Current Practice in Neurosciences

Advances in Neurorehabilitation for Persons with Traumatic Brain & Spine Injuries and Stroke

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Introduction AQ2,7

Neurorehabilitation is the process designed to aid in recovery from neurological injury and compensate for any functional limitations resulting from it. The model of care depends on the cause, stage of disease, premorbid status and often a multidisciplinary approach is required. Recovery from brain damage is a slow process that depends upon the extent of damage and the region of the brain involved(1).

According to global burden of disease study, the prevalences of stroke, traumatic brain injury (TBI) and spinal cord injury (SCI) are 93.8, 38 and 15.4 per 100,000 population. The age-standardized Disability Adjusted Life Years (DALY) for stroke decreased by 39% between 1991 and 2021, while for TBI, it decreased by 16% during the same period. Males are at a higher risk of developing stroke and TBI with a female to male ratio of 0.71 and 0.45 respectively.(2)

Persons with TBI, SCI or Stroke have a variety of impairments that cause limitations in activity and participation. Therefore, a multimodal rehabilitation approach is required that offers comprehensive neurorehabilitation.

ICF Model (International Classification of Functioning Disability and Health)

ICF displays interactive relationships between the impairment that an individual with a particular health condition might face, the functional consequence of the impairment, and the contextual factors that may mitigate or amplify the consequences. ICF offers a conceptual framework for understanding functioning and disability. In this framework, functioning is an umbrella term that encompasses all body functions and structures, activities and participation, while disability is an overarching term for impairments, activity limitations and participation restrictions (Figure 1). 'Impairments' are defined as problems in body function or structure; 'activity limitations' are difficulties a person may have in carrying out daily activities; and 'participation restrictions' are problems a person may experience when involved in life or social situations. A person's functioning and disability, including participation, are considered to arise from the interaction among health conditions and contextual or environmental factors (e.g. air quality, accessibility of the environment, peer relationships, service availability, etc.) and personal factors.(3)

Neural Plasticity

There are two different but related ways by which a patient improves after stroke(4). The first type of recovery, a reduction in the extent of neurological impairment can result from natural spontaneous recovery, which usually account for early spontaneous improvement after stroke within first 3-6months. This form of recovery manifests as improvement in motor control, language ability or other primary neurological functions(5). The underlying mechanisms include resolution of local edema, resorption of local toxins, restoration of circulation in ischemic penumbra, and recovery of partial damaged ischemic neurons(6). This sequence of recovery however can stop at any stage.

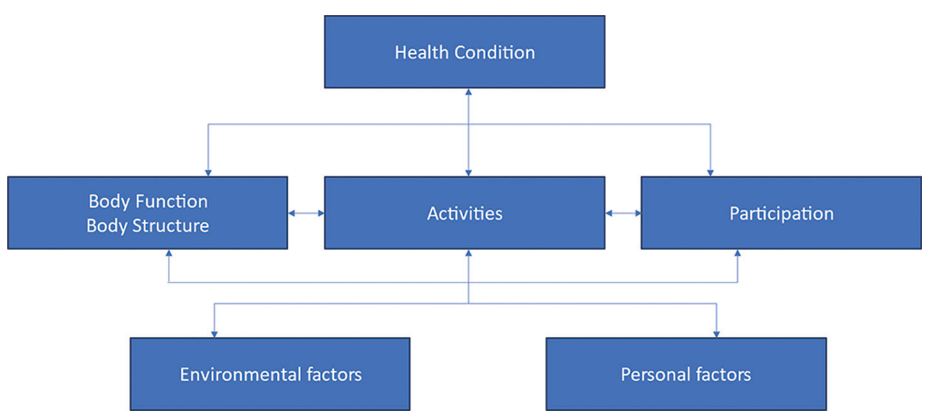

Figure 1: ICF model of functioning disability and health

The second type of recovery demonstrated in stroke patients is the improved ability to perform daily function in their environment, within the limitation of physical impairment. The underlying mechanism to explain the second type of recovery is neuroplasticity. Brain plasticity is the ability of nervous system to modify its structure and functional organisation. The two most plausible forms of plasticity are collateral sprouting of new synaptic connections and unmasking of previous latent pathways. Other mechanisms of plasticity include assumption of function by undamaged pathways, reversibility from diaschisis, denervation super sensitivity, remyelination, and regenerative proximal sprouting of transacted neuronal axons(7). Experimental evidence suggests that this plasticity can be altered by several external conditions, including pharmacological agents, electrical stimulation, intensive training and environmental manipulation(8). The ability to perform the task can improve through adaptation and training, in spite of presence or absence of natural neurological recovery. It is the element of recovery on which rehabilitation is believed to exert the greatest effect. The degree of recovery in independent functioning that occurs during rehabilitation is often greater than the expected by the reduction in neural impairments alone, which suggest that timely rehabilitation intervention probably plays important role in recovery(9).

Team Approach in Neurorehabilitation

Rehabilitation, defined as a problem-solving educational process to alleviate disability and enhance participation following disease or injury, is essential for preventing complications and enhancing individual independence (10). Neurorehabilitation is done with the patient, rather than to the patient.

There are three types of neurorehabilitation service delivery team models (table 1). The most suitable model is a dedicated, comprehensive and multidisciplinary rehabilitation team model. (Figure 2). Approaching from a patient-centred perspective, the multidisciplinary team establishes both short- and long-term goals. They strategically plan rehabilitation processes, administer suitable interventions, and continuously monitor and adjust them in response to the progression of the disease/recovery.

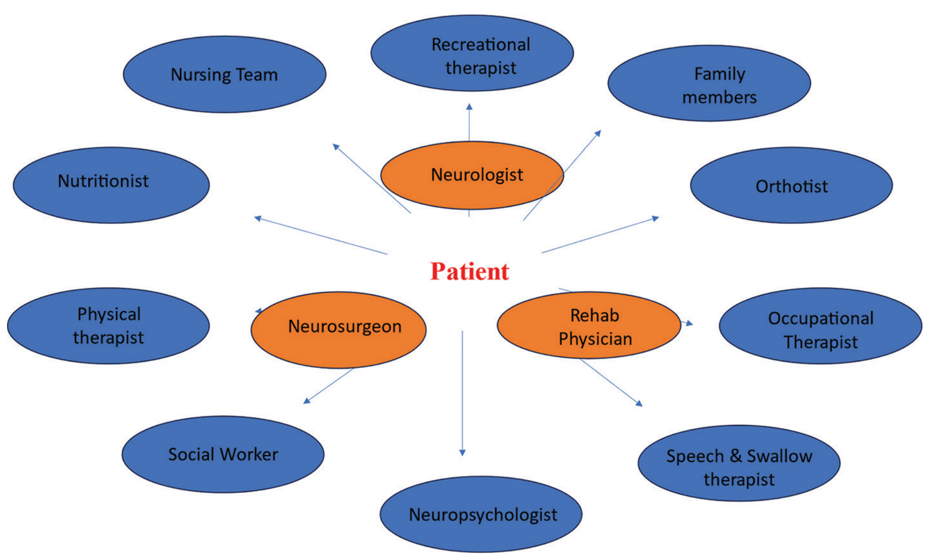

Figure 2: Patient centred rehabilitation approach

Table 1: Types of Team models in Neurorehabilitation

Types of Neurorehabilitation service models	
Multidisciplinary	Work undertaken with other disciplines in parallel or sequentially
Interdisciplinary	Work undertaken jointly with other disciplines
Transdisciplinary	Work integrated across many disciplines, and undertaken collaboratively.

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The rehabilitation plan is to be tailor-made as the problem areas and goals of rehabilitation vary from person to person. In this setting of goals is an important component and a core skill of rehabilitation professionals. (Table 2). The goals must be Specific, Measurable, Achievable, Realistic and Time bound. Rehabilitation is not a distinctly separate phase of care, beginning after acute medical intervention. Rather, it is an integral part of medical management and continues longitudinally through acute care, post-acute care up till the community reintegration ideally. The rehabilitation program may be offered in different settings, such as in intensive care or high dependency unit, an acute inpatient rehabilitation unit, a sub-acute rehabilitation inpatient unit, home care, or an outpatient centre (Table 3)(10). The acute rehabilitation setting is appropriate for those patients who meet the admission criteria and are able to tolerate 3 or more hours of active therapy per day. An acute setting is preferred if the patient requires close medical and nursing monitoring of the medical status (Table 4). If the patients' medical status is stable, but the patient is unable to tolerate more than one hour of therapy a day, a subacute rehabilitation setting is more appropriate. Other patients who require only minor degrees of assistance in self-care and mobility would be suitable for out-patient therapy or a home care program.(11)

In developing countries, where the expertise is concentrated in urban areas, it becomes difficult on part of the patient and the family to avail and sustain rehabilitation. Family based rehabilitation helps to bridge the gap and support the patient with the necessary rehabilitation program. The practice of staying in joint family reduces the caregiver burden stress on a single person as multiple people help the patient during rehabilitation. The caregiver in the family should be educated and counselled to provide physical, emotional, social and economic support to the patient. The training of multiple members in a family to provide rehabilitation reduces the fatigue in a particular care giver. Family based rehabilitation also reduces travel time and cost with improved economic viability(12).

Impairment based approach focuses on specific neurologic deficits simultaneously. This approach starts with identifying each impairment and then implementing targeted interventions designed to overcome these specific deficits. By utilising neuroplasticity, this approach seeks to enhance functional outcomes in daily life.

Rehabilitation Interventions for Symptom Management

Disorders of Consciousness (DOC)

DOC is classified in; Coma, Vegetative State (VS) which is also known as Unresponsive Wakefulness Syndrome (UWS), Minimally Conscious

Table 2: Goals of Neurorehabilitation

Goals of Neurorehabilitation
Continuity of medical care
Prevention, recognition and management of comorbid illness and intercurrent medical complications
Training for maximal functional independence in all respective domains or impairments
Facilitating psychosocial coping and adaptation by patient and the family
Promoting community reintegration, including resumptions of home, family, recreational, and vocational activities
Enhancing quality of life.

Table 3: Options for Rehabilitation

Options for rehabilitation
Acute inpatient rehabilitation
Subacute inpatient rehabilitation
Chronic inpatient rehabilitation
Outpatient rehabilitation
Family based rehabilitation
Community based rehabilitation

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Table 4: Criteria for admission to a comprehensive inpatient rehabilitation program

Criteria for admission to a comprehensive acute inpatient rehabilitation program
1. Stable neurologic status,
2. Significant persisting neurologic deficit,
3. Identified disability affecting at least two of the following: mobility, self-care activities, communication, swallowing, bowel or bladder control,
4. Adequate cognitive function to learn,
5. Sufficient communicative ability to engage with the therapist/s,
6. Reasonable physical ability and endurance to tolerate the active program, and
7. Achievable therapeutic goals.

State (MCS) or Emerging from MCS based on clinical evaluation. *Coma* is defined as absence of both arousal (spontaneous eye opening) and responsiveness and usually lasts less than four weeks. Patients in a coma can recover consciousness spontaneously in the acute period or transit to the VS or MCS. Some patients can regain full consciousness but still suffer from complete motor paralysis, a condition known as 'Locked in state' (LIS) where voluntary motor activity are restricted to movement of eye and blinking. As consciousness is not affected in this condition, LIS is not considered as a part of DOC.*UWS* patients show no behavioural sign of awareness, but have retained some level of arousal. They show eye-opening, have sleep-wake cycles, and are able to maintain vital functions unassisted. They may also show reflex responses to tactile, auditory, visual or painful stimuli, but fail to show any response to commands or any purposeful response. It can be a permanent state or can evolve into the MCS(13). *MCS* is characterized by inconsistent, non-reflexive behaviours indicating a form of fluctuating low-level awareness. MCS has been stratified into MCS+ (plus) and MCS− (minus), based on the complexity of behavioural responses. MCS− patients may show orientation to noxious stimuli or visual pursuit of moving or salient stimuli. Environmental stimuli may elicit appropriate affection responses, such as crying or smiling triggered by familiar voices or faces. MCS+ is characterized by more complex behaviours such as command following, language apprehension, intelligible verbalization, or verbal or gestural yes/no responses(1).

Brain activation in the absence of a behavioural response to spoken motor commands can be detected by EEG, also known as cognitive-motor dissociation (CMD). Patients with CMD demonstrate a vegetative state or a low level, minimally conscious state (restricted to nonreflexive behaviours, such as tracking, but lacking command following)(14).(Table 5)

First step is to ensure that the failure to demonstrate consciousness is not due to any reversible factors like medications, septic or metabolic disturbances or malnourishment. Multiple interventions are done in the acute/subacute phase to stimulate brain for improving consciousness in persons with DoC.

Standard Rehabilitation Measures

Non pharmacological interventions include standard therapy, multimodal sensory stimulation program, early mobilization, verticalization etc. (15–17) These interventions aim to activate undamaged but suppressed networks responsible for consciousness. In patients with intact neural network, optimal stimulation can be helpful in improving patients from vegetative state to minimally conscious state or emerge from the minimally conscious state.

Maintenance Therapy

These are therapy intended to reduce complications and include chest physiotherapy for improving airway clearance and lung expansion, stretching program to prevent contracture and maintain ROM of joints, strengthening program to avoid disuse atrophy of active muscle groups. Controlled breathing exercises, spirometer training and inspiratory muscle training (IMT) is useful in quadriplegics(18).

Early Mobilization

Mobilization of patients with early sitting improves the normal postural tone and proprioception. Patient's tolerance to supported sitting and standing increases, even

Table 5: Difference between types of disorders of consciousness

Behaviour	Coma	VS	MCS	CMD
Consciousness	Absent	Absent	Partial	Present
Eye opening	Absent	Present	Present	Present
Motor movements	Absent	Reflex/Non Purposeful	Purposeful	Non Reflexive/Lack command following
Visual response	Absent	Visual fixation	Visual Pursuits	Visual pursuit
Pain response	Absent/ Posturing	Posturing/ Withdrawal	Localisation	Posturing/Withdrawal
Comprehension	Absent	Absent	Inconsistent	Absent
Speech	Absent	Sounds	Words	Sounds

VS: Vegetative state. MCS: Minimally conscious state. CMD: Cognitive motor dissociation

when they are in an unconscious state. Adequate measures like strapping should be taken to support the head, trunk and limbs to prevent falls. In the acute phase, mobilization should be done under supervision to ensure hemodynamic and postural stability. Early mobilization while the patient is on mechanical ventilation can help in decreasing intensive care unit associated weakness(17).

Multimodal Sensory Stimulation Program

Multimodal Sensory stimulation is given to facilitate synaptic re-innervation and stimulate the RAS (reticular activating system) by peripherally activating the multiple arrays of sensory organs to promote awakening in patients with disorder of consciousness. Multiple methods of stimulation can be used for each sense. Visual, auditory, olfactory, gustatory, tactile, and kinaesthetic stimuli are given at different frequency and intensity. Commonly used programs have 30-minute sessions twice a day as part of the coma stimulation program.

In a Cochrane review of the sensory stimulation program, there was no strong evidence supporting the claimed efficacy of intensive multisensory stimulation programmes in the management of patients in coma or vegetative state(19). But newer studies have come up on the effectiveness of multimodal coma stimulation on patients with DoC, which suggest that receiving multimodal sensory stimulation 5 times a day yields better results than two times a day, and also both of these give superior results when compared with patients who receive only conventional rehabilitation measures(15). Therefore, multimodal sensory stimulation should be used as one of the standard rehab measures following TBI or stroke.

Verticality Training

Verticalization is a common therapeutic intervention during rehabilitation of patients with disorders of consciousness (DoC). It is considered an effective type of treatment to improve motor and cognitive recovery. It helps in recovery of the orthostatic autonomic control after a severe neurological injury. Due to the frequent occurrence of syncope, tilt table with BP monitoring are used for assessment as well as training for orthostatic hypotension (Figure 3). Body Weight Support (BWS) systems are available for patients to improve the feedback from verticality training by stimulating proprioceptive feedback along with verticality training. Advanced tilt table with a robotic stepper device for cyclic leg loading are currently available which can be used in ICU settings. They have Functional Electrical Stimulation to optimize active neuromuscular stimulation, with which patients can be trained intensively and safely in a very early stage of rehabilitation. The Erigo®Pro is one such example of a robotic tilt-table (RTT) with built-in stepping unit for the lower extremities to prevent orthostatic hypotension during verticalization(20).

Prescription of Orthosis

Individuals with Disorders of Consciousness (DOC) or stroke can present with spastic-dystonic tetraparesis or hemiparesis when undergoing rehabilitation. This condition makes them prone to developing significant contractures, particularly in the wrists, fingers, elbows, hips, knees, and ankles. To manage these issues, orthotic devices such as Solid Ankle Foot Orthoses, Rigid Knee Gaiters, Elbow Gaiters, and Resting Hand Splints are frequently prescribed. Additionally, reclining wheelchairs with proper cushioning and neck support extensions are commonly used to assist with patient mobility.

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Hyperbaric Oxygen Therapy

Hyperbaric oxygen therapy (HBOT) (Figure 4) is defined as the inhalation of 100% oxygen inside a hyperbaric chamber pressurized to >1 atmosphere pressure. This treatment may alleviate secondary injury after TBI through a variety of mechanisms. HBOT has been demonstrated to be neuroprotective in patients with TBI through increasing tissue oxygenation, suppressing inflammation, inhibiting apoptosis, decreasing intracranial pressure, and promoting neurogenesis and angiogenesis. Moreover, HBOT has been found to decrease the incidence of cognitive impairment, improve prognosis, and diminish mortality(21).

A cochrane review (2015) assessed the effects of HBOT as adjunct therapy for traumatic brain injury and reported an improvement of 2.68 points in Glassgow Coma Scale-GCS. HBOT can improve oxygen supply to the injured brain, reduce the swelling associated with low oxygen levels and reduce the volume of brain that will ultimately perish. It is, therefore, possible that adding HBOT to the standard intensive care regimen may reduce patient death and disability. The number required to prevent one mortality is to treat 7 patients.(22).

There are potential but minimal adverse effects of the therapy, including damage to the middle ear perforation and trigger new seizure., sinuses and lungs from the effects of pressure(23). Cindy Crawford et al studied the effectiveness of HBOT on traumatic brain injury and concluded that HBOT has weakly favorable evidence in improving level of consciousness in TBI(24).

Deep Brain Stimulation

Deep brain stimulation (DBS) is a neurosurgical procedure that allows targeted circuit-based neuromodulation and is commonly used for the treatment of movement disorders

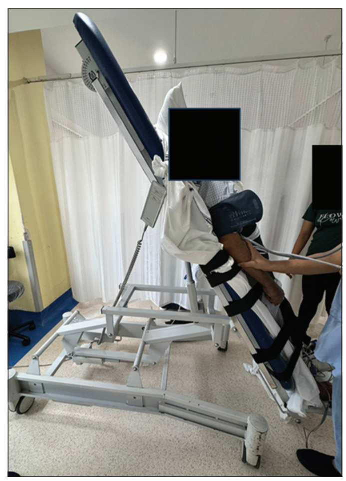

Figure 3: Verticalization using tilt table training

Figure 4: Hyperbaric oxygen therapy

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such as late Parkinson disease, tremor and dystonia(25). Several studies have reported regaining consciousness in TBI patients using DBS of subcortical structures or brainstem nuclei. It is associated with better outcomes in patients with MCS(26).

Repetitive Transcranial Magnetic Stimulation

Non-invasive Brain Stimulation can be delivered by electrical or magnetic medium. Repetitive transcranial magnetic stimulation(rTMS) consists of a transitory modulation of neural excitability with an effect that depends on the stimulation frequency.(27) Continuous low frequency rTMS ($\leq$1Hz) reduces cortical excitability in local stimulated regions and in correlated areas; while, intermittent high frequency rTMS ($\geq$5Hz) obtains the opposite effect.(28) Combined methods have been useful for studying the reactivity and connectivity of the cerebral cortex(29). rTMS for the treatment of patients with DOC has the potential to increase the CRS-R scores of some patients.(30) Also, it is a safe procedure with only transient and not severe side effects, namely, minor dizziness, discomfort at stimulation site, and mild headache. The usage of rTMS in DoC have been studied and the improvements in CRS (Coma recovery scale) was more remarkable in patients with MCS than in those with VS/UWS.(31)

Transcranial Direct Current Stimulation

Transcranial direct current stimulation-tDCS is a non-invasive technique used for neuromodulation. It involves delivering weak direct current to the cerebral cortex through electrodes, typically two, to modulate neural activity. Compared to other methods of neural control, tDCS offers portability, safety, low cost and ease of use(32). Anodal tDCS of the left DLPFC (Dorsolateral pre frontal cortex) is effective in promoting the recovery from prolonged unconsciousness in patients with MCS(minimally conscious state)(33). It is considered as a safe procedure with minimal to nil adverse effects(34).

Transcutaneous Auricular Vagus Nerve Stimulation

The afferent vagus nerve branches project into the nucleus of the solitary tract, which is attached to the thalamus, amygdala, forebrain and the medullary network. Anatomical studies have demonstrated that the vagus nerve has an afferent branch on the auricle(35). Certain case series which assessed the feasibility, safety and efficacy of trans auricular vagus nerve stimulation in patients with disorders of consciousness have concluded that it's use is feasible and preliminarily safe and may improve behavioural responses when applied to MCS patients. But systematic review has not shown favourable evidence of the efficacy of vagus nerve stimulation in facilitating the recovery of consciousness in DOCs(36).

Repetitive Median Nerve Stimulation

The median nerve serves as a peripheral gateway to the central nervous system and the sensory distribution of the hand exhibits a large cortical representation. Within the brainstem, the ascending reticular activating system (ARAS) maintains wakefulness and the spino-reticular component of the median nerve synapses with its neurons. The nearby locus coeruleus releases norepinephrine, resulting a monoaminergic arousal of the cortex directed to cortical layer I. The intralaminar nuclei of the thalamus are activated by acetyl cholinergic input from the ARAS. These intralaminar thalamic nuclei provide non-specific excitatory input to the cortical layer I, and are responsible, in part, for the initiation of awakening. The excited ARAS also stimulates the forebrain basal nucleus of Meynert which delivers diffusely spread acetylcholine to the cerebral cortex (37)(Figure 5).

Right or bilateral MNS promoted the recovery of consciousness disorders regardless of their cause. It also improved GCS scores, EEG scores, and cerebral blood flow while decreased Disability Rating Scores and number of days spent in ICU(38). Furthermore, stimulation of right MNS was more effective than bilateral MNS in improving GCS scores(39). This is a low-cost intervention and can be done bedside. It is done with a nerve stimulator with active electrode on volar aspect of right forearm and inactive electrode on volar aspect of lower 2/3 of right side forearm. Most commonly used is faradic current with amplitude of 25mA, frequency 40-5-Hz, duration of 300 microsec for 8 hours per day for 2 weeks.

Auditory Stimulation & Neurologic Music Therapy

Auditory stimulation can enrich the environment to improve arousal and awareness state in persons with DOCs and is widely used. Music is beneficial supporting

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Figure 5: Repetitive Median Nerve Stimulation

Neuroplasticity through engaging a global system of temporal, frontal, parietal, cerebellar, and limbic brain areas involved in auditory and language processing, emotion, attention, motor control, and memory.(40) Use of live music enables the manipulation of specific parameters of auditory stimuli (e.g., volume, pitch, timbre) thus optimising the possibility for gaining a more accurate picture of the DOC patient's auditory responsiveness.(41) Making music is a powerful way of engaging a multisensory and motor network and inducing changes and linking brain regions within this network.(42) Our pilot study have revealed that neurologic music therapy helps in improving arousal in persons with disorders of consciousness in standardised outcome measure(43). This is another low cost intervention which can be done bedside with trained family members.

Pharmacological Interventions

Neurostimulants are provided to manage arousal states with aim to enhance activity of neurotransmitters within CNS. They act by increasing the synaptic concentration of dopamine, serotonin, and noradrenaline in various brain regions. Potential benefits of neurostimulants include enhanced arousal, wakefulness, awareness, attention, memory, mental processing speed, and/or motor processing speed(44). A potential association between early stimulant therapy and risk of seizures or excite-toxicity in persons with acute DOC remains a hypothetical concern, but is not supported by current evidence. Amantadine is the only therapy that has been associated with the acceleration of recovery of consciousness in a randomized controlled trial of patients with DOC(45). Other medications like levodopa, modafinil, apomorphine, methylphenidate, bromocriptine, amphetamine are also being used in patients with acute DOC. Zolpidem is a GABA-ergic medication with a paradoxical awakening effect in some patients with subacute-to-chronic DOC(46). Evidence for efficacy of other neurostimulants alone or in combinations is inconclusive and derived from case reports, cross-over studies of short durations where the subjects serve as their own controls.

When a person with DOC regains consciousness, there can be multiple impairments which includes motor deficits, aphasia, dysphagia, neurogenic bowel and bladder, cognitive deficits, behavioural impairments which requires simultaneous multidisciplinary team rehab interventions.

Motor Recovery

There are different types of interventions that promote motor recovery post any neurological disorders including stroke/TBI. These include (table 6) (a)training interventions, (b)technological interventions, (c)pharmacological interventions and (d) neuromodulation interventions(47).

According to NICE guidelines, a patient should not be mobilised if systolic BP>180, GCS<8, Saturation <94% (<88 for COPD patients), HR <40 or >100bpm or if the patient has severe neglect making sitting outside unsafe. Similarly he can be mobilised out of bed to stand or walk if he is hemodynamically stable, is able to sit with assistance of up to 3 therapists, is alert and has appropriate level of understanding.(48)

Neurophysiological approaches

There are various neurophysiological therapy approaches, including Bobath, Proprioception Neuromuscular Facilitation, Brunnstrom, and Motor Relearning. Each approach is based on different rationales. Both Bobath and Proprioception Neuromuscular Facilitation (PNF) rely on neurophysiology and neuro-developmental sequences, while Brunnstrom is grounded in empirical observations of stroke patients, and Motor Relearning is focused on the kinematics and kinetics of normal movement control and motor control theory. (Table 7)

Training Interventions

A variety of approaches have been developed for *strength training* which have shown beneficial outcomes on motor recovery post stroke. Few of them include augmented exercise therapy with increased time spent on exercise in the first 6 months post-stroke, results in significant improvements in walking ability and speed as well as extended activities of daily living(49). *Task specific training* where tasks are practiced with a functional approach has proven effectiveness in motor recovery in upper limb and lower limb.

Constraint-Induced Movement Therapy

Constraint-induced movement therapy (CIMT) is designed to improve upper extremity motor functions after stroke. The basis of CIMT is to improve the function of the affected limb after a stroke by restricting the use of the healthy limb and forcing the use of the

Table 6: Interventions for motor recovery

Training Interventions	Technological Interventions	Pharmacological Interventions	Neuromodulation interventions
Structured task oriented training program	BWS training	SSRI	DBS
Modified CIMT	Robotic Gait training	Levodopa	rTMS
Functional strength training	Functional Electrical Stimulation	Fluoxetine	rTDCS
Mirror therapy	Brain Computer interface		
Biofeedback	Stem cell therapy		
	VR		

CIMT: Constraint induced movement therapy. VR: Virtual reality. SSRI: Selective serotonin reuptake inhibitors. DBS: Deep brain stimulation. rTMS: Repetitive transcranial magnetic stimulation. tTDCS: Repetitive transcranial direct current stimulation

Table 7: Neurophysiologic approaches

Items	Bobath	Proprioception Neuromuscular Facilitation	Brunnstrom	Motor Relearning
Rationale	Neurophysiology and neuro-developmental sequence	Neurophysiology and neuro-developmental sequence	Empirical basis from observations of stroke patients	Kinematics, kinetics of normal movement control, and motor control theory
Recovery	Hierarchical sequence (early, middle, and late recovery stage)	Hierarchical sequence (proximal to distal part, gross to fine motor function)	Identified 6 sequential recovery stages	7 sections of different functional tasks
Muscle tone and reflex behavior Sensory feedback	Prevention and inhibition Emphasis (handling)	No emphasis Emphasis (proprioceptors)	Facilitation early and correction later Emphasis (cutaneous stimulation and handling)	No emphasis Emphasis (practice with feedback)
Techniques of training	Movement pattern with key joint control	Spiral and diagonal movement pattern	6-stage recovery-dependent movement pattern	Functional task training

affected side. The core strategy of CIMT is the application of movement techniques, behavioural techniques and restriction methods to increase the frequency of use of the affected limb in stroke patients, improve the quality of movement of the affected limb in real-life scenarios, prevent or correct the learned non-use of the affected limb, and promote the recovery of motor function in the affect limb. In clinical practice, CIMT is mainly used to improve post stroke upper limb dysfunction by promoting the use of functionally impaired limbs after a stroke(50).

Mirror Therapy

Mirror neurons are a specific class of neurons that are activated and discharge both during observation of the same or similar motor act performed by another individual and during execution off motor act. Activation of these brain areas, namely inferior parietal lobe and ventral premotor cortex, facilitates movement execution subsequently, by directly matching the observed or imagined action. Mirror therapy works on this principle, it activates the mirror neurons and facilitates execution of movement.(51)

Mirror therapy (MT) is a type of rehabilitation approach where the reflection (visual input) of a moving non-affected limb gives the illusion of movement in the affected limb. This is achieved by placing a mirror between the arms or legs. MT has been studied to have effects not just on motor impairments but also on sensations, visuospatial neglect, and pain after stroke. Mirror therapy (MT) can be used in completely plegic as well as severely paretic stroke survivors, as it uses visual rather than somatosensory stimuli for producing a desired response in the affected limb. The role of MT in promoting normalisation of balance within the hemispheres post stroke by modulating the excitability of the primary motor cortex (M1) has also been hypothesised. During MT, both the affected limb movement and the passive observation of movement of the unaffected limb as reflected in the mirror influence M1 excitability(52).

Biofeedback

Biofeedback has been used in rehabilitation for many years and recent reviews have explored the evidence for this therapy in recovery of motor function after stroke. Electromyogram biofeedback (EMG-BFB) delivers an auditory or visual stimulus to the patient (generated from muscle activation) via electrodes placed on the skin, which can positively influence the patients use of their affected limb. A small number of studies of EMG-BFB combined with standard physiotherapy have described some benefits in motor power, functional recovery and gait quality. Short term benefit has also been reported for biofeedback in older patients for balance, gait and transfers,.(53)

The other strategies used are mental practice, action observation, bilateral arm training and circuit training.(54,55)

Technological Interventions

Body Weight Supported Treadmill Training

Body weight supported treadmill training (BWSTT) is a functional training method that is based on the reorganization of brain function and neuroplasticity. It involves using suspension devices to reduce the load on patients' lower limbs and using electric treadmills to enable patients' lower limbs to carry out repetitive and rhythmic gait cycle exercises(56). BWSTT in association with conventional rehabilitation have shown significant improvement in walking speed, endurance, balance, mobility and quality of life when compared with people receiving conventional rehabilitation alone (57).

Studies reveal that BWSTT shows a statistically significant improvement on locomotor outcomes even in chronic phase following stroke(58). Also BWSTT significantly improves the gait parameters of the patient when compared with patients on treadmill training without unweighing(59).

Rehab Robotics

Robots help to intensify motor rehabilitation of the upper and lower limbs after stroke. It intensifies the therapy without placing excessive demands on the therapist. It is mainly classified based on body part, design function and portability (Table 8).

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Robotic Assisted Gait Training

Robotic assisted step training is an advanced rehabilitation technique that provides coordinated movements of the lower limbs to simulate gait, offering stimulation for potential recovery. This method is safe for patients who have hemodynamic stability, postural control while standing, and sufficient lower limb tone to allow for a full range of motion(60).

Electromechanical devices for automated-assistive walking training can be differentiated into end-effector and exoskeleton devices. The definition of an end-effector principle is that patient's feet are placed on footplates, whose trajectories simulate the stance and swing phases during gait training whereas exoskeleton devices are outfitted with programmable drives or passive elements, which move the knees and hips during the phases of gait. Examples of exoskeleton type of devices are the "LOPES" (Lower Extremity Powered Exoskeleton) and the "Lokomat" (Figure 6). Example of end-effector devices are the "G-EO-system", the "Lokohelp" the "Haptik Walker" and the "Gait Trainer GT1"(61).

"Intensive, repetitive mobility-task training" is recommended by the AHA/ASA guideline (2016) for all individuals with gait limitations after stroke. Present recommendations are for the use of an end-effector–based device or an exoskeleton in combination with conventional physiotherapy and gait training. It has been demonstrated that robot-assisted gait training for stroke patients who are unable to walk independently improves their walking ability and performance of basic activities of daily living, compared to conventional therapy. Mechanically assisted walking may be considered in patients who are non-ambulatory or have low ambulatory ability early after stroke. Electromechanical (robotic) assisted gait training devices could be considered for patients who would not otherwise practice walking. They should not be used in place of conventional gait therapy. Consider the use of these mechanical devices mainly in the early sub-acute phase (up to 3 months) after stroke(62).

Robotic Assisted Upper limb Training

Robotic therapy has been proposed as a viable approach for the rehabilitation of the UL, (Figure 7,8) as a way to increase the amount and intensity of the therapy, and to standardize the treatment, by providing complex but controlled multisensory stimulation. Moreover, because of their built-in technology in terms of sensors and actuators, robotic devices can provide quantitative measure about the user's dexterity. Nowadays, the use of robotic rehabilitation in addition to conventional therapy is recommended in some of

Table 8: Classification of rehabilitation robotics

	Types	
Body Part	Upper Limb Robotics	Lower Limb Robotics
Design	Exoskeleton	End Effector
Function	Therapeutic	Assistive
Portability	Wearable	Fixed

Figure 6: Lokomat: Robotic assisted gait trainer

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Figure 7: Amadeo: Robotic assisted hand rehabilitation

Figure 8: Armeo Power, Robotic assisted upper limb training

the current stroke guidelines(63). The upper limb robotic devices can be exoskeleton or end effector types, (64). Electromechanical and robot-assisted arm training improved activities of daily living scores, arm function, and arm muscle strength. Electromechanical and robot-assisted arm training did not increase the risk of participant drop-out, and adverse events were rare. The test for subgroup differences between a subgroup of participants who received mainly training for the distal arm and the hand (finger, hand, and radioulnar joints) and a subgroup of participants who received training mainly of the proximal arm (shoulder and elbow joints) revealed no significant difference for either arm function or activities of daily living scores at the end of intervention. Effects on ADL could be substantiated for the subgroup treated during the acute and subacute phase, but not for the subgroup with participants in the chronic phase (i.e. more than 3 months after stroke) (66).

Functional Electrical Stimulation

Functional electrical stimulation (FES) is used as an adjunct therapy in both stroke and SCI rehabilitation. FES can be used to assist in the rehabilitation of motor activity (early stages after stroke or incomplete SCI) or as a neuroprosthesis (when voluntary motor activity can no longer be restored). Functional electrostimulation is divided into two categories: Functional FES and Therapeutic FES. Functional FES replaces the lost motor function while therapeutic FES prevents muscle atrophy and maintains helath of musculoskeletal system. Evidence shows that FES uses brain plasticity to restore the ability to perform voluntary movements after spinal cord injury and stroke(65).

The most promising method of applying FES technology to improve gait is FES-assisted walking therapy with stroke (Figure 9) and incomplete SCI patients. Positive results have also been reported for implanted and surface FES devices that are used as permanent orthotic systems. Although these systems have been found efficacious in a number of studies, a limited number of consumers are using these devices at home and in clinical settings(66). Some FES devices for hand in cervical spinal cord injury includes NESS H200, Bioness, Valenci CA which are used to provide grasp and release for individuals with cervical SCI. UE neuroprosthetic systems consist of a stimulator that activates the muscles of the forearm and hand and an input transducer and control unit(Figure 10). The control signal for grasp is derived from an action which the user has retained voluntary control, which can include joint movement, muscle activity, respiration, voice control, or cortical signals. A coordinated stimulation pattern is developed so that the muscles are activated in a sequence that produces a functional grasp.(67)

Brain Computer Interface

Brain-computer interfaces (BCIs) offer sensory feedback on ongoing brain oscillations, allowing stroke survivors to purposefully modulate their sensorimotor rhythms. A BCI converts electrical, magnetic, or metabolic brain activity into control signals for external devices, which can replace, restore, enhance, supplement, or improve natural neural output, thereby altering the interaction between the brain and its environment. BCIs can be categorized as invasive or non-invasive depending on the method used to measure brain activity. Invasive BCIs involve electrodes placed either on the brain's surface (electrocorticography or ECoG) or implanted within the cortex, while non-invasive BCIs use electrodes placed on the scalp (electroencephalography or EEG).

Figure 9: Therapeutic FES for lower limb

Figure 10: Therapeutic FES for upper limb

In a study involving stroke patients rehabilitated with non-invasive BCIs, a medium to large effect size was observed for upper limb motor function and improvement in Fugl-Meyer Assessment-Upper Extremity scores compared to conventional therapies. Additionally, several studies reported BCI-induced functional and structural neuroplasticity at a subclinical level, with some of these changes correlating with improved motor outcomes(68). BCI can also used for gaze tracking system in persons with locked in state or MCS (TOBI system / EEG Headgear system)(69).

Virtual Reality

In virtual reality-VR, advanced technologies are used to produce simulated, interactive and multi-dimensional environments. Virtual Reality (VR) can be non-immersive, semi-immersive and immersive depending up on the virtual environment, patient is exposed to and provides a unique medium suited to the achievement of several requirements for effective rehabilitation intervention.

A cochrane review concluded that the use of virtual reality and interactive video gaming was not more beneficial than conventional therapy approaches in improving upper limb function. Virtual reality may be beneficial in improving upper limb function and activities of daily living function when used as an adjunct to usual care (to increase overall therapy time)(70). Both therapists and users benefit from the ability to readily grade and document the therapeutic intervention using various systems. (71)

Trunk balance and posture are compromised in cervical and thoracic SCIs. VR can be used as an effective tool and technique in training these patients and improving posture and trunk balance. Sengupta et al reported the effect of training with semi-immersive VR in patients with tetraplegia and paraplegia in a case-control study. After 3 weeks of training patients in both the groups VR training showed significant improvement in trunk balance and posture with insignificant difference between the groups.(72)

Dynamic posturography

Posturography is the measurement of postural sway. It is usually recorded by force platform(s), measuring the center of foot pressure displacement during a given time period. Dynamic posturography" measures postural reactions in response to a translation/rotation of the support surface, visual surroundings, or both. This technique is used for analyzing postural reflexes and sensory re-weighing ability in older adults, stroke, and dizzy patients.(73)

Srivastava et al, 2009 evaluated the role of balance training on force platform with visual feedback technique (FPVF) in improving balance and functional outcome in chronic stroke survivors(Figure 11). It was concluded that Balance training by FPVF technique significantly improves balance and functional outcome even in chronic phase after stroke(74).

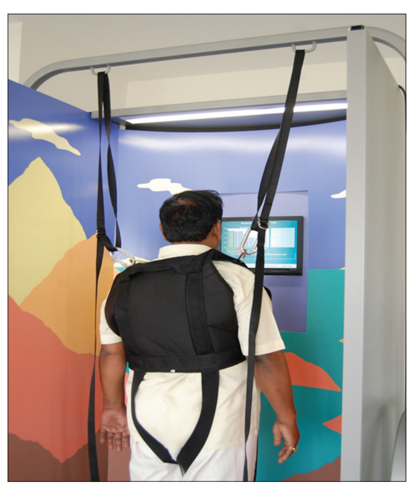

Figure 11: Dynamic Posturography

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Figure 12: Videofhuoroscopic Swallow Study (VFSS) showing UES spasm AQ4

Neuromodulation – Non Invasive Brain Stimulation

Non-invasive stimulation techniques such as repetitive TMS (rTMS) or transcranial direct current stimulation (tDCS) have the potential to modulate brain cortical excitability with long lasting effects. rTMS has been used to safely enhance motor performance in stroke patients as well as study the way that adjuvant rehabilitation interventions may facilitate adaptive brain plasticity. However, more studies are needed to determine optimal stimulation parameters and to understand how different patient characteristics influence response to non-invasive brain stimulation. It remains unclear which hemisphere is the optimal target for stimulation, or whether a combination of both stimulation sites should be considered(75). Some studies suggest that using rTMS to normalize interhemispheric imbalances in stroke patients may be an effective strategy to improve motor function. Thus, the alternative strategies include inhibiting the healthy hemisphere or enhancing excitability in the ipsilesional side may be an effective approach.(76)

tDCS can be applied focally to balance the level of hemispheric excitability and modulate spontaneous neuronal activity in a polarity-dependent manner. Excitability of a specific region can be increased by anodal stimulation or decreased by cathodal stimulation . Unlike TMS, which is both a neurostimulatory and a neuromodulatory application, tDCS seems to provide a neuromodulatory intervention only. The electrical currents in tDCS facilitate modulation of the neuronal resting membrane potentials. Anodal tDCS causes subthreshold depolarization and enhances the excitability of the affected hemisphere. Cathodal tDCS, on the other hand, induces hyperpolarization and reduces the excitability of the unaffected hemisphere. According to this model, inhibition of the unaffected hemisphere by cathodal tDCS or excitation of the affected hemisphere by anodal tDCS may normalize the poststroke bihemispheric imbalance of transcallosal inhibition(77)

Pharmacotherapy

Pharmacological intervention to enhance recovery from stroke has been investigated in animal models and clinical trials with focuses on the adrenergic, dopaminergic, and serotonergic pathways.

However, large-scale randomized controlled clinical trials of compounds to modulate these systems such as dextroamphetamine (d-amphetamine), L-3,4-dihydroxyphenylalanine (L-DOPA), and selective serotonin uptake inhibitors (SSRIs) have failed to reveal promising effects on recovery. Thus, the concept of pharmacological enhancement for motor rehabilitation in stroke needs to be reconsidered(78).

FLAME trial done for motor recovery in acute ischemic stroke with moderate to severe motor deficit, suggested the early prescription of fluoxetine with physiotherapy enhanced

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motor recovery after 3 months.(79) However, the larger meat analysis failed to show the same beneficial effect.

Cerebrolysin had a beneficial effect on function and global outcome in early rehabilitation of patients after stroke. Its safety was comparable with that of the placebo, suggesting a favourable benefit/risk ratio(CARS trial)(80). Meta analysis on the CARS trial also suggested cerebrolysin had a beneficial effect on motor function and neurological status in early rehabilitation patients after acute ischemic stroke.(81)

TALOS trial confirmed that SSRI is safe in ischemic stroke patients and treatment can be started subacute after stroke onset(82). European Academy of Neurology(EAN) & European Federation of Neurorehabilitation(EFNR) guidelines have weakly recommended use of citalopram 20 mg for early motor neurorehabilitation after acute ischaemic stroke.(83)

DARS trial studied the use of 100 mg of levodopa and 25 mg of carbidopa as an add on therapy to physical and occupational therapy. It concluded that usage of the same does not seem to improve walking after stroke(84).

Abnormal Tone

Spasticity or hypertonia is considered to be a positive sign of the upper motor neuron syndrome (UMNS), which refers to motor behaviours resulting from lesions proximal to the alpha motor neuron, therefore within the spinal cord or brain. Spastic dystonia is one of the positive phenomena of the upper motor neuron syndrome (UMNS). It is characterised by the inability to relax a muscle leading to a spontaneous, although stretch-sensitive, tonic contraction. A UMN injury leads to loss of inhibition downstream and hypersensitivity of the reflex arc within the spinal cord.

Secondary dystonia is usually due to injury of the basal ganglia and/or thalamus (rarely globus pallidus) either from trauma, stroke, or anoxia and can often have associated hemiparesis or quadriparesis. Hemidystonia affecting both the upper and lower extremity was the most common presentation following traumatic brain injury. Dystonia is more likely in younger patients and there is often a delay in its appearance from the time of injury.(85)

Spasticity affects approximately 35% of those with stroke, about 50% of TBI patients, 40% of SCI patients. Spasticity is frequently graded using the modified Ashworth scale, which is graded 0 to 4. Other commonly used scales include the Tardieu scale and Penn spasm frequency scale. Spasticity affects quality of life (QoL) and can be both diverse, and highly detrimental to daily functioning. Spasticity can result in urinary incontinence; limit sexual intimacy; interfere with walking, sitting, and standing, difficulty in self-care, personal hygiene and generally reduce a person's ability to undertake activities of daily living(86).

Treatment options are typically approached in a stepwise manner, beginning with conservative methods and progressing further if necessary. The initial step involves identifying and eliminating harmful stimuli, such as infections, pain, deep vein thrombosis (DVT), heterotopic ossification, pressure ulcers, urinary retention or stones, and ingrown toenails. Physical modalities and therapies are implemented, including stretching, splinting, serial casting, heat and cold therapies, direct tendon pressure, functional electrical stimulation, vibration, and biofeedback. Pharmacotherapy provides several options such as baclofen, tizanidine, dantrolene, and diazepam. These systemic medications are effective in managing mild to moderate spasticity, particularly in cases related to spinal cord injury (SCI), traumatic brain injury (TBI), or stroke.(87)

If not responding to conservative methods and pharmacology, we consider the possibility of diagnostic nerve blocks, chemical neurolysis, chemodenervation with botulinum toxin, and motor point blocks. These procedures are the typical choice for treatment of focal spasticity or when the systemic effects of the oral agents mentioned above are prohibitive at required treatment doses.

Another management option is an intrathecal baclofen (ITB) pump. This device allows for direct delivery of baclofen into the cerebrospinal fluid (CSF) in the intrathecal space. This allows a

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patient to receive a high concentration of the medication directly to the spine while decreasing the CNS risks associated with high oral doses of baclofen, with a ratio of 100:1 for the baclofen concentration at the spinal cord level when administered intrathecally versus orally(88).

Treatment of dystonia following brain injury may include anticholinergics and muscle relaxants such as benzodiazepines, baclofen, and tizanidine. Occasionally, there is mild symptom relief as these patients may also feel discomfort, but oral/enteral medicine is usually ineffective. However, there has been some improvement following botulinum toxin injections; therefore, it has become the treatment of first choice in patients with brain injury–associated focal dystonia(89)

Aphasia

Aphasia is a devastating consequence of stroke and affects approximately one-third of patients, where language reception or expression or both may be affected to varying degrees. Significant improvements can be achieved with Speech Language therapy-SLT, particularly with intensive delivery. Improvement in language may continue years after stroke onset. In recent years, newer approaches to therapy have been explored with positive results. Constraint-induced aphasia therapy (CIAT) is an intensive form of SLT where patients are not permitted to use compensatory strategies (e.g., drawing or writing) to communicate. CIAT primarily concentrates on two principles of constraints (force patients to use verbal language) and intensity (massed practice) due to patients with aphasia often making the least effort in communication and even solely using drawings or gestures instead of speaking out(90). CIAT has also been explored in conjunction with pharmacological therapy using memantine (an NMDA receptor antagonist which may counteract glutamate induced neurotoxicity seen in animal models of ischemic stroke). A placebo-controlled randomized trial showed that language improvements were most pronounced in the memantine (combined with CIAT) group, and this improvement persisted on long-term follow-up.(91)

Current evidence suggests that drugs, such as donepezil and memantine, can improve the prognosis of post stroke aphasia. Donepezil has a significant effect in improving the ability of auditory comprehension, naming, repetition and oral expression. Memantine has a significant effect in improving the ability of naming, spontaneous speech and repetition. Bromocriptine showed no significant improvements in the treatment of aphasia after stroke(92). The Canadian best stroke practice guidelines to improve language and communication are given in Table 9.

In patients with minimally conscious state+ status, efforts must be taken to introduce Augmentative and Alternative Communication (AAC) to improve patient participation and establish interaction between patients and caretakers. 'Yes-No' charts, Picture charts, Eye tracking devices can be tried once the patient is hemodynamically stable, can sit with assistance where needed and can otherwise communicate with eye blinks or other limited motor movements. For patients with preserved reading abilities, eye tracking technology can help in functional communication(93).

Table 9: Canadian Best Stroke Practice Guidelines

Canadian Best Stroke Practice Guidelines – To Improve Language & Communication
Persons with aphasia should have early access to a combination of intensive speech and language therapy and communication therapy according to their needs, goals and impairment severity [Evidence Level B]
Treatment to improve functional communication can include language therapy focusing on: • Production and/or comprehension of words, sentences and discourse, (including reading and writing) • Conversational treatment • Constraint induced language therapy • Use of non-verbal strategies, assistive devices and technology (e.g., I-Pads, Tablets, other computer-guided therapies) which can be incorporated to improve communication
Use of computerized language therapy to enhance benefits of other therapies.
Appropriate patients should be assessed for their potential to benefit from using augmentative alternative communication (e.g. iPad, tablet, electronic devices, alphabet board) or other communication support tools [Evidence Level C]

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Greener et al in Cochrane review assessed the effects of drugs on language abilities in patients with aphasia following stroke and concluded that Speech and language therapy (SLT) is the most common treatment for this disorder. The only drug with weak evidence of benefit was piracetam but there were concerns about its safety. There was inconclusive evidence about better effectiveness between piracetam and speech and language therapy(94).

Non-invasive brain stimulation techniques such as transcranial magnetic stimulation (TMS) and transcranial direct current stimulation (tDCS) have been employed to facilitate recovery by stimulating lesional and contralesional regions. There is compelling evidence that both TMS and tDCS may be of benefit in the treatment of aphasia without significant adverse effects. Both tDCS and TMS resulted in language improvements, including receptive and expressive modalities, may offer future supplementary approaches to conventional therapy (95).

Dysphagia

Dysphagia significantly affects quality of life and places patients at risk of pneumonia, malnutrition and death. Studies have shown incidence rates of dysphagia to range from 19% to 81% in stroke, 25-93% in TBI and 30-40% in acute cervical spinal cord injury.(96–98) The prevalence rates of dysphagia is 8.1–80 % of stroke patients, 27–30 % of traumatic brain injury patients, and 16-60% of SCI patients(98,99).

Swallowing requires food passage from the mouth through the esophagus and into the stomach without compromising the adjacent structures: nasal passages, larynx and the lower respiratory tract. The process starts after food ingestion and can be divided into four stages defined by the location of the bolus

Oral preparatory stage: prepare bolus for propulsion into pharynx

Oral propulsive stage: tongue pushes bolus through the fauces into the pharynx

Pharyngeal phase: pharyngeal structures move bolus through the upper oesophageal sphincter.

Oesophageal phase: oesophageal peristalsis and gravity move the bolus through the lower oesophageal sphincter into the stomach.(100).

Dysphagia, or swallowing impairment, is a common complication of many health conditions. To assess patients for dysphagia, we may use clinical assessments or instrumental swallowing assessments.

The Bedside Swallow Examination (BSE) is a crucial part of the clinical assessment process. It involves observing a dry swallow, testing swallows of food and liquid, and experimenting with behavioural and dietary adjustments. Liquid trials start with a small sip of water, and if the patient can handle it, larger sips and solid foods are introduced. During the oral phase evaluation, attention is paid to the labial seal, rotary chewing, presence of oral residue, and the length of the oral phase. Pharyngeal signs of dysphagia include delayed swallow initiation, coughing or throat clearing after swallowing, a wet voice, or difficulty breathing after the trials.

Instrumental swallowing assessments are more accurate and comprehensive, but they also require more time and resources (Table 9). The widely used instrumental assessments are a video fluoroscopic swallowing study (VFSS) and fibreoptic endoscopic evaluation of swallowing (FEES).

Videofluoroscopic Swallow Study (VFS), also known as Modified Barium Swallow (MBS), utilizes specialized VFS equipment to offer real-time visualization and assessment of the swallowing anatomy and physiology. It is considered the gold standard for evaluating dysphagia and ensuring swallow safety. VFS can also detect aspiration and silent aspiration (aspiration without a cough reflex), which is associated with a 20% mortality rate in elderly stroke patients within one year(101). Varying consistencies of barium sulphate along with food are utilised; however, barium aspiration can present safety concerns. Water soluble contrast agents such as Omnipaque are usually preferred, especially for those at high risk of aspiration.

In Flexible Endoscopic Evaluation of Swallowing (FEES), a fiberoptic nasopharyngo-laryngoscope is used to assess the anatomy and identify potential oropharyngeal

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dysphagia, while also evaluating sensory swallowing defects. Its portability makes it especially useful for bed-bound stroke patients. Similar to VFS, FEES uses real food to provide an accurate assessment of the patient's swallowing abilities. However, FEES is invasive and can cause discomfort, nosebleeds (epistaxis), and low blood pressure (hypotension). Additionally, visualization may be hindered by pharyngeal constriction, which can block the endoscope's tip and cause a "white-out" effect during swallowing(102).

After a stroke, up to 60% of patients experience dysphagia, which can lead to complications such as aspiration pneumonia, malnutrition, and poor functional outcomes. Protective measures to reduce these risks are central to treatment. Dietary modifications and proper oral hygiene are essential for lowering the risk of aspiration pneumonia, while nutritional supplementation, including tube feeding, may be necessary to prevent malnutrition. Rehabilitative approaches focus on improving swallowing function through various behavioral strategies, such as modifying food consistency, adopting compensatory postures, performing swallow exercises, and using swallow maneuvers. Research has also investigated the potential of pharmaceutical agents like capsaicin and other Transient-Receptor-Potential-Vanilloid-1 (TRPV-1) receptor agonists, which influence sensory perception in the pharynx. Additionally, neurostimulation techniques, including transcranial direct current stimulation, repetitive transcranial magnetic stimulation, and pharyngeal electrical stimulation, may enhance neuroplasticity within the sensorimotor swallowing network(103).Vitam Stim ™is a FDA approved device for neuromuscular electrical stimulation for pharyngeal muscles.

Dysfunction of the upper oesophageal sphincter (UES) is frequently detected in patients with dysphagia or globus sensation by means of video fluoroscopic swallowing study (VSS) (Fig 10). UES dysfunction is characterized by either incomplete or poorly coordinated opening of the UES during the pharyngeal phase of swallowing. This results in hypopharyngeal retention and sometimes to laryngeal penetration or tracheal aspiration of the swallowed food(104). Injection Onabotulinum toxin A into the cricopharyngeus muscle under ultrasound guidance is a successful therapeutic approach for patients with upper oesophageal sphincter spasm(105).

Timely Decannulation

Patients with severe DOC are managed with mechanical ventilation and are tracheotomised during the acute medical management. Once they are weaned off from ventilator, tracheostomy tube helps in management of tracheobronchial sections and to protect the airway against aspirations. But the tube itself can contribute to aspirations, dysphagia, pain, local complications like granulation tissue and increases the overall cost of medical care significantly. Timely decannulation is the removal of tracheostomy tube when the patient no longer needs it and it depends on patients swallow function, quantity of tracheal secretions and ability to breathe through nasal airway and maintain saturation on blocking of tracheostomy tube(106). A dye test can be used to objectively assess the risk of aspiration in patients with tracheostomy tube. It involves using a small drop of blue or green food colouring mixed with a bolus and to determine if there is aspiration by monitoring for the colour in tracheostomy tube suction. More comprehensive evaluation of swallow can be done using Video Fluoroscopic Swallowing Study (VFSS), otherwise known as modified barium swallow study**.** The patient is given feed of various consistencies mixed with barium, which allows the bolus to be visualized in real time on an X-ray during the swallow. It provides a direct, dynamic view of oral, pharyngeal, and upper oesophageal function. The size of tracheostomy tube is gradually decreased and the duration of tracheostomy blocking progressively increased before decannulation to evaluate the tolerance in patients who demonstrate adequate swallow function clinically. Transcutaneous neuromuscular electrical stimulation therapy can be used along with conventional swallow therapy for training of patients with mild to moderate dysphagia(107).

Cognitive Deficits

The pooled prevalence of memory and attention deficits after mild TBI is 31% and 20% in the acute phase and 26% and 18% in the subacute phase, respectively. It is 49% and 54% in the subacute phase and 21% and 50% in the chronic phase after moderate-to-severe TBI. The overall prevalence of information processing speed deficits after mild TBI in

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the acute and subacute phases is reported to bebetween 21% and 17%, respectively, and 57% in the chronic phase after moderate-to-severe TBI. The overall prevalence of executive dysfunction in the subacute and chronic phases is 48% and 38%, respectively, after moderate-to-severe TBI.(108). Various cognitive deficits are seen post neurologic injury(109) (Table 11).

Cognitive Assessment

There are numerous well-established tools for conducting cognitive assessments, each designed to evaluate specific neuropsychological domains, including memory, language, executive function, abstract reasoning, attention, and visuospatial skills. These assessment tools vary in scope, ranging from those focused on a single neuropsychological domain to mental status screens that assess multiple domains, to comprehensive neuropsychological exams that thoroughly evaluate each domain.

Most clinicians utilize established mental status screening tools like the Mini-Mental Status Exam (MMSE), Montreal Cognitive Assessment (MoCA), or Addenbrooke's Cognitive Examination (ACE) to identify potential cognitive impairment. If the results from these screenings are inconclusive or if additional information is needed, a full neuropsychological evaluation may be conducted. This comprehensive evaluation is designed to pinpoint specific cognitive deficits, distinguish between neurological and psychological causes, localize the impairments, and aid in developing a personalized management plan. The evaluation is non-invasive, involving a series of tests administered by a trained professional, and can take up to an entire day to complete.

Cognitive Retraining

Cognitive rehabilitation consists of diverse interventions. Studies have divided cognitive rehabilitation therapy into two components: Restorative and compensatory approach. The restorative approach aims at reinforcing, strengthening, or restoring the impaired skills. It includes the repeated exercise of standardized cognitive tests of increasing difficulty, targeting specific cognitive domains (e.g., selective attention, memory for new information). Compensatory approach teaches ways of bypassing or compensating for the impaired function. (Table 12)

Pharmacotherapy based on two principles, catecholaminergic and cholinergic augmentation has been found to be a useful adjunct in cognitive rehabilitation(110).

Table 10: Instrumental evaluation of swallow AQ3

Videofluroscopic Swallow Study (VFSS)	Flexible Endoscopic Swallow Study (FEES)
Allows real-time view of oral, pharyngeal and oesophageal phases of swallow	Oral phase not visible, can be seen only before and after the swallow
Evaluation of swallow biomechanics	Evaluation of vocal cord function on swallowing
Detects aspiration	Trace aspiration maybe missed
Radiation exposure	No radiation exposure
Sample of swallows may be small	Multiple swallows of different consistencies can be viewed
Requires patient participation	Decreased co0peration as invasive procedure

Table 11: Cognitive Impairments following TBI/Stroke

Common Cognitive Impairments following TBI, Stroke
Impaired attention
Decreased concentration
Easy distractibility
Impaired visual spatial conceptualization
Slow verbal/visual information processing
Impaired memory
Communication disorder
Poor judgment
Poor executive function
Loss of normal coherence

Enhancing cholinergic function is likely the most suitable pharmacological approach for improving arousal and cognition in traumatic brain injury (TBI). Amantadine may be considered to address deficits in attention, concentration, and overall cognitive functioning, particularly in cases of moderate to severe TBI. Cognitive impairments such as processing speed, sustained attention, and learning and memory deficits are likely to respond well to treatment with methylphenidate.

For individuals with executive dysfunction, bromocriptine has demonstrated some positive effects and is recommended to improve divided attention, initiation, and mental flexibility. In a rehabilitation setting, stimulant medications may enhance engagement in therapy, leading to better overall functional outcomes. For those whose primary complaints are memory and attention problems, cholinesterase inhibitors could be beneficial. Among these, donepezil is the most extensively studied and may be considered a first-line treatment for memory impairment(111). A study has shown that escitalopram may improve global cognitive function, especially in verbal and visual memory functions, and the effect might be independent of the antidepressant effect(112).

Several nonpharmacological treatments have proven effective in rehabilitating cognitive impairment. Aerobic exercises, which involve highly automated movements, can enhance cardiovascular and respiratory functions. A systematic review of trials examining the impact of aerobic exercise on post-stroke cognitive impairment indicates that engaging in aerobic exercise can improve overall cognitive abilities, as well as specific cognitive domains such as attention and memory.

Computer-assisted cognitive rehabilitation (CACR) is another highlighted cognitive rehabilitation intervention. Compared with the conventional methods, which are paper/pencil exercise, CACR has many advantages. Firstly, it has the flexibility to adjust the cognitive training on the basis of each patient's specific neuropsychological patterns so that the damaged location can be better stimulated, Secondly it can give instant feedback and shorten treatment time by incorporating video games and thirdly stroke patients might have more motivation for therapy. The clinical use of CACR has increased, and a number of studies show its efficacy in improving attention, memory, executive function, visuospatial neglect, and other cognitive declines(113).

Behavioural Issues

The new onset and persistence of disability can give rise to a variety of psychologic reactions in these patients, including sadness, grief, anxiety, depression, despair, anger, frustration, and confusion (Table 13). It is important to recognize the variety of reactions that might occur. While depression and sadness might occur with some frequency (estimates range between 30% and 60%, depending on study criteria), anxiety, guilt, stress, and other feelings are common as well.

Table 12: Cognitive Retraining

Compensatory	Restorative		Educational
Adapt to External Environment	Restore impaired function of patients		Family Member education program
	Domain Specific	General	
		Pharmacological	
		Non Pharmacological	

Table 13: Behavioural problems post stroke (140)

Emotional problems post stroke	Prevalence
Depression	30%
Involuntary emotional expression behaviour	20-30%
Catastrophic reaction	20%
Apathy	27%
Generalised anxiety disorder	22-28%
Post traumatic stress reaction	10-30%
Fear of falling	60%
Anger	17-35%

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One of the major factors influencing both the degree of participation in a therapy program and the outcome achieved is patient motivation. Patients who cooperate with therapeutic efforts and who have the determination to improve are more likely to participate in a therapy program. Therefore, behavioural problems should be addressed and it is a critical component of rehabilitation program.

Agitation

Agitation and restlessness are common during the early stages of recovery as survivors of traumatic brain injury begin to regain responsiveness. However, agitated behaviour is also associated with significant consequences such as destruction of property, potential harm to self or others, interference with daily activities, caregiver and family distress(114) and disruption of multidisciplinary patient care and rehabilitation. Agitation following a traumatic brain injury (TBI) typically lasts from 1 to 14 days, though it may persist longer in some cases. TBI often results in diffuse brain injury, commonly impacting the fronto-temporal regions and possibly involving subcortical and brainstem areas. These regions are crucial for regulating arousal, attention, memory, and limbic behaviors, and their disruption frequently leads to post-traumatic agitation. Dysfunction in the frontal lobe is associated with symptoms such as depression, withdrawal, overall changes in personality,(115) impulsivity, and spontaneous persistent aggression, as well as perseveration, disinhibition, amotivation, apathy, inattention, memory, planning, and problem solving.

Levels of agitation and sedation can be assessed using various scales like the Richmond Agitation Sedation Scale (RASS),(116) agitated behavioural scale(117). The RASS is a validated tool used to guide sedation therapy in hospitalized patients. The scale uses a rating severity from−5 (unarousable) to +4 (combative).

The primary goal of short-term management of agitation is to promptly control excessive psychomotor activity, typically using a combination of environmental and pharmacological restraints to quickly reduce dangerous behaviours. In long-term rehabilitation settings, however, these interventions can hinder therapy participation and negatively impact cognitive function. Therefore, the aim in this phase is to continue managing excessive psychomotor activity while minimizing the adverse effects of the treatments. This involves using a more tailored approach with a combination of environmental and pharmacological strategies(114).

Nonpharmacological strategies aim to provide consistency, predictability, and structure by incorporating familiar elements, routines, effective communication, distraction techniques, and physical restraint, all customized to the individual's needs. The Craig bed has been used for physical restraint for a long time. When medication is necessary, monotherapy is preferred to enhance compliance and reduce side effects. Managing agitation often requires a combination of pharmacological and non-pharmacological approaches. The principle of "starting low and going slow" is particularly crucial for individuals with TBI, as they are generally more sensitive to both the positive and negative effects of central nervous system medications.(118). Common medications includes atypical antipsychotic agents, anticonvulsant agents, antidepressant agents and beta-blockers. The most frequent first-line drugs for agitation included quetiapine, propranolol, olanzapine, sodium valproate and trazodone(119).

Depression

Post-stroke depression (PSD) is one of the common emotional disorders affecting stroke survivors. The prevalence of post stroke depression is high, with about one-third of stroke survivors suffering from it(120). The incidence of psychiatric symptoms, particularly depression, shows high variability, and is reported in 10-77% in patients with traumatic brain injury(121).

Several symptoms associated with PSD have been associated with reduced quality of life and have been known to interfere with stroke recovery, including changes in weight and appetite, disturbed sleep patterns, loss of energy, sense of worthlessness, suicidal ideation, anhedonia, psychomotor retardation, and/or agitation(122).

Depression following a traumatic brain injury (TBI) is linked to adverse outcomes in various aspects of societal participation. It is associated with reduced social activity, lower levels of community integration, decreased employment, and diminished participation in daily activities. Individuals with TBI who experience major depression for more than six months often show a decline in social functioning and the ability to perform daily living activities.(123)

Most commonly used screening tools are nine-item patient health questionnaire (PHQ-9) and the two-item patient health questionnaire (PHQ-2). These have good diagnostic reliability in the diagnosis of depression but it relies heavily on verbal communication. Other commonly used screening tools are Beck Depression Inventory (BDI), the Hamilton Rating Scale for Depression, and the Clinical Global Impression assessment by professionals.

Pharmacological therapy with antidepressants and psychotherapy should be considered as the first-line treatment for post-stroke depression (PSD). The two most commonly studied pharmacological interventions are selective serotonin reuptake inhibitors (SSRIs) and tricyclic antidepressants (TCAs). Among SSRIs, escitalopram and paroxetine are particularly effective. Cognitive behavioral therapy (CBT) is the most effective psychotherapeutic intervention for PSD. Prompt and appropriate use of antidepressants not only helps alleviate depression but also improves neurological outcomes and long-term prognosis(124).

In the 2015 update of the Canadian Stroke Best Practice Recommendations, it was advised that drug therapy should continue for at least period is 6 to 12 months if the chosen drugs are effective. The maintenance stage of treatment could be reduced, continuing 2 to 3 months after the depressive symptoms disappear(125). Preventive application of antidepressants, especially SSRIs, can significantly reduce the incidence of PSD and improve the prognosis of stroke patients.(126)

Escitalopram has shown the greatest reduction in depressive symptoms for individuals with traumatic brain injury (TBI), with sertraline also proving effective. Both of these antidepressants have minimal impact on seizure threshold. Stimulants like methylphenidate have been found to be more effective than antidepressants and psychological interventions in reducing depression severity. Non-pharmacological treatments such as psychotherapy and newer approaches like repetitive transcranial magnetic stimulation (rTMS) have also demonstrated effectiveness in managing depression after TBI. While the prevention of depression following TBI lacks strong evidence, existing literature suggests that prophylactic sertraline may be beneficial(127).

Neurogenic Bladder

The prevalence of urinary incontinence is 38-60% in stroke survivors in the acute phase. It is correlated with the size of the infarct or haemorrhage, the site of the lesion, the presence of cognitive impairment, aphasia, the morbidity & mortality, and the discharge destination of the patient(128)

Flisser *et al*. (129)divided patients with urinary complaints following stroke into four clinical categories:(Table 14)

Approximately 81% of SCI patients have some degree of impaired bladder function 1 year after injury. Patients with SCI, during the stage of spinal shock, often have urinary retention. They develop typical pattern of Overactive Detrusor with or without sphincter dyssynergia over time as spinal reflexes return. Detrusor over activity (DO) is the most common cause for urinary incontinence following neurological disease. Management depends upon the dysfunction of the individual(130).

Spinal cord lesions often cause neurogenic bladder dysfunction and interfere with activities of daily living, travel, sleep and personal relationship of the patients. The recovery of detrusor function and its control are of major importance to patients with myelopathy, family members, and health care providers. Depending on the level and severity of the injury, individuals use techniques like self intermittent catheterization, indwelling catheters, or suprapubic catheters to manage bladder function. Medications to relax the bladder or stimulate emptying are also added so as to achieve a timely regular complete voiding without any leaks.(131)

The treatment methods (Table 15) of the neurogenic bladder dysfunction include pharmacotherapy, training of the pelvic floor muscles, retention type catheter, sacral root electrical stimulation, selective sacral root rhizotomy, pudendal nerve stimulation, section of the external urethral sphincter and insertion of the artificial urethral sphincter, depending upon the type of bladder according to urodynamic evaluation. The goal is to maintain a low pressure, normal compliance of the bladder, eliminate the threat to the renal function and improve the quality of life.(132)

Neurogenic Bowel

Almost all people with spinal cord injury suffer from neurogenic bowel dysfunction (NBD), with a considerable impact on quality of life. Also Bowel dysfunctions increases significantly after stroke(133). Individual bowel management must be developed on the basis of an adequate diagnosis and considering the different lesion types. Due to the multifactorial influenceability of the intestine and the individual neurological deficit, various and complex bowel management programmes are the basis of the treatment of neurogenic bowel dysfunction. Often, more than one procedure is required to develop an effective bowel routine. A balanced, fairly high-fibre diet and sufficient fluid intake are important components of bowel management. In addition, rectal emptying techniques and emptying aids as well as physical measures constitute the conservative part of bowel management. Digital stimulation is the most commonly used method for upper motor neuron type of bowel dysfunction and digital evacuation is most commonly practiced in lower motor neuron type of bowel dysfunction following SCIs. Rectal or oral laxatives are often used to support these conservative approaches.

Surgical interventions such as sacral neuromodulation, deafferentations with anterior root stimulation, Malone stoma and colostomy are the final therapeutic options if conservative treatment is not sufficiently effective(134).

Quality of Life

TBI and stroke are the leading cause of long-term impairments and disabilities in functional, physical, emotional, cognitive, and social domains. There is high prevalence of psychological problems, including anxiety and depression. The social domain of QoL adversely affects functional abilities. Therefore, quality of life must be assessed so as to effectively intervene.

Table 14: Classification of neurogenic bladder

???	???
Type 1	No evidence of involuntary detrusor contractions on videourodynamics
Type 2	Involuntary detrusor contractions present, patient is aware of these contractions and able to abort them
Type 3	Involuntary detrusor contractions present, patient aware of the contractions and able to contract the sphincter but not abort the contractions
Type 4	Involuntary detrusor contractions present, patient unaware of the contractions and unable to contract the sphincter or abort the contractions

Table 15: Treatment in bladder dysfunction

	Storage Dysfunction		Voiding Dysfunction
	Urgency Frequency or incontinence	Stress Incontinence	
Conservative	Behavioural therapy Antimuscarinic agents Desmopressin OnabotulinumtoxinA into the detrusor Beta-3-receptor agonists Tibial neuromodulation	Pelvic floor muscle exercises Tricyclic anti-depressants with anti-cholinergic effects	Intermittent catheterization Indwelling catheterization Triggered voiding Alpha-blockers OnabotulinumtoxinA into the external sphincter
Surgical	Sacral neuromodulation Bladder augmentation Sacral deafferentation/ anterior root stimulation	Bulking agents Autologous/synthetic slings Balloons Artificial sphincter	Sacral neuromodulation Intraurethral stents External sphincter/bladder neck incision Transurethral resection of prostate

Health related quality of life (HRQL) reflects an individual's perception of how an illness and its treatment affect the physical, mental, and social aspects of his or her life. These three domains (physical, mental, and social functioning) are, however, regularly assessed without evaluating the consequences of impairment on a patient's life, so without a patient's evaluation of his functioning. Patients with neurological disorders requiring inpatient rehabilitation have impaired QoL that affects all domains of life. (135).

HRQL is usually assessed by questionnaires that will be filled out by the patient. Hence, more recently, these questions are referred to as patient-reported outcome measures (PROMs). HRQL instruments can be generic or disease-specific. Generic instruments do not take a particular condition into account and therefore allow comparisons with healthy individuals along with comparisons across various disease states. Disease-specific instruments take into account a patient's specific health condition and therefore may be more sensitive to the consequences of the condition and more relevant to patients. These instruments do allow comparisons with healthy individuals but not with patients with other diseases. A disease-specific HRQL measure for TBI, the Quality of Life after Brain Injury instrument (QOLIBRI) has been recently developed(136).

Therefore, quality of life following a stroke, SCI or TBI is a multifaceted experience that is influenced by a range of factors including physical recovery, psychological well-being, social support, and access to rehabilitation services. The caregiver and community support systems play a crucial role in enhancing outcomes. In a rehabilitation point of view, the visible and the invisible ailments must be addressed so that the patient can gain the utmost level of functional independence according to the injury.

Counselling, prognosticating and educating the family members

As rehabilitation care in general and neurorehabilitation in specific is not widely available especially in rural and semi urban settings, it is the role of treating doctor to educate the patient's family about the disease, its natural history, course, prognosis and the role of rehabilitation. Some patients will emerge towards consciousness but can still be left with significant cognitive and physical limitations. Spinal cord injury patients will have varied levels of dependence according to their neurological level of injury(NLI). The time for potential recovery and the level of recovery is difficult to predict on a case-to-case basis. Changes in neurological status is possible due to recovery from secondary effects like brain swelling, neuroplasticity leading to nearby functional brain areas taking up the lost function or by reorganisation of brain functions.

Dramatic improvements in consciousness are seen in some patients so an overly pessimistic prediction could result in premature withdrawal of life-sustaining therapies, leading to death in patients who might have reached acceptable outcomes if given sufficient time to recover(137). Avoiding misinterpretation of neuroimaging data and recognizing reversible changes are essential for accurate prognostication of patients with DOC. Several studies suggest that the cause of the injury, the age of the person at the time of injury, and how long the person has had a DOC may predict recovery. Traumatic aetiology and younger age are considered to have a better outcome with rehabilitation(138). Incomplete spinal cord injuries, lower levels of NLI, younger age are positive predictors of a better functional recovery(139). Family should be aware of the positive signs of recovery as well as red flag signs that require immediate medical attention. Common red flags are desaturation and persistent change in neurological status. The functioning of urinary catheter, nasogastric tube and tracheostomy tube as well as its hygienic maintenance and timely changes should be discussed before discharge to home care. Wherever feasible, professional family support should be provided via counsellor or peer support groups. Families need a realistic understanding of what to expect, including the best- and worst-case scenarios, recovery timelines, and possible complications. Accurate prognostication helps families set realistic expectations and plan for the future, whether it involves long-term care, adjustments to living arrangements, or financial planning.

Conclusion

Recent years have shown remarkable advancements in neurorehabilitation in patients with TBI, SCI and stroke, with advanced technologies contributing significantly to functional improvement and enhanced quality of life. These innovations, combined with traditional

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rehabilitation approaches and pharmacotherapy, can facilitate functional recovery and adaptability in patients. However, accessibility and affordability remain major concerns for many of these new technologies especially in a developing country like India with resource limitations. Therefore, further research and development are needed to provide conclusive evidence and ensure universal coverage and acceptance of these novel advancements.

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