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Advances in rehabilitation medicine

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ABSTRACT Rehabilitation medicine is the medical specialty that integrates rehabilitation as its core therapeutic modality in disability management. More than a billion people worldwide are disabled, and the World Health Organization has developed the International Classification of Functioning, Disability and Health as a framework through which disability is addressed. Herein, we explore paradigm shifts in neurorehabilitation, with a focus on restoration, and provide overviews on developments in neuropharmacology, rehabilitation robotics, virtual reality, constraint-induced therapy and brain stimulation. We also discuss important issues in rehabilitation systems of care, including integrated care pathways, very early rehabilitation, early supported discharge and telerehabilitation. Finally, we highlight major new fields of rehabilitation such as spasticity management, frailty and geriatric rehabilitation, intensive care and cancer rehabilitation.

Keywords: advances, disability, functional outcomes, rehabilitation

INTRODUCTION

The World Health Organization (WHO) has recently published the World Report on Disability.[1] It reports the staggering burden of global disability, with an estimated one billion people or 15% of the world's population experiencing mental or physical disabilities.[1,2] Furthermore, 190 million people worldwide have a severe disabling illness that has a considerable impact on survival, daily function, employment and quality of life.[2] Rehabilitation is a key component in disability management. It is defined as strategies that enable patients with health conditions to improve, optimise and maintain practical function in their interactions with the environment.[3] Rehabilitation medicine is the medical specialty that integrates rehabilitation as its core therapeutic modality.[1,3] Rehabilitation improves outcomes across a wide variety of diseases,[4] including stroke, traumatic brain injury, spinal cord injuries, arthritis, amputations and cancer.

There has been an exponential increase in rehabilitation research over the past two to three decades.[5-7] It is clear that the content and quality of rehabilitation is as important as the quantity delivered.[3] However, significant challenges in advocating and translating rehabilitation research remain. These include: (a) the lack of consensus on the components of human functioning and the definitions of what constitutes rehabilitation, (b) its overlap with many other disciplines, and (c) the sheer breadth of diseases and complications that rehabilitation medicine manages.[3,6,8]

A major milestone in the progress of navigating the heterogeneity of rehabilitation medicine and research is the recent development and endorsement of the WHO International Classification of Functioning, Disability and Health (ICF) for use in member states as the international standard to describe and measure health and disability.[9] ICF is an integrative biopsychosocial framework that addresses human functioning and disability (Fig 1). It describes the dynamic interaction between a health condition and its impact on body structures and function, as well as activity limitation and participation restrictions due to the health condition, which collectively comprises disability. Importantly, it incorporates personal and environmental contextual factors that intertwine with and affect the disability burden.[3,9]

Besides providing the conceptual basis for the definition, measurement and policy formulations for health and disability, ICF also provides a bird's-eye view of the field of rehabilitation medicine, as well as the advances and future challenges in this specialty. It also presents a workable framework, which we use to discuss the major contemporary research in this field. Due to the enormous breadth of the field, we focus on three themes that have come to the fore internationally, which have particular local relevance:

1. The changing paradigm of neurorehabilitation from compensatory strategies to restoration and recovery;
2. Systems of care in rehabilitation and integration across the rehabilitation continuum;
3. The rapid development of major new fields of rehabilitation concomitantly, with traditional emphasis on neurological and musculoskeletal rehabilitation.

CHANGING PARADIGM OF NEUROREHABILITATION

Prevailing traditional thinking in neurorehabilitation considers the brain and central nervous system (CNS) to be hardwired, nonadaptable and incapable of repairing itself once damaged.[10] In rehabilitation, the training of compensatory techniques tended to predominate after a CNS injury. For example, the loss of strength in one arm would involve training the unaffected arm in

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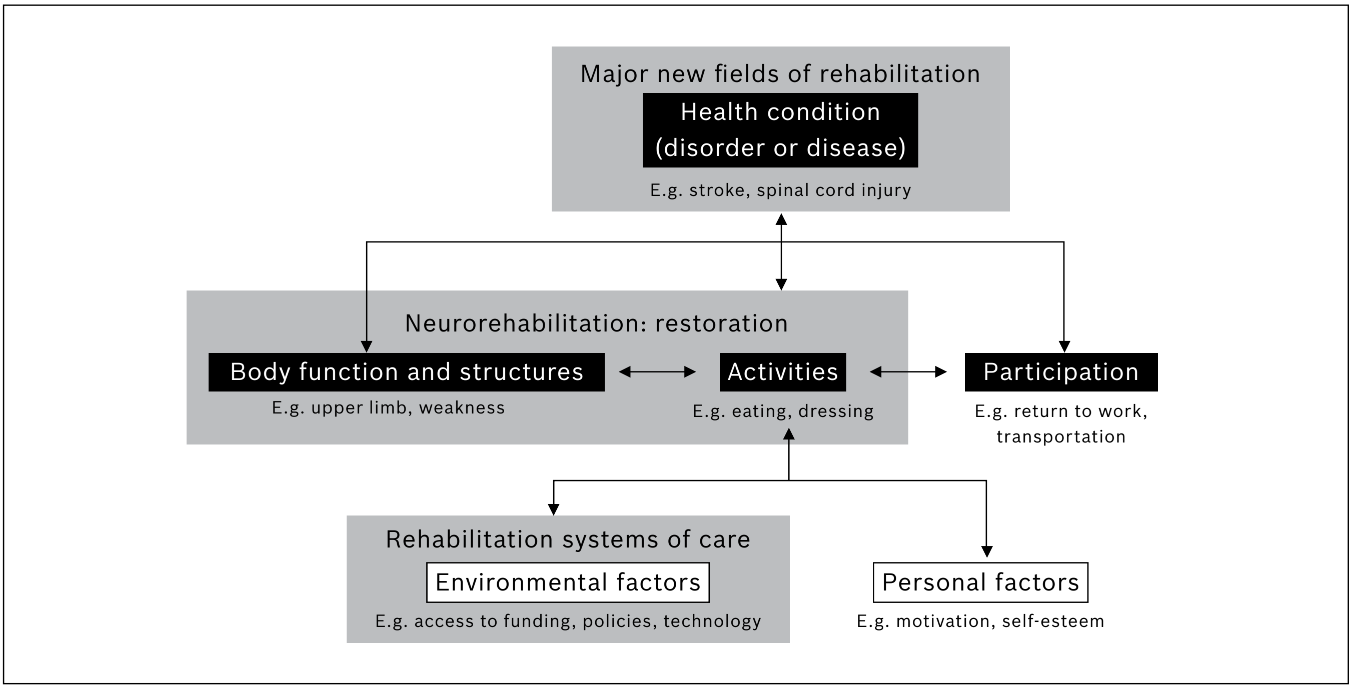

Fig. 1 Schematic diagram shows the International Classification of Functioning, Disability and Health,[1] which is a roadmap for advances and research in rehabilitation medicine. New emphasis is given to environmental and personal factors. Grey boxes represent major sections of discussion in this review.

activities of daily living. Similarly, weakness or ataxia in the lower limbs would necessitate the use of walking aids.[11] This view has existed since 1913, when Santiago Ramón y Cajal, the founder of modern neurobiology, coined the term 'neuron doctrine', which first described the neuron as the discrete, structural and functional unit of the nervous system. He considered nerve regeneration likely, but was pessimistic about the potential for adaptive plasticity in the CNS.[12]

The seeds of a conceptual change were planted by Donald Hebb in the late 1940s with Hebb's rule.[13] Hebb's rule describes a basic mechanism for synaptic plasticity, in which an increase in synaptic strength and efficacy results from the repeated and persistent stimulation of the postsynaptic cell. The phrase 'cells that fire together, wire together' was coined to describe this phenomenon. Learning with this model is now known as associative or Hebbian learning.[14] Further evidence that the brain can adapt and relearn after damage came from a series of landmark studies on primates by Nudo et al in 1996.[15] Repetitive retraining of the hand after an experimentally induced stroke resulted in the prevention of the loss of cortical representation of the hand territory, and even expansion of the hand territory into other regions previously occupied by elbow and shoulder representations.[14,15] These studies, together with advances in neuroimaging, provide evidence for what we know as neuroplasticity. Neuroplasticity is the structural and functional adaption of the nervous system to a change in environment, with a consequent change in behaviour.[14,16] There is now significant evidence that the brain is plastic post injury, and this potential to adapt forms the basis of contemporary neurorehabilitation.[5,10,14,16] The challenge in rehabilitation is to optimise conditions and prescribe rehabilitation that facilitates neuroplasticity and promotes restoration and recovery.

The ICF model as a framework provides clarity to discuss recovery and compensation.[1,5,17] At the health condition level, recovery is the restoration of lost function in damaged neural tissue, for example, post-diaschisis (brain shock) or activation of the penumbra.[18] Compensation occurs when alternate neural tissue acquires a new function after damage. Recovery at the body structure and functional level would then be the restoration of the ability to perform movements in the same manner prior to injury and the reappearance of premorbid movement patterns. Compensation at this level involves the performance of an old movement in a new way with altered strength or timing, such as muscle co-contraction and abnormal synergies post-brain injury. Finally, recovery at the activity level constitutes task completion with limbs or effectors as that in nondisabled individuals, whereby compensation indicates that task accomplishment is performed with alternate limbs or effectors.[5,11]

The most significant reason as to why recovery should be the aim is that patients tend to prioritise restoration over substitution and compensation. Using the increasingly popular goal-attainment scale as an outcome measure, studies indicate that patients' personal goals are usually to improve function in the affected limbs rather than compensating with their normal limbs.[19] Other reasons include premature limitation of functional gains, if compensatory techniques are instituted too early, and long-term complications, including pain, reduced joint motion and abnormal synergies.[5,17,20]

How then shall we optimise the brain's capacity for plasticity post injury for restoration and recovery? Broadly speaking, the myriad of rehabilitation interventions are categorised into two nonexclusive arms in the neuroplasticity paradigm (Fig. 2). The first arm comprises therapies based on the principles of motor

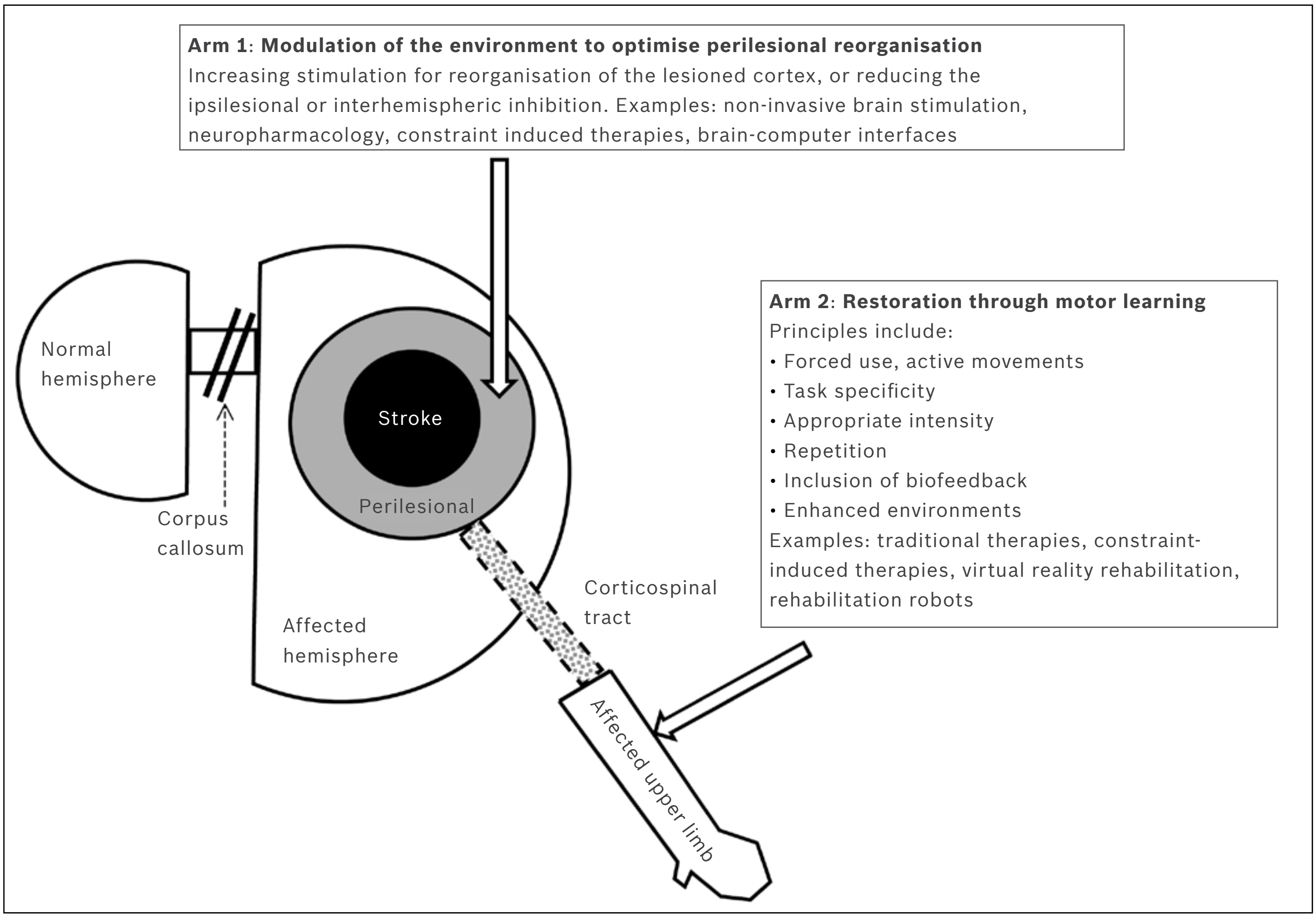

Fig. 2 Schematic diagram shows the two arms used to aid the understanding of the various interventions in neurorehabilitation. These arms are nonexclusive and various modalities of both arms are combined for synergistic effects on recovery.

learning in the promotion of recovery.[17] These principles include the forced-use paradigm, the need for active, repetitive, task-specific and functional movements, and the incorporation of biofeedback in training.[14,17,21] The second arm consists of interventions that neuromodulate the CNS to allow a more conducive and compliant environment for neuroplasticity to occur.[22] In this still-evolving field, these concepts are often termed 'regenerative neurology', or more accurately, 'restorative neurology' or 'neurorehabilitation'.[22] Major therapeutic modalities are described below.

Constraint-induced therapy

Constraint-induced therapy (CIT) arose from the work done on primates by Nudo et al,[15] which was described earlier, and further developed in humans by Corbetta et al[23] and Reiss et al.[24] As its core, CIT applies the forced-use paradigm in guiding CNS plasticity, popularly known as the 'use it or lose it' principle. There are two components in CIT. The first is the forced use of the affected arm by restraining the unaffected arm with either a sling or a mitten.[25] The second component is systematic massed practice of the affected arm through shaping – a therapy technique where the objective is progressively reached in small steps of increasing complexity and difficulty.[23-25]

Various protocols exist and most major trials involve stroke patients with impaired upper limb forearm and hand function. Well-designed randomised trials generally indicate a course with an active exercise component of two hours per day, five days a week, for three weeks. Restraints are applied for 90% of the waking hours.[25] Overall, meta-analyses report that arm motor impairment outcomes (body structure and functional level on the ICF) show moderate improvements compared to that of controls, although this only translated into minimal improvements in actual function (activity level on the ICF).[25] Critics further point out the narrow inclusion criteria – stroke patients need at least some wrist and finger extension for inclusion and significant patient frustration during long periods of restraint. However, it remains an important modality in neurorehabilitation, as improvements have been demonstrated years after a brain injury, with reasonable outcomes in combination with other forms of therapy. The forced-use paradigm has since been utilised in other areas of neurorehabilitation, such as aphasia treatment with constraint-induced speech therapy, with promising results.[26]

Rehabilitation robotics

The rise of rehabilitation robotics parallels the rapid advances in technology, computers and engineering.[10] Rehabilitation robotics further develops the forced-use principles by providing repetitive therapy to impairments, which reinforces associative learning. A major drive for development in this direction is the scarce availability of skilled labour to perform these repetitions that robots can perform.[7,10,21] Practical considerations, such as the need for body weight support during locomotor training in patients with significant spinal cord injuries, were also major drivers.[10,27] A significant advancement in this field is the ability of newer robotic devices to provide individualised programmes tailored to an objective amount of assistance required. This emphasises the active component of motor learning, whereby too much guidance results in diminished motor learning (guidance hypothesis) and reduces the burden on the learner to discover solutions.[7]

Since the development of the MIT-Manus arm robot two decades ago, there has been an exponential increase in rehabilitation robotic literature, especially with common robots such as the Lokomat® and Hybrid Assistive Limb® robots.[7,27,28] The categorisation and discussion of robot types is beyond the scope of this review, but it is suffice to say that this includes classification through body part (e.g. upper versus lower limbs) or joints controlled, exoskeletal versus end effector, treadmill- or overground-based, and type of assistance provided (e.g. force or directional assistance).[7,10]

Many individual trials report the efficacy of rehabilitation robotics, but the heterogeneity of robots and training protocols, as well as the variety of outcome measures at several ICF levels make comparison extremely difficult.[29,30] Although a number of well-designed trials have training protocols with hourly sessions five times per week for a duration of six weeks, there are large variations among these studies.[29] Reviews on upper limb robots reported that electromechanical training moderately improved upper arm function and the ability to perform activities of daily living, but the effects on arm impairments, including decreased strength, are unclear.[29,30] For lower limb robots, mobility reviews on their efficacy are even less convincing, with trials indicating that robot-assisted locomotor training is no more effective than standard physical therapy in improving functional gait.[10,31]

Although the efficacy of robotics compared to standard therapy is similar, a major discussion point is whether robotic therapy is cost-effective for manpower saving despite the high capital costs of robotic devices.[10] Economic analyses suggest that robotic interventions are still cost-effective in the long run, and electromechanical devices remain a very promising alternative in clinical rehabilitation as further research is developed.[32]

Virtual reality rehabilitation

Virtual reality (VR) rehabilitation is another newer modality currently employed in many rehabilitation centres worldwide.[33] This modality was simultaneously developed with the computer gaming industry, and its adoption in rehabilitation increased quickly with the decreasing costs and increased sophistication of newer consoles such as the Nintendo Wii™ and Microsoft Kinect™ platforms.[34,35] Proponents argue that it leverages the motor learning principles with its capacity to easily produce high-intensity, active, repetitive and task-orientated exercises.[34,35] VR rehabilitation can also deliver personalised gradated programmes and customisable biofeedback in a safe, enjoyable and motivating environment.[21,34] Rehabilitation with VR is often categorised as commercial off-the-shelf or customised, with various degrees of immersion or augmentation.[34,35] Immersive VR isolates the patient from the physical surroundings when interacting with the virtual environment, using equipment (e.g. head-mounted displays) or engagement in specially designed rooms. Some reports indicate that immersive VR is more effective than non-immersive systems, as patients are better able to focus due to less distractions.[36,37] Augmented VR, however, integrates virtual computer-generated images in real-world scenes for rehabilitation.

In various trials, a large variety of tasks were trained using VR. These include visuospatial skills, upper limb activities, driving and gait. Most protocols have sessions that average an hour, over a duration of four to six weeks. Like CIT and robotic therapy, statements of efficacy are clouded by a diverse range of outcomes. At the ICF body structure and functional level, arm movement, speed, range of motion, force and normalisation of abnormal patterns improved by about a ten percentage point more than controls that had traditional therapy alone. Activity outcomes focusing mainly on functional arm tests show moderately significant improvements compared to controls.[33,35,36] There is scarce literature published on long-term outcomes, direct comparisons between commercial and customised modules, immersive versus non-immersive VR, and augmented versus fully virtual systems.

A major development in the VR rehabilitation arena is the incorporation of various sensors and feedback devices into training programmes, apart from the usual optical and inertial measurement units that consist of accelerometers and gyroscopes. These include haptic feedback devices such as virtual gloves and electromagnetic sensors that can detect slight movements in finger joints, as well as neurophysiologic sensors that can detect electromyography and electroencephalography signals.[21,37] These devices confer diagnostic capabilities on VR rehabilitation systems, such that they are more than just a therapeutic modality. Another major advancement is its potential for testing and developing alterable algorithms in optimising training. For example, errors can be magnified as patients improve, making it more difficult for target attainment in progressively difficult tasks. These error amplification techniques may increase the speed of motor adaption and eventual motor learning toward the recovery of impairments.[7,38]

Noninvasive brain stimulation

Noninvasive brain stimulation (NIBS) techniques are being investigated for their ability to modulate and augment motor training-induced neuroplastic changes. The types of NIBS most commonly studied in neurorehabilitation are transcranial direct current stimulation (tDCS) and repetitive transcranial magnetic stimulation (rTMS). In tDCS, changes in neuronal firing are induced using low amplitude direct currents that are applied on the scalp. This changes the membrane resting thresholds and modifies spontaneous activity according to the direction of current.[39,40] Cathodal tDCS decreases cortical excitability whereas anodal tDCS increases it.[40,41] The after-effects of changes in excitability persist after tDCS is stopped, lasting from minutes to hours, depending on the duration and strength of the polarisation.[41] Consecutive sessions of stimulation induce behavioural effects that last for weeks.[42]

Similarly, rTMS has been shown to modulate brain cortex activity noninvasively such that low frequency rTMS (1 Hz) decreases the excitability of targeted cortical regions, resulting in measurable behavioural changes, while high frequency rTMS (20 Hz) has the opposite effect.[43] These effects are associated with long-term potentiation (LTP) and long-term depression (LTD), which are underlying mechanisms of synaptic plasticity.[44] Cathodal tDCS or low-frequency rTMS applied to the unaffected M1 motor cortex, or anodal tDCS or high-frequency rTMS applied to the affected M1 motor cortex, enhances motor learning in the stroke-affected arm and improves functional outcomes.[42,43,45]

With regard to stroke, the body of evidence in support of NIBS, which has focused on upper extremity motor recovery, is growing.[42,43,46] Applications to lower extremity motor recovery[47,48] and visuospatial deficits[49] have also been explored. Noninvasive brain stimulation has been employed in Parkinson's disease to improve gait parameters.[50,51] Further work is required to establish the efficacy of NIBS and define the optimum stimulation protocol and timing of stimulation in relation to other therapeutic interventions.

Neuromodulation with pharmacology

Amphetamines and methylphenidate

Prescribed in many clinical populations, amphetamines, methyphenidate and other related compounds are groups of neurostimulants, of which dextroamphetamine, methylphenidate and their derivates are widely used in cases of stroke and traumatic brain injury.[52-54]

Methylphenidate has structural similarities to cocaine, and it improves cognition, including attention and processing speed, in patients with traumatic brain injury.[53,55] It directly stimulates the release of dopamine and norepinephrine, and blocks catecholamine reuptake.[56] It acts through alpha-2 adrenoceptor and dopamine D1 receptors, and improves prefrontal cortical cognitive function.[57] Limited stroke trials have found that methylphenidate combined with physiotherapy may improve stroke severity and the ability to perform activities of daily living.[58,59] Methylphenidate is generally safe and well tolerated in appropriately selected patients despite anecdotal reports of seizures.[55,60] Despite the present lack of dosage guidelines on the use of methylphenidate in brain injury, methylphenidate remains a promising drug to enhance neuromodulation in cases of stroke and brain injury, particularly as its short half-life allows relatively immediate effects to be observed in appropriate patients.

Dopamine

Dopamine is a catecholamine neurotransmitter involved in many CNS pathways. The main dopaminergic structures are in the striatum of the forebrain and the motor cortex.[61,62] Dopamine plays a significant role in motor skill learning and synaptic plasticity, facilitating memory formation, reward-seeking behaviour and arousal.[63] Dopamine is partially metabolised to noradrenaline, which enhances functional motor recovery. Administration of dopamine is preferred to noradrenaline or amphetamines as the latter drugs result in putative dangerous cardiovascular side effects and seizures, coupled with a risk of dependence.[64]

Dopamine is available as the precursor drug, levodopa, and is administered with a peripheral decarboxylase inhibitor to boost absorption levels across the blood-brain barrier. In several trials, levodopa improved recovery from motor disability and general stroke impairments, as well as function two to six months after stroke.[52,64] Levodopa is generally considered safe for use. Common side effects are minor and include postural hypotension, nausea and vomiting.[64]

Acetylcholine and anticholinesterase inhibitors

Acetylcholine is a neurotransmitter found in virtually all brain structures. It is produced in the Meynert's nucleus, tegmental pontine reticular nucleus, cortex, hippocampus, amygdala, hypothalamus, cingulate gyrus and thalamus. Acetylcholine has effects on experience-induced cortical plasticity and facilitates long-term potentiation.[65] Donezepil is a reversible acetylcholinesterase inhibitor prescribed mainly for Alzheimer's disease. Limited studies report a positive effect on motor recovery and sensorimotor function in stroke patients.[66] A recent phase IIa trial of donepezil in conjunction with acute thrombolysis concluded that early administration of donepezil (within 90 days) produces favourable outcomes on impairment, in both the cognitive and physical domains.[67] In traumatic brain injury, improvements in the general measures of cognition (e.g. the Mini-Mental State Examination) and selective measures of attention and memory have been reported with the use of donepezil, rivastigmine and galantamine.[68] Mild side effects include insomnia, depression, nausea, loss of appetite and muscle cramps.[67,68]

Serotonin and selective serotonin reuptake inhibitors

Serotonin is a monoamine neurotransmitter mainly produced in the raphe nuclei of the brainstem and reticular formation. Serotonin is thought to regulate human emotions, memory and learning, while selective serotonin reuptake inhibitors (SSRIs) can modulate cerebral motor activity.[69,70] Serotonin and SSRIs modulate the CNS through regulation and induction of synaptic

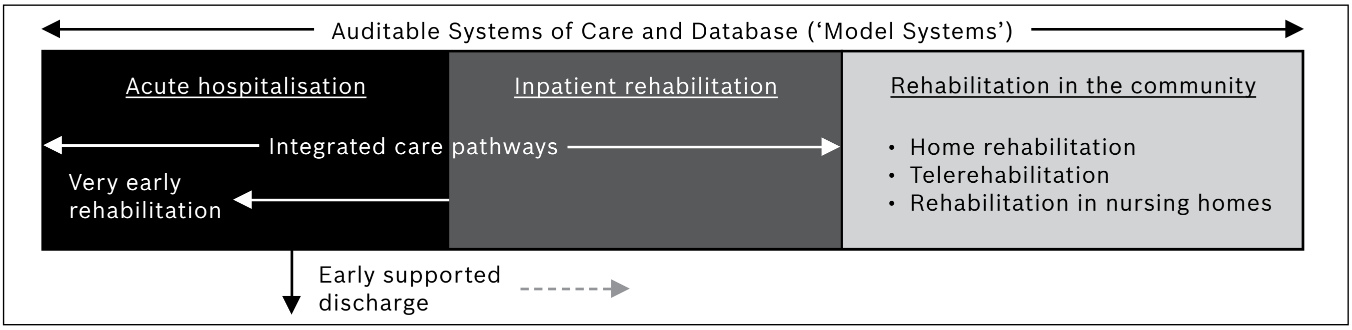

Fig. 3 Schematic diagram shows systems of care in rehabilitation and integration across the rehabilitation continuum. Recent research and initiatives in improving rehabilitation efficiency address contextual environmental factors in the International Classification of Functioning, Disability and Health.

activity, and may result in long-term potentiation of sensorimotor synapses.[70-72] Serotonin also increases neurogenesis and expression of neurotropic growth factors, and has a neuroprotective effect, as it reduces inflammation and enhances specific protein expression.[69] SSRIs can upregulate β-adrenergic receptors and potentiate the effects of the adrenergic system.[69,71]

Several trials have reported that SSRIs improve motor recovery independent of their effects on depression. Fluoxetine and citalopram improved upper limb impairment and function, general functional outcomes and gait scores when given at anti-depressant doses over a duration of three to four months in the immediate post-stroke period.[71-73] A decrease in the motor excitability of the unaffected hemisphere with resultant reduction in transcortical inhibition of neuroplasticity of the affected hemisphere is a postulated mechanism.[52]

Combination of modalities

The combination of modalities in both arms is intuitive, synergistic and a relatively new field for exploratory research. Examples of combinations include noninvasive brain stimulation with robotic training or constraint-induced therapy and pharmacologic treatments with traditional occupational therapy or VR rehabilitation.[74] Biofeedback elements should be incorporated into clinical trials. In addition, close collaboration with non-medical counterparts such as engineering, computer science, design and innovation centers is critical for advancements in these fields.

SYSTEMS OF CARE AND INTEGRATION

The development of effective systems of care and the streamlining of delivery of rehabilitation services are equally vital to effective rehabilitation. They are also important for the optimisation of scarce skilled rehabilitation resources. Research advances in rehabilitation medicine are futile if they cannot be translated into clinical practice. Newer concepts in rehabilitation systems promise important solutions to address needs. Fig. 3 illustrates some of these areas of rehabilitation health-services research.

Integrated care pathways

Clinical practice guidelines (CPG) are published for common disabling conditions, including stroke, hip fractures, joint arthroplasties and amputations.[75,76] Integrated care pathways (ICPs), variously termed clinical pathways, critical pathways or care maps, are often derived from CPGs and increasingly employed in routine clinical care. A key driver is the need to improve efficacy by streamlining services, as there is an increasing number of patients in need. Common to ICPs are inventories of structured steps and algorithms for progression, emphasis on documentation and incorporation of outcomes for quality improvement.[77,78]

ICPs incorporating rehabilitation components have several common features.[76,79] These include structured multidisciplinary care (based on the best available evidence with incorporation of education as a key component), specific rehabilitation outcomes, and a focus on caregiving and discharge planning through the rehabilitation continuum.[76,77,79] In general, ICPs do not reduce mortality rates or influence discharge destination.[77,78] However, most studies, especially in musculoskeletal conditions, demonstrate significant reduction in acute and rehabilitation lengths of stay and readmission rates.[75,80] A decrease in inhospital costs and charges is reported together with improvement in quality of life.[78,80] There is also a reduction in complications such as nosocomial urinary tract infections in stroke patients, as well as improved record documentation.[77,78]

It is disappointing that given the large body of evidence-based guidelines and CPGs in rehabilitation, there is scarce literature on the integration of more rehabilitation-specific practices in existing ICPs. Most ICPs delineate only generic instructions such as early referral for physiotherapy or occupational therapy, and appropriate screening by case managers. Such pathways should include the specification of weight-bearing and osteoporosis investigation plans post hip fracture, as well as the evaluation of caregiver burdens, bowel programmes and autonomic dysfunction in spinal cord injuries.[75,76]

Therefore, data from ICPs should be audited for processes and outcomes. Various national databanks incorporating rehabilitation parameters exist; these include the Spinal Cord Injury and Traumatic Brain Injury Model Systems in the United States and the Australasian Rehabilitation Outcomes Centre based in Australia.[81,82] They serve as powerful resources for maintaining efficiency and standards, rehabilitation resource planning and advocacy for the disabled.[77,78,81,82]

Very early rehabilitation

Very early rehabilitation (VER) breaks the existing paradigm of rehabilitation as the third phase of medicine after medical and surgical stability, and dispels the notion of rehabilitation as a step-down service.[83,84] A recent trend in rehabilitation medicine demonstrates the benefits of VER in an increasingly large number of neurological, musculoskeletal and cardiopulmonary diseases.[2] The hallmark of VER is the integration of comprehensive rehabilitation interventions, traditionally found only in dedicated rehabilitation programmes, into the acute management of conditions.[85,86] Some examples include inpatient rehabilitation exercise programmes for patients with acute exacerbations of chronic obstructive pulmonary disease (COPD) and early physical training for patients post spinal and cardiac surgery.[87-89]

Several reasons have been put forth to justify the adoption of VER. First, VER improves final function and earlier autonomy.[90] In neurorehabilitation, the brain is more plastic in the initial period after injury,[91] and genes responsible for synaptogenesis and neuroregeneration are increasingly expressed at a greater rate for a critical period after stroke. This has been shown in animal experiments where increased dendritic branching in the cortex is observed when rehabilitation is initiated earlier in the post-brain injury period, as opposed to later.[91,92] Second, VER can prevent the deleterious consequences of prolonged bed rest and its associated complications, including nosocomial infections, decubitus ulcers, venous thromboembolism and muscle fatigue.[90,92] Finally, VER allows for an early window of opportunity for rehabilitative interventions, when patients are more receptive to changing their health behaviour, hence enabling the modification of patients' risk factors. For example, it has been found that smoking cessation, and improvement of nutrition and quality of life interventions are more likely to be successful during comprehensive VER after an acute exacerbation of COPD.[93]

Also termed 'very early mobilisation' (VEM), VER is typically commenced within one to two weeks after the onset of illness. Trials have reported early mobilisation of stroke patients within 24 to 72 hours,[86,92] immediately after spinal surgery,[89] by the second day of hospitalisation for COPD exacerbation,[90] and within a week after cardiac surgery.[88] Although these programmes are not homogeneous, most incorporated early mobilisation as a consistent goal.[92] For instance, the AVERT (a very early rehabilitation trial) VEM trial for acute stroke stipulates that appropriate patients should sit out of bed at least twice a day within 24 hours after the onset of stroke.[86] Studies indicate that VER is generally safe at exercise intensities comparable to the levels of the chronic disabled populations.[90] However, patients should be stratified, such as according to the levels of cognitive deficits in neurologic disorders or cardiopulmonary fitness post myocardial infarction, with exercise intensity individualised according to illness severity in the relevant populations.[86,91,94]

Generally, studies indicate that VER results in faster recovery in the ability to perform activities of daily living and the return to walking in neurorehabilitation patients, as well as quicker rates of recovery from subsequent exacerbations in COPD patients.[87,92] Almost all studies report a shorter length of hospital stay.[86,89,93] Health-related quality of life and patient satisfaction also improved in cardiopulmonary and postsurgical patients, while inhospital complications were minimised and readmissions reduced after VER.[87,89] It has even been suggested that there is a reduction in mortality when VER is introduced in COPD patients.[87] However, there are exceptions; a study of high-dose constraint-induced movement therapy in patients with very acute stroke was associated with significantly poorer outcomes in the upper extremity, with excitotoxicity, lesion enlargement, overtraining, fatigue or decreased learning due to diminished rest time for consolidation being postulated as factors for the poor outcomes.[85]

As rehabilitation manpower resources are limited, a consequence of VER is the need for cross-training and transdisciplinary care in the acute ward setting. Physicians and nurses who are otherwise nonspecialised in rehabilitation are increasingly trained to conduct simpler rehabilitation assessments and follow through on basic therapy.[90] Prehabilitation is a related concept whereby rehabilitation is delivered prior to intervention or surgery to improve outcome post intervention.[89]

Early supported discharge

Early supported discharge (ESD) programmes provide coordinated, planned discharge from hospital with continued rehabilitation for patients in their homes. ESD programmes reduce long-term dependency and admission to institutional care, and substantially reduce the length of hospital stay, with no adverse impact on the mood and well-being of patients and their carers.[95] Stroke patients receiving ESD are more likely to be independent and living at home six months after stroke compared to those receiving conventional services. They are also more likely to be satisfied with the services rendered. ESD has been shown to be less costly than conventional care in some studies,[96,97] but this was not the case in other studies.[98] Nevertheless, the opportunity cost of freed hospital beds and the positive patient outcomes continue to make ESD attractive. Patients who benefit most from ESD are those with mild to moderate disabilities.[95] Programmes are typically multidisciplinary and overseen by a stroke physician. It is recommended that ESD teams be based in acute hospitals to facilitate cooperative and collaborative decision-making between ESD and acute services.[99] Indeed, the success of an ESD programme depends on the effective coordination and collaboration between the ESD and acute stroke teams.

Telerehabilitation

Telemedicine is the use of telecommunication technology for the exchange of medical information to improve patients' health.[100] Telerehabilitation, a subcomponent of telemedicine, provides remote support, assessment and intervention to disabled individuals in need of rehabilitation.[101,102] Telerehabilitation started developing only in the last decade with the reduction of technological costs, which was supported by funding for implementation research.[103,104] The minimal components required for a telerehabilitation service are computers with internet connection, preferably with wireless and high-speed broadband capability, a web camera and a microphone.[103] Add-on devices include various sensors and VR platforms.[105,106]

Many important factors drive advancements in this field. The first is improved access to specialised services and capacity for remote monitoring.[105,107] Skilled clinical manpower is often scarce and telerehabilitation has been employed for wheelchair prescription, musculoskeletal assessments and monitoring of pressure ulcers.[101,106,108] The provision of service stability with high staff turnover is an associated attraction.[105] A second factor is transportation difficulties affecting access to rehabilitation care.[100,105] It has been shown that less than one-third of patients continue to attend outpatient rehabilitation at three months post discharge.[109] Moreover, rural communities also experience transportation hazards during inclement seasons or weather, while urban residents often face traffic gridlocks and disabled-unfriendly surroundings.[106] Thirdly, telerehabilitation can also potentially overcome financial disincentives for less well-off families,[100] as funding and insurance costs for post-acute care is often limited and expensive. This modality promises lower costs by increasing the number of patients treated by a single rehabilitation unit at any one time.[103,110] The fourth driver of advancement in telerehabilitation is its ability to improve the delivery of rehabilitation education to remote clinicians and families, thus indirectly expanding the healthcare workforce.[105,110]

The most common telerehabilitation programmes are those for cardiac and neurological rehabilitation. The existing literature reports several telerehabilitation trials on post-stroke CIT and spinal cord injury populations.[102,103] Musculoskeletal conditions (e.g. degenerative arthritis) and rehabilitation post-joint replacement use this modality for assessments.[102,103] Telerehabilitation has also been used for movement patterns evaluation, visual gait analysis, preoperative home assessments, as well as orthotic prescription.[105,106] Most trials were successful, with significant improvements in clinical outcomes such as reduction of fatigue, better walking distances, improved upper limb function and amelioration of depressive symptoms.[100,102,104] High levels of satisfaction and comfort, as well as significant savings in travel time and costs were reported.[100,106]

However, many challenges remain. The first challenge is the establishment of clinician-patient rapport. As many patients prefer to receive in-person care, extra effort is required to establish this rapport through telerehabilitation.[105] End-user adoption is often difficult as it requires cultural and behavioural changes, which involve understanding and embracing technology.[110] There are also valid safety concerns, and thus the specialist clinician controlling assessments must defer decisions to the remote clinician or supervising attendant when safety becomes a concern.[101,105] In addition, network security protocols to protect patient data are still being refined.[100] Another major difficulty lies in the system and platform incompatibility across many providers, which has resulted in nonintegratable data and database conflicts.[101] Medicolegal issues associated with delivering care at remote places have also surfaced.[100] Finally, one needs to appreciate the limitations of telerehabilitation, which includes difficulties in detecting fine movements or tremors, as well as movements in certain planes such as ankle inversion and eversion.[105]

MAJOR NEW FIELDS OF REHABILITATION

Musculoskeletal, neurological and cardiopulmonary rehabilitation have formed the cornerstone of rehabilitation medicine over the past decades. Recently, post-transplant, intensive care and cancer rehabilitation are gaining prominence, with many programmes being developed in centres worldwide in order to meet the increasing demand for such services.[84] Subspecialties such as spasticity management and innovations to address the rehabilitation needs of the geriatric population have also recently come to the fore. In the following text, we address the salient points of some of these initiatives.

Spasticity syndrome

Spasticity is a common manifestation of upper motor neuron lesions. It is traditionally defined as resting hyperreflexia and hypertonia.[111,112] This definition, however, does not consider hypertonia that varies with posture and movement. It also excludes other clinically important phenomena, including spastic co-contraction of antagonist muscles, spasms and synkinetic movements. This has recently led to the broadening of the definition of spasticity as a consequence of disordered sensorimotor control.[113] Spasticity has rapidly transformed from a mere clinical sign to a comprehensive subspecialty with basic science research, new ways of assessment and a wide range of physical therapy, medical and surgical interventions.[113,114]

Spasticity causes pain, contractures, hygiene difficulties and impairments of function. For example, in patients with spinal cord injury or multiple sclerosis, excessive hip adductor spasticity impairs the ability to sit properly, increases the risk of skin breakdown and impedes perineal hygiene. The presence of hypertonia and hyperreflexia does not, however, equate to the need for treatment.[115,116] Instead, a directed focus on the impact of spasticity on function is necessary and dynamic assessment is required. For example, it is important to evaluate for synkinetic movements (e.g. excessive elbow flexion in stroke patients during gait) in both the standing and walking positions, as these are missed in the supine or sitting positions.

Multidisciplinary assessments are becoming a standard of care, and many comprehensive spasticity clinics and training fellowships have been established worldwide.[114,117]

The modified Ashworth and Tardieu scales are ordinal impairment scales that are widely used to measure spasticity, but they do not assess function. These scales should be complemented with other measures of function. One such measure that is gaining traction is the Goal Attainment Scale, which sets targets on the patient's own priorities from various interventions.[118]

The mainstay of spasticity management is physical therapy, which includes the judicious use of stretching, appropriate positioning and splints. Oral medications such as baclofen, tizandine and dantrolene sodium are prescribed for generalised spasticity. The advent of botulinum toxin has revolutionalised spasticity treatment, especially in patients with focal spasticity, and its use is strongly advocated in several national guidelines.[115,117] Botulinum toxin A inhibits the presynaptic release of acetylcholine and causes neuromuscular blockage that lasts 6 to 12 weeks, and possibly longer if given earlier post stroke.[119] Although it is generally safe, the downside is its high upfront cost; however, cost-effective studies have indicated long-term saving.

Intrathecal baclofen pump therapy offers relief for patients with severe and generalised spasticity, which responds poorly to the aforementioned measures, and it is now rapidly becoming the standard of care in appropriate patients.[116] These patients include those with spinal cord and traumatic brain injury. Baclofen is delivered intrathecally using a programmable pump implanted in the abdominal wall and is highly effective. Complications include infection and potential overdose with respiratory depression, but these complications are rare if compliance is exercised. Newer modalities, including the use of noninvasive brain stimulation and refinement of surgical techniques such as selective dorsal rhizotomies, are promising areas of research with direct clinical relevance.[119,120]

Frailty and geriatric rehabilitation

Frailty is a geriatric syndrome of increased vulnerability due to diminished physiologic reserves. With subsequent stressors, the frail elderly are highly susceptible to adverse health outcomes with risks of significant disability and death.[121,122] Frailty illustrates another paradigm shift in rehabilitation medicine, which addresses recovery through a holistic multisystem perspective rather than through the traditional approaches of a specific disease.[121]

This approach is important due to several reasons. Firstly, frailty is interconnected, but can occur independently of either comorbidity or disability.[123,124] For example, valuable resources may be exhausted when searching for causes of falls or generalised weakness where no single cause actually exists, as frailty reflects multisystem failure. Secondly, frailty is associated with an increased risk of readmission, nursing home admission, worse outcomes after surgery, postoperative complications, as well as higher risks of falls, dementia, general morbidity and mortality.[122,125,126] Thirdly, it is potentially reversible with specific interventions, rehabilitation and exercise.[125] Finally, frailty is an important consideration in the decision-making process for conditions, including interventions in cancer or even the triaging of patients for rehabilitation.[125]

Sarcopenia is a key feature of frailty and is defined as the age-related loss of muscle mass, strength, power, quality and function.[127] Age-related changes in the neurologic and endocrine systems, low-grade inflammation and loss of muscle homeostasis are thought to give rise to sarcopenia.[122,127] Clinically, frailty can be defined as three or more variables of a phenotype consisting of unintentional weight loss, self-reported exhaustion, low energy expenditure, slow gait speed and weak grip strength.[128] Frailty indices, which are cumulative deficit scores of multiple variables, including symptoms, signs, abnormal laboratory values, diseases and disabilities, are also used to define frailty.[123,129]

Previously, frailty was grimly associated with the desolation of irreversible ageing. However, this has changed and a number of trials on exercise have been conducted in the frail elderly. Resistance training, which has been best studied, is found to improve muscle strength with consequent better motor performance and gait speed.[124,125,130] Guidelines indicate that eight to ten exercises at least two to three times a week provide significant benefit.[124] The addition of an endurance programme consisting of moderate aerobic exercise such as jogging or swimming about two to three hours weekly improves maximal oxygen uptake and reduces fatigue.[125,130] Exercise in general also reduces chronic elevations in inflammatory mediators, lessens insulin resistance and stimulates muscle anabolic effects in the presence of amino acids.[122,125]

Nutritional interventions, including systematic nutritional assessments and supplementation with proteins such as leucine, address weight loss in frailty and may prevent falls.[121] Several pharmacologic agents for the treatment of frailty have been studied. These include the administration of testosterone or selective androgen receptor modulators to improve body composition and muscle strength in the hypogonadal elderly.[125] Myostatin inhibitors, ghrelin, angiotensin converting enzyme inhibitors and vitamin D supplementation may also have beneficial effects on enhancing musculoskeletal system functioning.[125]

Cancer rehabilitation

There is a mindset change with regard to the address of cancer patients as cancer survivors.[131] Advances in early detection, improvements in treatment regimens, better acute care and longer life expectancy have resulted in better survival rates of more than 50% over a five-year period for all cancers.[132] Previously considered acutely lethal, cancer is now a chronic disease with more survivors than the traditional rehabilitation fields of stroke, spinal cord injury and traumatic brain injury.[133]

Cancer survivorship is thus a distinct phase of cancer management with rehabilitation as a key component.[134]

There are a large number of short- and long-term effects of malignancy, or its treatment in the physical, cognitive and psychological domains.[132,135-137] Common physical issues include deconditioning, fatigue, lymphoedema, weakness, loss of joint range of motion, diminished function and mobility, pain, osteoporosis, and bladder and bowel dysfunction.[134] Frequent cognitive and psychosocial issues that need to be addressed are depression, anxiety, insomnia, low self-esteem, fear of recurrence and death, post-traumatic stress disorder and quality of life.[134,136,137]

Cancer-related fatigue deserves specific mention, as it occurs in 50% to 80% of patients and is highly distressing and disruptive.[133] It significantly affects activities of daily living and is strongly associated with health-related quality of life.[134,138] The management approach involves treating reversible causes such as anaemia, metabolic derangements and endocrine abnormalities, as well as correcting associated mood disorders, and emotional and sleep disturbances.[138,139] Psychosocial interventions, including cognitive behavioural therapy, support groups and nurse-led educational programmes are also useful. Recent research suggests that psychostimulants such as methylphenidate, modafinil and pemoline, antidepressants and even erythropoietin-stimulating agents may play a role in treating severe fatigue.[138,139]

The pivotal component of any good cancer rehabilitation programme is structured exercise.[134,135] Oncology patients have markedly impaired cardiorespiratory fitness due to surgery, radiation and the adverse effects of chemotherapy.[135] Strength and muscle mass are also significantly affected due to the paraneoplastic effects of cancer, immunosuppressants and deconditioning.[134,139] Programmes that incorporate an endurance training regimen of moderate intensity coupled with strength training at least three times a week improves a wide variety of outcomes.[133,135] These include fatigue, physical function and quality of life, with significant amelioration of the reduction of cardiorespiratory fitness during chemotherapy cycles.[135] Exercise reduces proinflammatory mediators (including cytokines), enhances immune function through macrophage and T-cell function, mediates hormonal regulation, and upregulates selective enzymes in carcinogen detoxification.[133] Moreover, exercise in cancer patients is safe and well tolerated.[135]

Several trials, including a local study, have reported significant improvements in overall function and symptoms among cancer patients who received rehabilitation, and the results are comparable to that of non-cancer cohorts, regardless of cancer stages and whether the tumours were solid or haematogenous.[136,140] In inpatient programmes, the length of rehabilitation stay for cancer patients is shorter than that for non-cancer populations, given the perceived shorter life expectancies and the compensatory rather than restorative approach in the cancer population.[136]

A persistent theme in the literature is the under-delivery and suboptimal results of cancer rehabilitation. Reasons for this recurring notion include the assumptions that exercise is too stressful and requires long-term commitment, and survival times are short and functional outcomes poor among cancer patients. Insufficient training of rehabilitation providers, poor awareness of the benefits of rehabilitation among oncologists and a lack of interaction to enable sharing of knowledge are some of the other reasons.[133,134] For example, few professionals are aware that localised pain in cancer is far more commonly due to usual musculoskeletal conditions such as degenerative joint disease than from metastases or cancer recurrence.[134,139] In such an instance, instead of increasing opioid doses or performing extensive workups, simple interventions such as administering nonsteroidal anti-inflammatory drugs or intra-articular injections would suffice.[134,139]

Future research in this subspecialty would help to establish the biomarkers associated with prolonged survival after rehabilitation. Currently, some of the factors that have been elucidated include a higher maximal aerobic capacity (i.e. VO_2 max) and cytokine levels associated with cancer progression.[135]

Rehabilitation in intensive care

The rapid progress in clinical management, technology and systems in intensive care units (ICUs) have significantly increased patient survival rates.[141] The impact of critical illness on disability and subsequent reintegration into society in patients who survive have only recently been appreciated.[141,142] The effects of the combination of immobility, critical illness, medications and ICU interventions on a patient's function persists even after the acute illness has resolved.[143]

Motor deficits, including weakness and diminished exercise capacity and endurance, remain in more than half of patients after ICU discharge.[144] Cognitive impairments such as memory, attention, problem-solving and decision-making deficits are common.[141] The prevalence of neuropsychiatric manifestations of post-traumatic stress disorder, depression and anxiety exceeds 40% in critical care, and these have further negative impact on physical activity and motor function.[142] Quality of life is especially affected in survivors on long-term mechanical ventilation, and their persistent impairments prevent them from returning to work and re-integrating into society.[141]

Muscle weakness deserves specific attention in ICU rehabilitation as it is a frequent complication associated with major disability and prolonged rehabilitation.[142,144,145] The causes of weakness are protean, mainly resulting from the use of neuromuscular blocking agents and corticosteroids, inflammatory syndromes (e.g. Guillain-Barré syndrome and encephalomyelitis), acidosis, uraemia, and electrolyte disturbances.[144,146] Critical illness myopathy (CIM) and critical illness polyneuropathy (CIP), well-known specific syndromes that afflict up to 50% of patients in ICUs, present with severe weakness that can involve the limbs, facial muscles and respiratory muscles.[141,144] Sepsis of all severities, particularly systemic inflammatory response syndrome and multiorgan failure, are the most common predisposing factors for CIM and CIP.[141]

Reviews of ICU rehabilitation are consistent in stating that rehabilitation is significantly under-delivered in ICUs.[141,145,147] Traditionally, rehabilitation assessments and programmes are only commenced after patients are extubated and transferred out of the ICU,[147] the main reason being the perception that critical care patients are too ill to participate in rehabilitation.[131] There are also communication difficulties with patients, an absence of exercise protocols, time constraints of nurses and therapists, as well as practical considerations such as numerous invasive vascular lines, catheters and restraints to navigate through.[147,148]

There are now several trials in ICU rehabilitation and these have some common themes. Firstly, they are distinguished by detailed, structured protocols with commencement of the rehabilitation programme by 24–48 hours post ICU admission.[141,147] Second, a clear sedation protocol is in place. This consists of consciously keeping sedation to a minimum and having daily, specifically timed interruption of sedation for rehabilitation assessment, interaction and exercise with the interdisciplinary team.[142] Another characteristic is a concentrated endeavour to assess and reverse the causes of ICU-acquired weakness. This involves early evaluation on relevant causes, including CIM and CIP, and may involve haematological and neurophysiological testings, or even muscle biopsies.[141,147] Most importantly, eligible patients are considered for a stepwise, progressive mobilisation programme in several phases.[146,148,149] This programme progresses from passive ranging and mobilisation in the unconscious phase to resistance training, increasing sitting tolerance, active transfers and walking.[146,148]

Innovative ways of delivering rehabilitation in ICUs, such as modified portable ventilators and hydraulic platform walkers for gait training, mobile assisted leg-presses, neuromuscular electrical stimulation protocols and video gaming, have been developed.[146,149,150] Results indicate a decline in the rates of failure to wean off mechanical ventilation, a reduction in patients requiring tracheostomy and an increase in ventilator-free days.[143,147,148] There were also improvements in mobility, rates of return to functional independence, number of delirium episodes, length of ICU and hospital stays, rates of readmission and overall care costs.[142,147,148] Patients found to be suitable for mobility must meet the inclusion criteria, including fraction of inspired oxygen concentrations (FIO_2) ≤ 60% and positive end-expiratory pressure ≤ 10 cm H_2O. The use of rehabilitation programmes in ICU is safe, and guidelines are available for termination of exercise with various cardiovascular and respiratory parameters such as hypotension or increasing FIO_2 requirements.[141,147]

CONCLUSION

Rehabilitation medicine has firmly shifted from the common perception of an empathic but slow-moving discipline to a rapidly developing science spanning the bench to bedside, with its practise in the acute illness phase through eventual reintegration into the community. The need for rehabilitation medicine clinicians will undoubtedly increase with better acute medical care and an ageing population. Close interdisciplinary collaborations with fellow medical specialties, nonmedical sciences and healthcare governing bodies continue to be essential for cost-effective, high-quality care. The breadth and depth of the field of rehabilitation are tremendous, and this brings hope to the multitude of disabled patients. We shall conclude with this heartfelt anecdote that indeed *"rehabilitation medicine is the easiest specialty to do badly and the hardest to do well."*

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