes	All-Cause Mortality	Short Term (2–6 wk)	Long Term (>6 wk)	Selective Reporting	
Abbasi, Mohammadi, & Sheaykh Rezayi (2009)	+	-	+	+	+	NA	+	-	+	
Cheng et al. (2013)	-	-	-	?	+	NA	+	-	+	
DeFina et al. (2010)	-	-	-	-	-	NA	+	+	-	
Di Stefano, Cortesi, Masotti, Simoncini, & Piperno (2012)	-	-	-	-	-	NA	+	-	+	
Megha, Harpreet, & Nayeem (2013)	+	+	-	-	-	NA	+	-	+	
Noé et al. (2012)	-	-	-	-	-	NA	+	+	+	
Oh & Seo (2003)	-	-	-	-	-	NA	+	+	-	
Urbenjaphol, Jitpanya, & Khaorophum (2009)	+	-	-	-	-	NA	+	-	+	

Note. Categories for risk of bias: + = low risk of bias; ? = unclear risk of bias; - = high risk of bias. NA = not applicable.

Table format adapted from "Assessing Risk of Bias in Included Studies," by J. P. T. Higgins, D. G. Altman, and J. A. C. Sterne, in *Cochrane Handbook for Systematic Reviews of Interventions* (Version 5.1.0, Chapter 8), by J. P. T. Higgins and S. Green (Eds.), 2011, London: Cochrane Collaboration. Retrieved from <http://www.cochrane-handbook.org>. Copyright © 2011 by The Cochrane Collaboration.

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**Supplemental Table 3. Risk of Bias for the Systematic Review Included in the Review**

Citation	"A Priori Design" Included?	Duplicate Study Selection/Data Extraction?	Comprehensive Literature Search Performed?	Status of Publication as Inclusion Criteria?	List of		Characteristics of Included Studies Provided?	Quality of Studies Assessed and Documented?	Quality Assessment Used Appropriately?	Methods Used to Combine Results Appropriate?	Likelihood of Publication Bias Assessed?	Conflict of Interest Stated?
					Included/ Excluded Studies Provided?	Excluded						
Meyer et al. (2010)	+	+	+	+	-	+	+	+	+	NA	-	-

Note. Responses to risk of bias questions: + = yes; ? = unclear; - = no. NA = not applicable.

Table format adapted from "Development of AMSTAR: A Measurement Tool to Assess the Methodological Quality of Systematic Reviews," by B. J. Shea, J. M. Grimshaw, G. A. Wells, M. Boers, N. Andersson, C. Hamel, . . . L. M. Bouter, 2007, *BMC Medical Research Methodology*, 7, p. 10.

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